

Mood Disorders in Pregnancy and Postpartum

William Watson, MD, FCFP

Family Physician, St. Michael's Hospital

Simone Vigod, MD, MSc, FRCP(C)

Staff Psychiatrist, Women's College Hospital

OCFP-ASA, Toronto

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Faculty/Presenter Disclosure

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 - No relationships to declare



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- Dr. Vigod receives salary support from the Ontario Mental Health Foundation and the Department of Psychiatry Women's College Hospital University of Toronto, and has served on the planning committee for a Women's Health CME Initiative for MDH Consulting

Speaker Bios

- Dr. Watson is an Associate Professor, Department of Family and Community Medicine, University of Toronto, and Staff Physician at St. Michael's Hospital Family Practice Unit. He has an interest in Postpartum Depression and has contributed to a number of review publications and workshops on the topic
- Dr. Simone Vigod is a scientist at Women's College Research Institute and a psychiatrist at Women's College Hospital. She is an assistant professor in the [Department of Psychiatry at the University of Toronto and an adjunct scientist at the Institute for Clinical Evaluative Sciences \(ICES\) in Toronto, Ontario. In addition, she is the recipient of the inaugural Shirley Brown Chair in Women's Mental Health Research Clinician-Scientist Award, and an Ontario Mental Health Foundation New Investigator Award.](#)

Objectives

- To learn about updated risk factors for PMD in the family practice context
- To learn about new screening tools for early detection of PMD
- To learn about newer approaches to management, including psychotherapy and drug treatment.

Why know about perinatal mood disorders?

- An important public health issue
 - Risk of a Major Depressive Episode is up to 10% in pregnancy, 15% postpartum (higher than age-matched point prevalence in the non-pregnant population)
 - Risk of bipolar disorder relapse is high in pregnancy and very high in the postpartum period

From: Episodes of Mood Disorders in 2,252 Pregnancies and Postpartum Periods

American Journal of Psychiatry 2011; 168:1179-1185 doi: 10.1176/appi.ajp.2011.11010148

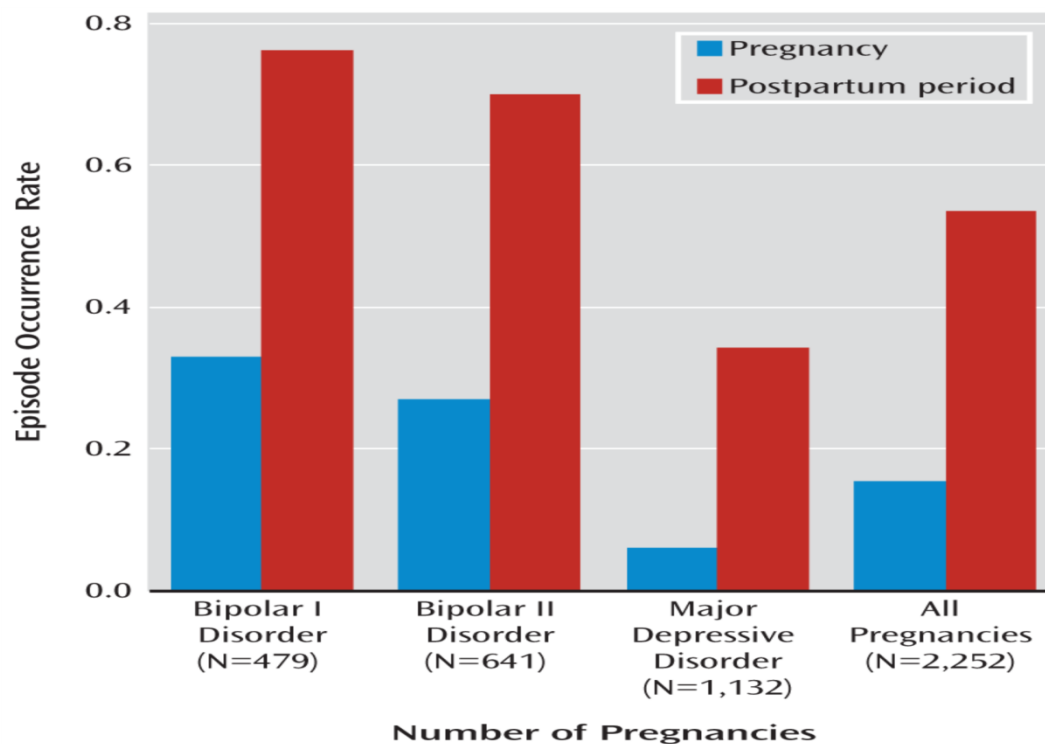


Figure Legend:

Episode Occurrence Rates of Major Affective Episodes During Pregnancy and During the Postpartum Period in 1,162 Women With Bipolar I, Bipolar II, or Major Depressive Disorder^a

Why should family docs know about perinatal mood disorders?

- Potential Impact of untreated mood disorders on mother, baby and family can be profound:
 - Pregnancy: spontaneous abortion, poor prenatal care, substance use, poor fetal growth, preterm labour, suicide
 - Postpartum: poor attachment/parenting, delayed infant motor, language and cognitive development, child behaviour problems, suicide/infanticide

Spectrum of Illness

- Entire range of psychiatric disorders occur during the perinatal period
 - Perinatal period generally defined from onset of pregnancy until ~ 1 year postpartum
 - Management often begins at pre-conception counseling for women with a personal history of mental health problems

Context in Family Practice

- Hospital/office setting
- Well baby, well family exam
- Other family members/relationships
- Resources

Outline

1. Preconception – prevention for mother and baby
2. Pregnancy – prevention and treatment
3. Postpartum – prevention and treatment

Case 1-Preconception

- 36 y.o G0P0, married, planning pregnancy
- Has history of 2 episodes of major depression, treated with sertraline 100mg
- She asks you: “Should I stop my medication now that I am trying to get pregnant?”

What is your approach?

Risks of Continuing medication

Weigh risk/impact of
relapse

vs.

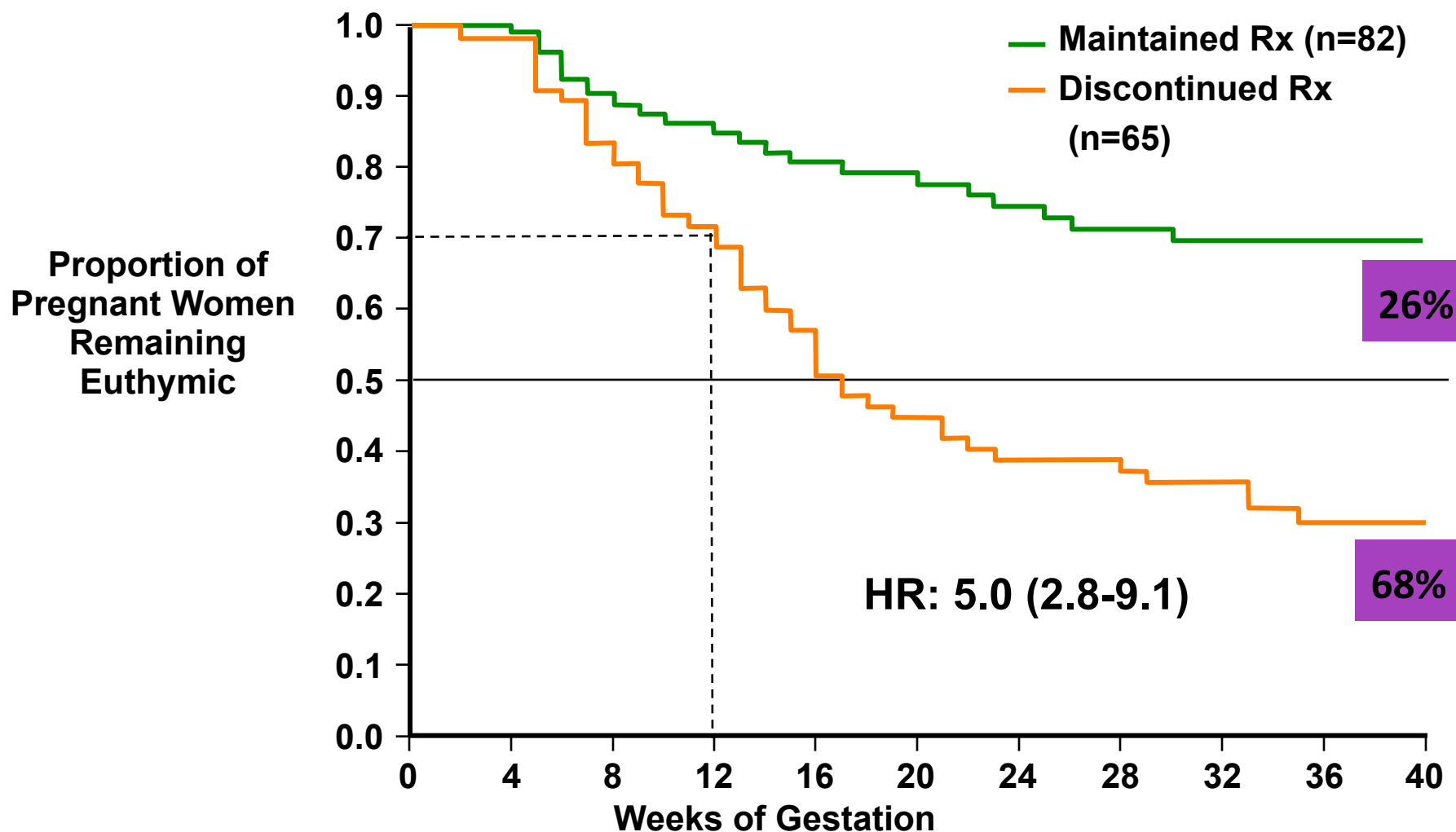
Potential risks of
medication use



Mood Disorders in Pregnancy

- Not necessarily a high risk time for new onset
 - Although, in general, the 3rd and 4th decades of life are high risk for onset of mood disorders in women
 - Unplanned pregnancy, marital or financial instability may pose risk
- Relapse rates of existing disorders are high
 - Risk Factors for Relapse (Viguera 2011)
 - Younger age at onset
 - Previous postpartum episodes
 - Fewer years of illness
 - Bipolar disorder
 - Fewer children, and
 - Not being married

Relapse of Major Depression when Antidepressants are Discontinued



Depression in Pregnancy

- But....In the Cohen et al. study, the overall relapse rate was 43% and ~ 75% of the women had 3+ prior episodes of depression
- In a sample that included women who were less severely ill Yonkers et al., 2011
 - Relapse rate = 16%
 - Women with 4 or more episodes before pregnancy were at highest risk of depression in pregnancy
 - Discontinuation of antidepressants in pregnancy did not have a strong effect on the development of a major depressive episode

Depression in pregnancy

- Take Home Points:
 1. History of recurrent depression increases risk of depression in pregnancy
 2. Severity may be an effect modifier with respect to medication discontinuation:
 - In women with severe and/or recurrent depression, discontinuation of medication represents risk of relapse
 - In women with less severe histories of depression, the impact of medication discontinuation may not be as dramatic

Case 2-Pregnancy

- 32 year old G2P1, with 19 month old son
- Works full-time, husband travelling ++, Now 22 weeks GA in semi-planned pregnancy
- No clear history of depression, but always very “independent”, “hard on self”
- Very overwhelmed, tired, irritable, anhedonic, can't sleep, passive suicidal ideation
 - What to do?

Choosing a treatment option

Weigh impact of
depression in
pregnancy (or risk of
relapse)

vs.

Potential risks of each
treatment option



Untreated Depression

Advantages

- No concern about fetal exposure to medication
- No need to commit time or resources to psychotherapy
- May have spontaneous remission

Disadvantages

- Negative effects of depression on daily function, sense of well being, experience of pregnancy
- Reduced antenatal care attendance,
- Increased smoking, substance and alcohol use
- Increased risk of postpartum depression
- Possible negative effects on child in infancy and early childhood

Psychosocial/Psychological Treatments in Pregnancy

- Tested interventions include antenatal classes, group psycho-education, nondirective counseling, interpersonal psychotherapy (IPT), and cognitive behavioral therapy (CBT)
- Despite methodological insufficiencies in some studies, these data indicate that individual psychotherapy is helpful for pregnant women with mild–moderate depression
- Evidence is strongest for structured psychotherapies, particularly IPT and CBT

Psychotherapy in Pregnancy

Advantages

- Effective for mild (and sometimes moderate) symptoms of depression
- No need to be concerned about medication exposure for the fetus

Disadvantages

- Not likely to be effective on its own (i.e. without medication) for moderate or severe symptoms
- Takes time... while fetus may be exposed to effects of illness
- Requires access and resources

Antidepressants in Pregnancy

- First line for moderate to severe depression in pregnancy
 - SSRI or SNRI with most data on older medications (e.g. fluoxetine, sertraline, *paroxetine*, citalopram)
- Second Line
 - Other first-line antidepressants (e.g. Bupoprion, Mirtazapine):
Much less data but nature and magnitude of risks likely similar
- Third Line
 - Tricyclic Antidepressants: need monitoring during pregnancy
 - Other (e.g. Mono amine oxidase inhibitors) very rarely used

Antidepressants in Pregnancy

Advantages

- Effective for moderate and severe depression (> 50%)
- Can have response within 2 weeks
- Minimal maternal side effects for first and second line medications

Disadvantages

- Maternal side effects
- **3 theoretical** risks for fetus:
 - Teratogenesis (~1st TM)
 - Neonatal toxicity/withdrawal (3rd TM)
 - Developmental effects with latent childhood manifestations

SSRI/SNRIs in Pregnancy

From [observational](#) studies (many with methodological problems related to confounding by indication):

- Teratogenicity (T1)

- Spontaneous abortions ---- recent meta-analyses NO association
- Cardiovascular malformations ---- ARI 5/1000 to ~ 8/1000, although recent NEJM stud NO association (Likely class effect despite early focus on paroxetine)

- Toxicity/Withdrawal (T3)

- Persistent Pulmonary Hypertension of the Newborn (PPHN) ---- ARI 1.2/1000 to ~2.4/1000
- Neonatal Adaptation Syndrome ----- up to 30% (vs. 10%), usually mild & self-limited

- Developmental Effects

- Preterm birth ---- no high risk of < 36 weeks, ARI 60/1000 to 70-90/1000
- Lower birthweight ---- by 200-300g
- Long term outcomes – recent concerns about increased risk of autism, but 2 largest and best designed studies suggest that association is due to shared genetic liability with depression

Neonatal Adaptation Syndrome

- **Set of neurobehavioral signs occurring ~ 30% of SSRI/SNRI exposed full term babies vs. 10% of non exposed babies**
- **Possible symptoms**
 - Usually mild: Insomnia or somnolence ; Agitation , tremors, jitteriness, shivering and/ or altered tone; Restlessness, irritability & constant crying; poor feeding, vomiting/diarrhea
 - Severe syndrome that consists of seizures, dehydration, excessive weight loss, hyperpyrexia (poor temperature control), or intubation (due to tachypnea/respiratory distress) is rare in term infants (1/313 quantifiable cases)*
- **Duration Usually short lived**
 - Median duration of 3 days, and 75 % complete resolution by 5 days (max 4 weeks)'
 - **Premature babies** are more vulnerable to NAS, and are more likely to develop signs, which may be more severe.
 - Weak evidence that severity of symptoms may be dose related
- **Management supportive**

Neonatal Signs After Late In Utero
Exposure to Serotonin Reuptake
Inhibitors. Moses-Kolko et al.JAMA 2005;
293; 2372-2383

Benzodiazepines

- May be required for concurrent management of anxiety and/or sleep in severe cases
- Contradictory data on increased risk of cleft palate/lip with 1st trimester exposure
 - Best to avoid in 1st trimester
- Theoretical risk of neonatal withdrawal and of toxicity in breast-feeding
 - Use shorter half-live drugs – lorazepam, clonazepam
 - Monitor infants

Alternative Treatments

- If there is benefit, then it is likely for women with mild depressive illness
 - Limited support for some non-pharmacologic alternatives to psychotherapy: Dietary calcium, Exercise, Massage therapy, Bright light therapy
- Early enthusiasm for omega-3 fatty acids
 - Most randomized clinical trials to date have failed to show that the active treatment differs from placebo

Alternative Treatments

- Repetitive Transcranial Magnetic Stimulation (rTMS)
 - Investigated widely for severe or treatment-resistant depression
 - Magnetic fields have been associated with increased risk of miscarriage --- there is a theoretical risk to administering transcranial magnetic stimulation in pregnant women
 - However, it is under study in pregnant populations
- There is a clear need for safe and rapidly effective treatments for women with depression in pregnancy

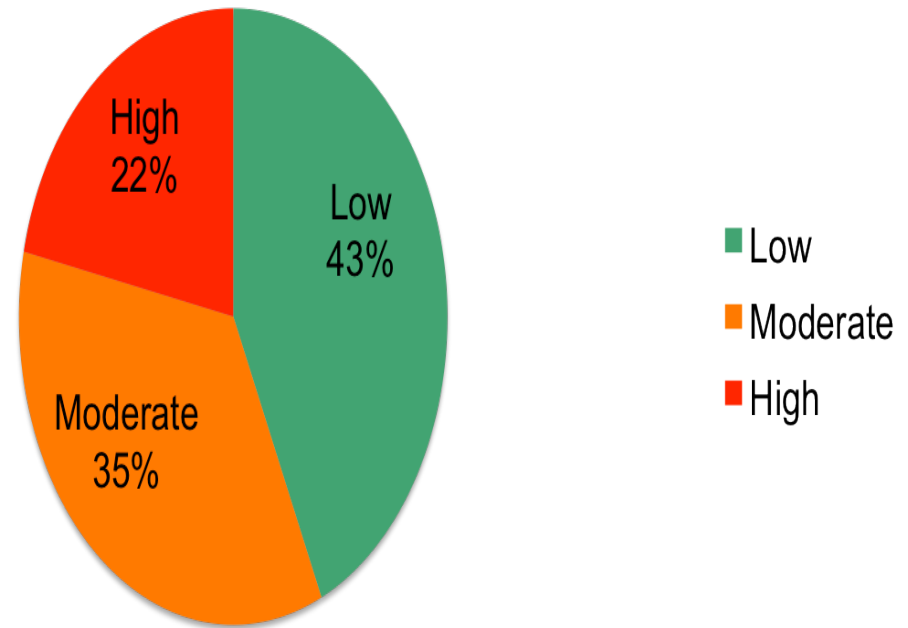
ECT

- Efficacious, but has side effects and requires general anesthetic
- Risk is minimal but not non-existent
 - Case reports suggest potential associations with adverse cardiovascular events and some adverse neonatal outcomes
- Use in pregnancy usually limited to: severe treatment-resistant depression, acute suicidality, psychotic depression, or severe dehydration/malnutrition secondary to a depressive syndrome

Among depressed pregnant women ...

- As few as 20% of women accept treatment
 - Misinformation and concern about harms and benefits
 - Stigma/Pressure from family, friends, media and providers

Decisional Conflict



Walton, Ross, Stewart, Grigoriadis, Dennis, Vigod.
Archives of Women's Mental Health, 2014

Summary



1. Depression in pregnancy is common and associated with negative consequences
2. Existing treatment options have harms and benefits, rendering decision-making difficult for many women
3. Treatment rates are low, with antidepressant medications particularly unacceptable
4. Leaves a GAP for new treatment options

There is a clear need for (a) help with decision-making; and (b) new safe and rapidly effective treatments that are acceptable to women with depression in pregnancy

Enter our 2 pilot studies

1. An electronic patient decision aid (PDA) for antidepressant use in pregnancy
2. Transcranial direct current stimulation (tDCS) for depression in pregnancy

PDA Background

- Neither information nor clinical care alone is sufficient for assisting women deciding whether or not to start or continue antidepressant medication in pregnancy
 - High **decisional conflict** among >50% women even after consultation with a psychiatrist
- Well-designed patient decision aids (PDAs) are used to **supplement** clinical consultation
 - Aim to prepare individuals to make **complex health decisions**
 - No existing PDAs for antidepressant use in pregnancy, but women want to play an active role in decision-making

Patient Decision Aid Study Intervention

- Sections of the PDA
 - (1) Information about depression in pregnancy, each treatment option, and procedure
 - (2) Information on risks and benefits of both untreated depression and antidepressant treatment, including exercises to help women determine which risks/benefits are most important to her
 - (3) Summary section that outlines information reviewed and risks/benefits deemed most important



Depression in Pregnancy:
Introduction



What is depression?



How common is depression in
pregnancy?



Who is at risk of depression in
pregnancy?



What are the options for treating
depression in pregnancy?

Continue



Who is at risk of depression in pregnancy?

Several different factors may affect a woman's risk of developing depression during pregnancy. Strong risk factors include having a personal history of depression.

In addition, stress such as poor social support, financial instability, unemployment, single parenting or marital instability, history of interpersonal violence, unplanned pregnancy and obstetrical complications may increase risk.

Let's Begin

You may or may not be engaged in current non-medication treatment for depression such as supportive counseling or a form of psychotherapy. As such, you may be facing multiple decisions about how best to treat your symptoms of depression.

However, you are using this electronic decision aid because you, or your health care provider, has indicated that antidepressant medication in pregnancy may be an option for you.

Decision are you considering

Please choose the option that best describes the decision you are currently facing **regarding the use of antidepressant medication** in pregnancy.



Not currently taking any anti-depressant medication and considering **Starting** new medication(s)



Currently taking anti-depressant medication and considering **Stopping** my medications(s)

Continue



Other problems that come along with depression in pregnancy

Problem	Out of 1000 women with untreated depression	Out of 1000 women with no depression
Poor Sleep	200	100
Smoking	300	50
Alcohol or Drug Problems	120	50
Postpartum Depression	670	80

Poor nutrition and poor antenatal care are also more common among women with depression.

postpartum depression that could affect the health of my baby. [Read about this](#)

Reasons NOT to choose" each option?

Start Antidepressant Medication

Reasons to choose [i](#) click

Reasons NOT to choose

- Possible effects of antidepressant medication on the baby including slightly increased risk for *heart malformations* [i](#) *preterm birth or low birthweight* [i](#) *persistent pulmonary hypertension of the newborn* [i](#) *neonatal adaptation syndrome* [i](#) and *long-term problems with child health* [i](#)
- Potential side effects of antidepressants for me. [Read about this](#) [i](#)
- Need to remember to take daily medication
- Cost of medication

After reading about your options, where you are in your decision making process now?

I do not currently take antidepressant medication and I am deciding whether or not to start antidepressant medication in pregnancy:

I will definitely not start taking antidepressant medication
I am undecided
I will definitely start taking antidepressant medication

Continue



Enter tDCS

- Transcranial direct current stimulation (or tDCS) is a non-drug treatment for depression.
- The treatment directly stimulates a part of the “affective circuit” that functions abnormally when an individual is depressed
- It has been shown in multiple treatment trials to improve depression symptoms over 2 to 3 weeks of treatment
- It is a **focal** treatment. tDCS directly has been shown to directly stimulate the dorsolateral prefrontal cortex and does not cause changes to a patient’s heart rate, blood pressure or body temperature.

tDCS



Bipolar Disorder

- 27 year old woman, G1P0, with history of bipolar disorder, type 1.
- Multiple episodes of mania with psychosis, with several hospitalizations, stabilized finally on Lithium (level ~0.4) and Quetiapine 300mg per day
- Pregnancy unplanned, but wanted
- Concerned about fetal exposure to medication

Bipolar disorder in Pregnancy

- Relapse risk high
 - 25-75% depending on population studied
 - Up to $\frac{3}{4}$ episodes depressed/mixed and $\frac{1}{2}$ in 1st trimester (for women euthymic at conception) (Viguera 2007)
- ... and related to medication discontinuation
 - Recurrence risk two-fold greater in those who **discontinued medication** with median time to recurrence 4x shorter
 - Median time to recurrence 11 times shorter if meds discontinued abruptly vs. gradually

Risks of Continuing medication

Weigh risk/impact of
relapse

vs.

Potential risks of
medication use



Mood Stabilizers

- Lithium

- Only slightly increased risk of cardiac defects (e.g. ebstein's anomaly) when used in pregnancy
- Need to attend to ECF changes in pregnancy AND massive ECF contraction at delivery
 - Some recommend discontinuation of Lithium with onset of labour and restart day 2 postpartum
- Passes into breast milk and toxicity can be substantial therefore CLOSE monitoring if used

Mood Stabilizers

- Valproate
 - Teratogenic (neural tube defects - NTD)
 - Recent reports of developmental delay in breastfed infants
- Lamotrigine
 - Risk of NTD
 - Passes into breast milk (up to 30% of maternal levels) → theoretical risk of rash

Anti-psychotics

- Pregnancy:
 - Haloperidol best studied – not thought teratogenic
 - Main Issue with newer anti-psychotics is potential for weight gain and gestational diabetes
 - FDA warning re: Extra-pyramidal symptoms (EPS) in newborns for all typicals and atypicals
- Minimal data in breast-feeding
 - Clozapine and Olanzapine not recommended due to risk of blood abnormalities and EPS respectively

Postpartum mood disorders



Postpartum Mood Disorders

- Risk appears to be substantially higher than in pregnancy both for **new onset** and **recurrent** mood disorders
- Why?
 - Biological factors such as genetic predisposition to rapid change in hormones at delivery
 - Psychosocial risk factors: social support, life stressors, etc...

Postpartum Mood Symptom Spectrum

- Baby Blues: up to 75%, within days, resolves within first month without treatment, likely hormone-related
- Postpartum Depression (PPD): major depressive episode (MDD) with onset in the 1st postpartum year (requires treatment)
- Postpartum Psychosis: psychotic episode, 90% occurring within first 3 months postpartum, likely a bipolar disorder presentation (*Psychiatric Emergency*)

Case Identification/Screening

- NICE (UK)

- During the past month, have you often been bothered by feeling down, depressed or hopeless?
- During the past month, have you often been bothered by having little interest or pleasure in doing things?
- **If the woman answers 'Yes' to both questions a further question should be asked:**
- Is this something you feel you need or want help with?
-

- EPDS (10 Qs)

- **In the past seven days:**
- I have been able to laugh and see the funny side of things
- I have looked forward with enjoyment to things
- *I have blamed myself unnecessarily when things went wrong
- I have been anxious or worried for no good reason
- *I have felt scared or panicky for no very good reason
- *Things have been getting on top of me
- *I have been so unhappy that I have had difficulty sleeping
- *I have felt sad or miserable
- *I have been so unhappy that I have been crying
- *The thought of harming myself has occurred to me
-

Case 3-Postpartum: Maria, aged 22

- You are seeing Maria, a new mother, with her five-day-old baby boy for a checkup. She had a normal pregnancy and delivery, and her baby is healthy but has lost 100 g since birth. John, the baby's father, accompanies Maria and the baby. Maria is breastfeeding and having difficulty with the baby's latch, and she thinks she doesn't produce enough milk. She looks very tired and on the verge of tears.
- Maria says she hasn't been out of the house since the baby was born, and that she has been crying frequently. She worries about the house being a mess when visitors arrive. John is bewildered by her tears and asks you if her tearfulness is normal. He is concerned about how she is feeling and quietly asks if she is depressed.

How do we know what is normal?

- Affective upheaval: joy, fear, ambivalence
- Redefinition/transformation :
 - self: redefinition as mother- Who will I be?
 - child: as “part of & apart from her”
 - relation to her :
 - Mother- return to experiences of mother (conflicts, ambivalence)
 - body, mortality, partner, father, children, culture

-Ballou

Formulation

- Bio: psych history, family history, medical (anemia, thyroid), substances, pregnancy, delivery
- psycho: psychological maturity, separation, attachment, body, personality
- social: supports, work, intimate relations

Case 4-Mrs. C

- A 35 year old teacher
- Brought to the office by her husband of 10 years
- He has noticed that since the birth of their one month old daughter, Mrs. C. has not been her normal self-he is worried
- Mrs. C starts to cry after you ask her about the baby
 - She feels overwhelmed, a bad mother, and especially guilty about having had a baby
 - Most of the time she is irritable and anxious
- Personal hx of abusive (psychological) mother
- You note she is tearful, frustrated, poor mother-infant interaction



Post-Partum Depression

Onset: DSM IV TR indicates within 4 weeks of delivery, genetics work suggests onset 6-8 weeks and clinically, even later onset observed

Risk Factors: Untreated depression/anxiety in pregnancy, poor sleep , poor social support, stressful life events

Symptoms: same as major depressive episode

- 50% with anxiety – panic, obsessive ruminations
- Themes of incompetence, obsessional harm (differentiate from psychosis)

Management

1. Prevention: social support, sleep protection, some advise longer stay with rooming out of baby for high risk mothers but evidence limited for this strategy
2. Safety Assessment: mother, baby (+/- other kids)
3. Treatment: based on nature and severity of illness
 - Psychotherapy: Strongest evidence for Interpersonal Therapy (IPT) where focus is on role transition to parenthood and improving communication abilities and social support
 - Psychotropic medication: as indicated, consider passage into breastmilk and risk of toxicity
 - Somatic Therapies

Case 5-Bridget

- Bridget is a single mother who has just given birth to a 4-kg, healthy baby girl. In hospital, Bridget seemed somewhat anxious. Before you see her the next day, the nurses take you aside and relate that she was acting strangely and had paranoid thoughts that someone was trying to take her baby away. When you visit her in her room, you notice that she is dishevelled and appears restless and irritable. She is speaking quickly and swearing which is unusual for her.
- Her mother mentions that Bridget had a “nervous breakdown” when she was 18 and was hospitalized for two weeks because of acute excitement. She was discharged with medication that she took for six months. In addition, her father had a history of “manic-depressive” illness.

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Bipolar Disorder Postpartum

- Relapse 30-50% - acute and severe
 - mostly depressive
- Risk Factors (other than medication discontinuation):
 - Younger age, primiparity, sleep/biological rhythm disturbance (so protect sleep)
 - Psychosocial risk factors play less of a role
- Increased risk of postpartum psychosis
 - 90% within 4 weeks of delivery
 - Marked by confusion, thought disorder
 - Small but serious risk of suicide/infanticide
 - THIS IS A PSYCHIATRIC EMERGENCY – DON'T LET HER LEAVE, ENSURE SAFETY OF BABY AND MOTHER, PSYCHIATRIC ASSESSMENT NEEDED

Summary

- There are substantial risks to untreated mood disorders in the perinatal period
- Choice of treatment involves a risk-benefit analysis unique to each patient
 - Do not underestimate effect of decisional conflict, stigma and lack of support for women faced with these decisions about medication use

Useful References

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Resources

- <http://womensmentalhealth.org/>
- <http://www.motherisk.org/women/index.jsp>

Questions/Discussion

