WOMEN'S MENTAL HEALTH

Still Not A Priority, Still Not Good Enough

GP Mental Health
Masterclass
Psychscene Meeting
Feb 3rd 2018

Prof J.Kulkarni
Monash Alfred Psychiatry
Research centre
www.maprc.org.au

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Mental Illness in Australian Women

- In Australia in 2007, 43 per cent of women (3.5 million) had experienced mental illness at some time in their lives.

- 22% of Australian women compared to 18% of men experienced symptoms of a mental disorder during the previous twelve-months

(**National Survey of Mental Health and Wellbeing: Summary of Results, 2007)**

Women and Mental Health

2X more women **attempt suicide** than men

2X as likely as men to develop **depression**

Anorexia and **Bulimia** are **3X** more common in women than men

2X as likely as men to suffer **anxiety disorders**

1/12 women will develop **alcohol dependence** during their lives

2X more likely than men to experience **Post Traumatic Stress Disorder**

The Cost of Mental Illness in Women

- The economic impact of depression/ anxiety in women in Australia due to direct lost productivity is estimated to be $22 billion per year (ABS 2012 data)
- Add in costs of treatments, lost earnings, cost of loss of effective parenting of children, divorce, loss of care of elderly and other…….

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GENDER & MENTAL HEALTH

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- Mental health (like physical health) is clearly gendered.
- Men and women have different patterns of mental illness and other forms of mental distress and they are exposed to different risk factors and vulnerabilities.
- A number of different theories have been proposed for the gender differences in the prevalence of mental health problems

Theories to Explain Gender Differences in Mental Illness

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Social theories

Biological theories

Psychological theories

Women and Mental Disorders

- SOCIAL: Violence, poverty, gender inequities in wages, power, social roles
- BIOLOGY: Hormone impacts, gender differences in drug metabolism systems, brain circuitry and genetic transmission.
- PSYCHOLOGY: Psychiatric illnesses may present very differently in men and women because of gender differences in psychological responses and defences

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GLOBAL SOCIAL IMPACTS on WOMEN'S MENTAL HEALTH

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RUSSIA

Domestic abuse in Russia

- 600,000 women victims of domestic abuse every year
- 14,000 die from injuries inflicted by husbands or partners each year

Source: Russian interior ministry estimates

Feb 9 2017

RUSSIAN President Vladimir Putin has signed into law a controversial bill easing punishment for domestic violence, which critics say will make holding abusers accountable even more difficult.

IRELAND

- “You cannot separate out the issue of having no reproductive rights from a woman’s mental health,” - **Veronica Keane, Irish Times 1st March 2017**
- “In Ireland we have a Men’s Health Strategy, but we don’t have a women’s health strategy.” **Orla O’Connor, Irish Times 1st March 2017**

“Rights, Resilience, Recovery” is the theme of the 2017 World Congress on Women’s Mental Health taking place in the RDS from March 6th-9th

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INDIA

NEWS

Indian Politician, Babulal Gaur, Reveals His Thoughts On Rape: 'Sometimes It's Right, Sometimes It's Wrong'

06/06/2014 17:24 | Updated 12 June 201

The Huffington Post UK

MAIL TODAY VIA GETTY IMAGES

Just a week after the gang rape and murder of two teenagers, an Indian politician has said rape is "sometimes it's right, sometimes it's wrong."

The Huffington Post UK 6th June 2014

SUDAN

'True hell' of mass rape in Darfur revealed in report on Sudan

Rape by Sudanese forces in Darfur revealed in Human Rights Watch report as agency says UN and African Union should take urgent steps to protect civilians

Women in Tabit in Sudan's North Darfur state. Human Rights Watch says mass rape in the town could amount to crimes against humanity. Photograph: Mohamed Nureldin Abdallah/Reuters

The Guardian Feb 11th 2015

CHINA

- “In 1995, China hosted the Fourth World Conference on Women, which produced the Beijing Platform for Action, a document outlining concrete measures to achieve gender equality worldwide.
- Yet today China’s authorities are actively thwarting women’s ability to act to achieve their goals.
- On March 8, 2015, International Women’s Day, police detained women’s rights activists planning an action to raise awareness about sexual harassment on public transportation”.

Ref: Inequality in China and the impact on women’s rights March 19, 2015 8.35pm AEDT by Eileen Otis, Associate Professor, University of OregonThe Conversation

HOW ARE WE DOING IN AUSTRALIA?

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VIOLENCE AGAINST WOMEN: HOW AUSTRALIAN PSYCHIATRIC UNITS PERPETUATE VIOLENCE AGAINST VULNERABLE WOMEN

October 13, 2016 · by Jayashri Kulkarni · in Research & Technology

Since the 1960s, psychiatric inpatient units in many parts of the world have housed male and female patients together. The level of illicit drug and alcohol use in the inpatient population, both prior to and during hospitalisation, heightens the level of behavioural disinhibition in the inpatient population.

Embed from Getty Images

Increasing rate of abuse of girls in Australia

- There is an increasing number of early – mid teenaged girls with incidences of maltreatment – sexual abuse, physical violence and/or neglect. *
- The biological, psychological and social impact of this is long – lasting, with obesity, poor education attainment, health services engagement due to self harm and rage with resultant poor quality of life.

*(ABS data 2011 v ABS data 1996)

PRECOCIOUS SEXUALISATION

TODDLERS & TIARAS
CONTESTANT – AGED 4

Miley Cyrus aged 9

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EARLY SEXUALISATION OF GIRLS & Mental Illness

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- Premature sexualisation is linked with serious mental health problems like eating disorders, low self-esteem and depression.
- Sexualisation puts girls in danger. It contributes to exploitation and violence against girls and women. It increases sexism, sex bias, and sexist attitudes.

Ref : Womensforum Australia 2013

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BIOLOGICAL IMPACTS ON WOMEN'S MENTAL HEALTH

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Hormones and the Brain

- Estrogens, progesterones, androgens – are all potent neurosteroids
- Significant evidence for modulation of dopamine, noradrenaline, serotonin, glutamate and acetylcholine by estradiol, progesterones and androgens.
- Longstanding clinical/ anecdotal evidence for biological hormone impact on mental state

Specific Mental Illnesses in Women

- Depression related to reproductive events:
  - PMS/PMDD
    - Depression and the OC Pill
      - Postnatal Depression
        - Perimenopausal Depression
- Borderline PD/ Complex Trauma Disorder
- Relapses of Psychosis related to estradiol fluctuations

Premenstrual Dysphoric Disorder (PMDD)

- A real entity
- 80% of women have some challenge relating to menses, 40% have PMS,10-15% have PMDD
- IT DOES NOT FOLLOW A CLEAR PREMENSTRUAL ONSET WITH OFFSET AT MENSES
- Look for cyclical onset with rapid onset and offset
- Listen to your patient – she often keeps a diary

PMDD TREATMENTS

- For severe PMDD (NOT PMS, not another psychiatric condition), vitamins, herbal treatments, lifestyle changes are ineffective
- Hormone treatments very important – suggest trying first line:

  - A) OCP – continuous. We favour “Zoely” – natural estradiol +nomegestrol acetate

  - B) OCP plus estradiol

PMDD

2nd Line treatments:

•SSRIs – use short half life drugs, less agitating ones – eg:citalopram, sertraline. Test with pharmacogenomic testing www.genesfx.com.au

3rd Line treatments

•SSRI + estradiol

•SSRI + aldosterone

4th Line treatments

•GnRh agonist drugs (eg: Synarel) + add back estradiol (chemical menopause)

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Mood & Oral Contraceptives - Is There a Relationship?

An Observational Trial With Australian Women

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AIMS

- To determine whether
  - The use of hormonal contraception is associated with negative mood change
  - Progestogen-only contraceptives are more or less likely to be associated with negative mood change than combined oral contraceptives
  - Newer progestogenic compounds are less likely to be associated with negative mood change than older types of progestin
- To establish any predisposing factors for hormonal contraceptive-related negative mood change

STUDY DESIGN

- Observational cross-sectional design
- Collection of both quantitative and qualitative data
  - Quantitative data from standardised, self-administered mood rating scales
  - Qualitative data from an interview process
- Variables
  - Independent variable = type of contraceptive medication being (or not being) used
  - Dependent variables = scores on a battery of mood rating scales and the GAF

EE_2 DOSE VS. NON-USERS

- Significant differences in BDI, CESD-R, POMS and GAF scores between different EE_2 dose groups and non-users ($p < 0.05$)
- Users of 20μg COCPs had significantly higher mean scores on all mood rating scales than all other groups ($p < 0.05$, partial $eta^2 > 0.15$)
- Users of 20μg COCPs had significantly lower mean GAF score than all other groups ($p < 0.05$, partial $eta^2 = 0.12$)
- SUMMARY: **Low dose estradiol pill (20μg) assoc with more depression. Older progestins also assoc with more depression**
- **In our Clinic – we use ZOELY (estradiol 30mcg + nomigestrol)**

Which “Pill” is best for mood?

- From our studies (ongoing) and clinical practice:
- Low dose estradiol (20mcg) – worse for depression
- Drospirenone (Yaz,Yasmin) – worse for aggressive behaviours
- Norethisterone, levonorgestrel, medroxyprogesterone in OCs – not great for mood
- Progesterone –only - worst of all for mood (especially depot provera or Implanon(etonogestrel)
- Multiphasic OCs worse for mood than monophasic OCs
- Best so far for mood is ZOELY (nomegestrol + 1.5mg oestradiol). But has weight gain and acne side effects
- **STILL WAITING FOR A GOOD OC FOR MOOD AND OTHER ADVERSE EFFECTS**

Danish Pill Study 2016

Research

JAMA Psychiatry | Original Investigation

Association of Hormonal Contraception With Depression

Charlotte Wessel Skovlund, MSc; Lina Steinrud Mørch, PhD; Lars Vedel Kessing, MD, DMSc; Øjvind Lidegaard, MD, DMSc

IMPORTANCE Millions of women worldwide use hormonal contraception. Despite the clinical evidence of an influence of hormonal contraception on some women's mood, associations between the use of hormonal contraception and mood disturbances remain inadequately addressed.

OBJECTIVE To investigate whether the use of hormonal contraception is positively associated with subsequent use of antidepressants and a diagnosis of depression at a psychiatric hospital.

DESIGN, SETTING, AND PARTICIPANTS This nationwide prospective cohort study combined data from the National Prescription Register and the Psychiatric Central Research Register in Denmark. All women and adolescents aged 15 to 34 years who were living in Denmark were followed up from January 1, 2000, to December 2013, if they had no prior depression diagnosis, redeemed prescription for antidepressants, other major psychiatric diagnosis, cancer, venous thrombosis, or infertility treatment. Data were collected from January 1, 1995, to December 31, 2013, and analyzed from January 1, 2015, through April 1, 2016.

EXPOSURES Use of different types of hormonal contraception.

MAIN OUTCOMES AND MEASURES With time-varying covariates, adjusted incidence rate ratios (RRs) were calculated for first use of an antidepressant and first diagnosis of depression at a psychiatric hospital.

RESULTS A total of 1 061 997 women (mean [SD] age, 24.4 [0.001] years; mean [SD] follow-up, 6.4 [0.004] years) were included in the analysis. Compared with nonusers, users of combined oral contraceptives had an RR of first use of an antidepressant of 1.23 (95% CI, 1.22-1.25). Users of progestogen-only pills had an RR for first use of an antidepressant of 1.34 (95% CI, 1.27-1.40); users of a patch (norgestrolmin), 2.0 (95% CI, 1.76-2.18); users of a vaginal ring (etonogestrel), 1.6 (95% CI, 1.55-1.69); and users of a levonorgestrel intrauterine system, 1.4 (95% CI, 1.31-1.42). For depression diagnoses, similar or slightly lower estimates were found. The relative risks generally decreased with increasing age. Adolescents (age range, 15-19 years) using combined oral contraceptives had an RR of a first use of an antidepressant of 1.8 (95% CI, 1.75-1.84) and those using progestin-only pills, 2.2 (95% CI, 1.99-2.52). Six months after starting use of hormonal contraceptives, the RR of antidepressant use peaked at 1.4 (95% CI, 1.34-1.46). When the reference group was changed to those who never used hormonal contraception, the RR estimates for users of combined oral contraceptives increased to 1.7 (95% CI, 1.66-1.71).

CONCLUSIONS AND RELEVANCE Use of hormonal contraception, especially among adolescents, was associated with subsequent use of antidepressants and a first diagnosis of depression, suggesting depression as a potential adverse effect of hormonal contraceptive use.

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Supplemental content

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Perimenopausal Depression

Under recognised and underrated

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PERIMENOPAUSAL DEPRESSION

- Very high incidence of first onset depression in perimenopause. Even higher relapse risk of depression in women with past history.
- Overall depression rates increase up to sixteen times in 42-52 year old women.
- Second highest completed suicide group –in Australia – women aged 45-52
- Declining/ chaotic HPG axis function occurring from age 43-55. CNS changes first – up to 5 years before hot flushes, amenorrhoea

PERIMENOPAUSE DEPRESSIVE SYMPTOMS

- Plummeting self – esteem
- Paranoid ideation
- Aggressive
- Disconnection
- No libido
- Irritable / agitated
- Weight gain
- Poor sleep (compounded by hot flushes)
- Memory/ concentration changes
- Anxiety /Panic

Aetiology of Perimenopausal Depression

- A subset of women seem to be predisposed to experience mood disturbances triggered by hormonal fluctuations.
- This subset includes women with a history of mood disorders or of premenstrual and postnatal mood-related symptoms or a female family history of mood disorders related to hormone events.
- Women with no previous history of mood disorders at all can develop severe perimenopausal depression de novo.
- Not found with usual HPG axis lab investigations – this is CNS estradiol fluctuation

PERIMENOPAUSE DEPRESSION MANAGEMENT

- Depression in middle aged – multifactorial
- Antidepressants or MHT? Usually both, but if possible better to start with MHT
- Sleep regulation
- Natural medicines
- Psychotherapy

Menopause Hormone Treatment

- Currently, the evidence base in terms of clinical trials conducted with menopausal hormone treatments in actual perimenopausal depression is limited.
- MHT is useful in treating perimenopausal depression
- MHT Practice Suggestions: International Menopause Society (IMS) guidelines updated in 2016
- The MHT types that are available for use in perimenopausal depression treatment include – conjugated equine estrogen (CEE) or transdermal estradiol 75–100 mg/day or oral ethinylestradiol Micronized progesterone can be administered as a cyclic regimen.

MHT Practice Suggestions

- International Menopause Society (IMS) guidelines updated in 2016
- The MHT types that are available for use in perimenopausal depression treatment include – conjugated equine estrogen (CEE) or transdermal estradiol 75–100 mg/day or oral ethinylestradiol.
- Micronized progesterone can be administered as a cyclic regimen.

COCs for Perimenopausal Depression

- In early transition to menopause, the combined estrogen/progestogen contraceptive pills (COCs) are useful treatments, although it is important to keep in mind that many COCs may be associated with increases in depression.
- Zoely as a COC has less depression than other COCs

TIBOLONE

- Tibolone is a synthetic steroid and has a mixed hormonal profile. Its estrogenic potency is about 1/50 of that of ethinyl-estradiol, its progestogenic potency is 1/8 that of norethisterone acetate and the androgenic potency is about 1/3 that of norethisterone. It has been proven to relieve climacteric symptoms and improve libido as well as assist in the management of perimenopausal anxiety and mild depression

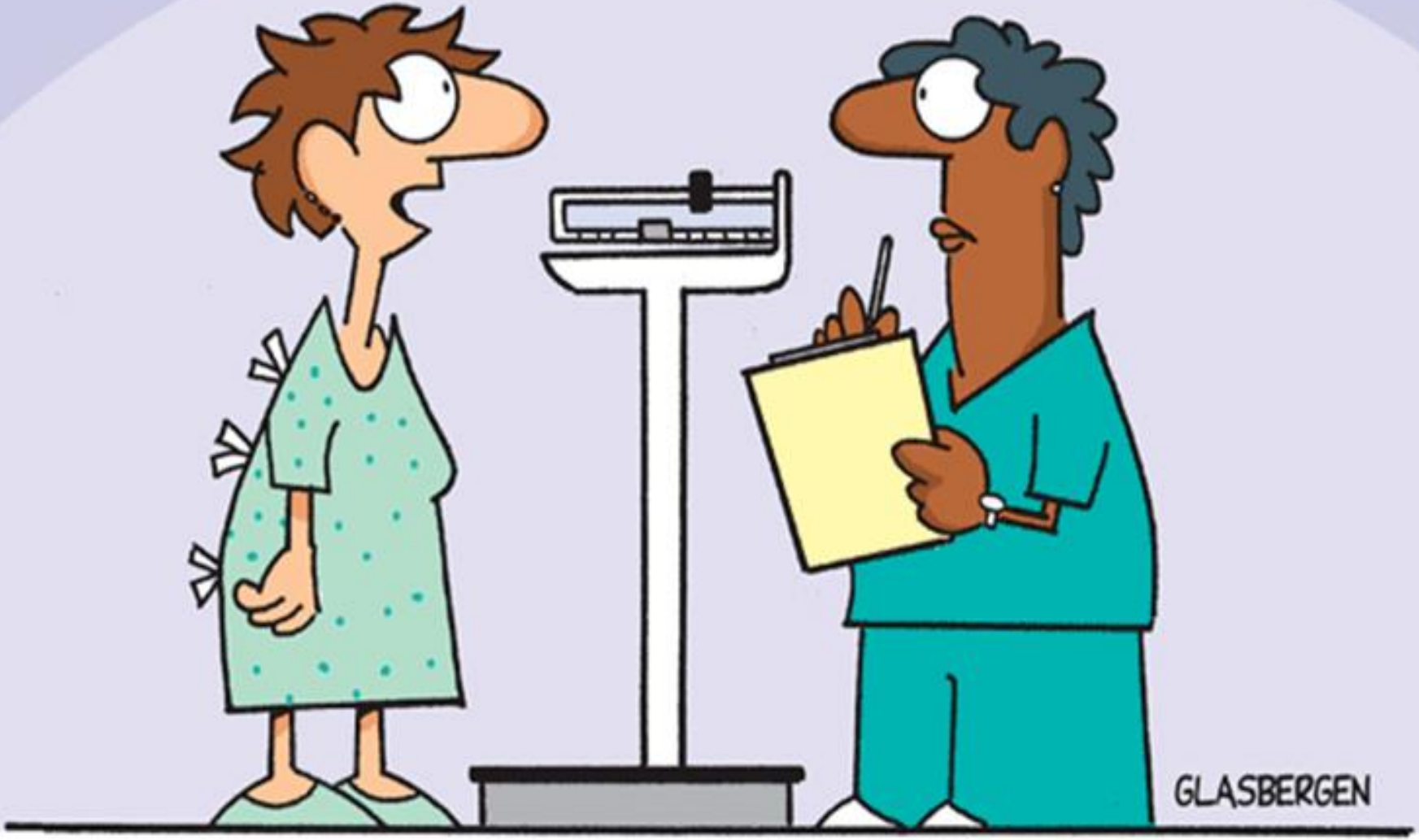
- Adverse effects with tibolone is intermenstrual bleeding. but an advantage of tibolone treatment is that it does not cause increased breast density.

MHT for Depression

- The risks and benefits of MHT differ for women during the menopause transition compared to those for older women. Bioidentical hormones are not recommended by the IMS because of standardization and dosing issues.

Treating women with new depression related to perimenopause

- Assess and monitor severity (including suicidality) – new doesn't mean less severe
- HT more acceptable to most women
- Natural therapies
- Psychotherapies - support but don't treat this depression
- Combinations of the above
- Address weight gain and physical health issues



"I'm a wife, a mother, a daughter, an executive, a cook, a housekeeper, a teacher, a chauffeur, and a soccer coach. *That's only 19 pounds per woman!"*

Antidepressant Use - Depression in Perimenopause

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- Commonly used to treat anxiety, depression, sleep problems, hot flushes
- SNRIs popular (low dose venlafaxine)
- Issues – discontinuity problems, blunting, aggression, problems with tachyphylaxis
- Match symptom with antidepressant eg: agitation worsened by fluoxetine
- Consider circadian rhythms restoration

NEW APPROACHES : OUR RESEARCH

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- Recognition of the condition
- Safe, shorter –term hormone treatment
- Different antidepressant approach (on/off)
- Physical health overview – tackle weight gain, wine consumption, lack of exercise
- Working with natural medicines too

CASE STUDY

- Kate is a 48 year old nurse, who has three children aged 17, 14 and 12.
- Married for 21 years.
- No past history of any psychiatric illness, no family history
- Symptoms were tiredness, tearfulness, poor sleep pattern, weight gain, excessive alcohol use, constant anxiety

CASE STUDY

- Kate, was working in a private hospital as a theatre nurse and found that she couldn't concentrate – although she had done this work well for the past 15 years.
- "I felt so tired and foggy all time – but also 'wired and edgy' at the same time"
- Sleeping pattern changed – woke up about 3-4 times per night, then ruminating over the days work, household issues, children, husband
- Changed from Theatre to Recovery work – not enjoyed as much, felt like a "demotion"
- Gained 5 kg
- Drinking nearly one bottle red wine per night – to "drown out everything"

CASE STUDY

- Kate began to think about her life as being futile
- She often thought about methods of committing suicide
- She attended her GP and told him about her symptoms and her thoughts of suicide
- Kate started on fluoxetine – agitated, felt worse, despairing. Dose increased every 4 days to 80mg/day – even worse (poor sleep, agitation)
- Discussing suicide ideas daily with husband, she took sick leave, not able to care for children
- Referred to WMH Clinic

CASE STUDY

Diagnosis: Perimenopausal Depression

Treatment:

Risk Assessments done

HRT - Tibolone started

- Decreased dose of Fluoxetine to 40mg/day(with aim to cease over time) (www.genesfx.com testing showed slow metabolism)
- Low dose quetiapine (12.5mg nocte)
- Psychotherapy (with husband as well)
- Alcohol withdrawal programme

CASE STUDY

After 3 months:

- Kate's comment : "I feel better, and nearly myself again"
- Sleeping, eating better. No suicidal ideation
- No alcohol

After 8 months:

- "I'm back"
- Continuing on tibolone
- No quetiapine
- No fluoxetine
- No alcohol

WHAT HAPPENED TO JENNY?

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- **Biological**
- Hormone shifts related to perimenopause
- Depression related to change in brain neuroendocrinology
- **Psychological**
- No particular psychopathology, but self-esteem plummeted
- **Social**
- Life roles, relationship changes, work

PERIMENOPAUSE

- A biopsychosocial approach is imperative
- A time of great upheaval for many

BUT

- Happy endings are very possible

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EMMA

EMMA

- Emma, now 26 – was raised by her single mother.
- Her father left when Emma was 5.
- She was sexually abused by her mother's boyfriend when she was aged 8 to age 14.
- She told her mother who did not believe her.
- Emma left home at age 16 and has a history of amphetamine abuse, alcohol abuse.

Emma

- She cuts her arms and wrists and says this makes her feel “alive”.
- Emma could not complete school and said she was unable to concentrate and has a “bad memory”.
- She feels empty inside and often looks “dazed”.
- Emma has angry outbursts over minor things.

EMMA

- Emma is very overweight.
- She has made 11 suicide attempts.
- Emma has had 4 admissions to psychiatry wards.

EMMA

Emma has a diagnosis of "**BORDERLINE PERSONALITY DISORDER**".

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What is BORDERLINE PERSONALITY DISORDER?

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- The DSM 5 term is “Borderline Personality Disorder”.
- What a useless term!!
- A better term is **COMPLEX TRAUMA DISORDER.**

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Symptoms of BPD/ CTD

- Deep feelings of insecurity
- Fear of abandonment and loss
- Rage & anger
- Fragile sense of self / feel fragmented
- Dissociation with stress.
- Self-harm
- Persistent impulsiveness
- Confused, contradictory feelings.

Symptoms of BPD/ CTD

- May experience **anxiety** or **mood disorders**.
- May experience **psychotic symptoms**
- Re-appearance of symptoms at **menopause.**
- **THIS CONDITION IS COMPLEX, HARD TO DIAGNOSE. CONTAINS MANY SYMPTOMS THAT OCCUR IN OTHER CONDITIONS**

What Causes CTD/BPD?

85% of cases

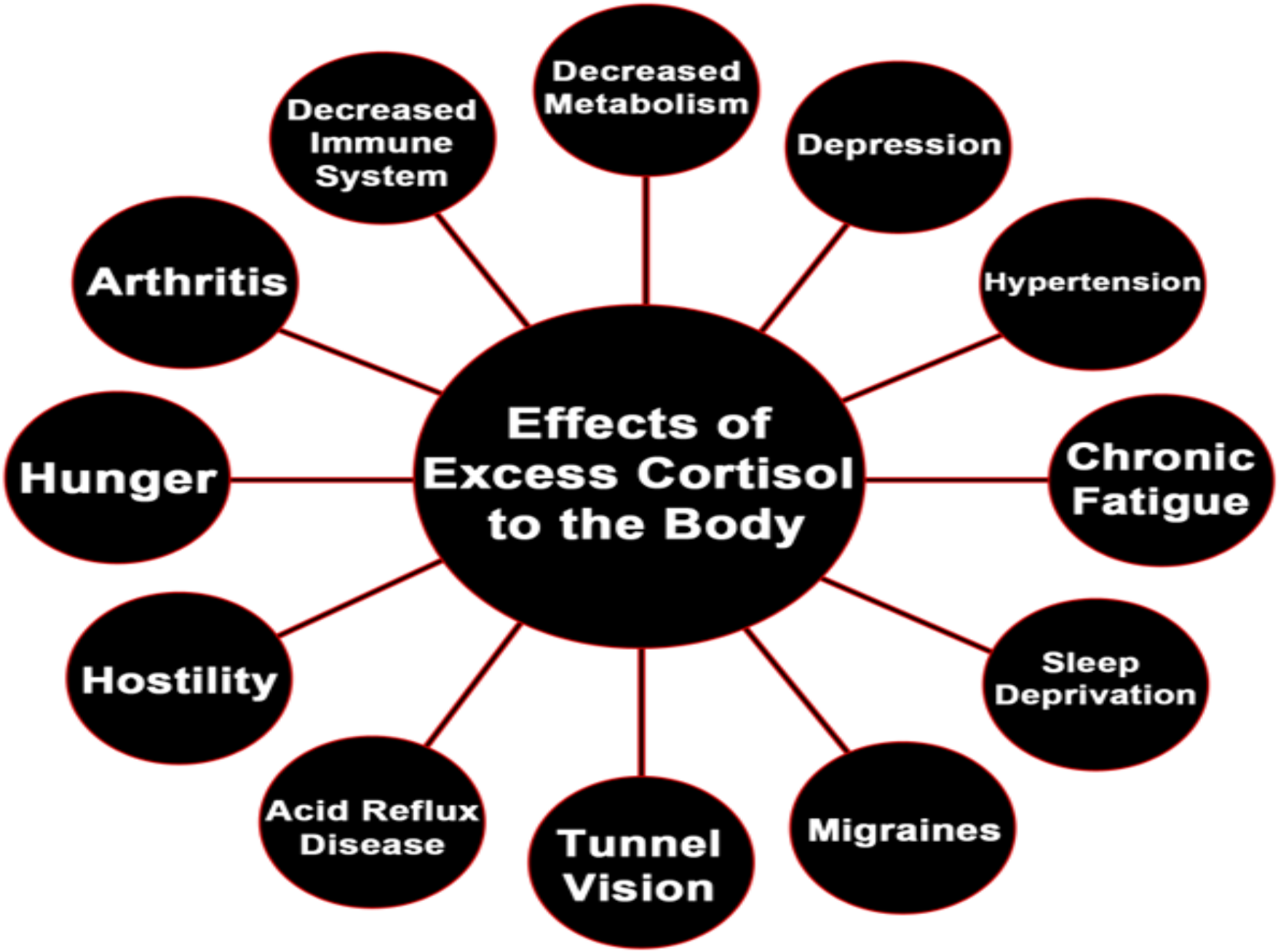
- Early Life Trauma (many types)
- Early Life Deprivation (loss of, disruption of primary care)
- Early Life Privation (no real primary care)

15% of Cases

- ?Genetic factors

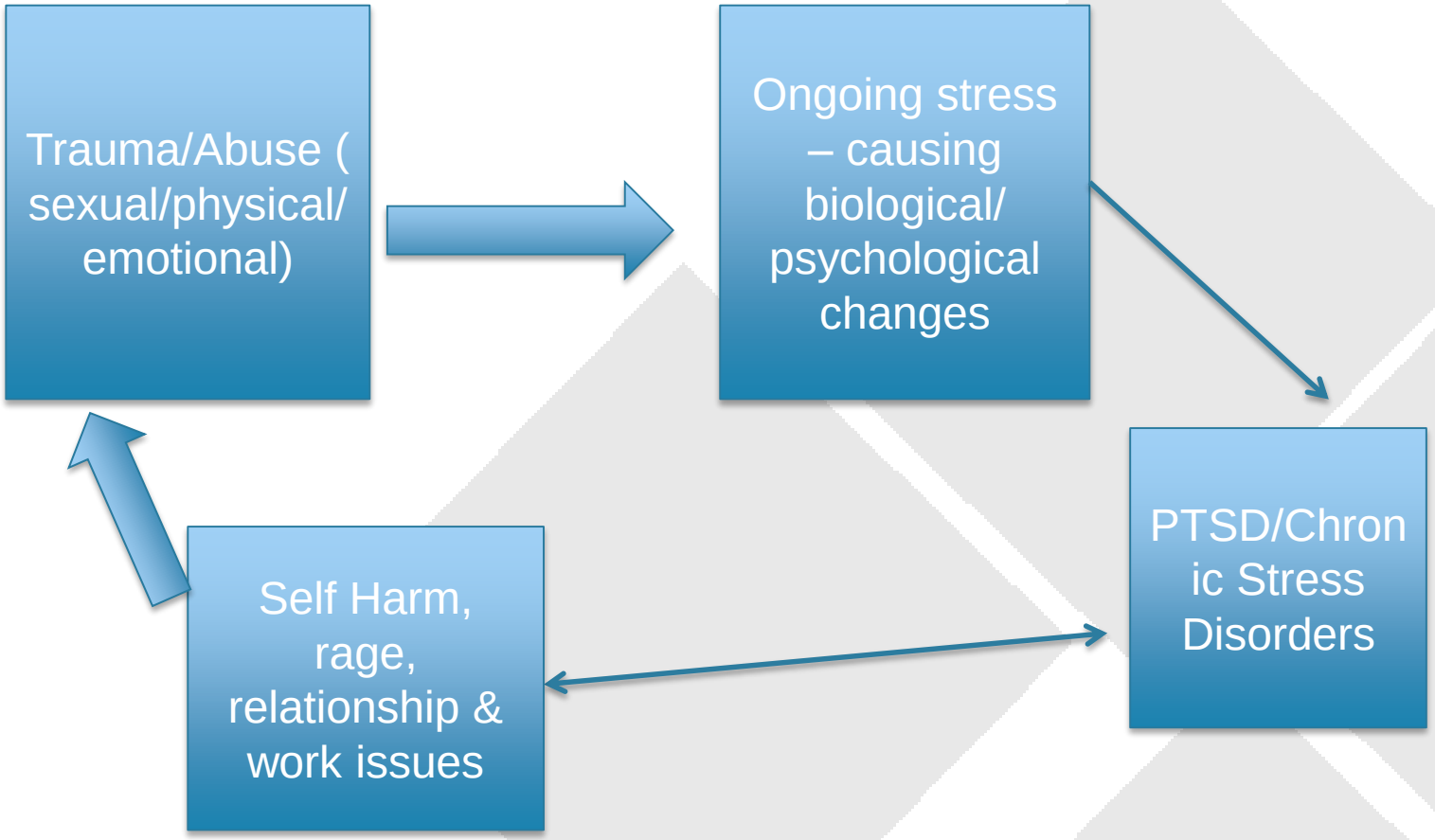
MANY BIOLOGICAL ISSUES IN WOMEN WITH CTD/BPD

- Obesity
- Diabetes
- Infertility
- Abnormal menstrual cycles
- Chronic fatigue
- Fibromyalgia
- Increased susceptibility to infections



Cortisol - The Stress Hormone

Relationship between Abuse/Stress and CTD



A BIOPSYCHOSOCIAL MODEL FOR BPD/ CTD

- To date, BPD sufferers have not received rational “bio” treatments, nor a clear explanation of the “social” (often about violence) aspect of aetiology
- Treatment has mainly been ”psychological” – with patchy, difficult to access, long treatments

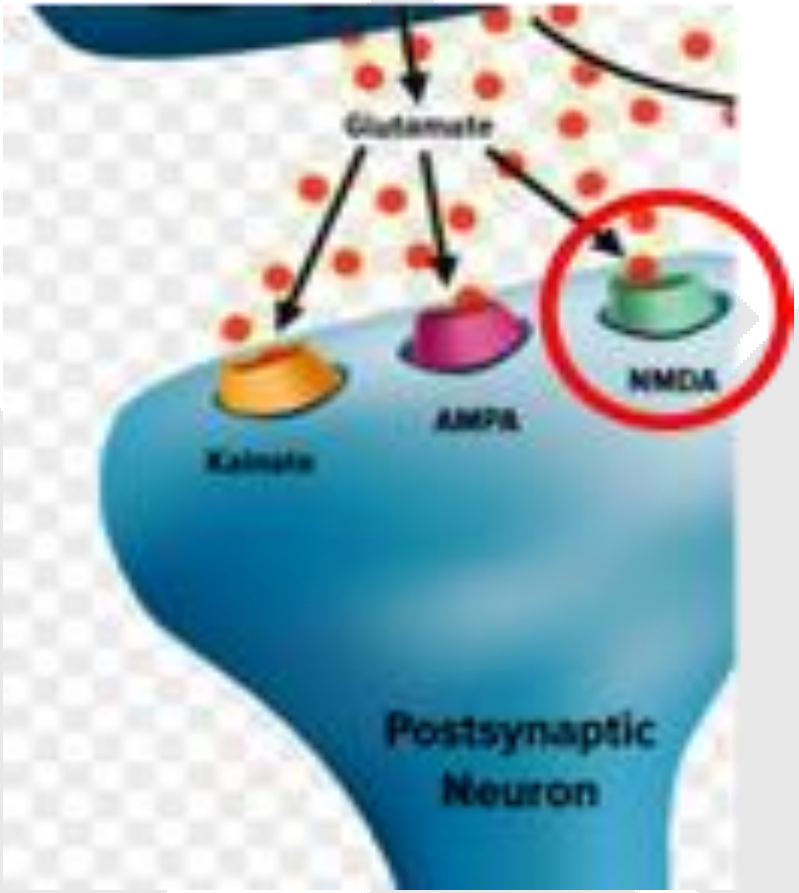
CTD/BPD “Bio”Aetiology

- Childhood maltreatment can trigger major neurobiological destabilization
- Disruptions in neuroendocrine, neurochemical and neuroimmunological systems with feedback system loops between all of the critical central nervous system anatomical and neurochemical pathways *
- Growing evidence that glutamate dysregulation is critical in the development of the hallmark symptoms of BPD*.

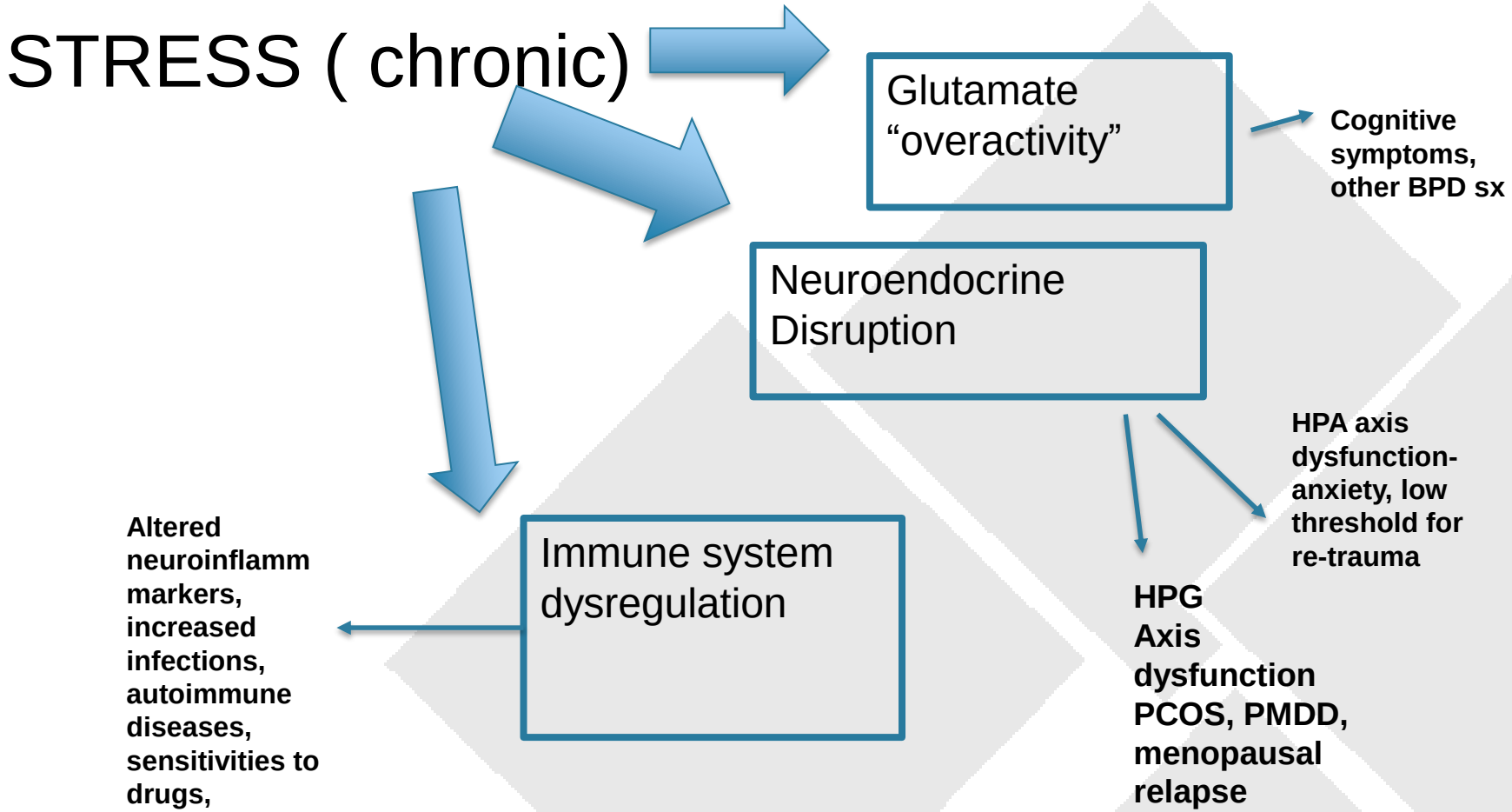
- *Grossjean B 2007

Glutamate & BPD/CTD

- The **NMDA receptor** is a glutamate receptor. Activated when glutamate and glycine (or D-serine) bind to it.
- The glutamatergic system, in particular, the NMDA subtype receptor, has major role in cognition and memory, and its critical role in experience-dependent neuroplasticity. *
- *Javitt D 2004



Theoretical "Bio" Aetiology of BPD/CTD

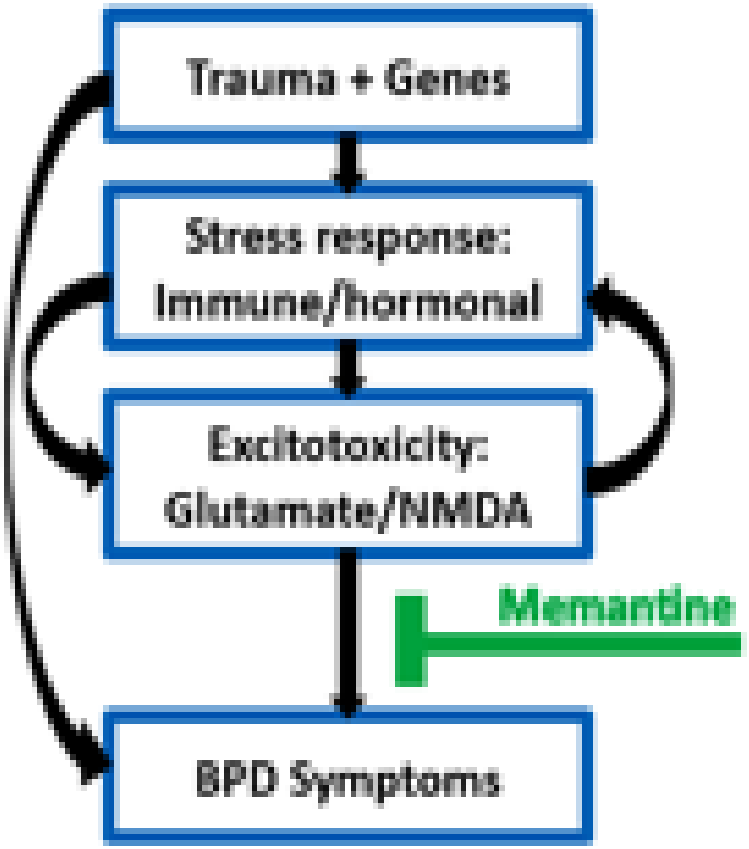


In summary

- **Early traumatic experiences and genetic vulnerability lead to stress-related neuroendocrine, immune and cognitive changes thereby contributing to the development of BPD and ongoing symptoms.**
- **Altered glutamate signaling appears to be a key event in the pathophysiology of BPD,**
- **Molecular mechanisms capable of regulating glutamate release represent novel and potentially promising treatment targets.**

Memantine – an NMDA antagonist

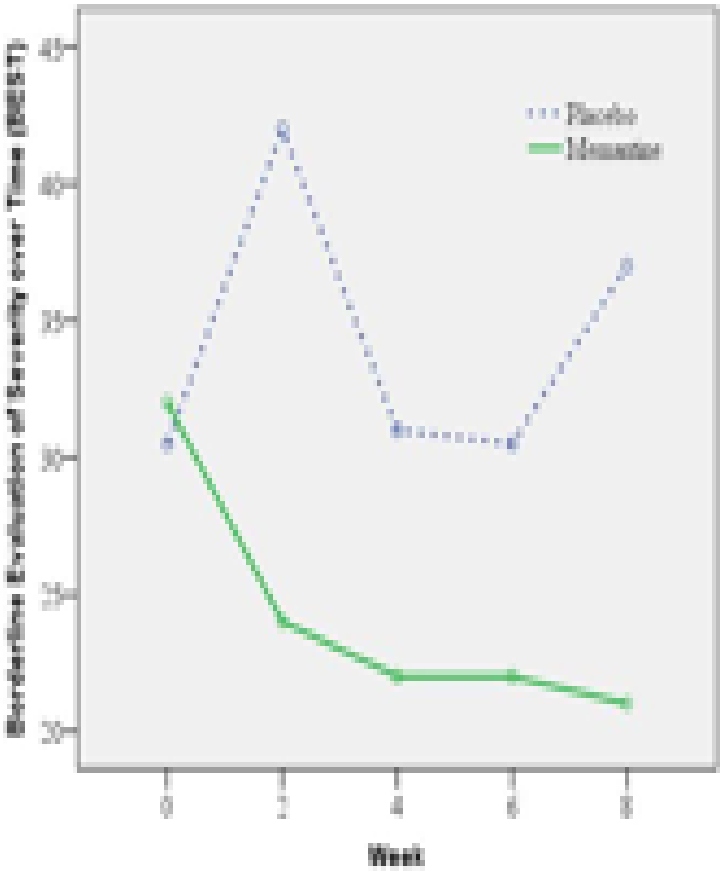
- Memantine – a cognitive enhancer used in Alzheimer's
- NMDA antagonist
- Doesn't cause dissociation –like ketamine



- NHMRC Project grant 2016

Study underway

- Small numbers to date (N=8) – but shows promise
- Recruitment ongoing
- Stay tuned!!



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Our RESEARCH in CTD

- New treatments being developed for people with CTD with NMDA receptor modulator
- Hormone treatments for women with CTD
- New clinical approach by linking trauma with biological changes, renaming the condition
- Special psychotherapy
- Education of health professionals, general public about CTD

WE NEED TO DO BETTER FOR EMMA

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SOME OTHER CURRENT WMH RESEARCH

- Estrogen and “brain estrogen” treatment in women with schizophrenia
- Hormone treatment for Women with Bipolar Disorder
- Menopause & Anxiety
- Women’s safety in our inpatient wards
- Educating GPs and other clinicians on the assessment of Domestic Violence
- Brain stimulation treatment for women
- Many, many other projects in women’s mental health….

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MAPrc Women's Mental Health Research Team

Cutting edge research into women's mental health. We also have a tertiary specialist Women's Mental Health Clinic that won the 2012 Vic Health Minister's Award for Outstanding Achievement

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WHERE TO FROM HERE?

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New Approaches Needed Now

- One size does not fit all!
- Specific mental health approaches **for women** urgently needed

An Integrated, Tailored Approach

- We need to tackle the culture – to decrease violence, decrease drug and alcohol use, increase productivity for good mental and physical health for women and men.
- Pursue Women's Health and Women's Mental Health agendas vigorously.
- Provide new women focused treatments through more research
- Provide more advocacy
- Address safety, privacy and treatment access issues for women with mental ill health
- Continue with "White ribbon" programmes and more.
- Pursue gender equality in pay, social responsibility and equity domains.

Women's Mental Health
Let's make it a national priority.

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