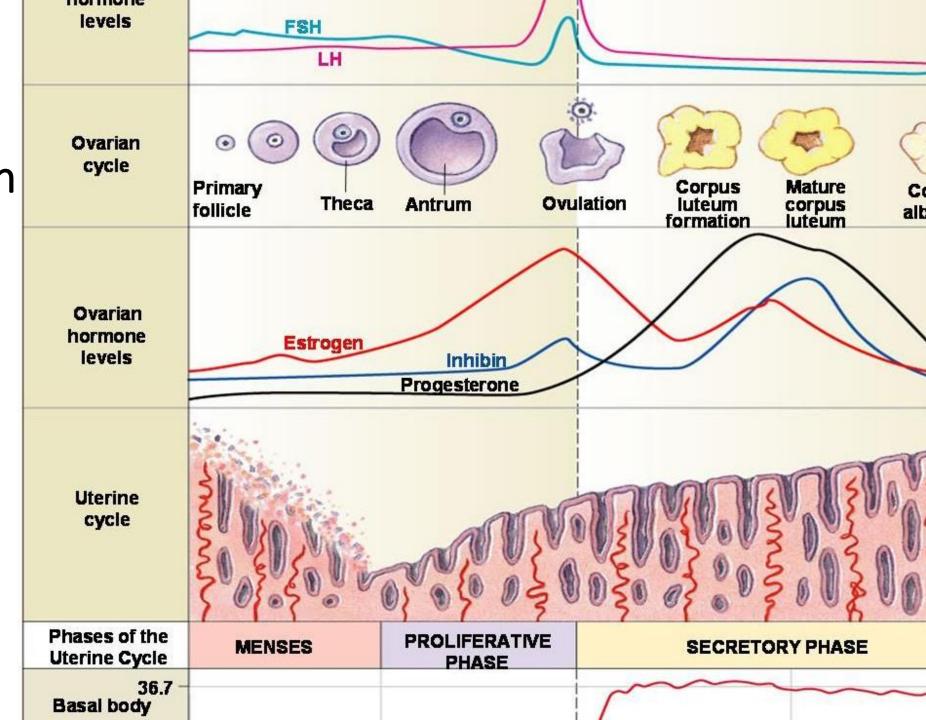
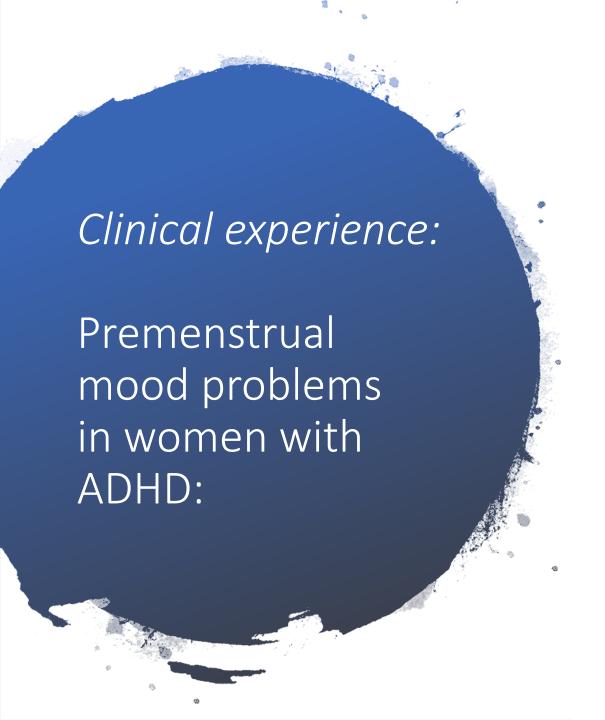


No conflict of interest

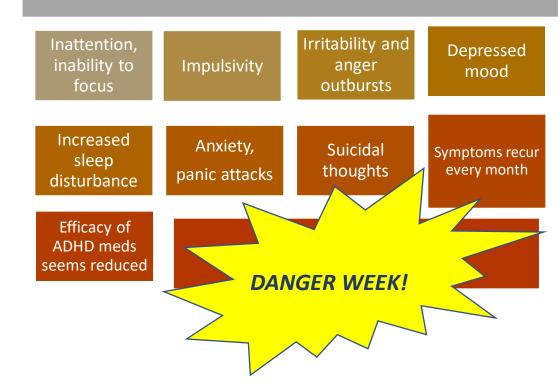
Hormonal Mood Changes in women with ADHD







Women with ADHD report
severe premenstrual
mood instability &
increased severity of ADHD:





Besides premenstrual, also postnatal & perimenopausal mood changes

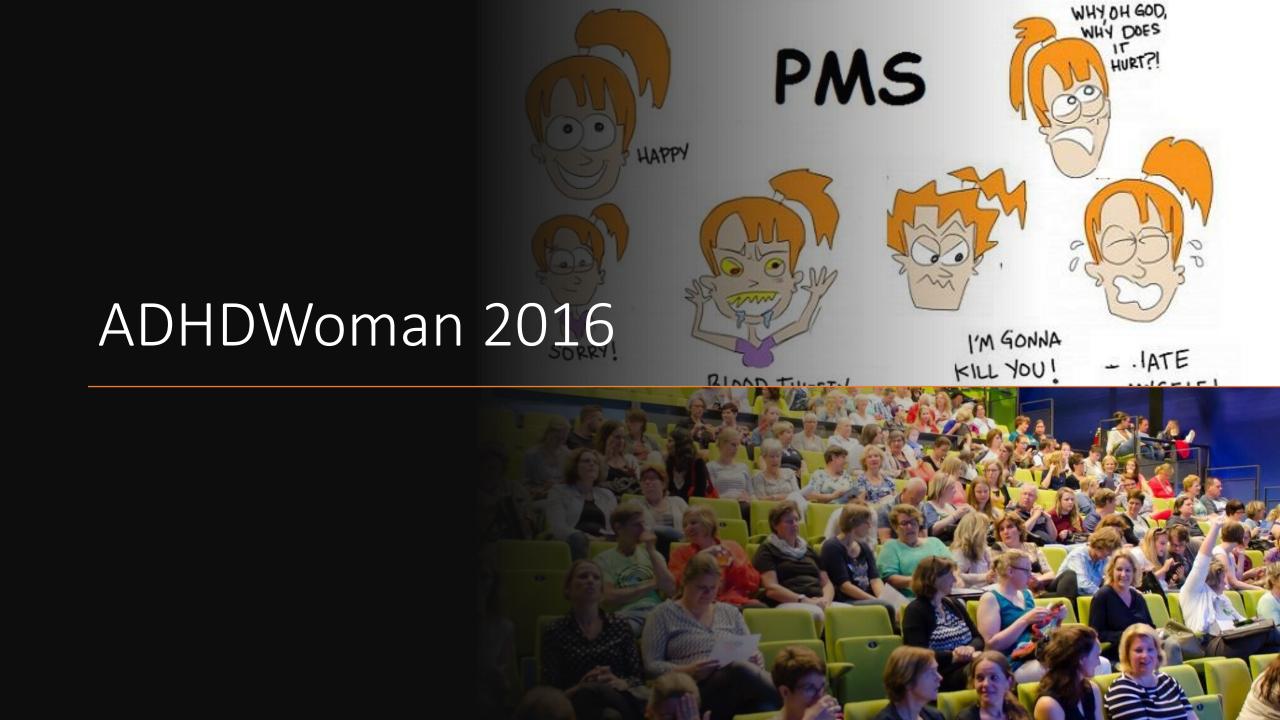
 According to clinical experience, postnatal depression and perimenopausal depression also seem more severe and more frequent than normal

But no data so far ...

Research question:

Are hormonal mood problems indeed more severe and more frequent in women with ADHD compared to women without?

General female population:
 Premenstrual Dysphoric Disorder (PMDD) in 29%



Women with ADHD were asked to vote for their most urgent question to science:

Highest votes for hormonal mood changes during the lifecycle



1st study on mood x female hormones in ADHD, 2016

N=200 participants at the Dutch ADHDWoman Conference

Self report questionnaire on mood changes to the level of clinical depression during:

- the menstrual cycle : premenstrual dysphoric disorder (PMDD) (=more severe than PMS)
- the postnatal period : postpartum depression (PPD)
 - the perimenopausal period

Questionnaire consisted of validated scales, adapted for selfreport



Neuropsychiatric Interview Plus version 5.0 (M.I.N.I. Plus) for Premenstrual Dysphoric Disorder (PMDD)



Edinburgh Postnatal Depression Scale (EPDS) for life-time Post Partum Depression (PPD)



Greene Climacteric Scale (GCS) for Perimenopausal Mood Symptoms



Munich Chronotype Questionnaire (MCTQ) for sleep characteristics

Results

PMDD,
PPD and
climacteric
mood symptoms
in women with
ADHD

- N=200 women
- Selfreport questionnaires
- Comparing women with ADHD symptoms to women from the general population

Results:

- 62% indication for PMDD, versus 29% in controls
- 67% indication for PPD, versus 13-19% in controls
- (Peri)menopausal women with ADHD: 2 fold increased severity of mood, somatic and sexual symptoms compared to controls

Replication study

Women with a diagnosis of ADHD at PsyQ

- Outpatient Clinic Adult ADHD at PsyQ, the Hague, the Netherlands
- N=209 women with diagnosed ADHD
- Age 18-71 years
- Same questionnaires
- Expectation: lower prevalences compared to 1st pilot study

> J Psychiatr Res. 2021 Jan;133:10-15. doi: 10.1016/j.jpsychires.2020.12.005. Epub 2020 Dec 3.

Prevalence of hormone-related mood disorder symptoms in women with ADHD

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Farangis Dorani <sup>1</sup>, Denise Bijlenga <sup>2</sup>, Aartjan T F Beekman <sup>3</sup>, Eus J W van Someren <sup>4</sup>, J J Sandra Kooij <sup>5</sup>
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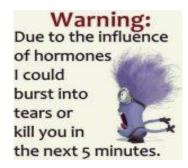
Affiliations + expand

PMID: 33302160 DOI: 10.1016/j.jpsychires.2020.12.005

Abstract

This is the first study to assess the prevalence of symptoms of premenstrual dysphoric disorder (PMDD), episodes of postpartum depression symptoms (PPD) after first childbirth, and climacteric mood symptoms in Attention-Deficit/Hyperactivity Disorder (ADHD). 209 consecutive women (18-71 years) with ADHD completed the PMDD chapter of the Neuropsychiatric Interview Plus version 5.0.0 to assess PMDD, the Edinburgh Postnatal Depression Scale to assess PPD, and the Greene Climacteric Scale to assess climacteric symptoms. Comorbid psychiatric disorders, medication use, and chronobiological sleep characteristics were also assessed. The prevalence of PMDD and PPD were

Results 2nd study







Women with diagnosed ADHD compared to women from the general population

- Indication of PMDD in women with ADHD: 46% versus 29%
- **PPD**: **58**% reported lifetime postnatal depressive symptoms, versus **13-19**% in the general population
- Perimenopausal depression: 3-fold increased number of symptoms of anxiety, depression, somatic & sexual complaints vs women from the general population

Summary



- Confirmation of 2-3 fold increased PMDD, PPD and perimenopausal mood symptoms in ADHD women in a clinical sample
- Three periods of hormonal changes during lifetime
- Why are mood symptoms more severe in women with ADHD?
- How can we treat them better?

Why?

+ 0

Little research on hormonal influences on the brain in women

Cycle often exclusion criterion in research due to changing hormonal levels;

So more research in males

No studies in women with ADHD

Female Hormones & ADHD Symptoms Across the Menstrual Cycle

- 32 <u>control women</u>, 18-22'yrs, regular cycle
- Relationships between estrogen, (E)
 progesteron (P), testosteron (T) and daily
 ADHD symptoms
- Higher impulsivity and inattention when E is low
- Higher inattention in luteal phase of cycle
- NB Stimulant response may also differ across the cycle

Roberts 2018

How?

- Low dopamine levels in certain brain regions in ADHD
- Estrogen & progesteron modulate neurotransmitters like serotonin and dopamine
- Sex hormones have been implicated in brain development and maintenance
- Ovarian hormones also directly effect the brain regarding cognition, memory, learning and emotion, and influence reward-related motivation, impulsivity, and temporal decision-making
- Estrogen influences blood flow and metabolic rate of glucose, and this changes during the cycle

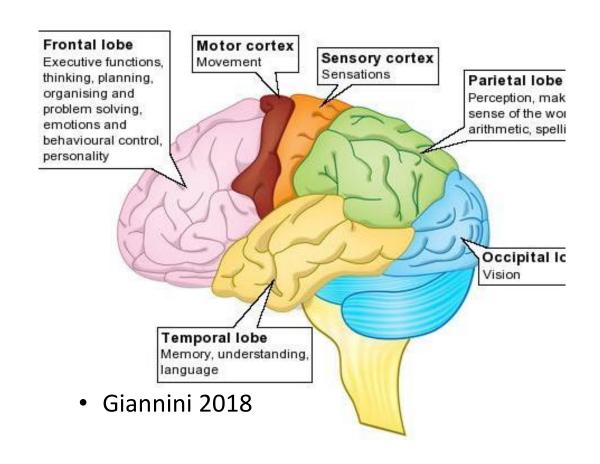
Estrogen & Progesteron INTERACT with Dopamine

Estrogen:

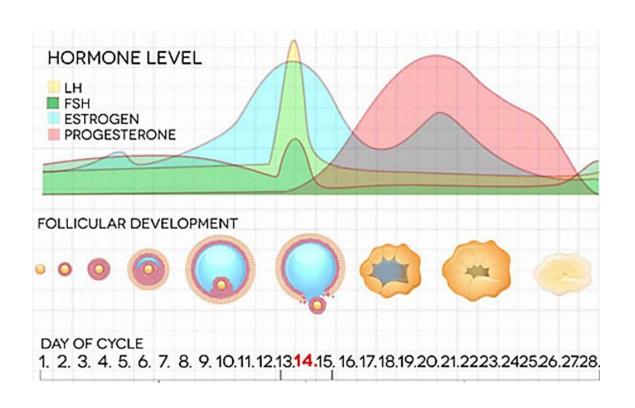
- Increases dopamine synthesis and decreases its degradation
- **Upregulates** dopaminergic receptors
- Effect of estrogen esp. in Prefrontal Cortex
- Impacts working memory function by affecting dopamine levels
- Effects on limbic regions: estrogen influences emotional and motivational behaviors

Progesteron:

 Effect of progesterone on dopaminergic systems depends primarily on the previous priming by estrogen



Why increased Mood Changes during the cycle in ADHD women?



- Estrogen acts as dopamine agonist, increases dopamine activity!
- In ADHD women: low prefrontal dopamine AND low estrogen in 3rd + 4th week of the cycle: reinforce each other

Premenstrual week:

- 2x 'low': ADHD women may be more impaired
- May explain increased mood instability and increased ADHD severity ...

Menopause Timetable

Women may enter menopause earlier than they realize. Estrogen levels usually drop before menopausal symptoms are seen. Below, the typical ages for various symptoms.

SYMPTOM	AGE -35	40	45	50	55	60	65	70	
Dropping estrogen levels		0-						-	•
Menstrual irregularity		0							
Mood swings		ОО							
Loss of concentration)	0							
Hot flashes		ОО							
Vaginal dryness		0							
Last period		O							
Osteoporosis		O							
Heart Disease						0-			→

Sources: "Perimenopause: Preparing for the Change" by Nancy Lee Teaff and Kim Wright (Prima Publishing, 1996); "Perimenopause: Changes in Women's Health After 35" by Drs. James E. Huston and L. Darlene Lanka (New Harbinger, 1997).



PMDD

- Contraceptives, continuously (without stopweek), esp. for somatic symptoms
- SSRIs for mood symtpoms
- Temporary higher dose of ADHD meds??

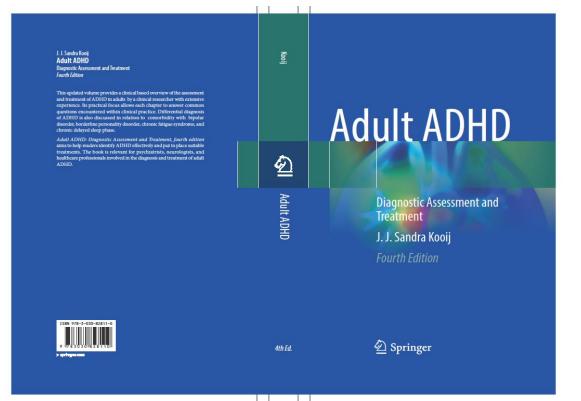
PPD

- SSRIs
- Estradiol (sublingual, transdermal)

Climacteric Mood Symptoms

- SSRI / SNRI
- Estradiol
- SSRI + estradiol
- DHEA

Ryu 2015; Barrett-Connor 1999; Santoro 2005; Schmidt 2005; Cohen 2006; Soares 2006; Soares & Zitek 2008; Gregoire 1996; Ahokas 2001







Thank you!



