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Late onset of Psychosis in Perimenopause and Menopause

5 February 2025, 6.30-8.30pm

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Welcome

Sarah Sullivan

Co-director,

Psychosis Health Integration Team

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Housekeeping

- Fire alarm: please follow the exits down the stairs and outside
- Toilets: through the door at the back of this room, down the corridor on left, also at top of stairs
- Respect and welcome diversity of thought

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What is the Psychosis Health Integration Team?

- A group of health care professionals, researchers, service providers and people with lived experience, supported by Bristol Health Partners, who together try to improve research in our region.
- The team wants to:
  - improve research that results in changes to services that promote a greater emphasis on psychological and trauma informed approaches.
  - bring together medical/biomedical research with social/environmental research and work towards addressing this division

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Purpose of this event

Learn

Think

Share

Discuss

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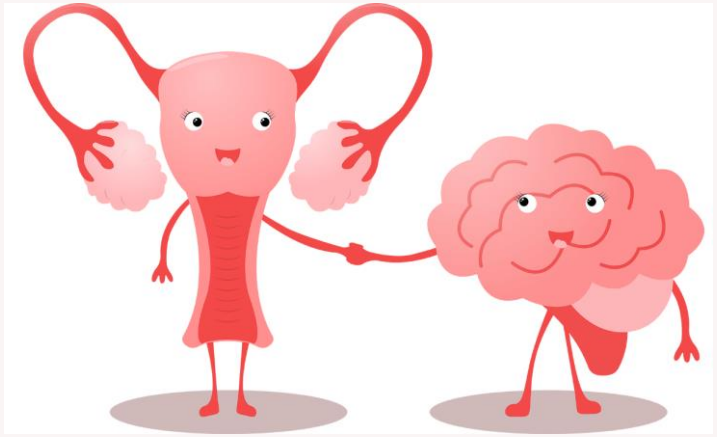

Psychosis and Peri/menopause

Dr Ruta Kuzminskyte, Avon & Wiltshire Mental Health Partnership NHS Trust

Dr Sophie Behrman, Oxford Health NHS Foundation Trust

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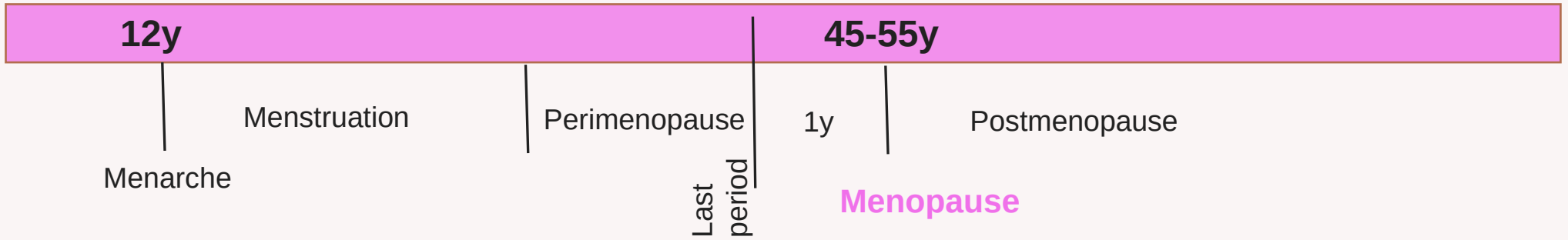
Menopause

- **What is the definition of the menopause?**
  - One year since last menstrual period
  - End of a woman's reproductive age
  - When ovaries stop producing eggs



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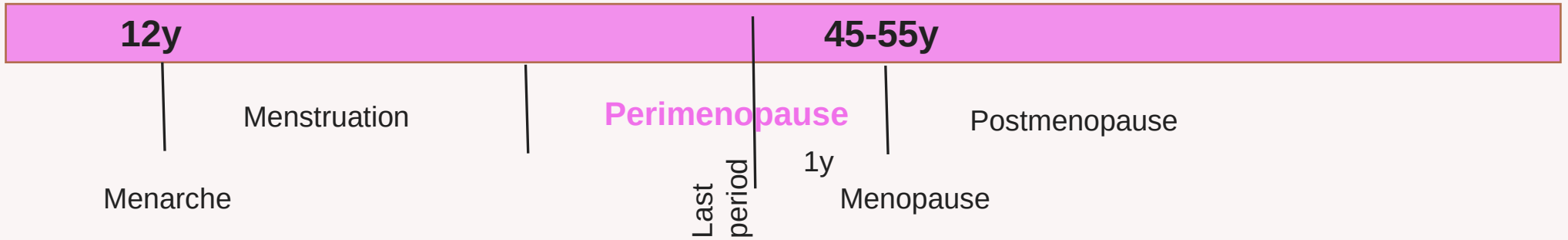
Menopause

- “Menopause transition” – the period when the timing of menstrual cycle wobbles and hormonal and clinical symptoms of menopause begin
- Perimenopause – a phase that starts toward the end of menopausal transition and continues into the first year after the final menstruation period.
- Postmenopause – the stage starting 12 months after the last period



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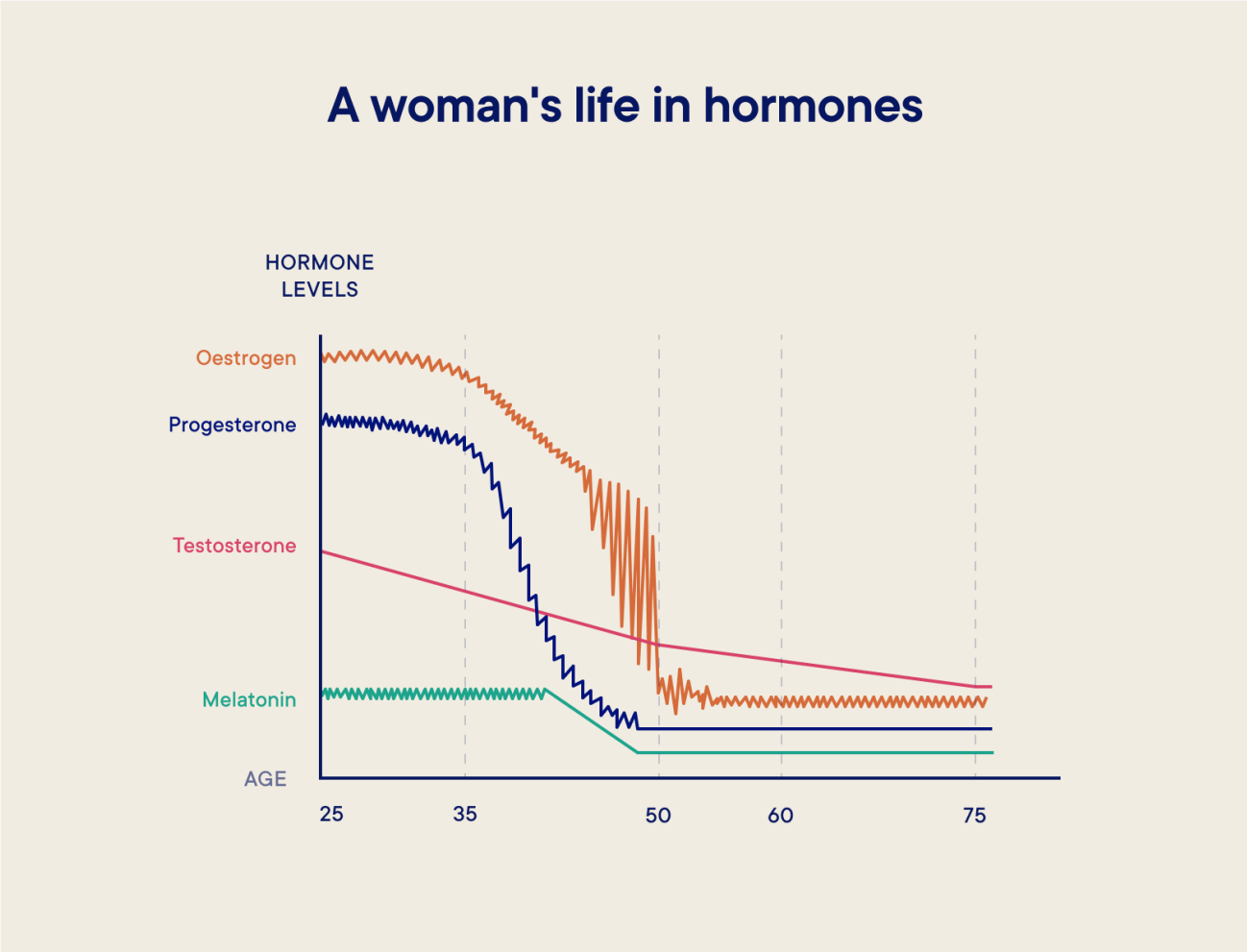
Menopause

- Natural menopause
- Early menopause (before 45y)
- Induced / medical menopause: radiation, chemotherapy, oestrogen blockers, aromatase inhibitors
- Surgical menopause

A woman’s life in hormones



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Symptoms of perimenopause

- Changes in menstruation and frequency
- Genitourinary: vaginal dryness, painful intercourse, stress incontinence, overactive bladder
- Muscular: joint and muscle pain, stiffness, aches
- Cardiovascular: irregular pulse, palpitations
- Weight gain
- Gastro: bloating, reflux, nausea
- Thinning hair, dry skin, itchiness
- Dry, burning mouth
- Tinnitus
- New allergies
- Neurological: fatigue, dizzy spells, headaches, migraines

Brain related

- Hot flashes (vasomotor) 80-85%
- Body temperature
- Mood
- Sleep
- Libido
- Cognitive performance

- Depression (20%)
- Anxiety
- Panic attacks

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“Normal” perimenopause

- Mood swings
- **Diminished ability to cope** with everyday hassles
- A sense of overwhelm
- Irritability -- rage
- Sadness
- Emotional flatness
- Lack of motivation

Fear of going crazy

Brain fog (60%)

- Brain feels like mush
- Fogginess in thinking
- Difficulty in processing information
- Hard to absorb and recall information
- Short term memory
- Difficulty to concentrate
- Shorter attention span
- Mental fatigue
- Trouble multitasking
- Word finding difficulties
- Trouble following the flow of conversation
- Lack of energy

Fear of early dementia

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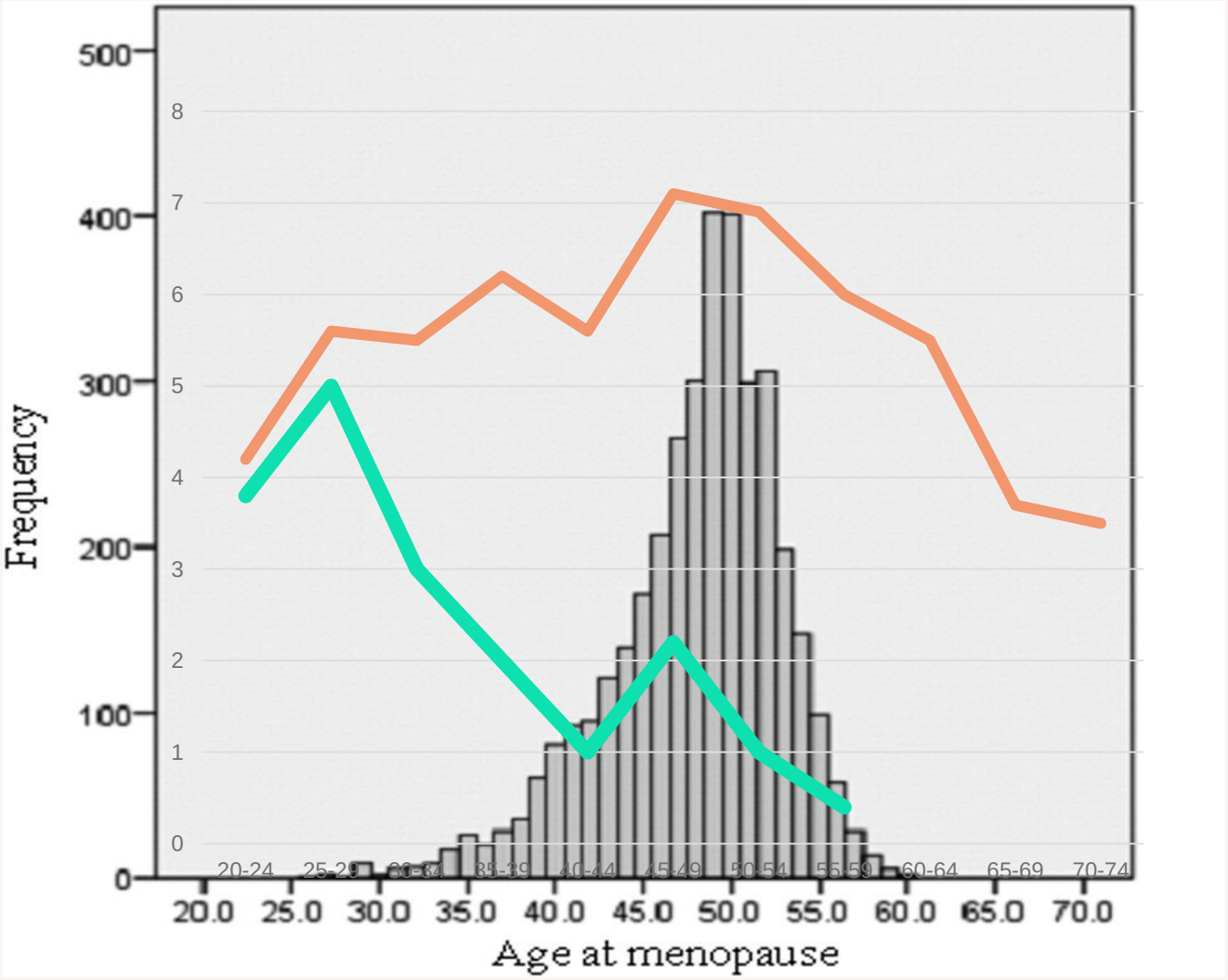
Why do we need to care about menopause?

Bar chart- age of menopause (Pokoradi 2011)

first admission for schizophrenia (women) (Hafner 1993)

reported suicides (women), England and Wales (ONS 2020)

Dr Sophie Behrman



What do we mean when we say Psychosis?

- Psychosis is a mental state where a person loses touch with reality. It can involve hallucinations, delusions, disorganised thinking, and difficulty to distinguish between what is real and what isn't. (ChatGPT)

  - Acute stress induced / drug induced
  - Schizophrenia like
  - Severe depression with psychosis
  - Mania / bipolar affective disorder

AWP South Glos Early Intervention: Perimenopause, Menopause & CBT for Women with Psychosis

Dr Hanna Van Der Woude, Clinical Psychologist for AWP & Co-Director Bristol Psychosis HIT

Claire Dickens, CBT Therapist South Glos EI

Ellie Spare, CBT Therapist South Glos EI

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South Glos Early Intervention Service

- 3 years ago we began to work with over 35s as part of moving to an ageless service
- We noticed an unexpected increase in women that were referred for a first episode psychosis and “At risk mental state” (vulnerability to psychosis)
- In fact, 72% of over 40s were women, compared with 28% men. (The under 40s = 65% male 35% female)
- This coincided with an increasing awareness of peri-menopause within team members and conversations started

What factors might make a woman more likely to develop psychosis over 40?

- Early experiences of trauma (makes everyone more vulnerable)
- Overlap between psychosis and the symptoms of perimenopause
- Change in role
- Life stressors
- Caring responsibilities
- Change in fertility – coming to that point in your life, meaning of this for the person
- Hormonal changes
- Society pressures of ageing – how does this vary in other cultures?
- Physically signs of aging – pain, less mobility , meaning on how we see ourselves
- Feeling less capable
- There is an increase in women over 40 noticing problematic ADHD, difficulties with concentration

Factors that increase vulnerability to developing psychosis

- Ethnicity
- Gender (male)
- Migration
- Poverty and social deprivation
- Growing up in an urban environment
- Socio-economic deprivation
- Social Isolation
- Lack of social support
- Victimisation
- Adverse Childhood Experiences (ACE's)
  - CSA, CPA, Emotional abuse, neglect, parental separation / loss, parental MH issues
- Adverse Life Experiences in adulthood
- Substance Use

Themes

- Trauma shapes the beliefs we develop about self, others and the future
- Intergenerational transmission of trauma
- Attachment
  - Impacts on relationships
  - Impacts on emotional regulation skills
  - Intergenerational patterns passed down the line
- Resilience and protective factors

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The relationship between Trauma & Psychosis

- There appears to be a link between the type of traumas experienced and how the distress manifests *(Bentall et al., 2012; Varese et al., 2012)*
  - CSA related to greater degree of voice hearing
  - CPA related to greater degree of paranoia
- The content of anomalous experiences may fully match that of the trauma experienced (12.5%) or may be thematically linked (45%) *(Hardy et al., 2005)*
- Psychosis itself (and associated experiences) can also be trauma inducing

The relationship between Trauma & Psychosis

50 – 98% of individuals who have experienced psychotic symptoms have also experienced trauma *(Read et al., 2005)*

Prevalence of PTSD in people with psychosis is approximately 15%, which is up to five times the general population rates *(de Bont et al., 2015)*

ACE's increase the risk of psychosis by 2.8 times on average and childhood trauma as a major risk factor probably adds 33% to the onset of psychosis in society *(Varese et al., 2012)*

Dose response relationship – the more frequent and substantial the experience of trauma, the more significant the difficulties are likely to be. Those subjected to the most extreme levels of trauma are 48% more likely to develop psychosis *(Bentall et al., 2012; Varese et al., 2012)*

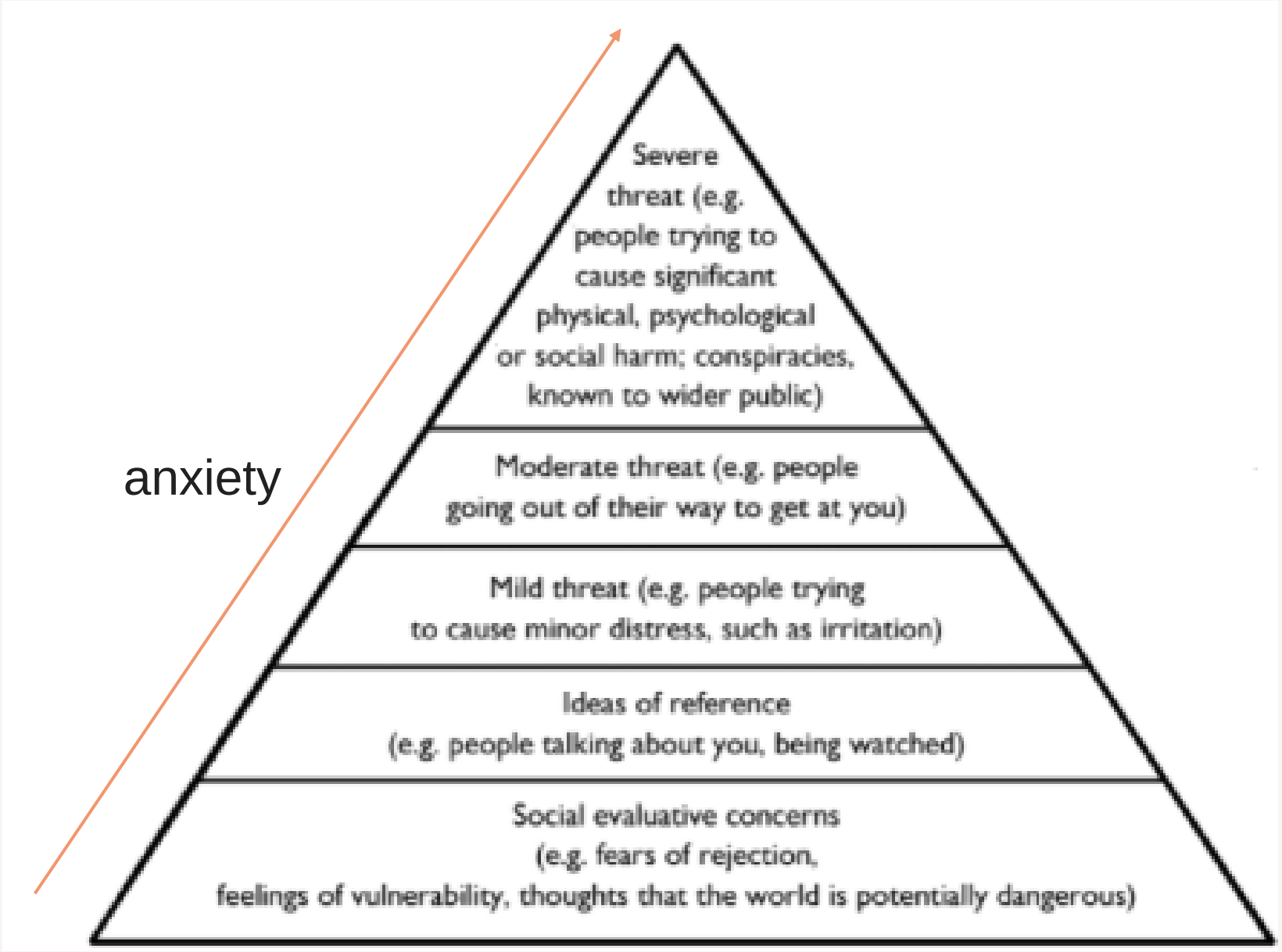
People who experienced 5 types of trauma were **193** times more likely to become psychotic *(Shevlin et al., 2007)*

Perimenopause, Menopause and Trauma

- A systematic review on the bidirectional relationship between trauma-related psychopathology and reproductive aging *(Arnold et al., 2024)*
- Does childhood maltreatment or current stress contribute to increased risk for major depression during the menopause transition? *(Bromberger et al., 2022)*
- Association between perimenopausal age and greater PTSD and depression symptoms in trauma-exposed women *(Michopoulos et al., 2023)*

Menopause, trauma and psychosis

Menopause symptoms	Trauma & PTSD symptoms	Experience of psychosis
Increasing anxiety Difficulty sleeping Low mood/ depression Difficulties with concentration Short term memory changes brain fog Impact on thinking Physical aches/ joint pain Feeling isolated Lack of motivation tiredness	Heightened anxiety Heightened threat system- worry about being harmed again Voice hearing Paranoia Low mood Negative beliefs about self, others and world Negative thinking Heightened emotional arousal Sleep difficulties Nightmares Intrusions/ flashbacks Feeling isolated Reduced motivation	Heightened anxiety Heightened threat system- worry about being harmed again Paranoia Misinterpretation of symptoms Voice hearing/ hallucinations Sleep difficulties Nightmares Intrusions Low mood/ heightened emotional arousal Difficulties with concentration Feeling isolated Lack of motivation Impact on thinking



Understanding the link between anxious thinking and paranoia

(Freeman et al (2005) paranoia hierarchy)

Main themes

- Peri-Menopause and anxious thinking → paranoia and psychosis
- Impact of sleep
- Developments of meaning that match previous trauma?

= “perfect storm”

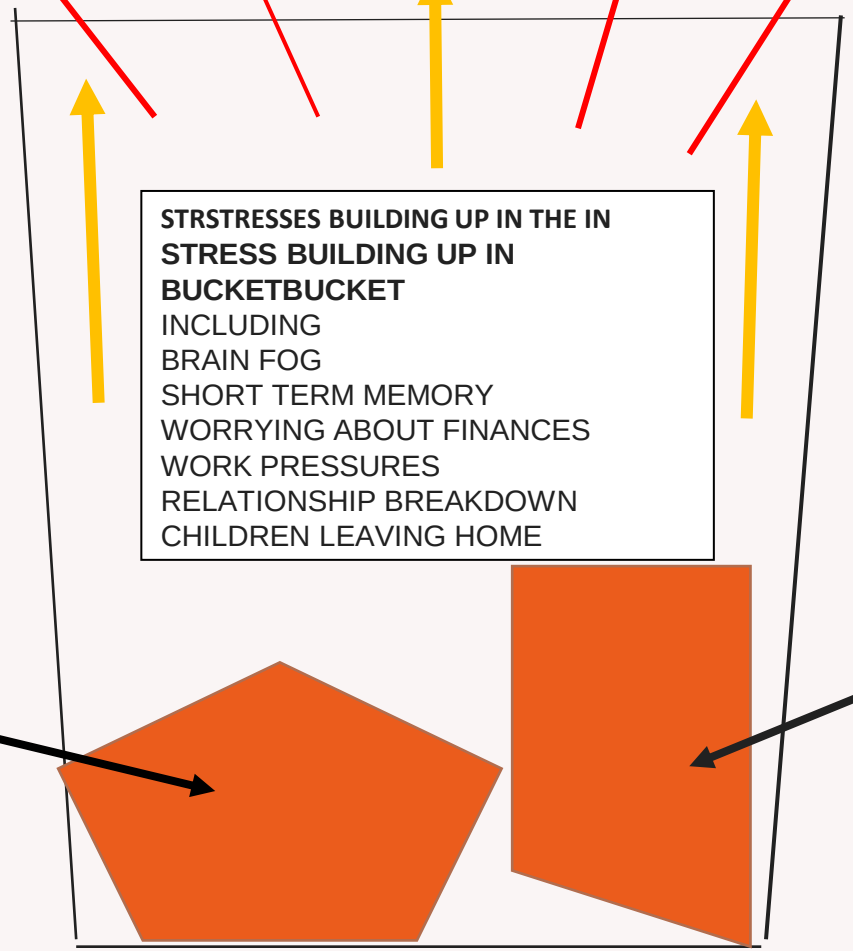
Example of Stress Bucket for EI

STRESS OVERFLOWS..
FEELING ANXIOUS , PANIC AND CAN'T SLEEP

STRESS OVERFLOWS..
FEELING CRAP- CAN't THINK STRAIGHT

STRESS OVERFLOWS….
BELIEVING OTHER PEOPLE ARE TAKING THINGS FROM HOME

STRESS OVERFLOWS….
WORRY OTHERS WANT TO HARM ME



STRSTRESSES BUILDING UP IN THE IN STRESS BUILDING UP IN BUCKETBUCKET
INCLUDING
BRAIN FOG
SHORT TERM MEMORY
WORRYING ABOUT FINANCES
WORK PRESSURES
RELATIONSHIP BREAKDOWN
CHILDREN LEAVING HOME

ROCKS TAKING UP SPACE IN BUCKET

DOMESTIC VIOLENCE
GROWING UP
ADVERSE CHILDHOOD EXPERIENCES

ROCKS TAKING UP SPACE IN BUCKET

BULLYING
POVERTY
BELIEFS ABOUT SELF, OTHERS, WORLD AS A RESULT OF THOSE EXPERIENCES

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What have we noticed in our service delivering CBTp

- The women we see come from a varied socio-economic background, differing education attainment, some in employment some not, mix of family backgrounds and roles.
- Most describe distress around paranoid thinking as their primary concern, fewer have voice hearing
- There is some commonality in the meanings that are drawn: “I Therefore, cope; I am a failure; I am vulnerable; I am powerless”
- Therefore, we stick to the principles of CBT with a curiosity about the relevance of peri-menopause, as we would any other life events and subsequent meaning.
- CBTp framework of assessment, normalisation, information sharing and interventions.
- The goals for therapy are varied and not often directly related to peri-menopause.
- Interventions that come from the research into persecutory delusions are very relevant (e.g. Freeman et al, Feeling Safer : Worry, Sleep, Building Self-Confidence.
- This illustrates the complexity of an individual’s life and the importance of an individualised approach.

Going forward

- Culture and ethnicity– we don’t have enough information
- We don’t all ask the same questions at the same time
- Stigma around perimenopause
- Other outcome measures we have to use but there is no current questionnaire for perimenopause symptoms in routine practice
- The importance of demystifying what is going on, normalising symptoms and experiences
- The earlier the better: so we can proactively support women before they reach crisis point and need to access MH services.

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What does research into this topic tell us?

Sarah Sullivan
Ruta Kuzminskyte

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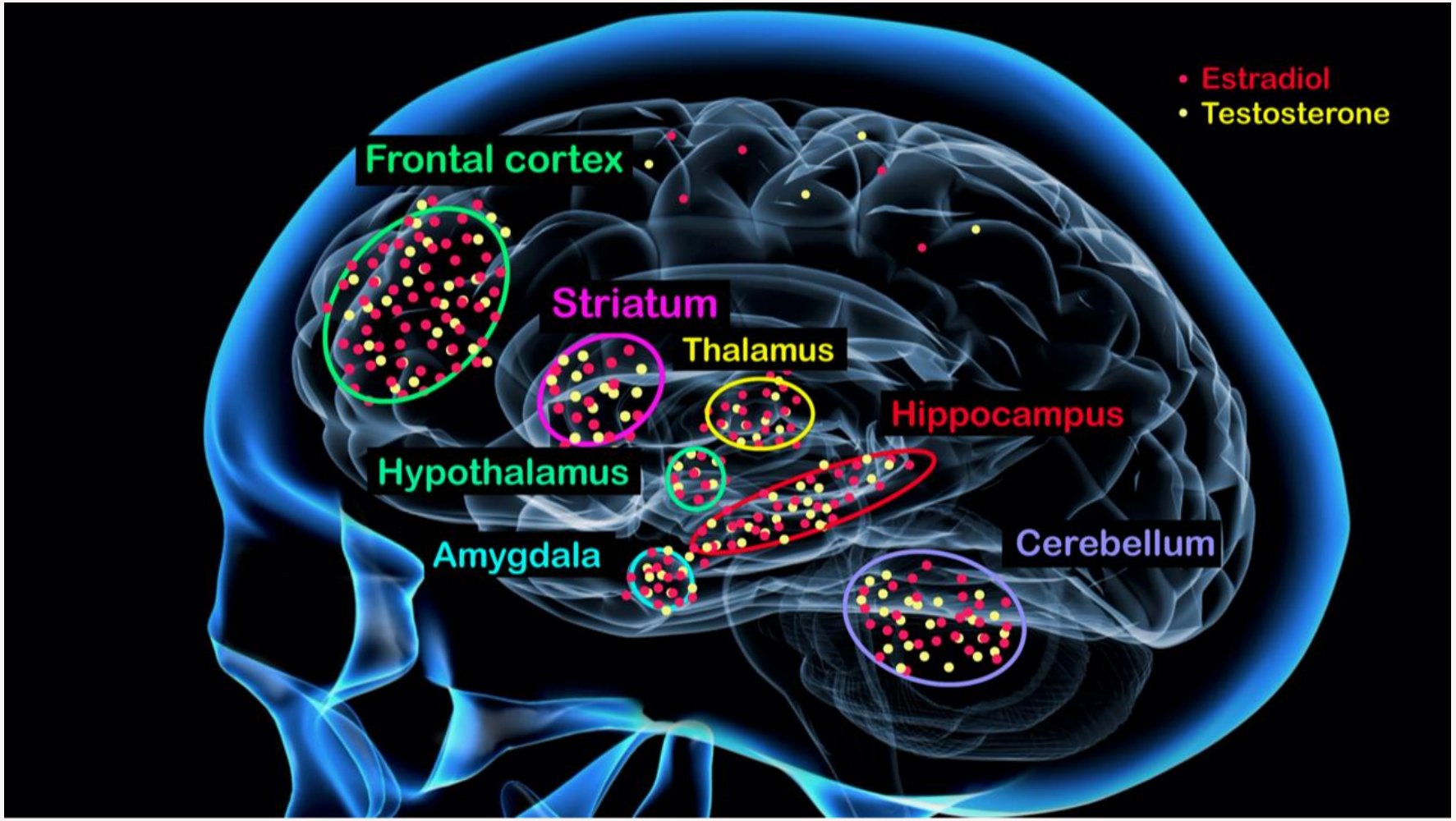
Hormone receptors in the brain

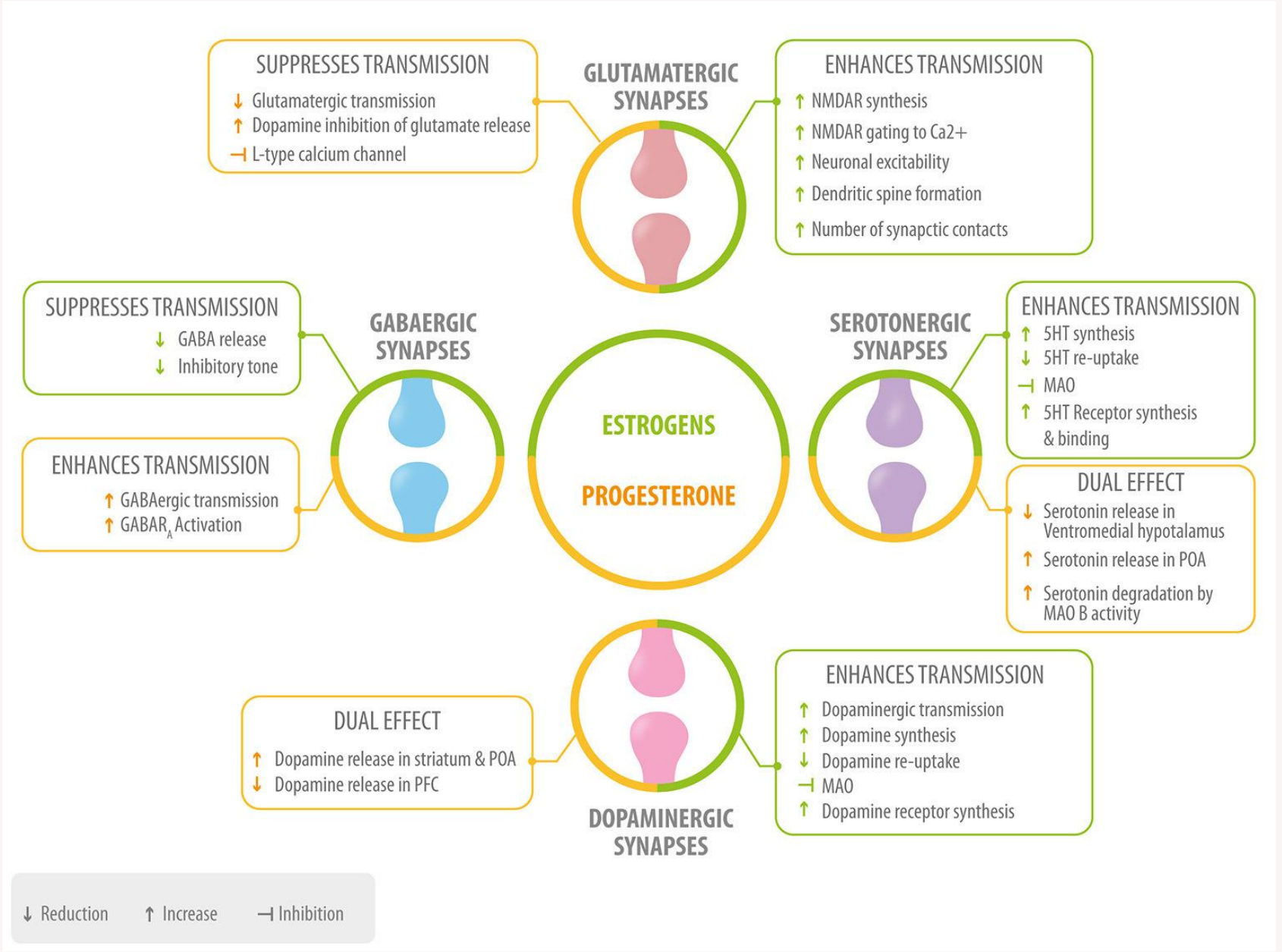


Oestrogen and neurotransmitters

Oestrogen modifies neuronal activity in a non-permanent manner

Regulates levels of neurotransmitters:

- Acetylcholine
- Dopamine
- Glutamate
- GABA (Gamma-aminobutryic acid)
- Serotonin



Juan Pablo Del Río et all: Steroid Hormones and Their Action in Women's Brains: The Importance of Hormonal Balance

	Oestrogen	Clinical effects	Progesterone	Clinical effects
Glutamate	Increases release	Increases neuronal excitability –improving memory, learning	Inhibits	Decreases neuronal excitability
GABA	Supresses	Increases synaptic transmission in glutamate and dopamine neurons	Potentiates	Anti-anxiety effects
Serotonin	Promotion of serotonin synthesis, inhibits degradation, inhibits reuptake	Increased availability	Decreases serotonin levels	However oestrogen followed by progesterone enhances serotonergic synaptic activity
Dopamine	increases synthesis, decreases degradation, reuptake, upregulates receptors	esp PFC – working memory, emotional and motivational behaviours, decrease impulsive behaviours	Depends on previous priming with oestradiol and location of activity in the brain	

What is the research evidence?

- Animal studies show that oestrogen modulates brain dopamine
  - Psychotic symptoms partly due to increased dopamine activity

- Human evidence sparse and inconsistent
  - 3 studies show peaks in incidence after age 50 in women but not men
  - 1 study reporting reduced premorbid fertility in women with first episode psychosis – probably a biological cause (apparently)
  - 1 study showed reduced oestrogen in bloods of women with psychosis
  - **No studies** to date on age of menopause and risk of psychosis

Literature references

1. Seeman, P et al (1976) Nature 261(5562)
2. Hafner H.B. et al (1991) Psychiatry Res 38(2)
3. Arad M & Weiner I (2010) Neuropharmacology 35(7)
4. Kirkbride et al (2012) PLoS One 7(3)
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6. Kohler S et al (2009) Schizo Res 113(2-3)
7. Van der Leeuw C et al (2013) Schizo Res 143(1)

Research: Late onset psychosis

- “Exploration of first onsets of mania, schizophrenia spectrum disorders and major depressive disorder in perimenopause” Lisa M. Shitomi-Jones, Clare Dolman, Ian Jones, George Kirov, Valentina Escott-Price, Sophie E. Legge & Arianna Di Florio 2023

Research: Course of pre-existing psychosis

Schizophrenia

- More severe menopause symptoms S. Tiwari et al 2023 review
- Higher negative symptoms MA Whooley et al 2000
- Menopause can worsen positive symptoms A Szeliga et al 2021
- Starting at age 45–50, women were consistently more often hospitalized for psychosis than their male peers. While younger women have a lower risk of relapse and generally need a lower antipsychotic dose to prevent rehospitalization than men, antipsychotic effectiveness declines in women after the age of 45. Finish register study. I Sommer et al 2023
- Time since menopause was significantly negatively associated with antipsychotic response in postmenopausal schizophrenic women, suggesting a decline in antipsychotic response after menopause. A Gonzalez-Rodriguez 2016

Schizophrenia and menopause

	Premenopausal women	Postmenopausal women
Antipsychotic dose	Women require lower doses of antipsychotics than men	Need higher doses of antipsychotics than premenopausal women
Clinical symptoms	Women have fewer negative and cognitive symptoms than men	Show increased psychotic symptoms Symptoms worsen with postmenopausal duration
Treatment response	Overall response is better in women than in men	Antipsychotic response worsens at menopause and continues to worsen with time

Review: The Effect of Menopause on Antipsychotic Response. A González-Rodríguez et al 2022

Research: pre-existing psychosis and oestrogen

- Low oestrogen in schizophrenia occurs in women with and without antipsychotic-induced hyperprolactinemia N Bergemann et al 2005
- Postmenopausal women treated with HRT compared to not treated needed lower dose of antipsychotic, had same positive symptoms, less severe negative symptoms LA Lindamer et al 2001
- Superior efficacy was found for adjunctive estrogens in female patients on total symptom severity, positive and negative symptoms Begemann et al 2012
- HT during the perimenopause in women with schizophrenia ameliorates psychotic and cognitive symptoms. A Brzezinski et al 2017
- Adjunctive treatment with transdermal estrogen showed significant improvement in schizophrenia and schizoaffective psychotic symptoms in perimenopausal age range (38-46), but not in younger women Weiser at all 2019

Perimenopause in the brain

- Changes do not occur after menopause, they start during perimenopause
- Perimenopause is a warm-up act; research shows that this is exactly when brain is going through the most profound changes – a state when the brain is in a state of adjustment, even remodelling

- Brain energy changes
- Brain structure changes
- Regional connectivity

Lisa Mosconi et al In vivo brain estrogen receptor density by neuroendocrine aging and relationships with cognition and symptomatology Nature 2021

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Q&A discussion session

Sarah Sullivan

Ruta Kuzminskyte

Hanna Van Der Woude

Ellie Spare

Claire Dickens

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Thank you

Provide feedback

smartsurvey.co.uk/s/M1QO70/

Get in touch

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