DR NINA FULLER SHAVEL

Precision Health and Integrative Medicine Approaches to Supporting Trauma Recovery

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Brief introduction

- Degrees in Natural Sciences and Medicine from the University of Cambridge
  - Background in cellular and molecular biology, distinction in Pathology, winner of the Henry Roy Dean Prize
- Postgraduate degrees in nutrition and integrative medicine and additional qualifications in functional medicine, herbal medicine, yoga and mindfulness
- Fellow of the College of Medicine, Co-Chair of the British Society for Integrative Oncology (BSIO)
- Founder and Director of Synthesis Clinic (UK) – an award-winning multidisciplinary integrative medicine practice specialising in women's health and integrative cancer support for solid tumours; podcast co-host for the Synthesis Clinic Podcast
  - Innovation Leader of the Year at the UK Business & Innovation Awards 2022
- Research interests in integrative medicine and precision health (incl. current MSc Precision Cancer Medicine and Pg Dip Health Research at the University of Oxford)
- Member of national and international conference committees in integrative medicine and guideline development boards in integrative oncology, editorial board member for the Nutritional Medicine Journal
- Educator – training for medical and nutrition professionals in integrative medicine for women's health (e.g. Hormone GATeway®) and integrative oncology (Systems Approach to Cancer®)

Disclosures

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  - Dr Stephen Porges
  - Dr Ruth Lanius
  - Dr Pat Ogden
  - And many more researchers in this important field

nicabm National Institute for the Clinical Application of Behavioral Medicine

Session outline

- Brief introduction to neurobiology of trauma from a practical perspective
- The role of the MDT (multidisciplinary team) in supporting trauma recovery
- Nutrition and lifestyle considerations in trauma recovery and practical applications, including a brief case study review
- Looking to the future

Trauma

- An event or series of events that overwhelm the coping capacity of an individual, key aspects are profound powerlessness and inescapability.
  - The event itself may matter less than how it is perceived by the individual
  - Worldwide, around 70% of people will experience a traumatic event, yet the lifetime prevalence of PTSD is around 5%
- Has also been defined as 'life-threatening powerlessness' but does not have to be life-threatening
  - Spectrum of over and under-use
- Results in profound mind-body dysregulation – initial event's impact and initial 'in the moment' adaptive response becomes frozen in time and often plays out in a maladaptive way subsequently

PTSD – key categories of symptoms

- <u>Four main categories:</u>
  - intrusion symptoms
  - avoidance symptoms
  - arousal and reactivity symptoms
  - cognition and mood symptoms

PTSD DSM 5 (over age 6)

- A. **Exposure to actual or threatened death, serious injury, or sexual violence** in one (or more) of the following ways:
  - Directly experiencing the traumatic event(s).
  - Witnessing, in person, the event(s) as it occurred to others.
  - Learning that the traumatic event(s) occurred to a close family member or close friend. In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental.
  - Experiencing repeated or extreme exposure to aversive details of the traumatic event(s), e.g. first responders and emergency servicers

PTSD DSM 5 (over age 6)

- B. Presence of one (or more) of the following **intrusion** symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred:
  - Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s). **Note:** In children older than 6 years, repetitive play may occur in which themes or aspects of the traumatic event(s) are expressed.
  - Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s)
  - Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring. (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings.)
  - Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).
  - Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).

PTSD DSM 5 (over age 6)

- C. Persistent **avoidance of stimuli associated with the traumatic event(s)**, beginning after the traumatic event(s) occurred, as evidenced by one or both of the following:
  - Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).
  - Avoidance of or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).

PTSD DSM 5 (over age 6)

- D. **Negative alterations in cognitions and mood** associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:
  - Inability to remember an important aspect of the traumatic event(s) (typically due to dissociative amnesia, and not to other factors such as head injury, alcohol, or drugs).
  - Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world (e.g., "I am bad," "No one can be trusted," "The world is completely dangerous," "My whole nervous system is permanently ruined").
  - Persistent, distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame himself/herself or others.
  - Persistent negative emotional state (e.g., fear, horror, anger, guilt, or shame).
  - Markedly diminished interest or participation in significant activities.
  - Feelings of detachment or estrangement from others.
  - Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, or loving feelings).

PTSD DSM 5 (over age 6)

- E. **Marked alterations in arousal and reactivity** associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:
  - Irritable behavior and angry outbursts (with little or no provocation), typically expressed as verbal or physical aggression toward people or objects.
  - Reckless or self-destructive behavior.
  - Hypervigilance.
  - Exaggerated startle response.
  - Problems with concentration.
  - Sleep disturbance (e.g., difficulty falling or staying asleep or restless sleep).

PTSD DSM 5 (over age 6)

- F. Duration of the disturbance (Criteria B, C, D and E) is more than 1 month.
- G. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- H. The disturbance is not attributable to the physiological effects of a substance (e.g., medication, alcohol) or another medical condition.

PTSD DSM 5 (over age 6)

- With or without dissociative symptoms
  - **Depersonalization:** Persistent or recurrent experiences of feeling detached from, and as if one were an outside observer of, one's mental processes or body (e.g., feeling as though one were in a dream; feeling a sense of unreality of self or body or of time moving slowly).
  - **Derealization:** Persistent or recurrent experiences of unreality of surroundings (e.g., the world around the individual is experienced as unreal, dreamlike, distant, or distorted).

C-PTSD – complex PTSD

- C-PTSD is caused by ongoing trauma that lasts months or years, often in childhood.
- Usually multi-event chronic trauma, often on a background of poor attachment

How common is PTSD?

- 2014 Adult Psychiatric Morbidity Survey of Mental Health and Wellbeing in England, in the large general population sample, 3.7% of men and 5.1% of women screened positive for PTSD – **average around 4%**
- UK Armed Forces Mental Health Report – 0.1-0.2% PTSD but recent studies looking specifically at veterans report 7.4% (Stevelink et al., 2018)
- Compare this to:
  - Field Trials for the Fourth Edition of the DSM found that **22% of cancer survivors** suffer from some level of lifetime cancer-related PTSD
  - Unfortunately, PTSD does not often disappear once treatment is finished, even if the patient is cancer-free. A recent study by Chan et al. (2018) reported over 1/3 of cancer patients diagnosed with PTSD six months after diagnosis developed chronic or full PTSD by the four-year mark.
  - It has been estimated that 12-25% of people who experience life-threatening illness develop medically-induced PTSD (Edmondson, 2014)

Trauma presentation in clinic

- Always be trauma-aware
- Particular attention to below but clinical history is essential (beware blank ‘childhood was fine’)
  - History of life-threatening or life limiting illness - acute or chronic
  - History of mental health disorders, including addiction
  - Chronic pain
    - And more – not forgetting occupational and family history

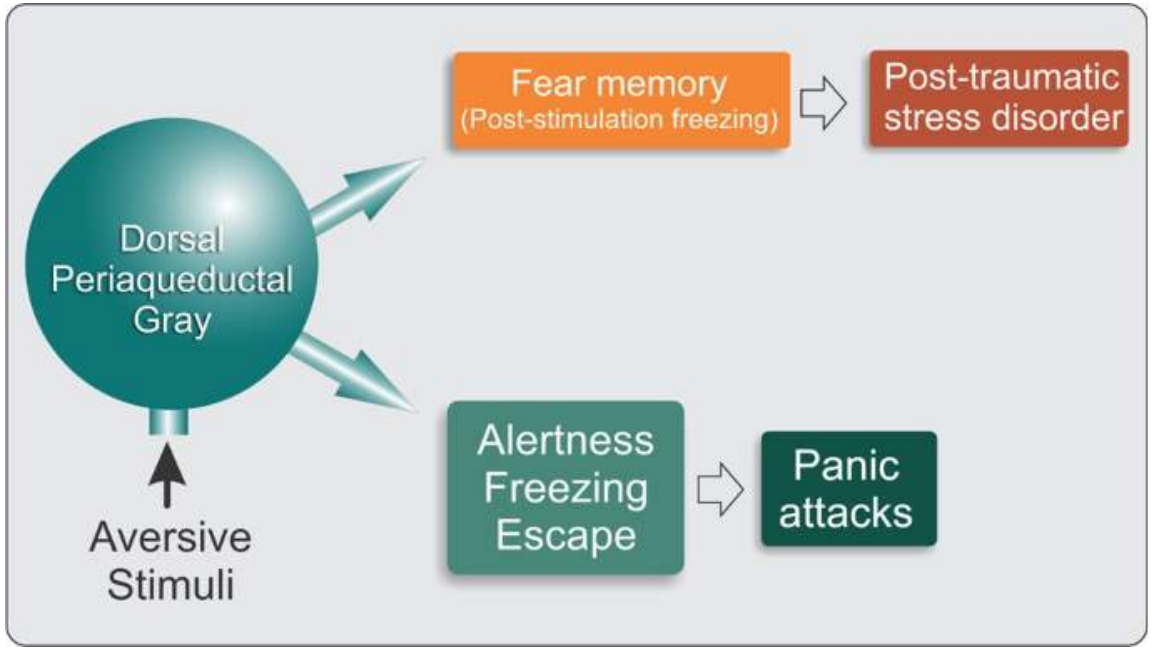
PTSD risk factors

- Exposure to a traumatic event — the type of event affects the risk of PTSD, with higher rates reported following rape and physical assault than following an accident.
- Severity of the incident — in general, the more severe the traumatic event (and the greater the perceived threat to life) the higher the chance of PTSD.
- Female sex
- Younger age
- Previous experience of trauma (ACEs)
- Presence of multiple major life stressors
- Low social support, social disadvantage — meta-analyses have identified level of social support as one of the strongest predictors of PTSD
- History of a mental health disorder

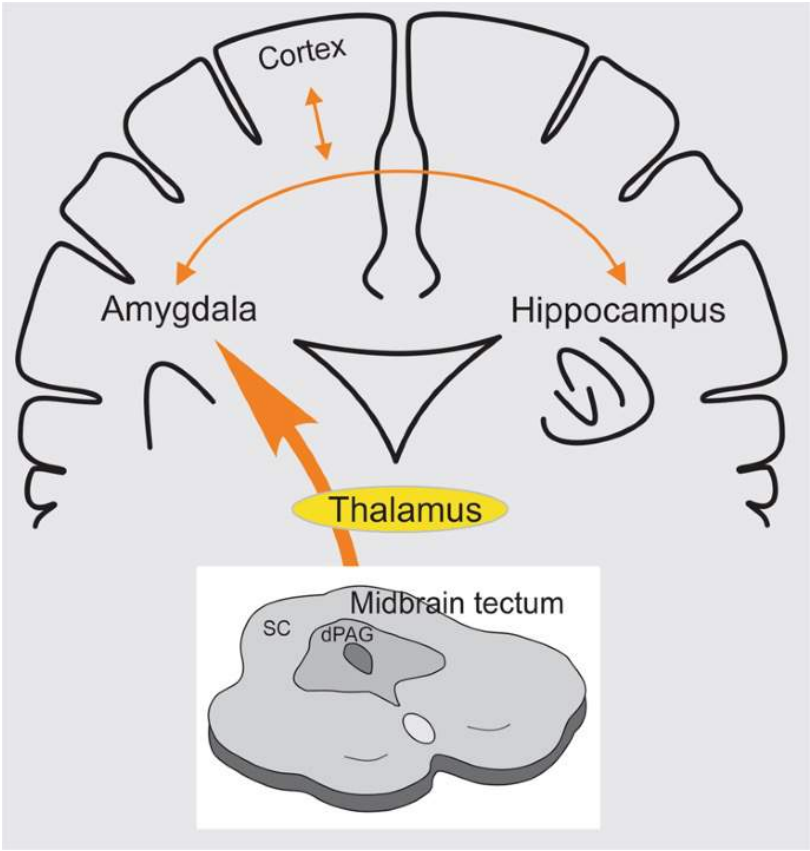
Some key concepts

- Structural and functional abnormalities within fear-processing regions within the forebrain in patients with PTSD, particularly within the prefrontal cortex (PFC), anterior cingulate, insula, hippocampus and amygdala.
  - Deficits in the extinction of fear memory
- First responses happen below the conscious level – SC orients to threat, activation of PAG in midbrain
  - PAG usually acts as a hub that integrates a vast array of bodily functions that are directed toward the survival – essential for controlling cardiovascular and respiratory function, temperature regulation, micturition, vocalisation, sexual behaviour, and responsiveness to pain etc.
    - It is a key centre for integrating emotional behaviours, such as anxiety, aggression, and defensive reactions when individuals face with a proximal or approaching threat

PAG and its connections



M. L. Brandão & T. A. Lovick (2019)

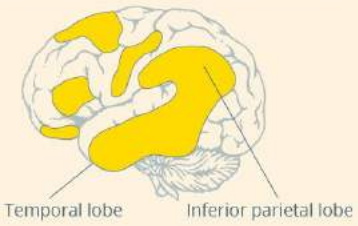
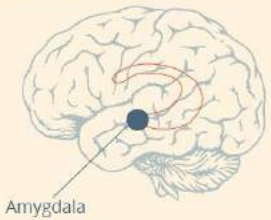
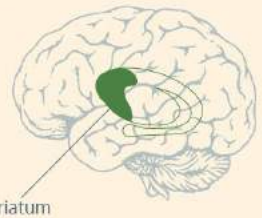


Amygdala sends a distress signal to the hypothalamus - activation of SNS and HPA axis

Understanding trauma neurobiology

- Three key networks affected:
  - Default mode network
  - Central executive network
  - Salience/emotional processing network

How Trauma Impacts Four Different Types of Memory

EXPLICIT MEMORY		IMPLICIT MEMORY	
SEMANTIC MEMORY	**EPISODIC MEMORY**	**EMOTIONAL MEMORY**	**PROCEDURAL MEMORY**
What It Is The memory of general knowledge and facts.	**What It Is** The autobiographical memory of an event or experience – including the who, what, and where.	**What It Is** The memory of the emotions you felt during an experience.	**What It Is** The memory of how to perform a common task without actively thinking
Example You remember what a bicycle is.	**Example** You remember who was there and what street you were on when you fell off your bicycle in front of a crowd.	**Example** When a wave of shame or anxiety grabs you the next time you see your bicycle after the big fall.	**Example** You can ride a bicycle automatically, without having to stop and recall how it's done.
			
How Trauma Can Affect It Trauma can prevent information (like words, images, sounds, etc.) from different parts of the brain from combining to make a semantic memory.	**How Trauma Can Affect It** Trauma can shutdown episodic memory and fragment the sequence of events.	**How Trauma Can Affect It** After trauma, a person may get triggered and experience painful emotions, often without context.	**How Trauma Can Affect It** Trauma can change patterns of procedural memory. For example, a person might tense up and unconsciously alter their posture, which could lead to pain or even numbness.
Related Brain Area The temporal lobe and inferior parietal cortex collect information from different brain areas to create semantic memory.	**Related Brain Area** The hippocampus is responsible for creating and recalling episodic memory.	**Related Brain Area** The amygdala plays a key role in supporting memory for emotionally charged experiences.	**Related Brain Area** The striatum is associated with producing procedural memory and creating new habits.
			

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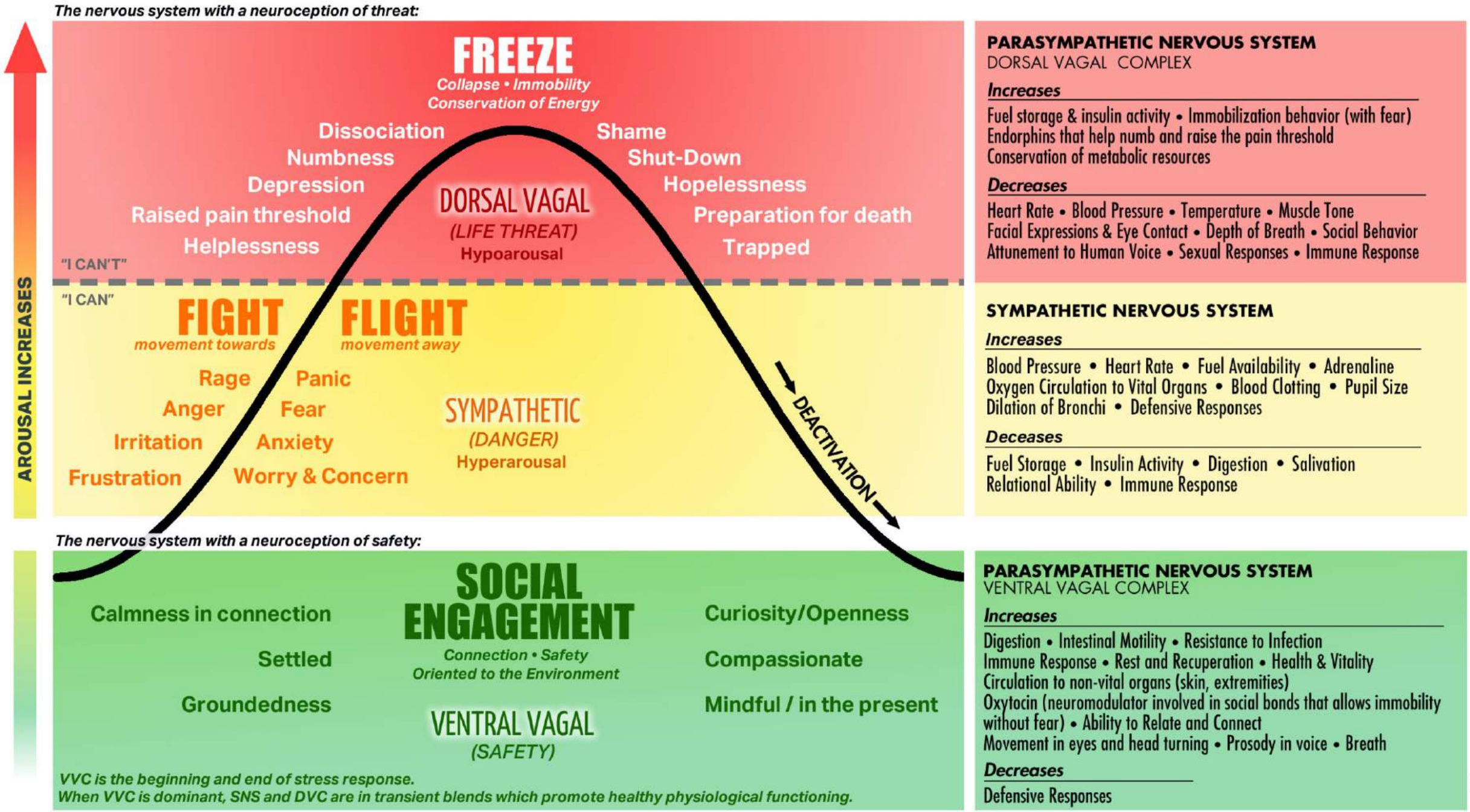
Understanding trauma neurobiology

POLYVAGAL CHART



PARASYMPATHETIC NERVOUS SYSTEM
DORSAL VAGAL COMPLEX

Increases

Fuel storage & insulin activity • Immobilization behavior (with fear)
Endorphins that help numb and raise the pain threshold
Conservation of metabolic resources

Decreases

Heart Rate • Blood Pressure • Temperature • Muscle Tone
Facial Expressions & Eye Contact • Depth of Breath • Social Behavior
Attunement to Human Voice • Sexual Responses • Immune Response

SYMPATHETIC NERVOUS SYSTEM

Increases

Blood Pressure • Heart Rate • Fuel Availability • Adrenaline
Oxygen Circulation to Vital Organs • Blood Clotting • Pupil Size
Dilation of Bronchi • Defensive Responses

Deceases

Fuel Storage • Insulin Activity • Digestion • Salivation
Relational Ability • Immune Response

PARASYMPATHETIC NERVOUS SYSTEM
VENTRAL VAGAL COMPLEX

Increases

Digestion • Intestinal Motility • Resistance to Infection
Immune Response • Rest and Recuperation • Health & Vitality
Circulation to non-vital organs (skin, extremities)
Oxytocin (neuromodulator involved in social bonds that allows immobility without fear) • Ability to Relate and Connect
Movement in eyes and head turning • Prosody in voice • Breath

Decreases

Defensive Responses

ver 9.0

Adapted by Ruby Jo Walker from: Cheryl Sanders, Anthony "Twig" Wheeler, and Steven Porges.

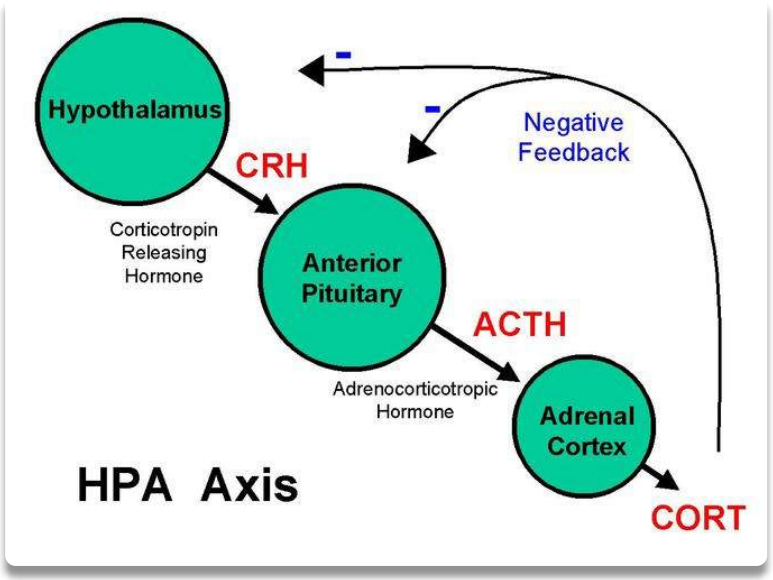
rubyjowalker.com

Stress response and PTSD – points of interest

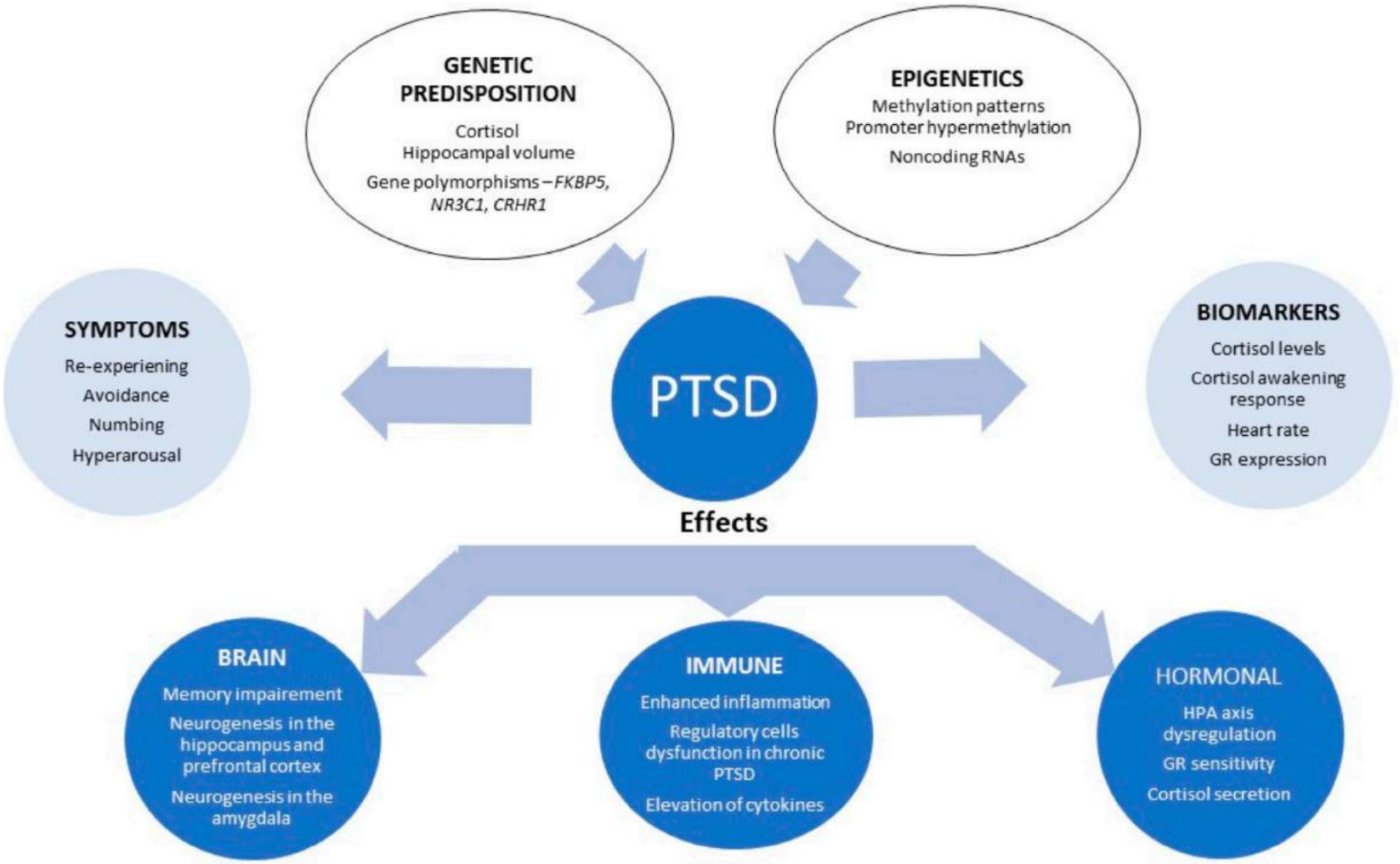
- Initial excitement about propranolol use in blocking memory reconsolidation of the traumatic event. According to memory reconsolidation theory, retrieval of memory under certain conditions leads to its labilisation and subsequent re-storage which could be disrupted by drugs.
  - Mixed studies – it is likely that there is a subpopulation that may benefit (Raut SB et al, 2022)
  - Hydrocortisone explored in secondary prevention and treatment settings – appears to be most effective given IV within 6-12 hours of exposure (hypothesis is that exogenous high GC levels following trauma may inhibit retrieval of fear memories, resulting in less intrusion, avoidance and hyper-arousal)
- Chronically PTSD may be associated with blunted CAR and lower morning and 24hr cortisol levels (particularly in those with childhood trauma), as well as GR sensitisation, although not all studies are consistent (individual assessment); higher DHEA and DHEA-S levels have also been observed

Trauma, genetics and epigenetics – examples

- **Heritability of PTSD around 30%** - complex polygenic influences
  - Key HPA axis genes identified in recent meta-analysis – **FKBP5 and GR (NR3C1**); specific SNPs in these are not only associated with PTSD risk but may also predict psychotherapeutic outcomes; CRHR1 also plays a role
- Several variants in **FKBP5**, a co-chaperone protein for the GR, have as key SNPs for PTSD risk (higher FKBP5 – more GR resistance and reduced negative feedback for stress response termination).
  - FKBP5 polymorphisms have also been associated with MDD after adverse life events, suicide attempts and certain dissociation symptoms, so it may serve as a global vulnerability indicator, as well as more specifically impacting fear learning and extinction in PTSD.
  - A meta-analysis of 14 studies on GxE interactions of FKBP5 variants identified that among adults who had been exposed to early life trauma, carriers of the T-allele of rs1360780 (6 studies), C-allele of rs3800373 (4 studies) or T-allele of rs9470080 (5 studies) were all at higher risk for developing PTSD.
- **Altered methylation of NR3C1 (GR)** may be a relevant factor in trans-generational and early life trauma -hypermethylation of NR3C1 at exon 1F has been identified in most studies of children and adults who experienced adversity during childhood or in utero, affecting GR-mediated CRH inhibition. In contrast to this, in adult non-combat PTSD studies have found lower levels of NR3C1 methylation with PTSD symptoms.



PTSD - inherent complexity + importance of individual assessment



BDNF plays a multifactorial role as both a regulator and target of stress hormone signalling within the brain

Castro-Cale & Carvalho (2020)

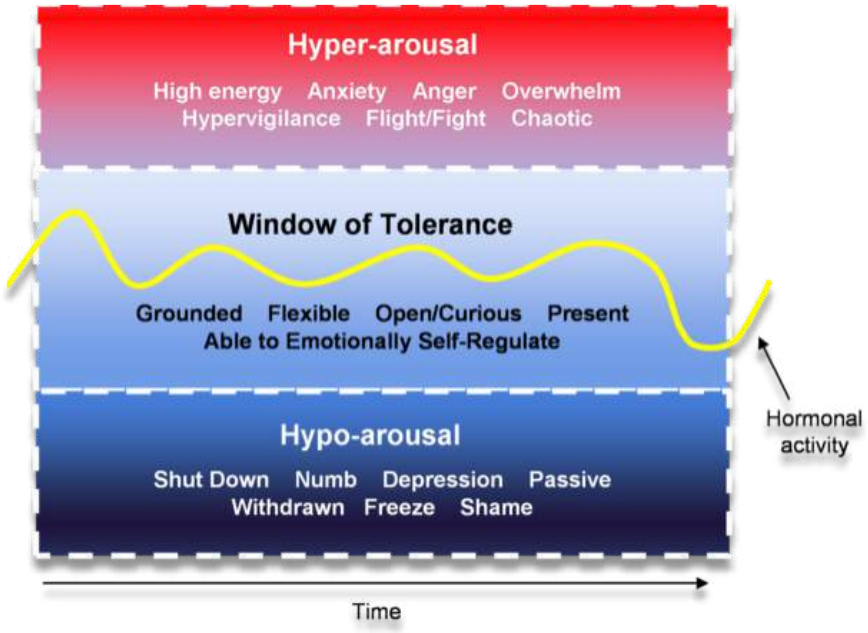
Physiological burden of PTSD

- Alterations in HPA axis, immune, nervous system and GI function, telomere shortening and accelerated ageing
- Associated with increase in:
  - Osteoporosis
  - Migraines
  - Sleep disorders
  - CVD and metabolic syndrome
  - Respiratory disorders
  - Autoimmune disease
  - Early death from unknown cause

What do our clients with trauma need?

- Individual assessment – look at all systems and wider context, look at specific needs and symptoms as much as possible with overall resilience support in mind
- Sense of safety – this is NOT just being nice
- Compassionate non-judgmental attitude and presence
- Clinical competency and relevant training, as well as keen attention to scope of practice and safety netting

Creating safety within the therapeutic relationship



- Choice making as the first step – simple choices fostering a sense of agency, e.g. where the person would like to sit, whether they would like water or tea
- Predictability and reliability is important, as well as the overall environment
- Pacing – go slow and keep within the window of tolerance
- Remember that your state is essential to help with co-regulation

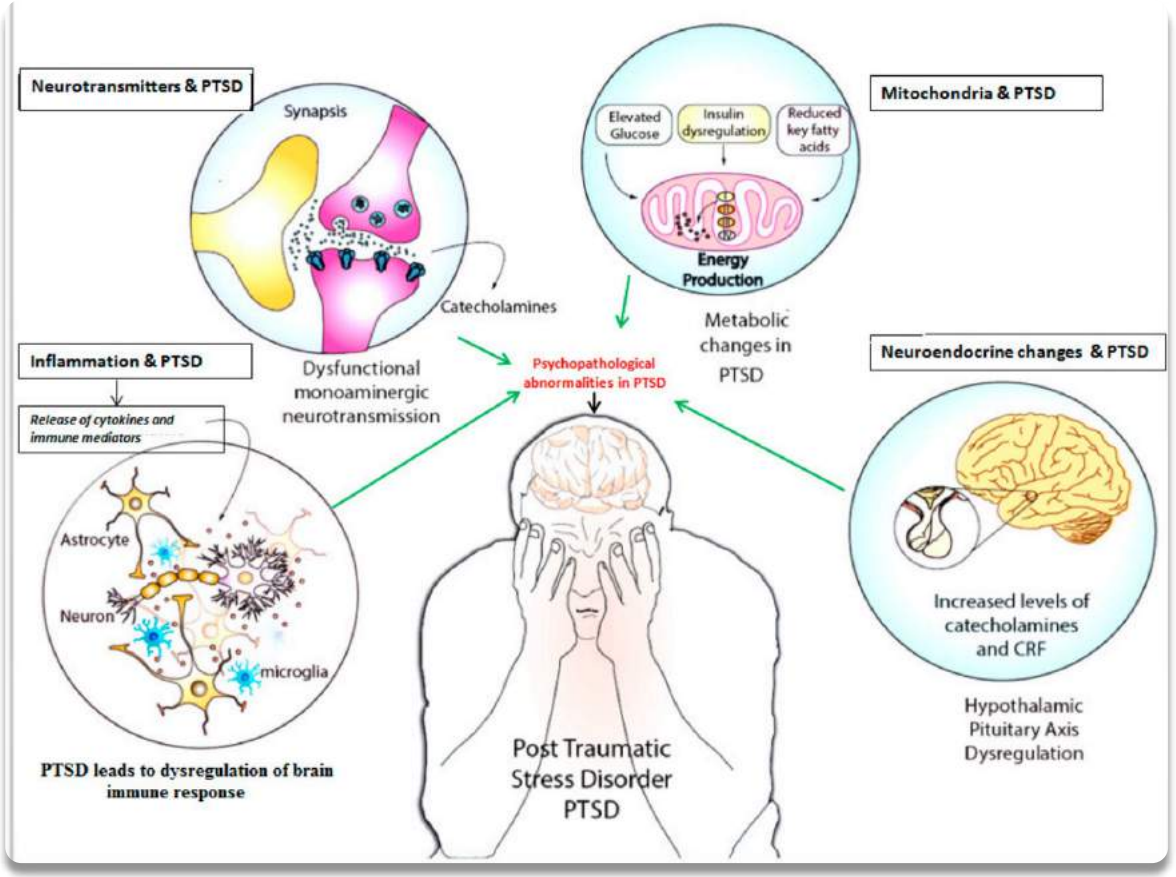
The role of the MDT in trauma recovery

- Psychological therapy input – trauma specialist, not generic therapy or counselling
  - Ideally a trauma specialist psychologist if formal PTSD/C-PTSD
  - Integration in approach is important – often most effective is a personalised and dynamic combination of 'top-down' and 'bottom-up' approaches, may include appropriate EMDR protocols
    - All therapy is not created equal – don't assume, ask!
- Medical input, e.g. GP, psychiatry, integrative medicine
- Nutrition and lifestyle support
- Mind-body and other supportive modalities, e.g. yoga therapy for trauma (IAYT), acupuncture, neurofeedback, creative approaches (art/music therapy)
- Social support
- And many more options, depending on individual assessment and need

Important aspects to consider in trauma impact

DOD Systems Biology of PTSD study

- Metabolism
- Inflammation
- Gut microbiome
- Mitochondrial dysfunction



Aliev et al (2020)

Considerations for baseline assessment

- Thorough clinical history (may include ACE score if comfortable) – timeline and systems review
  - Should include up-to-date medication review and medication history, as well as any communications from the medical or psychological team involved and full assessment of co-morbidities
- Baseline bloods – general health profile, e.g. FBC, LFTs, Us&Es, fasting cardiometabolic risk assessment (at minimum fasting glucose and lipids, HbA1c), hsCRP where possible, vitamins D, B12 and folate
- Consideration given on a personalised basis to hormone assessment, incl. HPA axis, detailed nutrient and metabolic assessment, GI work-up etc

Nutrition and lifestyle in trauma recovery

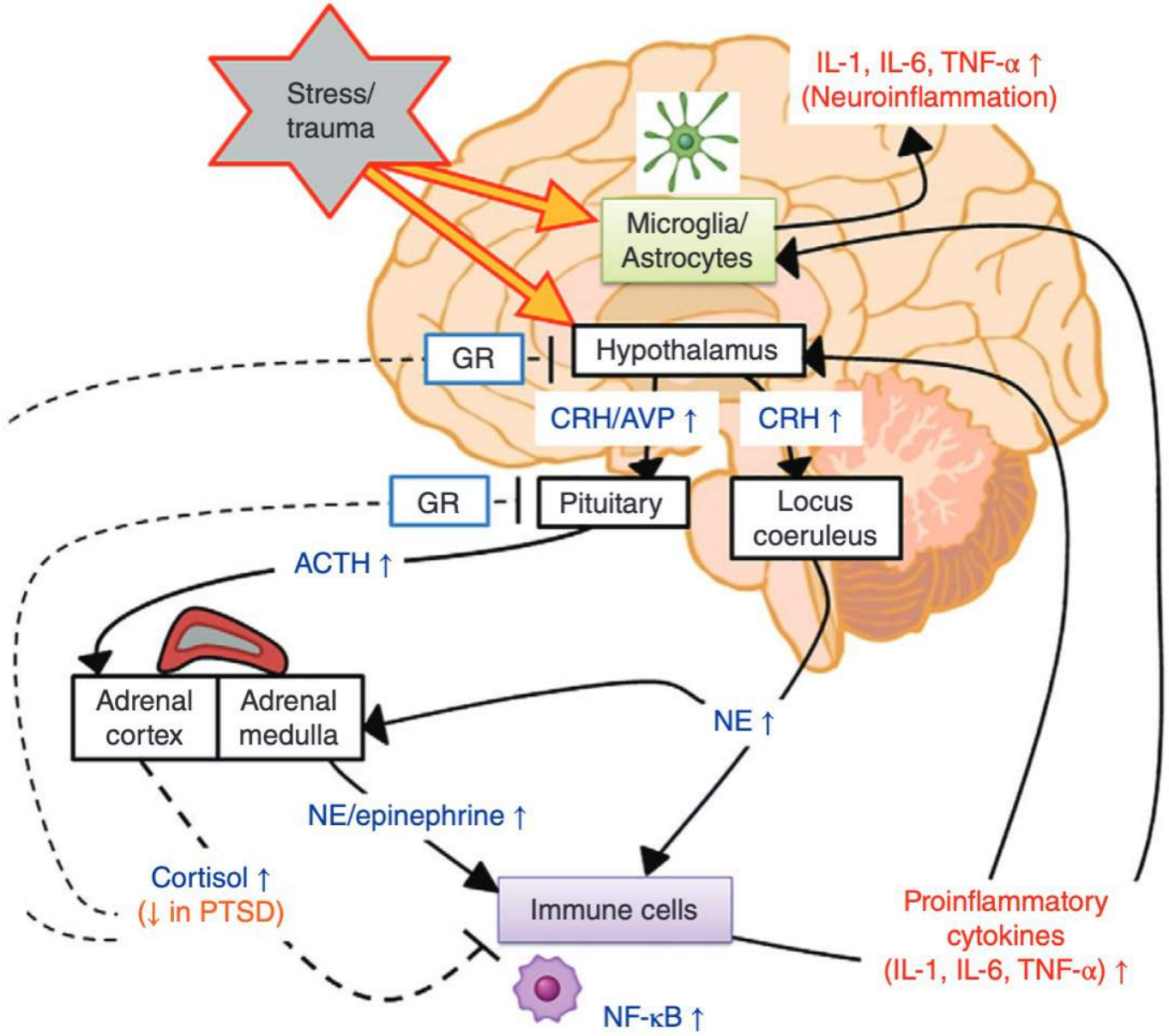
- PTSD is unsurprisingly associated with reduced healthy eating and physical activity and increased obesity and smoking, which is at least in part responsible for increased rates of **cardiometabolic disease**.
  - Medication may contribute, e.g. antipsychotics in particular
- Starting with the basics may be helpful in ameliorating these consequences, e.g. anti-inflammatory phytonutrient- and omega-3 rich Mediterranean-style diet, regular movement, sleep and psychology-guided self-regulation and stress management techniques, as well as minimisation/avoidance of risky behaviours.
  - Fasting can be tricky – remember distress tolerance may be low and keeping within the window of tolerance is important
- Early research in dysregulation of 1C metabolism – assess homocysteine and nutrient levels and address methylation appropriately
- Vitamin D deficiency was positively (OR = 2.02; p = 0.028) associated with PTSD (also GC SNP alleles with higher risk association for AA in rs4588 and TT for rs7041) – assess and address

Supporting resilience through HPA axis

- Very little evidence for adaptogen use in PTSD
- However, clinically assessing and supporting HPA axis and overall resilience is useful in our clinical experience
  - Nutrition, movement and circadian rhythm regulation (light exposure and sleep support, both generally and medical use of melatonin, which can address Lo Deep sleep deficiency) as foundations alongside appropriate therapeutic input
  - Addition of personalised adaptogen and nervine support may be appropriate – caution with interaction checks, less is more

Working on inflammation and neuroinflammation

- Several studies have reported that compared to healthy controls, individuals with PTSD exhibit significantly elevated levels of proinflammatory markers, such as IL-1β, IL-6, TNF-α, and CRP.
- IL-6, TNF-α, and IL-1β are shown to influence the brain at multiple levels, affecting, for example, neurogenesis, synaptic plasticity, and memory/learning.
- Inflammation-related activation of the kynurenine pathway – increased QA production may lead to NDMA-R-mediated neurotoxicity
- Elevated levels of oxidative stress
- Example approaches may include omega-3, numerous phytochemicals (curcumin, resveratrol, hesperidin and more), umPEA…



Hori & Kim (2019)

Supporting healthy BDNF levels

- Common BDNF Val66Met polymorphism modulates stress susceptibility
  - BDNF stress-sensitivity hypothesis - disruption of endogenous BDNF activity by common factors (such as the BDNF Val66Met variant) potentiates sensitivity to stress and, by extension, vulnerability to stress-inducible illnesses
  - Relative to Val/Val homozygotes, Met allele carriers reported greater severity of lifetime and current PTSD symptoms, specifically re-experiencing symptoms BUT greater engagement in physical exercise moderated this so Met allele carriers who exercised had significantly lower severity of PTSD symptoms compared to those who did not exercise.
  - Exercise-induced improvement of BDNF level might alter mitochondrial function, neuroplasticity, and the rate of apoptosis in the hippocampus.
- Another example - 12-week yoga- and meditation-based lifestyle intervention (albeit in MDD) showed significant increase in BDNF levels
- Address inflammation, oxidative stress and metabolic dysregulation as contributory factors to BDNF level
- Consider adjuncts, e.g. omega-3, curcumin etc

Addressing gut health

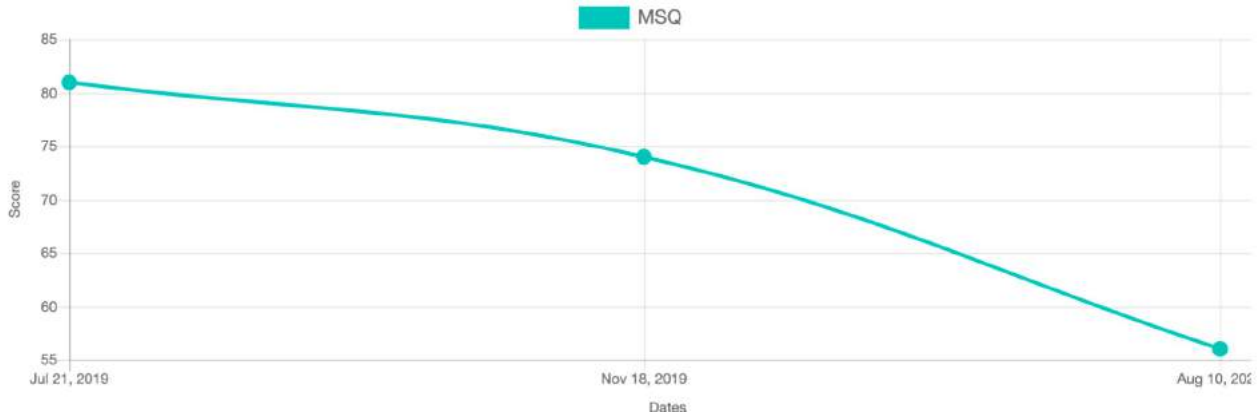
- Bi-directional relationship with inflammation is important, as well as consideration of enteric nervous system impact
- Studies in PTSD thin on the ground
  - Example - pilot RCT in = 31 PTSD+ mild TBI of intervention (*Lactobacillus reuteri* DSM 17938) or placebo supplementation (daily for 8 weeks +/- 2 weeks) – near-significant decrease in CRP but no VAS stress responsivity difference
- Therefore, currently personalised interventions targeted at overall presentation from the individual would be most appropriate

Brief case vignette 1 – a message of hope

- 21 y.o. male diagnosed with FND, multiple NES episodes, non-verbal, fluctuating gait impairment, multiple episodes of dissociation and agitation daily, severe circadian dysregulation
- History highlighted TBI (SPECT ordered by us later showed clear R-sided perfusion differential) followed by trauma secondary to bullying and the final trigger of URTI (likely Streptococcal) leading to acute presentation to secondary care
- At baseline, poor methylation with low folate, profound vitamin D deficiency at 24.8 nmol/l, diurnal cortisol dysregulation with low morning cortisol and high cortisol PM and at night, normal hsCRP and metabolic status apart from low HDL
- Multidisciplinary approach
  - Psychology – resourcing, then trauma therapy as function improved (ecosystem)
  - Integrative medicine – nutrition, lifestyle, sleep/circadian rhythm support, supplementation, overall context
  - Acupuncture initially followed by physiotherapy and Pilates-based physical rehabilitation

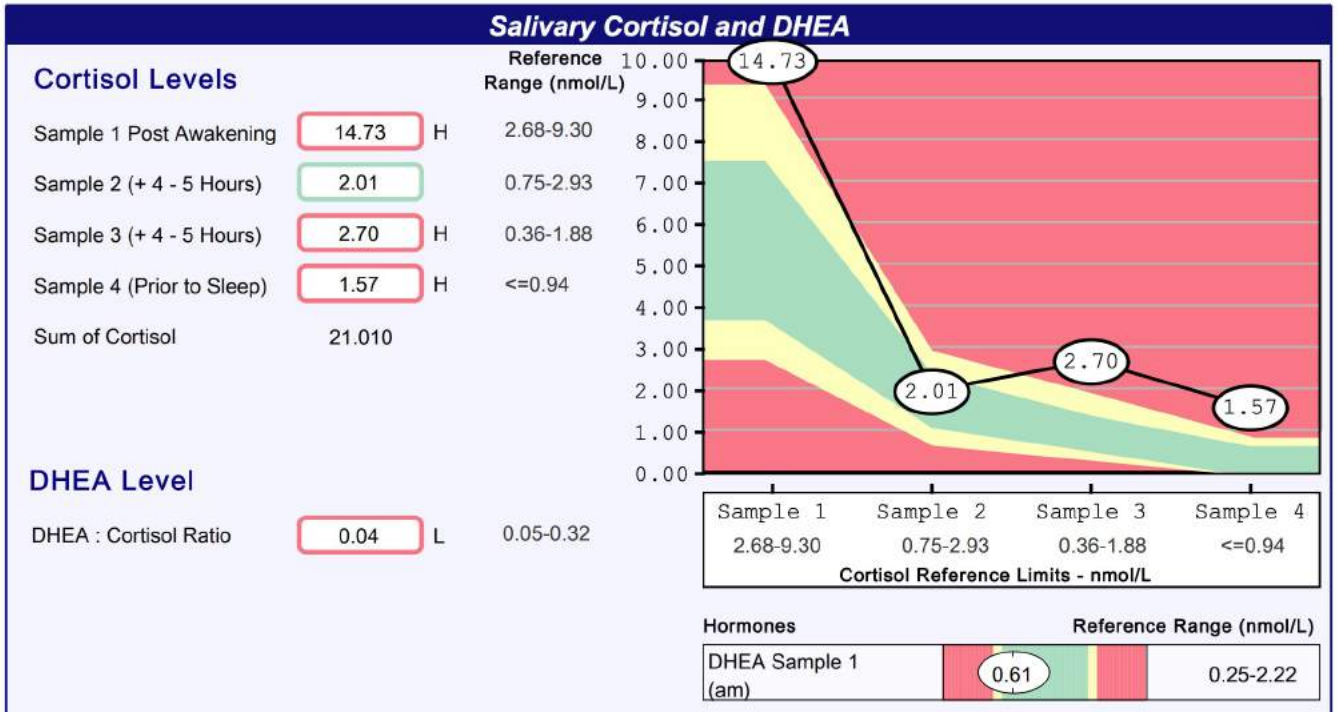
Brief case vignette 1 – a message of hope

- Over the course of a year



- 1/3 reduction in symptoms as measured by MSQ but clinically a much more dramatic difference
- Normalisation of multiple parameters, including methylation and vitamin D status
- Verbal, moving regularly and starting to engage with rehab, starting to play guitar
- Caution – HPA and NS reactivity still brittle and increased dissociation if stretched

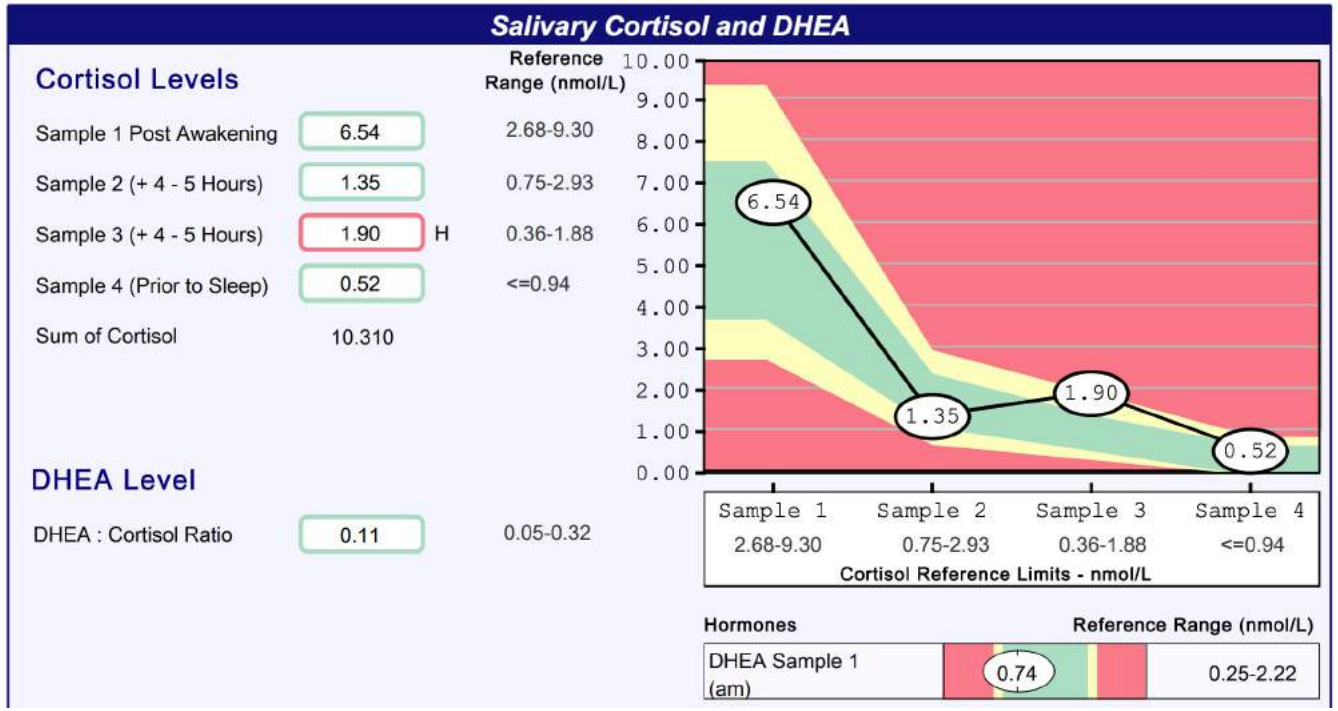
Brief case vignette 2– burnout and dissociation



Case 2 programme

- Nutrition – low GL anti-inflammatory high nutrient density plan, PFC balance at every meal and snack, reduction in refined sugar, hydration
- Exercise – small amounts spread through the day according to tolerance, no high intensity work, yoga as able to
- Stress/sleep – time out of work, rest, sleep support (melatonin + PS at night), phased return, cautious reintroduction of breathwork ONLY during the sympathetic phase (not dorsal vagal)
- Supplementation
  - B complex, D3, omega-3 with CoQ10, magnesium (citrate for constipation), Rhodiola complex AM and Reishi-Cordyceps with PS at night
- Integrative work with our clinical psychologist

Case 2 – 6 months later



And the work continues – focus on the gut-brain axis

Looking to the future

- Emerging directions to be aware of – just a few examples:
  - Psychedelic assisted psychotherapy, e.g. MDMA - by reducing activation of the amygdala and insula and increasing connectivity between the amygdala and hippocampus, MDMA may allow for reprocessing of traumatic memories and emotional engagement with therapeutic processes
  - Rapid EMDR protocols
  - Vagus nerve stimulation
  - Intranasal oxytocin

Summary

- Trauma broadly and PTSD more specifically is common – 4/100 in the UK population as an average
- Being trauma-aware in general and particularly in complex chronic and life-limiting and life-threatening illness is aware
- Key components to consider:
  - Individual assessment – look at all systems and wider context, look at specific needs and symptoms with overall resilience support in mind (particular attention to communication, cardiometabolic, inflammation, energy and GI nodes with others as appropriate)
  - Supporting a sense of safety, offering compassionate non-judgmental attitude and presence
  - Pacing – go slow and keep within the window of tolerance
  - Clinical competence and relevant training, as well as keen attention to scope of practice and safety netting
- MDT approach is essential, ideally with regular cross-communication and aligned and dynamic strategy
- Evidence base for specific nutrition and lifestyle interventions in PTSD is limited but rapidly evolving

References

- Aliev G, Beeraka NM, Nikolenko VN, Svistunov AA, Rozhnova T, Kostyuk S, Cherkesov I, Gavryushova LV, Chekhonatsky AA, Mikhaleva LM, Somasundaram SG, Avila-Rodriguez MF, Kirkland CE. Neurophysiology and Psychopathology Underlying PTSD and Recent Insights into the PTSD Therapies-A Comprehensive Review. J Clin Med. 2020 Sep 12;9(9):2951. doi: 10.3390/jcm9092951.
- American Psychiatric Association, D.S. and American Psychiatric Association, 2013. Diagnostic and statistical manual of mental disorders: DSM-5 (Vol. 5). Washington, DC: American psychiatric association.
- Atwoli L, Stein DJ, Koenen KC, McLaughlin KA. Epidemiology of posttraumatic stress disorder: prevalence, correlates and consequences. Curr Opin Psychiatry. 2015 Jul;28(4):307-11. doi: 10.1097/YCO.0000000000000167.
- van den Berk-Clark C, Secrest S, Walls J, Hallberg E, Lustman PJ, Schneider FD, Scherrer JF. Association between posttraumatic stress disorder and lack of exercise, poor diet, obesity, and co-occuring smoking: A systematic review and meta-analysis. Health Psychol. 2018 May;37(5):407-416. doi: 10.1037/hea0000593.
- Bersani FS, Mellon SH, Lindqvist D, Kang JI, Rampersaud R, Somvanshi PR, Doyle FJ, Hammamieh R, Jett M, Yehuda R, Marmar CR, Wolkowitz OM. Novel Pharmacological Targets for Combat PTSD-Metabolism, Inflammation, The Gut Microbiome, and Mitochondrial Dysfunction. Mil Med. 2020 Jan 7;185(Suppl 1):311-318. doi: 10.1093/milmed/usz260.
- Brandão, M.L., Lovick, T.A. Role of the dorsal periaqueductal gray in posttraumatic stress disorder: mediation by dopamine and neurokinin. Transl Psychiatry 9, 232 (2019). https://doi.org/10.1038/s41398-019-0565-8
- Bremner JD, Moazzami K, Wittbrodt MT, Nye JA, Lima BB, Gillespie CF, Rapaport MH, Pearce BD, Shah AJ, Vaccarino V. Diet, Stress and Mental Health. Nutrients. 2020 Aug 13;12(8):2428. doi: 10.3390/nu12082428.

References

- Brenner LA, Forster JE, Stearns-Yoder KA, Stamper CE, Hoisington AJ, Brostow DP, Mealer M, Wortzel HS, Postolache TT, Lowry CA. Evaluation of an Immunomodulatory Probiotic Intervention for Veterans With Co-occurring Mild Traumatic Brain Injury and Posttraumatic Stress Disorder: A Pilot Study. Front Neurol. 2020 Oct 20;11:1015. doi: 10.3389/fneur.2020.01015.
- Castro-Vale I, Carvalho D. The Pathways between Cortisol-Related Regulation Genes and PTSD Psychotherapy. Healthcare (Basel). 2020 Oct 1;8(4):376. doi: 10.3390/healthcare8040376.
- Chan CMH, Ng CG, Taib NA, Wee LH, Krupat E, Meyer F. Course and predictors of post-traumatic stress disorder in a cohort of psychologically distressed patients with cancer: A 4-year follow-up study. Cancer. 2018 Jan 15;124(2):406-416. doi: 10.1002/cncr.30980.
- Dunlop BW, Wong A. The hypothalamic-pituitary-adrenal axis in PTSD: Pathophysiology and treatment interventions. Prog Neuropsychopharmacol Biol Psychiatry. 2019 Mar 8;89:361-379. doi: 10.1016/j.pnpbp.2018.10.010.
- Edmondson D. An Enduring Somatic Threat Model of Posttraumatic Stress Disorder Due to Acute Life-Threatening Medical Events. Soc Personal Psychol Compass. 2014 Mar 5;8(3):118-134. doi: 10.1111/spc3.12089.
- Hori H, Kim Y. Inflammation and post-traumatic stress disorder. Psychiatry Clin Neurosci. 2019 Apr;73(4):143-153. doi: 10.1111/pcn.12820. Epub 2019 Feb 21. PMID: 30653780.

References

- Kolacz J, Kovacic KK, Porges SW. Traumatic stress and the autonomic brain-gut connection in development: Polyvagal Theory as an integrative framework for psychosocial and gastrointestinal pathology. Dev Psychobiol. 2019 Jul;61(5):796-809. doi: 10.1002/dev.21852.
- Miller MW, Lin AP, Wolf EJ, Miller DR. Oxidative Stress, Inflammation, and Neuroprogression in Chronic PTSD. Harv Rev Psychiatry. 2018 Mar/Apr;26(2):57-69. doi: 10.1097/HRP.0000000000000167.
- Morris MC, Hellman N, Abelson JL, Rao U. Cortisol, heart rate, and blood pressure as early markers of PTSD risk: A systematic review and meta-analysis. Clin Psychol Rev. 2016 Nov;49:79-91. doi: 10.1016/j.cpr.2016.09.001.
- Notaras M, van den Buuse M. Neurobiology of BDNF in fear memory, sensitivity to stress, and stress-related disorders. Mol Psychiatry. 2020 Oct;25(10):2251-2274. doi: 10.1038/s41380-019-0639-2. Epub 2020 Jan 3. PMID: 31900428.
- Osali A. Aerobic exercise and nano-curcumin supplementation improve inflammation in elderly females with metabolic syndrome. Diabetol Metab Syndr. 2020 Mar 30;12:26. doi: 10.1186/s13098-020-00532-4. PMID: 32256716; PMCID: PMC7106798.
- Paduchová Z, Katrenčíková B, Vaváková M, Laubertová L, Nagyová Z, Garaiova I, Ďuračková Z, Trebatická J. The Effect of Omega-3 Fatty Acids on Thromboxane, Brain-Derived Neurotrophic Factor, Homocysteine, and Vitamin D in Depressive Children and Adolescents: Randomized Controlled Trial. Nutrients. 2021 Mar 27;13(4):1095. doi: 10.3390/nu13041095. PMID: 33801688; PMCID: PMC8066966.

References

- Pitts BL, Whealin JM, Harpaz-Rotem I, Duman RS, Krystal JH, Southwick SM, Pietrzak RH. BDNF Val66Met polymorphism and posttraumatic stress symptoms in U.S. military veterans: Protective effect of physical exercise. Psychoneuroendocrinology. 2019 Feb;100:198-202. doi: 10.1016/j.psyneuen.2018.10.011. Epub 2018 Oct 17. PMID: 30388593.
- Rauch SAM, King A, Kim HM, Powell C, Rajaram N, Venners M, Simon NM, Hamner M, Liberzon I. Cortisol awakening response in PTSD treatment: Predictor or mechanism of change. Psychoneuroendocrinology. 2020 Aug;118:104714. doi: 10.1016/j.psyneuen.2020.104714.
- Raut SB, Canales JJ, Ravindran M, Eri R, Benedek DM, Ursano RJ, Johnson LR. Effects of propranolol on the modification of trauma memory reconsolidation in PTSD patients: A systematic review and meta-analysis. J Psychiatr Res. 2022 Apr 4;150:246-256. doi: 10.1016/j.jpsychires.2022.03.045.
- Ross MC, Cisler JM. Altered large-scale functional brain organization in posttraumatic stress disorder: A comprehensive review of univariate and network-level neurocircuitry models of PTSD. Neuroimage Clin. 2020;27:102319. doi: 10.1016/j.nicl.2020.102319.
- Schumacher S, Niemeyer H, Engel S, Cwik JC, Laufer S, Klusmann H, Knaevelsrud C. HPA axis regulation in posttraumatic stress disorder: A meta-analysis focusing on potential moderators. Neurosci Biobehav Rev. 2019 May;100:35-57. doi: 10.1016/j.neubiorev.2019.02.005.
- Seo JH, Park HS, Park SS, Kim CJ, Kim DH, Kim TW. Physical exercise ameliorates psychiatric disorders and cognitive dysfunctions by hippocampal mitochondrial function and neuroplasticity in post-traumatic stress disorder. Exp Neurol. 2019 Dec;322:113043. doi: 10.1016/j.expneurol.2019.113043. Epub 2019 Aug 22. PMID: 31446079.

References

- Sessa B, Higbed L, Nutt D. A Review of 3,4-methylenedioxymethamphetamine (MDMA)-Assisted Psychotherapy. Front Psychiatry. 2019 Mar 20;10:138. doi: 10.3389/fpsyt.2019.00138.
- Sheerin CM, Lind MJ, Bountress KE, Marraccini ME, Amstadter AB, Bacanu SA, Nugent NR. Meta-Analysis of Associations Between Hypothalamic-Pituitary-Adrenal Axis Genes and Risk of Posttraumatic Stress Disorder. J Trauma Stress. 2020 Oct;33(5):688-698. doi: 10.1002/jts.22484.
- Stevelink SAM, Jones M, Hull L, Pernet D, MacCrimmon S, Goodwin L, MacManus D, Murphy D, Jones N, Greenberg N, Rona RJ, Fear NT, Wessely S. Mental health outcomes at the end of the British involvement in the Iraq and Afghanistan conflicts: a cohort study. Br J Psychiatry. 2018 Dec;213(6):690-697. doi: 10.1192/bjp.2018.175.
- Sugasini D, Yalagala PCR, Subbaiah PV. Plasma BDNF is a more reliable biomarker than erythrocyte omega-3 index for the omega-3 fatty acid enrichment of brain. Sci Rep. 2020 Jul 2;10(1):10809. doi: 10.1038/s41598-020-67868-9. PMID: 32616795; PMCID: PMC7331585.
- Tolahunase MR, Sagar R, Faiq M, Dada R. Yoga- and meditation-based lifestyle intervention increases neuroplasticity and reduces severity of major depressive disorder: A randomized controlled trial. Restor Neurol Neurosci. 2018;36(3):423-442. doi: 10.3233/RNN-170810. PMID: 29614706.
- de Vries GJ, Lok A, Mocking R, Assies J, Schene A, Olff M. Altered one-carbon metabolism in posttraumatic stress disorder. J Affect Disord. 2015 Sep 15;184:277-85. doi: 10.1016/j.jad.2015.05.062.
- van Zuiden M, Haverkort SQ, Tan Z, Daams J, Lok A, Olff M. DHEA and DHEA-S levels in posttraumatic stress disorder: A meta-analytic review. Psychoneuroendocrinology. 2017 Oct;84:76-82. doi: 10.1016/j.psyneuen.2017.06.010.