

South London
and Maudsley

NHS Foundation Trust



Institute of
Psychiatry

at The Maudsley

KING'S
College
LONDON

Oestrogen, Progesterone and The Mind

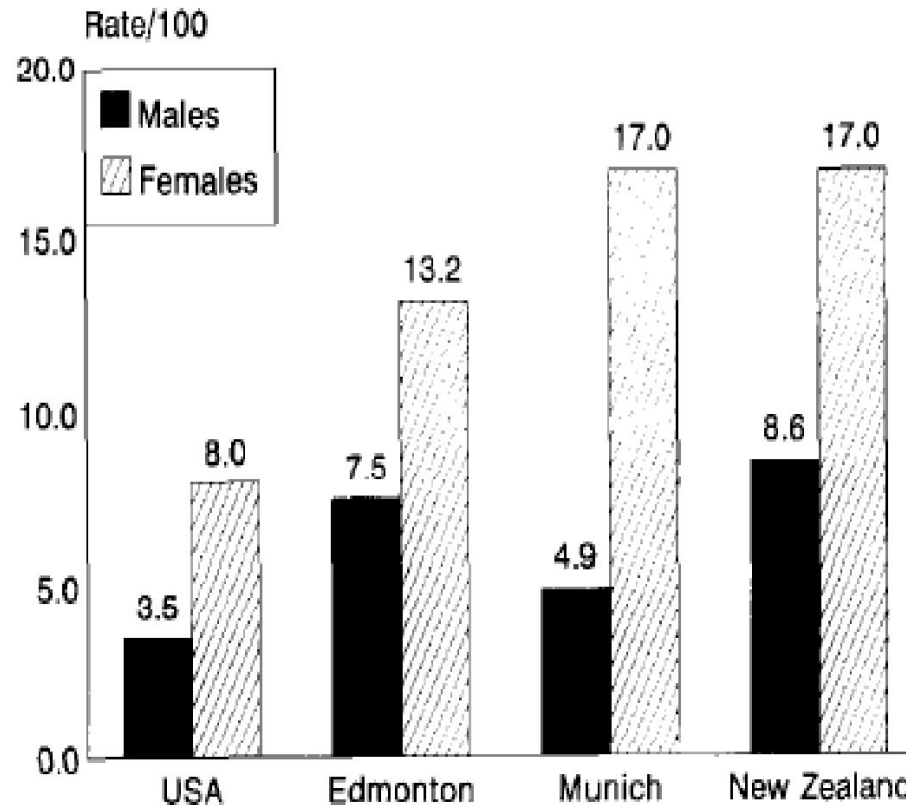
Michael Craig PhD FRCOG FRCPsych

Professor of Translational Reproductive & Neurodevelopmental
Sciences, IoPPN KCL

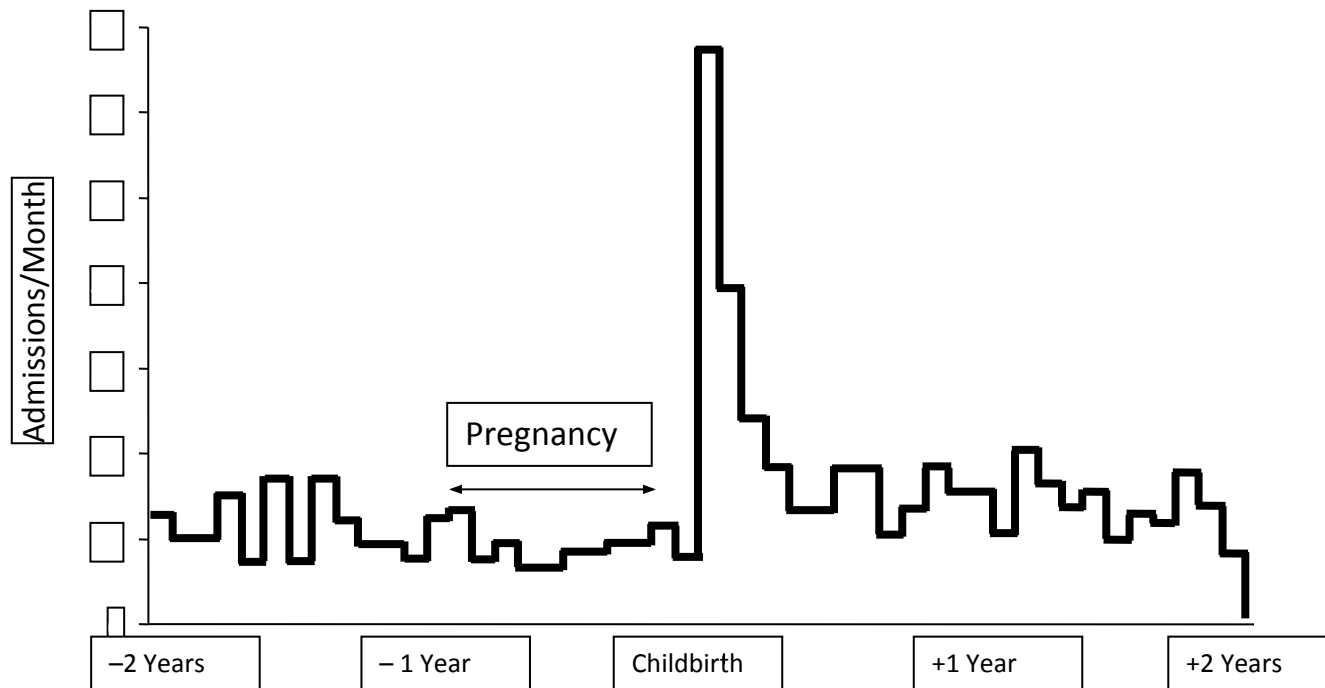
Clinical Lead, National Female Hormone Clinic,
Maudsley Hospital

Depression (1:2)

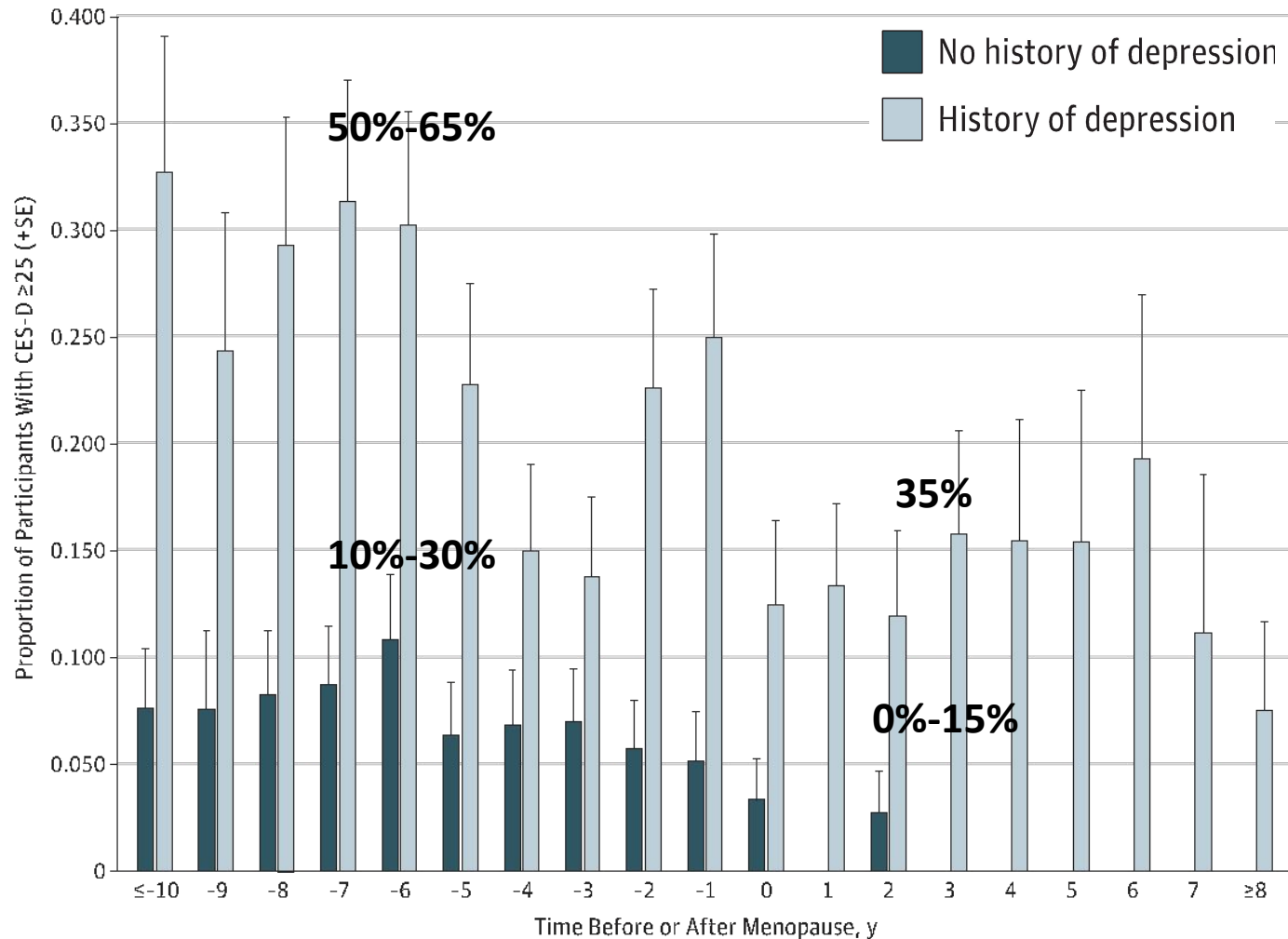
Lifetime rate/100 of major depression, males & females age 26-64,



Epidemiology of Postpartum Episodes

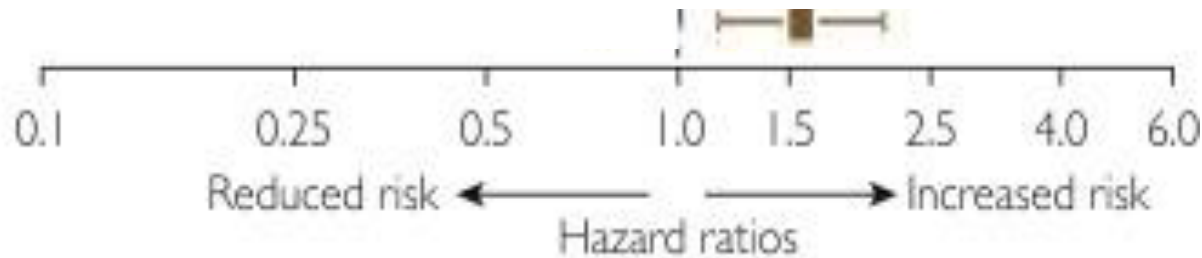


Depressive *Symptoms* Around Natural Menopause



Depressive Disorder

Post surgical menopause



01/01/1988 - 31/12/2007

Olmsted County, Minnesota

Premenopausal < 50 years
old

BSO vs. matched referent.

Median 14y follow up

REPRODUCTIVE DEPRESSION



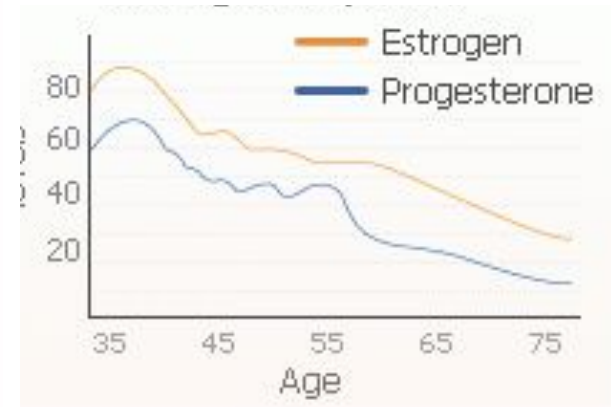
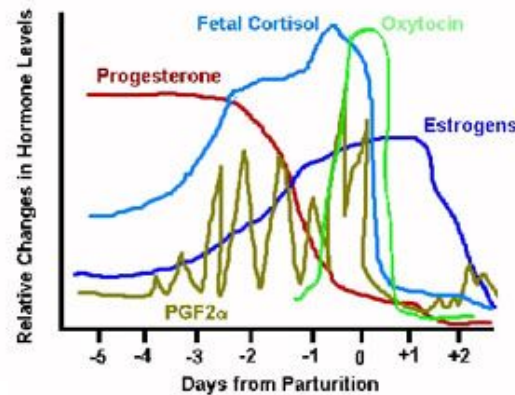
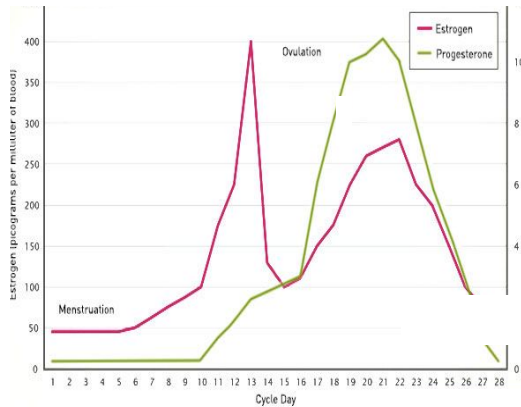
**Premenstrual
Dysphoric Disorder**
5%



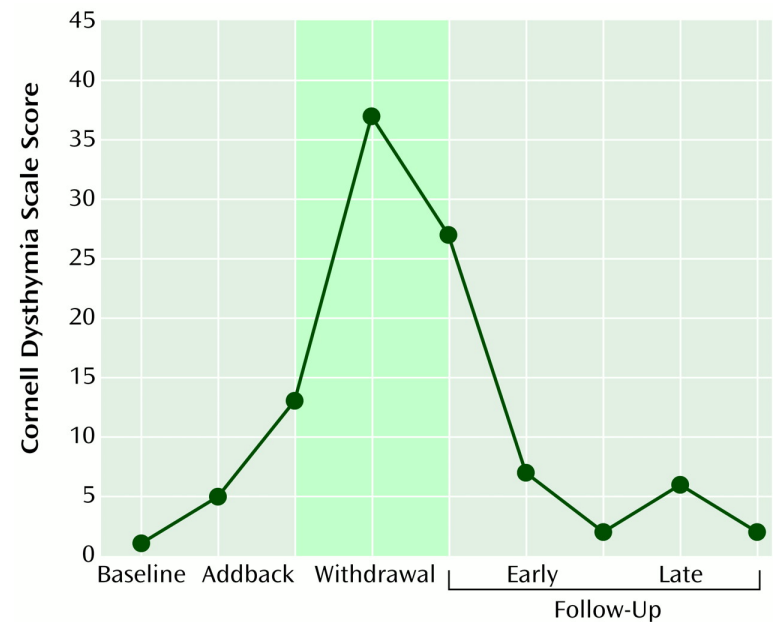
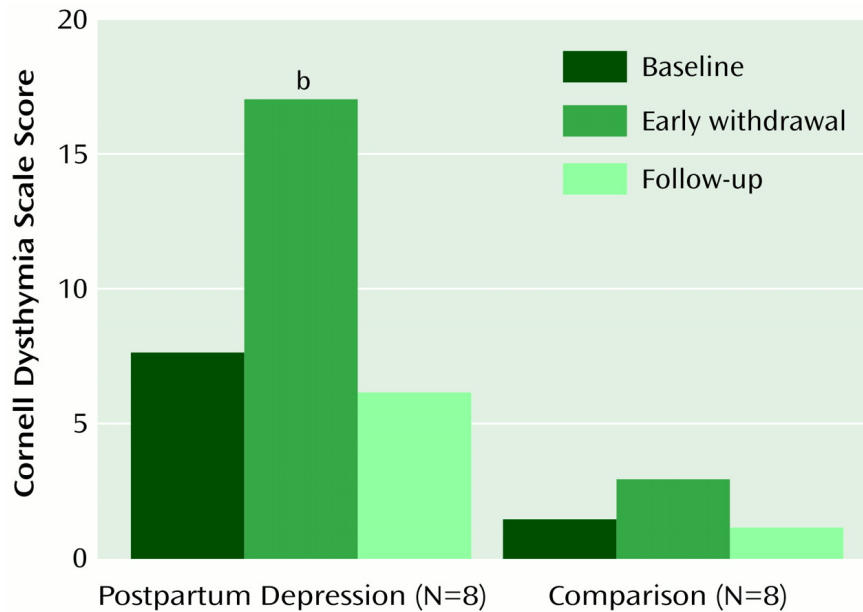
**Postnatal
Depression**
15%



**Perimenopausal
Depression**
15%



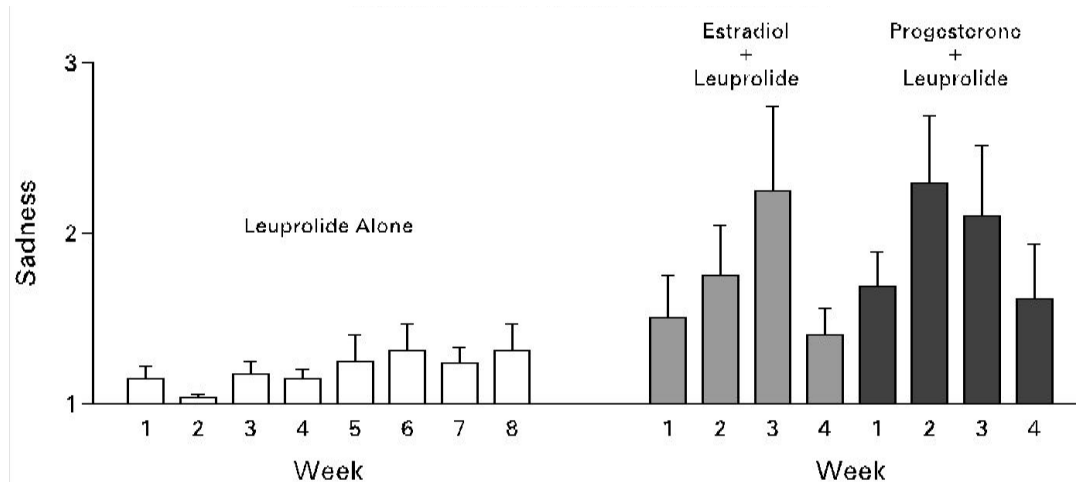
Postnatal Depression



P1: Sudden drop in sex hormones
triggers low mood in past PND

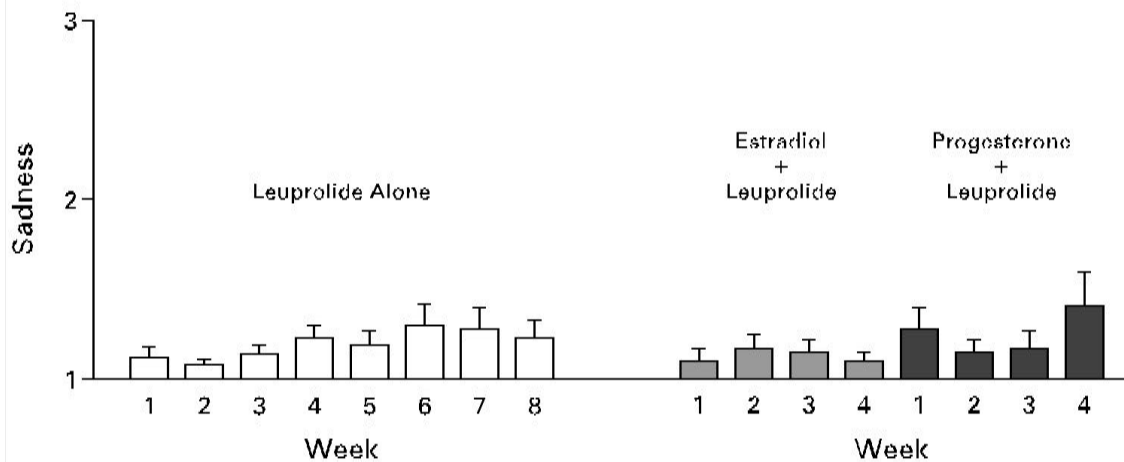
Premenstrual Dysphoric Disorder

PMDD

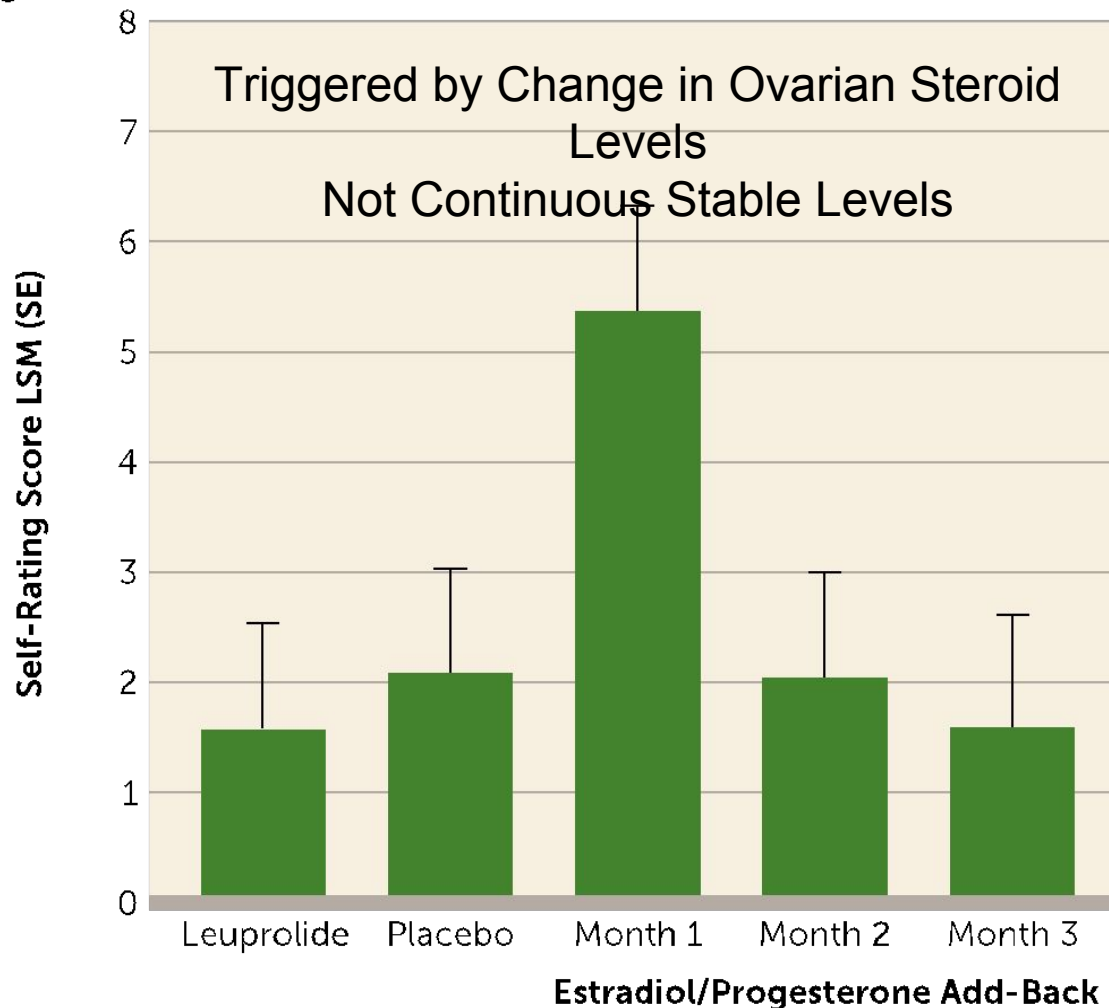


P2: Sudden increase in sex hormones leads to PMDD

CONTROL



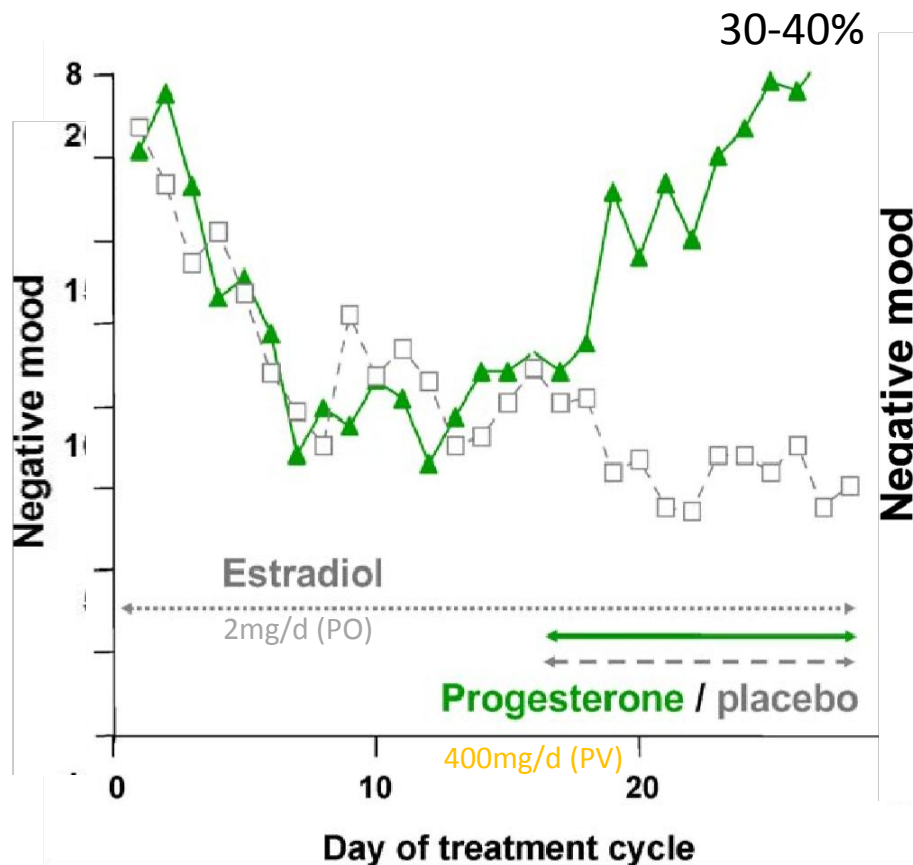
Premenstrual Dysphoric Disorder



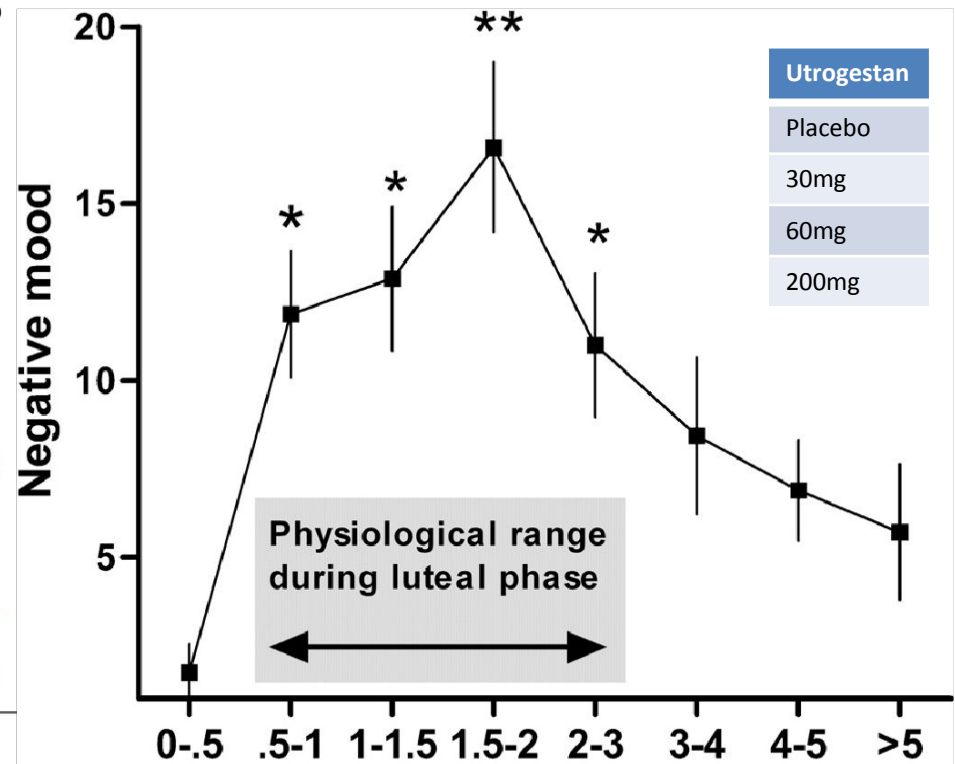
P3: After 1 month symptoms settle

Progesterone

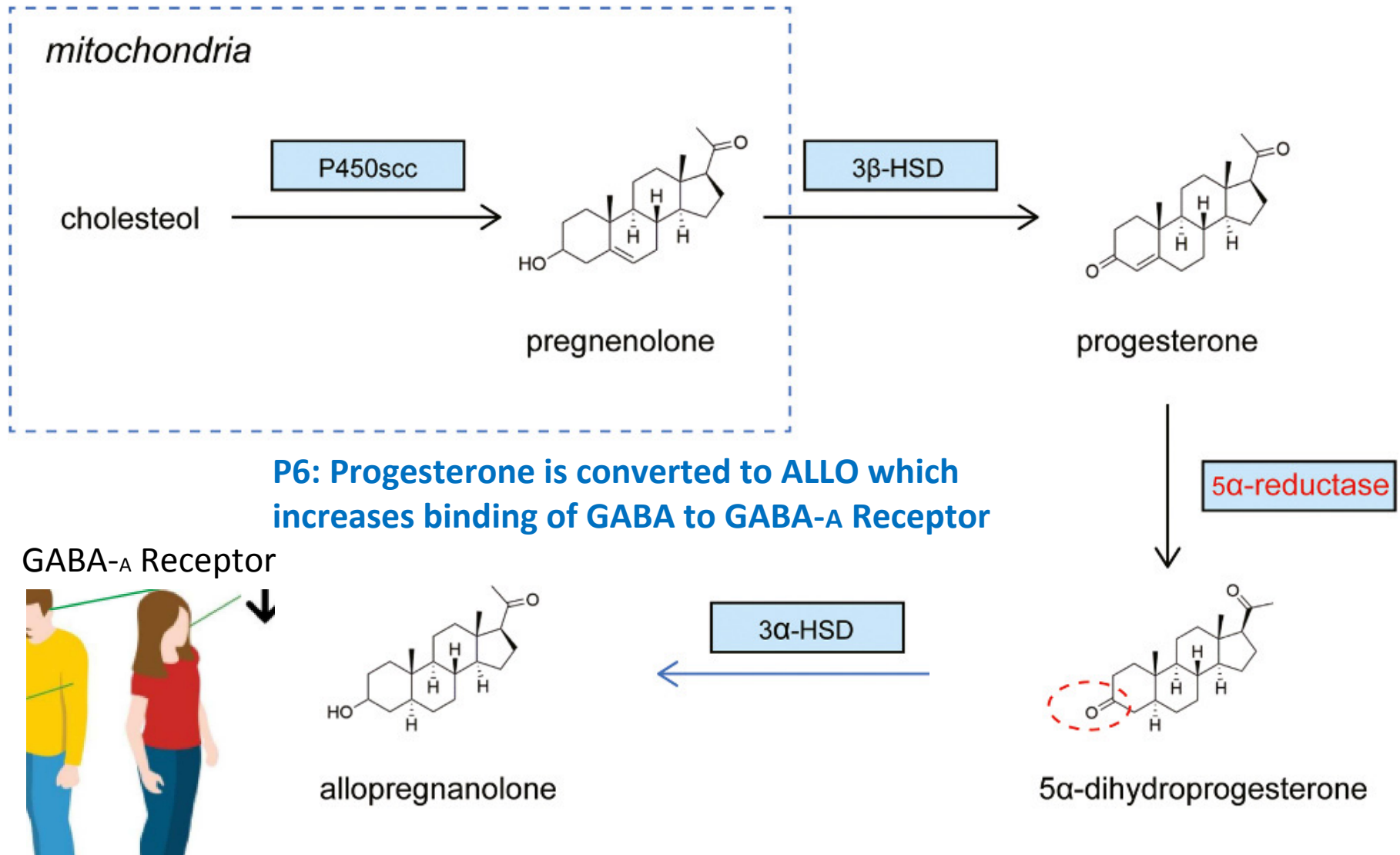
P4: Some women are particularly sensitive to progesterone



P5: The dose of progesterone is important (i.e., biphasic effect)

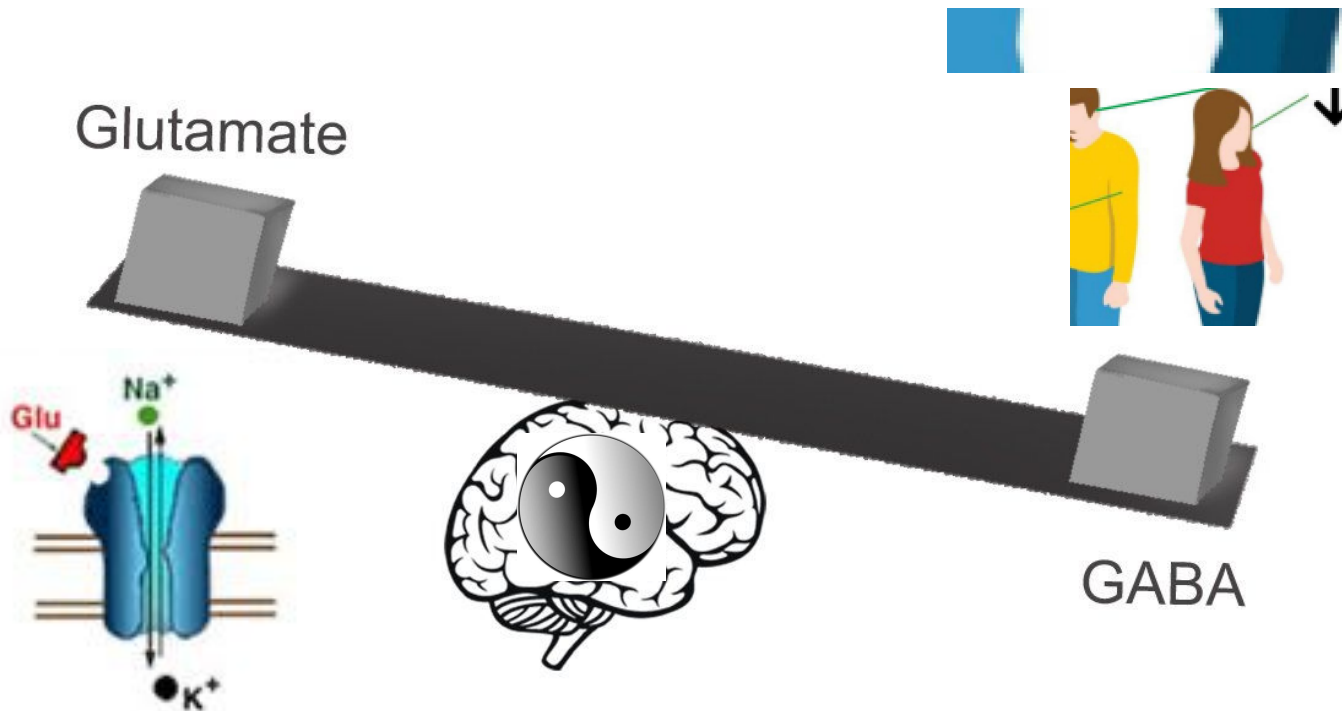


GABA-A Receptor

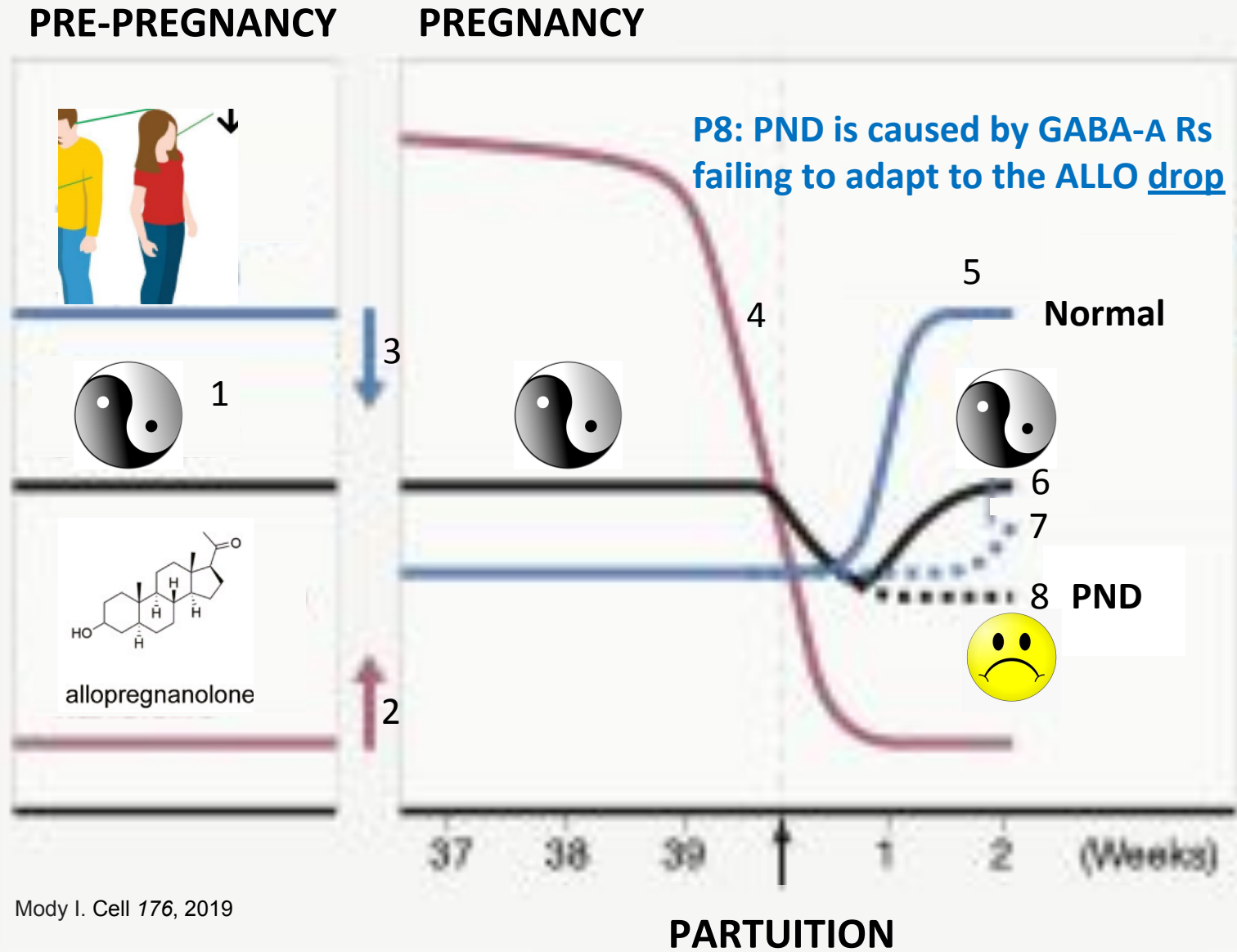


The Zen Brain

P7: The brain is balanced when
GABA and GLU are balanced

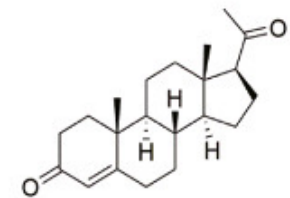
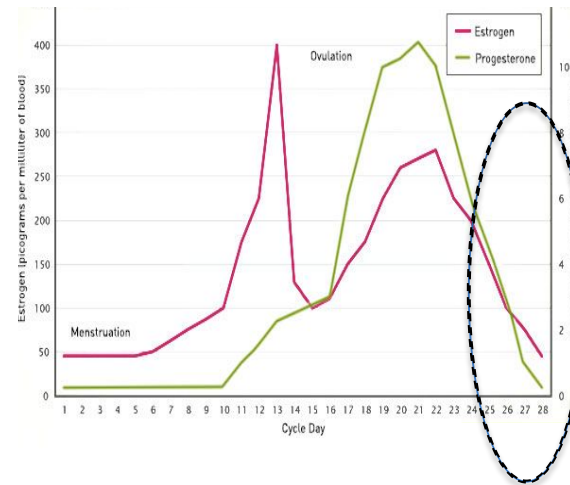


Postnatal depression (PND)



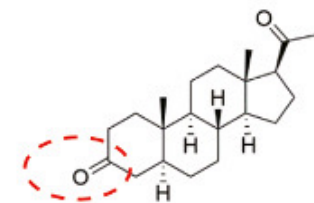
PMDD

P9: PMDD is also caused by GABA-A Rs failing to adapt to the ALLO drop



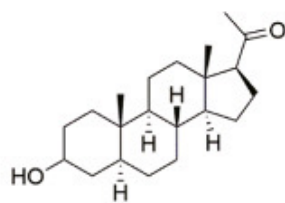
progesterone

5 α -reductase



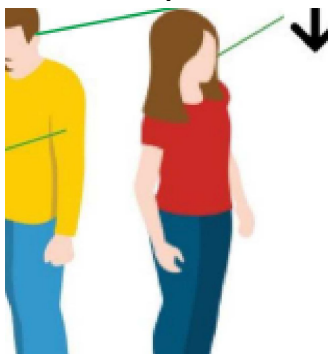
5 α -dihydroprogesterone

3 α -HSD



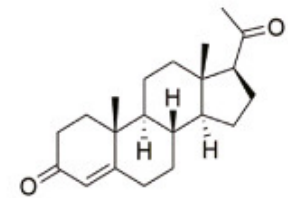
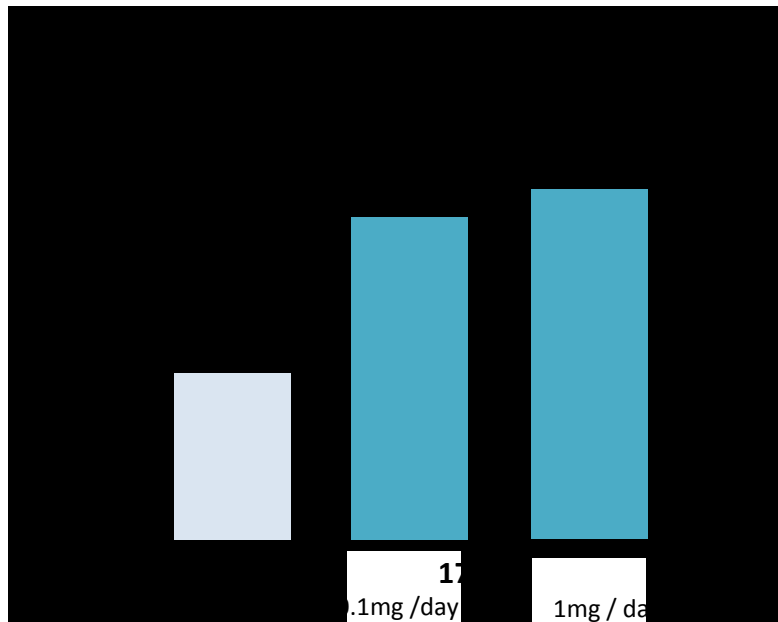
allopregnanolone

Poor adaptation



STOP THE DROP

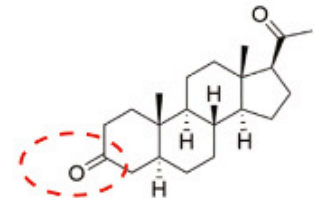
HIPPOCAMPUS



progesterone

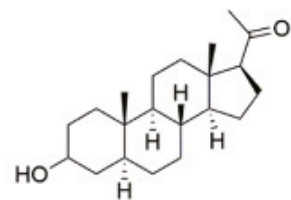
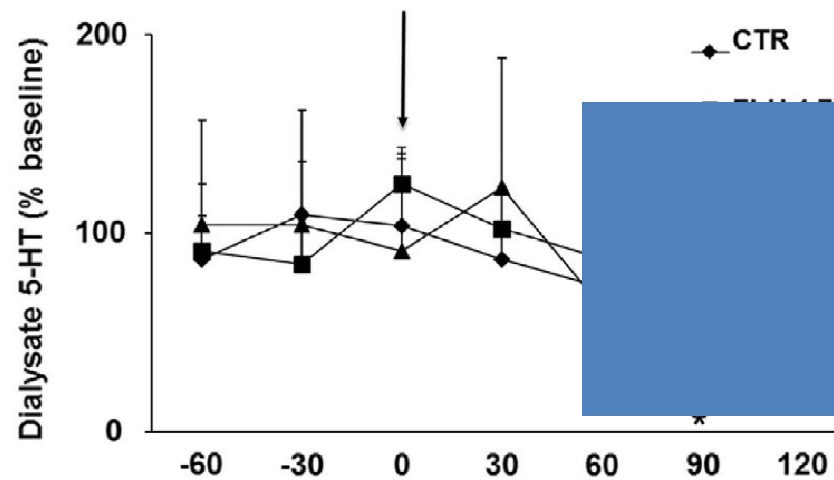
Oestradiol

5 α -reductase

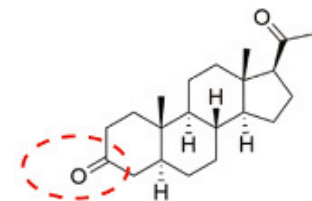


5 α -dihydroprogesterone

STOP THE DROP

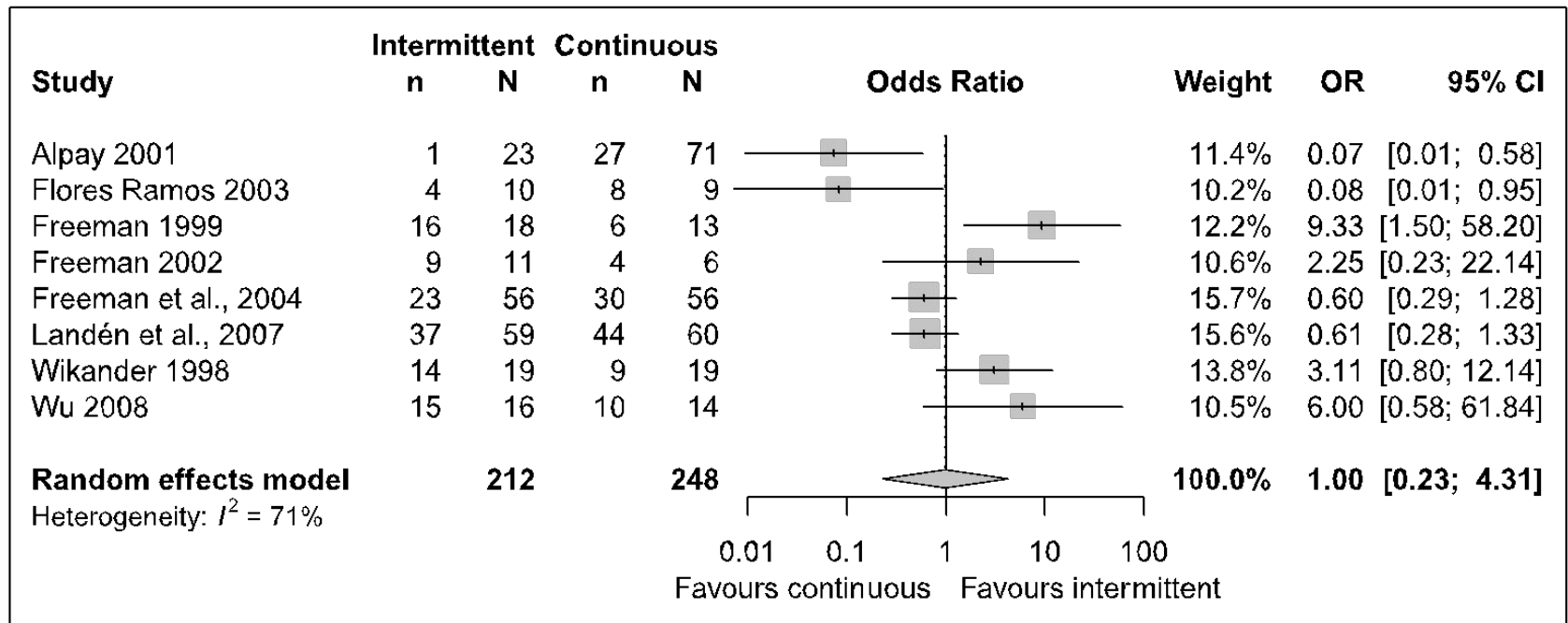


allopregnanolone



5 α -dihydroprogesterone

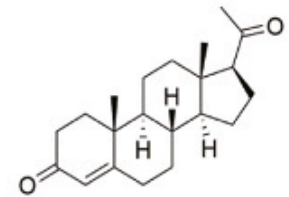
Intermittent SSRIs for PMS: A systematic review + meta-analysis



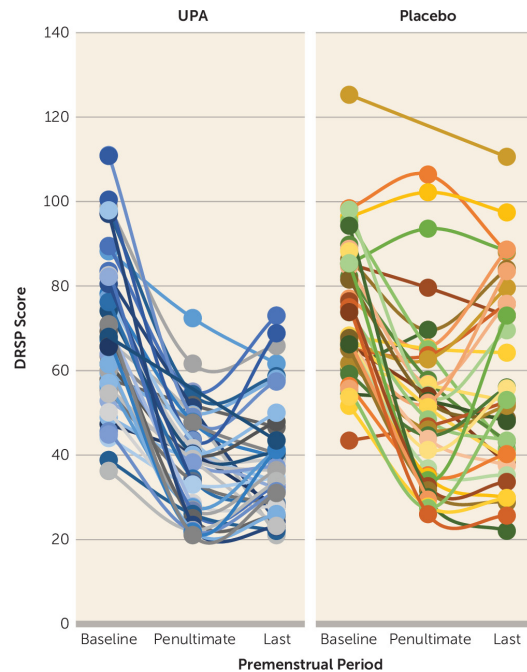
STOP THE DROP

Ulipristal Acetate

Selective prog. receptor modulator



progesterone



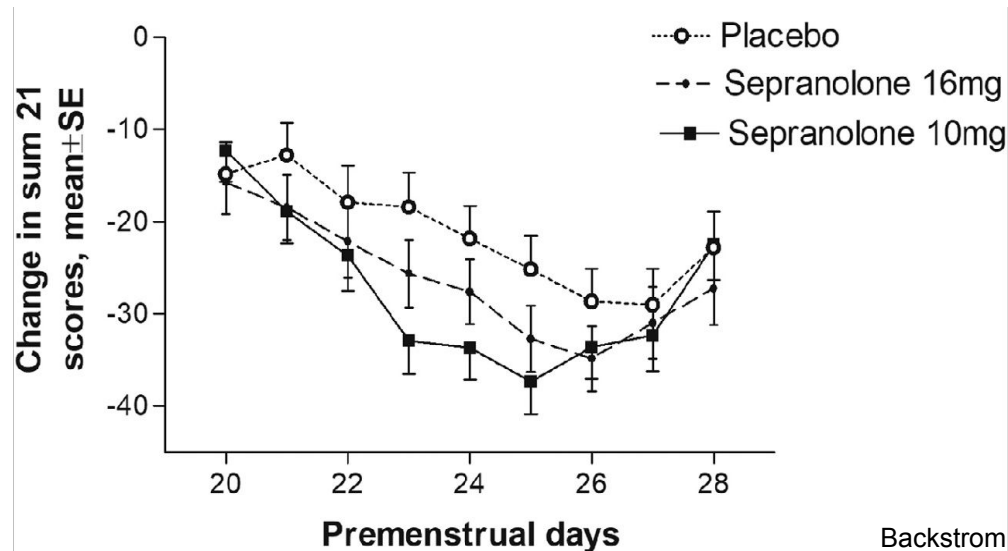
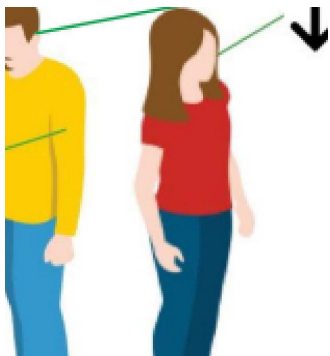
N= 95 (PMDD)
UPA 5 mg/day or placebo (RCT)
3 cycles

85%: complete / partial remission
replication + larger populations needed

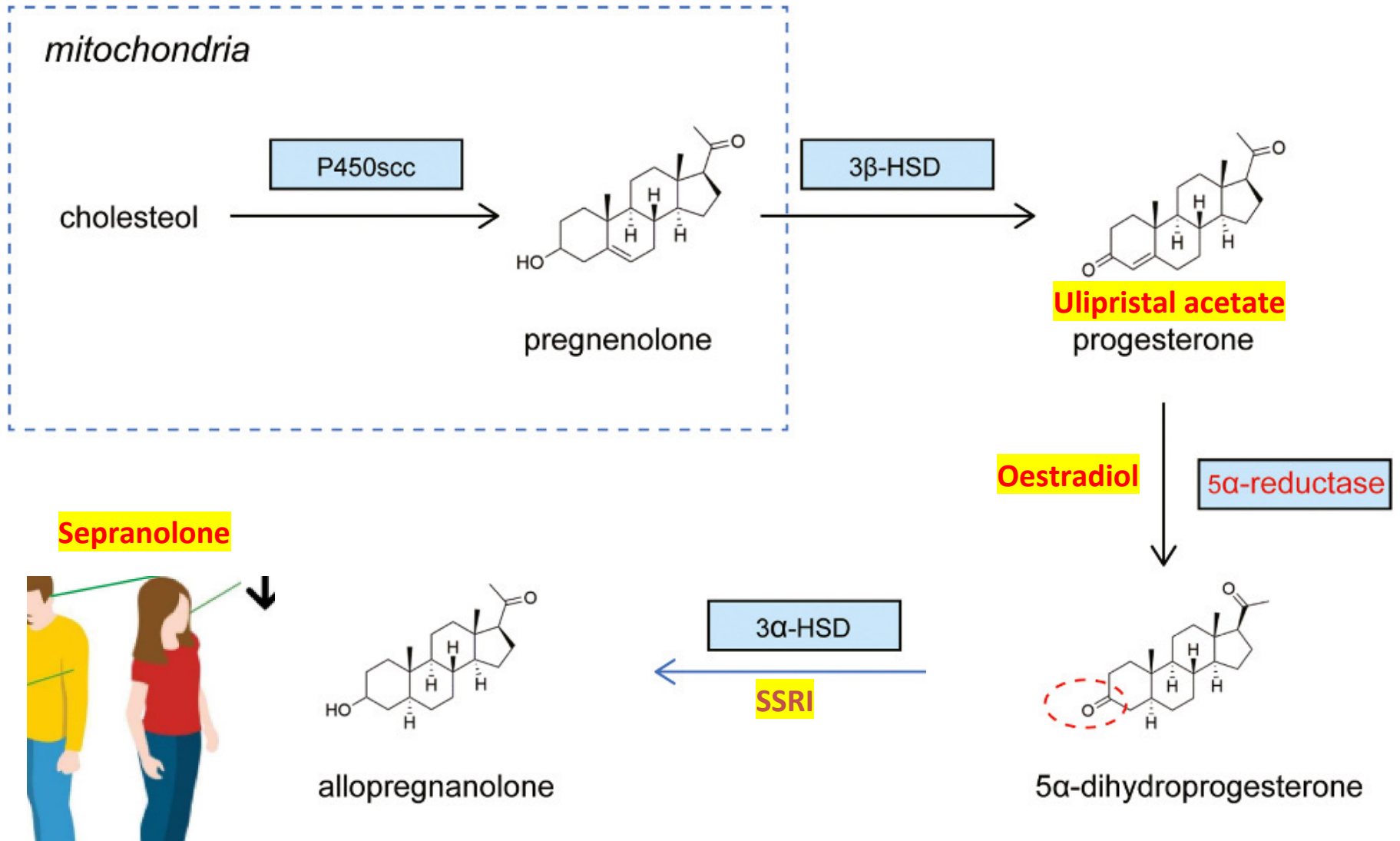
BLOCK THE DROP

GABA_A receptor modulating steroid
antagonist
Sepranolone

N = 206 (PMDD)
10mg, 16mg, placebo (s/c)
every 48 h for 14 days
3 cycles



SUMMARY



Attention Bias



DEPRESSION: Brain activation

Sad face



AMYGDALA

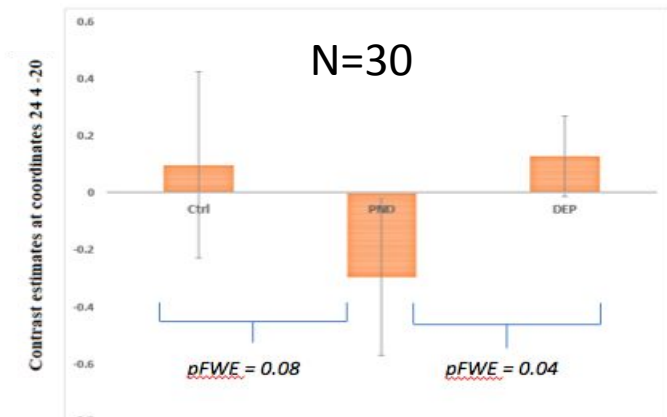
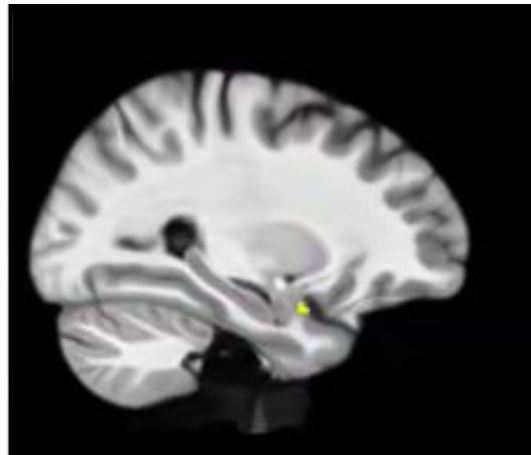
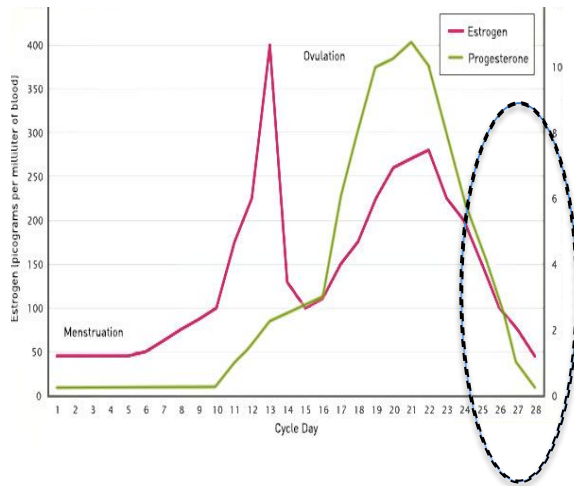


PH

F

Reproductive Depression

Happy face



Reproductive depression

Failure of GABA-A receptors to adapt to acute changes in ALLO

Treatments involve blocking this change or their effects on GABA-A receptors.

Associated with negative attention bias

Female Hormone Clinic

A national service for women who suffer from serious mental health disorders, including psychosis and severe depression, at times of hormonal change (e.g. premenstrual, peri and post-menopausal).

“Dr Craig’s interdisciplinary initiative is both brave and welcome. It is not about showing that women become a little moody at the time of the month, but about improving the care of those whose quality of life and health is severely impaired by treatable medical problems.” The Times, 2008