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Oral presentations

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The "Wiener Schmääh" in stress resilience: From Selye to Nobelists Guillemin (1977) and Kandel (2000)

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The "Wiener Schmääh" refers to the conceptual framework with many roots and branches developed in the beginning 20th century. Its impact on the foundation of stress resilience and brain research brought groundbreaking understanding into the human mind-brain-body interplay is still little-known. 2025 marks the 50th anniversary of the International Institute of Stress (IIS) at McGill University (Canada), founded by Hans Selye (1907–1982). Selye was born in Vienna, and his intellectual development was in the former Austro-Hungarian institutions (in present-day Slovakia and the Czech Republic): MD (1929) and PhD (1931) in biochemistry at the University of Prague. This shaped his early life, influenced his aspirations, inventive nature, and passion for creativity. It helps with rapid integration into research in the New World. Connections with well-established institutions (Johns Hopkins University and McGill University, Canada) fostered his creativity. His originality of work reveals a keen sensitivity to innovations, and his efforts to gain better opportunities for the scientific community and healthcare by founding IIS. Prof. H. Selye was a pioneer in the fundamentals of stress response and “cross-adaptation” as well as insight into stress as the basis of post-traumatic stress disorder (PTSD) [1]. Selye’s PhD student, Roger Guillemin, studied hypothalamic neuropeptides and hormones involved in stress responses (Nobel Prize, 1977) [2]. The other direction of emotional "color" of eustress or distress and their memorizing was done by “Wiener Schmääh” native scientist Eric Kandel (Nobel Prize, 2000). His work helps to understand the complex relationships between brain activity, synaptic plasticity, influencing behavior, mental and visceral health, and their outcomes on stress resilience, emphasizing the necessity of a multidisciplinary approach in research [3]. These forgotten episodes of intellectual influence of Vienna on early stress resilience research indicate the importance of the early carrier period in a professional journey. However, Selye's legacy didn't include official recognition in the form of a Nobel Prize; his impact on science and his serving as the President of IIS later in his career remains extremely influential today.

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Arts and medicine

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There is a complex relationship between the arts and medicine in history as well as in the present. Both share an interest in the human body, both rely on the training of the eye and hand, both combine aesthetics and diagnostics. The art and science of anatomic wax modeling was not possible without the dissection of cadavers. The idea behind the wax models was that once the whole body could be studied on a model, it would not be necessary anymore to perform dissections in order to learn the anatomy and further medical sciences. An idea which also prompted the Grand Duke Pietro Leopoldo of Tuscany (later Emperor Leopold II) to finance the wax modeling workshop in the observatory “La Specola”. To know the human body was necessary for physicians, but also a prerequisite to artistic creation. Great artists like Leonardo da Vinci, Michelangelo or Raphael are known to have studied anatomy. Wax was cheap and an easy matter to work on and used since ancient times.

The “Josephinum” in Vienna has been founded 1784 by Emperor Joseph II as medical surgical Academy to train military surgeons and thus revolutionized medicine in the 18th century. The Josephinum was an innovative institution, especially regarding the various teaching tools of the age of enlightenment used in the training of the students. The most important part of these teaching aids and still today of unique bearing are the anatomical and obstetric wax models which were ordered by Joseph while visiting his brother Pietro Leopoldo in Florence. All models – 1.192 single

pieces - were carried across the Alps in a convoy of men and mules to Linz and then travelled upstream via the Danube to Vienna.

Still today, the building reflects its significance and serves now as a gate to the historic collections of the Medical University of Vienna. It houses the world-famous anatomical wax models from Florence, as well as surgical instruments, valuable books, important estates and other documents in the field of the history of medicine. The Medical University of Vienna is one of the few medical institutions worldwide with such an eminent cultural heritage. The Josephinum with its permanent collections and – among them - the permanent collection of anatomic and obstetric wax models as well as with temporary exhibitions is open to the public as Medical History Museum Vienna.

Hans Selye: A peculiar man

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Many of his contemporaries described János Selye as a peculiar, strange man. In terms of his world view and unusual research methods, he was standing in the 19th century with one foot and in the 21st century with the other. In my lecture I will go through the stages of Selye's life that made him one of the most distinguished and respected researchers, as well as one of the most popular speakers of his time, regarding his public and scientific activities.

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From the discovery of Hans Selye to modern concepts of distress & eustress.

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Hans Selye (1907, Vienna - 1982, Montreal) first published his seminal papers in 1936 (*Nature*) & 1937 (*in Science*) that described the three stages of stress reaction (i.e., alarm reaction, resistance & exhaustion) in rats exposed to cold, forced immobilization or toxic agents. He identified the adrenals & the pituitary as the main endocrine glands involved in this nonspecific reaction. He also knew & documented that although the sudden release of epinephrine (adrenaline) from the adrenal medulla plays a critical role in the initial alarm reaction, but the long-term effects of stress reaction are due to the enhanced synthesis & release of glucocorticoids from the adrenal cortex. Based on this mechanistic reasoning he described in his first publications what has later become known the “morphologic stress triad”: adrenal hypertrophy, gastric erosions/ulcers & thymolymphatic atrophy. Furthermore, what we call today ‘stress-related diseases’ in man, he described these in the 1940s & 1950s as ‘diseases of adaption’ in rats. In the last stages of his productive life, Selye realized that virtually all the stressors (i.e., stress-causing agents) he used in experimental animals were unpleasant, negative factors that caused ‘distress’. Thus, in his last scientific book (1974) “Stress without distress” he called distress the stress reaction caused by negative, unpleasant factors & eustress (from ‘euphoria’) the similar reaction triggered by positive, pleasant factors like joy over major rewards, receiving surprising good news. Namely, we learned during the last about 40 years that our pituitary gland cannot distinguish between positive & negative stimuli to release ACTH (only our brain cortex, amygdala & hippocampus may perceive the difference). Because of these stress-related creative discoveries Hans Selye is known as ‘father of biologic stress’ and although most of his original experiments were performed in rats & mice, the human relevance has quickly become relevant, e.g., starting with the sudden increase in hospitalizations due to performed gastroduodenal ulcers after the German rocket attacks & during the air-raids in London in the early stages of World War II (1942-43). More recently, many clinicians realized that the three stages of stress reaction (i.e., alarm reaction, resistance & exhaustion), as described by Hans Selye, can be recognized in severe cases of COVID-19 infection. Namely, in the initial stages of these viral infections, large elevations of blood cortisol concentrations were detected, & as the disease progressed, the damaged adrenal cortex ‘exhausted’, glucocorticoid synthesis dropped more drastically than in other ICU patients & if these patients were given synthetic glucocorticoids, their quality of life not only improved, but were often discharged alive from the hospital. These recent clinical recognitions were not surprising to most pathologists who knew that the adrenal cortex was similarly affected in the early stages of AIDS epidemic in the 1980-90s & if those patients were treated with daily glucocorticoids, their average lifespan was expanded by about 6 months. Thus, Selye was a much more creative & visionary scientist than is generally considered.

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Orchestration of the bodily response to stress: Focus on corticotropin releasing factor

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Stress may cause behavioral and/or psychiatric manifestations such as anxiety and depression and also impact on the endocrine and autonomic nervous systems and visceral organ function including the gastrointestinal and cardiovascular systems. During the past decades substantial progress have been made in the understanding of the underlying mechanisms recruited by stressors. Experimental studies point to the activation of the corticotropin-releasing factor (CRF) signaling system being implicated in a large number of stress-related endocrine, behavioral and visceral responses. This is supported by neuroanatomical reports showing that the CRF system (ligands and receptors) are expressed in specific brain nuclei and at peripheral sites. In particular, CRF receptors are expressed in hypothalamic, limbic and pontine circuitries regulating, pituitary secretion, anxiety, and autonomic outflow to the viscera. In the gastrointestinal tract CRF receptors are located in myenteric neurons, mast cells and enterochromaffin cells. Functional studies using the exogenous injection of CRF agonists and selective antagonists to CRF receptors unraveled the importance of brain CRF signaling in the stress-related endocrine (activation of pituitary-adrenal axis), behavioral (anxiety/depression), autonomic nervous system (activation of sympathetic system and sacral parasympathetic, decreased vagal activity), and immune responses. In the gut, the administration of CRF agonists recapitulate stress-related alterations of gastrointestinal function including in the stomach, the inhibition of gastric transit, and in the colon, the induction of diarrhea, enhanced motility, mucus secretion, mucosal permeability to macromolecules, bacterial translocation, and mast cell activation which in turn promote visceral hypersensitivity. Moreover, CRF antagonists pretreatment blocked all stress-related gastrointestinal alterations and visceral hyperalgesia. Clinical studies indicate that CRF administration can induce irritable bowel syndrome (IBS)-like symptoms in healthy subjects and heighten colonic sensitivity to colorectal

distention in IBS patients. However so far, there is still an unmet need for the use of CRF antagonists to treat stress-related disorders.

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The good & bad metabolic elements of distress

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One of the recent discoveries in understanding stress response is related to the brain-gut-fat axis. This newly discovered pathway serves as a highway for complex metabolic elements that can trigger diverse physiological and pathological processes. Adipocytes, the primary cellular components of fat, perform numerous physiological functions and contribute to resilience and pathogenesis of various diseases [1]. The differences between patients where disease manifestation is related to fat mass vs dysregulated adipose functions show help to catch heterogeneity in obesity. Obesity phenotypes are complex, multifactorial conditions that often coexist. There is a growing body of evidence that links the cytoprotection of white and brown adipose tissues (WAT and BAT, respectively) to the resilience of nervous tissue to exogenous and endogenous pathological challenges. Modifying WAT and BAT can alter stress response, which in turn determines the progression and outcome of neurological disorders [2]. While body mass index (BMI) is less important for understanding metabolic risk, the distribution of WAT and BAT is more crucial. Changes in compensatory mechanisms of WAT and BAT can optimize energy balance, promote mind-body well-being, and delay aging. Alterations in metabolically active BAT in adults can lead to long-lasting physiological changes that contribute to distress. Regaining new BAT improves insulin sensitivity, endothelial health, and reduces low-grade inflammation, enhancing the thermogenic capacity of adipose tissue. The tips on how to maximize physiological BAT activity, minimize its loss, and adapt to the complex metabolic challenges associated with distress.

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Metabolic syndrome: Sex, age, medication and stress response specific pathophysiological mechanism

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Metabolic syndrome is a gender-specific group of pathophysiological mechanisms that includes the development of insulin resistance in various organs, metabolic changes affecting the utilization of fat, carbohydrates, and proteins, low-grade systemic inflammation, and the onset of type 2 diabetes and cardiovascular diseases. Chronic exposure to stress, observed in both rodent models and humans, is linked to anxiety, metabolic imbalance, and fluctuations in weight. One key pathophysiological mechanism connecting stress response and metabolism involves the opposing actions of insulin and cortisol/corticosterone: insulin promotes glucose storage in cells, while the stress response depletes energy reserves, leading to cellular starvation. Therefore, the activation of the neuroendocrine axis and increased sympathetic tone contribute to the development of metabolic syndrome. Conversely, metabolic disturbances that cause cellular starvation can activate stress response. Medications that directly or indirectly modulate stress responses such as corticosteroids, antipsychotics, beta-blockers, and antidepressants - may have metabolic syndrome as a potential side effect. In our study, middle-aged Sprague-Dawley rats exposed to a high-fat, high-sucrose diet, despite early treatment with metformin or liraglutide, developed prediabetes.

Moreover, female rats treated with liraglutide exhibited reduced fat mass but developed type 2 diabetes, which was associated with an increased stress response and adrenal gland enlargement. While one-point corticosterone measurements did not show significant differences between the groups, the insulin tolerance test indicated that the liraglutide-treated groups maintained higher glucose levels, likely due to a sensitized stress response. An increase in adrenal size was observed in all treated and untreated female groups but not in male groups. This finding aligns with studies suggesting that females exhibit a higher stress response, which intensifies with aging. Therefore, careful titration of medications that influence metabolism or modulate the stress response is essential for female sex and elderly.

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Stress and psychiatric disorders

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Stress and Psychiatric Disorders are intimately connected. As part of any psychiatric examination, a core question is always directed toward any "psychosocial stressors." It has long been observed clinically that stress can trigger the onset of or exacerbate psychiatric disorders. Mood disorders such as Major Depressive Disorder and Bipolar Disorder, Psychotic Disorders such as Schizophrenia, Development conditions such as Tourette's Disorder and Stuttering and by definition, Posttraumatic Stress Disorder and other conditions. Emerging evidence reveals the biologic mechanisms underlying stress in psychiatric disorders including structural brain changes, neuroinflammation, and disruption in neurotransmitter/hormones. Treatments involve psychotherapy and psychopharmacology. Therapies targeting neuroplasticity through psychedelic assisted psychotherapy are currently being studied.

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Stress-related diseases: Focus on the microbiota-gut-brain axis

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The effects of stress on digestive functions are associated with modifications of visceral sensitivity, intestinal permeability, gut microbiota, local inflammatory response and gastrointestinal motility. Irritable bowel syndrome (IBS) is a stress-related disease assimilated to a dysfunction of gut-brain

interaction. Stress has also a role in the pathogeny of inflammatory bowel disease (IBD; Crohn's disease and ulcerative colitis). In particular, early-life trauma are frequently reported in IBS and IBD and are involved in their pathogeny. IBS and IBD are biopsychosocial models. Anxiety and depression are often reported in such patients. The medical treatment of IBS is rather disappointing and behavioral treatments such as hypnosis and cognitive behavioral therapies are of interest while biological therapies have revolutionized the treatment of IBD. However, there are still unmet needs of drugs in the treatment of IBS and IBD. Stress is able to induce a perturbation of the microbiota-gut-brain axis through the autonomic nervous system, and the hypothalamic pituitary adrenal axis. Such a perturbation can facilitate a disruption of the homeostasis both at the level of the body and the gut. Since there is a bidirectional communication between the microbiota, the gut, and the brain, the consequences of stress can be localized at the level of the gut and/or the brain, so that it can be difficult to know what the primary impact of stress is. Thus, medical management can be rather problematic, in particular for IBS. For example, the medical treatment of IBS after failure of firstline therapies such as antispasmodics, transit modifiers, probiotics, focuses on central neuromodulators. Fecal transplantation is still a research topic but is not used in the current practice in IBS and IBD. Regulating the autonomic nervous system is of interest in IBS and IBD either through bioelectronic medicine or behavioral therapies.

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Structural & functional stress-related GI diseases

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Hemorrhagic gastric erosions & ulcers which developed in rats exposed to severe stress were one of three components of the initial 'triad of stress' that Hans Selye first described in 1936. Erosions are superficial mucosal lesions that usually heal spontaneously in 3-4 days after distress, while ulcers are deep lesions that penetrate the muscularis mucosae of the gastrointestinal (GI) tract. The healing of deep ulcers requires an angiogenesis-dependent

production of granulation tissue, over which proliferating & migrating epithelial cells complete the healing in about a week – unless the stomach is infected by *Helicobacter pylori* that markedly delays the healing, hence it requires the elimination of these bacteria by antimicrobial drugs. It's important to note that in rodents (e.g., rats, mice) even the most intensive distress produces only gastric lesions & not duodenal ulcers, for the reproduction of which specific duodenal ulcerogenic chemicals are needed in rodents (e.g., propionitrile, cysteamine or their derivatives, that I discovered still in Selye's institute in Montreal). In humans, on the other hand, the stress- & drug-induced duodenal ulcers are more frequent than gastric ulcers, in most countries of the world (except in Japan). Thanks, in good part, to the discovery of these animal models of duodenal ulcers, as well as to investigating the many forms of stress-induced gastric erosions & ulcers in humans & experimental animals, the pathogenesis of these lesions are relatively well understood: it is generally agreed that they are triggered by the increased secretion of catecholamines & glucocorticoids during severe stress, where vascular & motility factors play a critical role, with a small, if any, contribution by enhanced gastric acid secretion. Healing of these ulcers in humans is delayed because of inability of angiogenic growth factors (e.g., bFGF, PDGF, VEGF) to exert their normal healing capability, in part due to ulcers being infected by *H. pylori*.

Inflammatory bowel disease (IBD), like ulcerative colitis (UC), Crohn's disease (CD) involve parts of small intestines, in addition to the colon, have become topics of clinical & experimental investigations in the second part of the 20th century. As their names indicate, IBD involves the lower parts of the GI tract, i.e., small & large bowel but their pathogenesis is incompletely understood. Stress & environmental factors play a role in the pathogenesis of UC, while genetic & immunological elements are more important for the development of CD.

Functional GI diseases, like irritable bowel syndrome (IBS) is even more recently recognized as an entity of stress-related GI diseases. Their clinical manifestations, pathogenesis & therapeutic options will be presented at this conference by Prof. Bruno Bonaz.

Erosions & ulcers: superficial vs. deep lesions. (Rate limiting step of maintained blood flow & importance of “granulation tissue”).

- **Gastric ulcers vs. gastritis:** Role of *H. pylori*
- **Duodenal ulcers:** Most frequent form of “peptic ulcers” & not only due acid excess; role of gastroduodenal dysmotility.
- **IBD (ulcerative colitis & Crohn disease):** Clinically most relevant & challenging; critical role of angiogenesis.
- **IBS (irritable bowel syndrome):** A functional, often very painful GI disorder, with poorly understood pathogenesis.

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Vagus nerve stimulation & hypnosis for IBS & IBD

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The gut and the brain communicate bidirectionally through the autonomic nervous system. The vagus nerve (VN) is a key component of this gut–brain axis and has numerous properties such as anti-inflammatory, antinociceptive, and antidepressive effects. A perturbation of this gut–brain communication is involved in the pathogeny of irritable bowel syndrome (IBS), and inflammatory bowel disease (IBD). Stress plays a role in the pathogeny of these diseases, which are biopsychosocial models. The gut–brain axis can be targeted for therapeutic purposes in IBS and IBD through non-drug therapies, such as hypnosis and VN stimulation (VNS), opening up possibilities for responding to patient expectations. We have shown that VNS, approved in the treatment of drug refractory epilepsy and depression, is able to improve an experimental model of colitis in rats. In a translational approach, we have performed a pilot study of VNS in patients with active Crohn’s disease and shown, for the first time, that VNS is of interest in such patients. In the same way, we have shown that VNS is of interest in IBS patients, notably by improving abdominal pain. Gut-oriented hypnosis is well known to improve IBS patient symptoms. Few data are available regarding the use of hypnosis in IBD patients. We have performed a clinical study evaluating the effect of hypnosis on the quality of life of patients with Crohn’s disease. In an intermediate analysis, our results are encouraging as they suspect an effect of hypnosis on short-term quality of life, clinical symptoms, acceptability of the disease, perception of benefit from the disease and physiological stress. We are waiting for the final results to propose a standardized hypnosis protocol to our patients. In conclusion, VNS and hypnosis are of interest for IBS and IBD patients and should be considered in the management of such patients.

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Building resilience from the gut up: Microbiome and integrity alterations in stress-susceptible rats

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Introduction: Posttraumatic stress disorder (PTSD) is a prevalent and debilitating brain disorder. Since only vulnerable individuals develop symptoms after trauma, identifying predictive markers is crucial for prevention. The gut-brain axis enables bidirectional communication, and alterations in gut integrity or microbiome composition can impact brain function [1]. Thus, the gut may serve as a novel therapeutic target in PTSD. Methods: We used electric footshock as a trauma model and measured freezing behavior as the main outcome. In Long-Evans rats, we investigated gut-related vulnerability markers (microbiome composition, intestinal integrity [2]). In CD1 mice, we examined the effects of post-trauma sucrose drinking (2%, 16%, 32%) and chronic treatments: an antibiotic (AB) cocktail (28 days in drinking water) or a probiotic (Pro) mixture [3] (14 days via cookie). Results: In rats, vulnerable animals had the thinnest intestinal villi without changes in tight junction proteins (ZO-1, occludin, claudins) or inflammatory markers (TNF- α , IL-1 β , IL-10, TLR-4). However, gut-regulatory markers differed: Muc2 mRNA (mucin production) was highest and Reg3 β mRNA (epithelial integrity) lowest in vulnerable rats. Akkermansia muciniphila, a mucin-associated bacterium, was more abundant in this group. Short-chain fatty acid levels were unchanged. In mice, 16% and 32% sucrose (but not 2%) consumed for 24h post-trauma reduced freezing behavior the next day, but not two weeks later. AB (but not Pro) was initially aversive, causing weight loss, but animals adapted. Chronic treatment didn't affect locomotion or anxiety.

Fourteen days post-trauma, AB reduced freezing and jumping behaviors, while Pro had no effect. Conclusion: Our findings suggest gut integrity and microbial composition influence PTSD-like symptoms via brain-gut interactions. Immediate high-calorie intake may transiently reduce stress responses but not prevent PTSD development. AB treatment showed a delayed behavioral benefit, highlighting a potential therapeutic pathway through the gut-brain axis.

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Understanding and reducing work-related distress

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The world is changing - people are living longer, and spend around 45 years of their lives at work.

In today's fast-paced environment, workplace stress is affecting employees across different industry sectors and job roles. While some stress can be motivating, excessive stress often leads to burnout, lower productivity, and serious mental and physical health issues. In the U.S. about 65% of employees report work as a major stressor, with 35% experiencing chronic stress - costing \$27 billion annually in lost productivity. In the UK, work-related stress accounts for 35% of workplace illness and 43% of days lost. Globally, only 57% of employees report good overall health. Research

since the 1970s examining the relationship between work stress and well-being has been showing clear links between work-related stress and a variety of physical and mental disorders. A meta-analysis by Nixon et al. (2011) identified correlations between work stressors e.g., role conflict, long working hours, interpersonal conflict, lack of control, organizational constraints, with physical complaints such as fatigue and sleep disturbance, backache, headache, eye strain, dizziness, fatigue, appetite loss, and gastrointestinal problems. Common causes of stress include high workload, lack of managerial support, and organizational changes. Importantly, it's not just the job itself, but the fit between individual and environment that matters. While stress remains a challenge, our ability to manage it is improving. Interventions at both individual and organizational levels—ranging from stress management programs to supportive leadership and flexible work structures - are critical for breaking the cycle of distress. Stricter regulations and growing awareness are pushing companies to adopt healthier practices, enhancing resilience and long-term success. According to the McKinsey Health Institute (2024), organizations that address workplace stress not only improve employee well-being but also benefit from reduced absenteeism and turnover, and increased productivity.

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The experience of a psychiatrist

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Mental health and mental disorders exist on a continuum, rather than as absolute, separate categories. Contemporary understandings of mental disorder development are grounded in the biopsychosocial model, which aligns with the stress-diathesis model. According to this framework, mental disorders emerge when an individual's vulnerability to stress exceeds their capacity for resilience. Vulnerability and resilience to stress are shaped over the course of life through cumulative environmental influences and the individual's stress responses. While prolonged and

unprocessed distress - particularly during critical early life periods - can heighten vulnerability to stress in later life, post-traumatic growth following adversity can enhance resilience. When major psychosocial stressors- such as the death of a loved one, chronic illness, or divorce - trigger significant distress, this can evolve into clinical mental illness. Stress thus serves as a common denominator in many mental disorders. It plays a central role not only in conditions traditionally associated with stress, such as anxiety disorders and post-traumatic stress disorder, but also in those often viewed through a more biological lens, including schizophrenia, bipolar disorder, and major depression. This presentation will explore the connection between stress and mental disorders using clinical case examples.

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Overcoming the stress of stuttering: A primer of resilience & stress management

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Stuttering is a neurodevelopmental disorder that affects 5% of all children and persists to affecting over 1% of all adults. Stuttering has existed through the course of human history and knows no boundaries--occurring at similar rates throughout the world. It has long been known that stress adversely affects stuttering symptoms AND that stuttering itself leads to stress. Emerging evidence also shows that individuals who stutter experience significant trauma from bullying, ridicule, stigma and discrimination. What has contributed greatly to stuttering being misunderstood is that individuals can nearly uniformly be in a state of fluency through singing or reading aloud in chorus. From such, speech has been postulated related to two loops of neuronal connections--a medial system, which appears to be dysfunctional in stuttering, and a lateral system which is preserved. The medial system involves the natural timing and initiating of speech through the basal ganglia--namely the striatum.. The amygdala is activated in stuttering and plays a central role in reaction

to stress. The lateral system can be activated through an external timer such as singing thereby bypassing the stress-prone striatal circuit.

Stuttering is now known to be a heterogeneous condition with multiple etiologies. One clear cause of stuttering is of autoimmune origin related to the development of anti neuronal antibodies during development in reaction to streptococcal infection. Such neuroinflammation may explain why stuttering symptoms tend to be variable. Inflammatory responses and stress appear to exacerbate stuttering.

Future directions of research are to outline the subtypes of stuttering and the direction of targeted multidisciplinary treatment approaches. Pharmacologic treatments have shown promise as well as neuromodulation such as Transcranial Magnetic Stimulation. Adjunctively, cognitive behavioral psychotherapy and acceptance commitment therapy are utilized primarily to reduce the stress exacerbation of stuttering. Future therapies may involve neuroplasticity through novel agents-- thus repairing the regions of the brain that did not fully develop and are easily prone to stress.

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The SEMART approach from childhood to advanced age: Connecting physiological and psychological insights for lifelong wellbeing

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Worldwide, every third person has metabolic disorders, and for every 10th mental disease, an increased number of post-traumatic stress disorders (PTSD) after experiencing traumatic events during wartime, forced displacement, or extremal conditions. This highlights the need to provide future physicians a solid understanding of lifestyle diseases with focus on self-care, age differences in PTSD and stress management in medical education [1]. To address this, the School of Medicine of the American University of Health Sciences, Signal Hill/Long Beach, CA, USA developed the course “SEMART” (Stress Education, Management and Resilience Training). In this course, stress reduction techniques, mental disorders related to stress, PTSD, and burnout phenomena in health care practitioners will practically be examined and linked to underlying physiological and psychological mechanisms [2]. Through orientation sessions, Problem-Based Learning (PBL) each week, and an integrative medicine interdisciplinary approach (1 hr/week classes) students will explore the modulation of autonomic body functions through the synchronization of neural activities in stress resilience activities. Moreover, it is important to learn the basic concepts of how emotional factors influence pain perception, metabolic health, sleeping quality; stress – attention, processing speed, and memory, and their clinical relevance from childhood until advanced age and stress resilience development. This seems to be a promising approach to build new skills and develop additional competencies [3], enhance medical students mental health as well as their motivation and improve learning success in modern medical education.

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Stress reduction & work stress management

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Stress management involves a variety of strategies aimed at preserving health through the maintenance of a healthy lifestyle. Key components include a balanced diet, regular physical activity, strong social connections, effective coping mechanisms, adequate sleep, laughter, and relaxation techniques. However, when facing significant life stressors, stress management may also require a deeper process of psychological adaptation, similar to the stages of grief. This process can include denial, anger, bargaining, sadness, and ultimately acceptance—leading to post-traumatic growth and increased resilience. Failure to complete this process, known as maladaptation, can result in chronic distress and heightened vulnerability to future stressors. Psychotherapy can support this adaptation by fostering greater self-awareness, self-acceptance, and the development of healthier behavioral patterns. In the workplace, excessive strain can lead to burnout for some individuals. Both organizational-level interventions and personal strategies play a vital role in achieving a healthier work-life balance and improving stress management. This presentation will explore various examples of stress management, with particular focus on managing work-related stress.

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Traditional Chinese medicine approaches to stress management: A historical and clinical perspective

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Traditional Chinese Medicine (TCM) offers a holistic approach to stress that complements modern biomedical models. Rather than focusing solely on neuroendocrine or psychological factors, TCM views stress as an imbalance of qi (vital energy) and disharmony among internal organs. Common diagnostic patterns include liver qi stagnation, heart-spleen deficiency, and disharmony between the heart and kidney—each associated with emotional and physical symptoms such as anxiety, insomnia, fatigue, or irritability.

Traditional Chinese medicine has significant effects in stress management and treatment of stress-related diseases. This presentation will introduce how acupuncture (Amorim D et al. 2018), herbal medicine (Lin J et al. 2022), and movement-based therapies like Qigong (Wang C et al. 2010) are applied to regulate qi, calm the spirit, and restore emotional balance. By integrating historical insights and modern clinical practices, this talk aims to foster dialogue between Eastern and Western medical traditions and offer innovative perspectives for managing stress in diverse patient populations.

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Stress and Alzheimer's disease: Nutraceutical guidelines for prevention and therapy

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Stress-induced zinc deficiency increases the risk of COVID-19 morbidity and mortality (Schloss 2023). Survivors of COVID-19 are at substantially higher risk of developing AD (Aleman et al. 2025). Stress-related deficiencies of zinc and niacin (pyridine nucleotides) impair dolichol biosynthesis at dolichol kinase (DOLK, free Zn^{2+}), polyprenol dehydrogenase/dolichol dehydrogenase (DHRSX, NAD/NADH), and polyprenol reductase (SRD5A3, NADPH) leading to protein glycosylation dysfunction (e.g., amyloid precursor protein, tau, and voltage-gated calcium channels) and impaired function of the central nervous system (Wilson et al. 2024). While oxidative stress is a recognized contributor to Alzheimer's disease progression (e.g., lower levels of NADPH and reduced glutathione), the involvement of dolichol biosynthesis dysfunction as a major risk factor and the roles that zinc, and pyridine nucleotides play in dolichol-mediated disease progression are only beginning to be recognized. Nutraceutical supplements that normalize dolichol pathway function, such as precursors and cofactors (e.g., polyprenol, NAD, NADPH, Zn^{2+} , and CTP), are reported to help prevent Alzheimer's disease and improve cognition after onset.

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Future horizons in stress resilience: Focus on integrating AI and personalized health management

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Lifestyle diseases and influence of catastrophic outcomes of wars, wildfires and post pandemic events are global health challenges with rising incidence of metabolic disorders, mortality of cardiovascular and oncology diseases. Future horizons in their prevention and care must focus on improving stress resilience. The economic burden of obesity sub-phenotypes and its comorbidity in adults and childhood is critical for modern public health and health care. Therefore, early detection, prevention and long-term management strategies are crucial for effective interventions which require involvement of healthcare providers, educators and innovative technologies like artificial intelligence (AI). This multimodal approach with personal involvement could help detect food intake, physical activities, sleeping quality and real-time glucose-responsive neuromodulation while minimizing medication dependence for obesity, like GLP. Traditional anthropometrical methods such as body weight index (BWI) or blood-based biomarkers like HbA1c or saliva cortisol level are insufficient for capturing early changes in body's fat mass and lean mass, short-term glycemic fluctuations or visceral fat. Advanced imaging data as DEXA (Dual-Energy X-ray Absorptiometry) scanning technology are still unavailable for routine use for public. The more precise metrics such as bioelectrical bioimpedance analysis of body's weight, Glucose Variability (GV) and Time in Range (TIR), Continuous Glucose Monitoring (CGM) and AI integration offer real-time data analytics and personalized treatment plans. Empowering patients through AI-driven self-management and community support is crucial for sustainable improvements of prevention different sub-phenotypes of obesity. Creating a system of daily routine on promising physiological based activities as food selection, physical activities, brown fat stimulation, mental health-related techniques, represents a paradigm shift in stress resilience management. Understanding multifactorial impact of lifestyle, and integrative strategies may benefit the care and management of obesity. AI-driven care integrating these innovations into healthcare systems can improve more precise prediction of obesity and prevent its outcomes.

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Poster session

Sex difference in daily cortisol fluctuation during COVID-19 lockdown of foreign students from I. Horbachevsky TNMU

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During COVID-19 lockdown, people faced different daily routines, inability to go out, and emotional challenges from social isolation, family conflicts, and loss of loved ones (1). During the lockdown 200 foreign students at I. Horbachevsky Ternopil National Medical University, Ukraine (TNMU) were confined to dormitories. This stress may have altered their cortisol secretion patterns in a sex-specific manner (2,3). To investigate this, two months after the lockdown began, saliva cortisol of 96 male and 93 female students was sampled 5 times a day, starting at 7 am and continuing in 4-hour increments, and measured using ELISA. The investigation of cortisol level from all subjects together showed that cortisol levels peaked at the 2nd measuring point (11 am - 1 pm), which is a deviation from the normal daily cortisol fluctuation with highest peak before waking up (corresponding to the 1st measuring point). Males had significantly higher cortisol levels than females at the 3rd ($p=0.017$, $U=2988$, $z=2.38$) and 4th measuring points ($p=0.009$, $U=2920.5$, $z=2.59$). The cortisol fluctuation data were then subjected to mathematical modelling using Mathematica software (ver. 12.0, Wolfram Research, Inc., Champaign, IL, USA) which

grouped data into 5 male and 5 female clusters (π_1 - π_5). Assuming that the detection of the morning peak was missed in cluster π_1 , clustering showed that 62% of male and 76% of female subjects (clusters π_1 and π_2) had actually normal cortisol fluctuations, while others deviated (38% of male and 24% of female subjects). Cortisol peaks in all female clusters were higher than in male clusters, except in male- π_5 where it peaked at mid-day. Mathematical modelling effectively grouped subjects by typical and atypical cortisol fluctuation and assessed sex-specific differences. Most subjects' cortisol secretion remained unchanged during the lockdown, but it is unclear if lockdown stress altered the proportion with atypical fluctuations.

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Age and sex matter: Chronic stress impairs memory via lipid raft disruption in aged female rats

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Chronic stress induces long-term metabolic changes, contributing to various pathologies. Research in this area faces challenges, including ethical considerations, translational relevance, accurate stress measurement, and appropriate model selection. Sex hormones modulate the stress response, creating sex-specific, age-dependent metabolic imprints. This study investigated chronic stress response in young and aged Sprague Dawley rats of both sexes, aiming to determine if stress, sex and/or aging caused memory impairment and altered cellular membrane microenvironments crucial for cognitive function. Premenopausal stressed females exhibited memory impairment. Increased amyloid precursor protein expression and dysregulation of the hippocampal immune system, evidenced by changes in astrocyte and microglia counts in this animal group. Given that immune system dysfunction can disrupt synaptogenesis, neuroplastin expression and its lipid environment were analyzed using a novel Python script method. Stress reorganized the glycolipid microenvironment in hippocampi of old females, impacting neuroplasticity. These findings highlight the vulnerability of premenopausal females to chronic stress, linking immune dysregulation, altered lipid environments, and memory decline.

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Emotional impact of crisis pregnancy on women's mental health in Ireland

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INTRODUCTION: Crisis pregnancy is an unplanned pregnancy, or a planned one that becomes distressing due to changing circumstances, which leads to psychological stress⁰. Chronic stress from work, unstable relationships, or limited access to reproductive healthcare can impair decision-making, increasing the risk of crisis pregnancy. Such pregnancies often exacerbate existing psychological distress through emotional turmoil, stigma, and uncertainty⁰. This distress may lead to anxiety and depression, especially among women facing social and economic disadvantage⁰. Therefore, this study was conducted to assess emotional impact of crisis pregnancy among women with suicidal ideation in Ireland using Mental Health Inventory (MHI-5) scale. **METHODS:** Cross-sectional analysis of data on telephone interviews from a census-based Irish Contraception and Crisis Pregnancy Study (ICCP-2010) was conducted. Quota sampling was applied, and analyses were conducted using MHI-5 scores on Likert scale to assess psychological impact. IBM SPSS was used, employing nonparametric tests (Mann-Whitney U, Kruskal-Wallis, Spearman's correlation) and Chi-square tests to examine suicidal ideation. **RESULTS:** Among 241 women who experienced crisis pregnancy, 107 (44.4%) reported suicidal ideations, reflecting high level of emotional distress. Data further showed that financial and emotional difficulties had a significant influence on mental health. Women who reported emotional or financial challenges surrounding their pregnancy had significantly poorer mental health outcomes, as measured by MHI-5. The most affected group were those facing emotional difficulties, with lowest median MHI-5 score of 32, indicating severe psychological distress. Financial hardship was significantly associated with poorer mental health, with low MHI-5 scores linked to financial difficulties as a reason for crisis pregnancy ($p = 0.008$). **CONCLUSION:** Crisis pregnancy is serious external stressor in a women's life with severe mental health implications. Results highlight the detrimental impact of stress on women's psychological well-being, emphasizing the need for supportive interventions to reduce stressors to greatly improve mental health outcomes.

References:

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