THE XXVII
SIGNE AND ANE
GYLLENBERG SYMPOSIUM

Psychosomatic Medicine Revisited

SEPTEMBER 19TH-20TH 2024
AT THE HANAHOLMEN CULTURAL CENTRE
ESPOO, FINLAND

SIGNE&ANE
GYLLENBERG
FOUNDATION

PROGRAM

Thursday 19th September 2024

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THEME 1	**WELCOME AND INTRODUCTION** **Chair: Henrik Enckell**	**THEME 2**	**MECHANISMS** **Chair: Tom Pettersson**
9.00–9.10	Welcome from the organizers Per-Henrik Groop Professor of Internal Medicine Chairman of the Board Signe and Ane Gyllenberg Foundation	13.30–14.15	Keynote lecture: Can Science Speak for Itself? **Professor Simon Wessely**
9.10–9.55	Keynote lecture: Mentalization, Resilience and Psychosomatic Symptoms **Professor Peter Fonagy**	14.15–14.45	Stress, Fatigue, and Illness Behaviour **Professor Mats Lekander**
9.55–10.40	Keynote lecture: Mind, Brain and Body in the Cultivation of Well-being as a Skill **Professor Richard Davidson**	14.45–15.15	Structural and Functional Autonomic Disorders are on a Different PAGe **Professor Thomas Chelimsky**
10.40–11.10	Coffee break	15.15–15.45	Coffee break
11.10–11.50	Keynote lecture: Current Understanding and Management of Functional Somatic Symptoms **Professor Peter Henningsen**	15.45–16.15	Placebo and Nocebo **Professor Luana Colloca**
11.50–12.00	Q&A and discussion	16.15–16.45	Placebos and Placebo Effects: Making Sense of the Conceptual Confusion **Professor Pekka Louhiala**
12.00–13.30	Lunch	16.45–17.15	From Mechanisms to Clinical Practice **Adjunct Professor Helena Liira**
		17.30–19.00	Buffet dinner at Hanasaari

PROGRAM

Friday 20th September 2024

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THEME 3 **CLINICAL SYNDROMES**
Chair: Markku Sainio

9.00–9.30 Functional Neurological Disorders – Past, Present and Future
Professor Jon Stone

9.30–10.00 Environmental Intolerance
Adjunct Professor Markku Sainio

10.00–10.30 Why Does Pain Persist?
Professor Eija Kalso

10.30–11.00 What is the Legacy of 'Getting It Right' for People with Functional Symptoms
Professor Mark J Edwards

11.00–11.30 Coffee break

11.30–12.00 The Neurobiology of Stress-Mediated Gastrointestinal Dysfunction in Disorders of Gut-Brain Interaction
Professor Qasim Aziz

12.00–12.15 The Non-pharmacological Management of Disorders of Gut-Brain Interaction (DGBI)
Professor Gisela Chelimsky

12.15–12.45 Long COVID and Chronic Fatigue Syndrome
Professor Markku Partinen

12.45–14.00 Lunch

THEME 4 **CLINICAL CARE AND MANAGEMENT OF FUNCTIONAL DISORDERS**
Chair: Viveca Söderström-Anttila

14.00–14.30 Frida's Pain: a Biopsychosocial Perspective
Professor Judith Rosmalen

14.30–15.00 A Novel, Concentrated Treatment Approach for Chronic Health Challenges
Professor Gerd Kvale

15.00–15.50 Panel discussion with short introductions:

Implementations into Practice
- Somatic Symptoms and Syndromes in Healthcare Systems
- Somatic Symptoms and Syndromes and Health Insurance
- What's next?

Chair: Markku Partinen
Participants: Professor Helena Liira, Associate professor Lena Thorn, Professor Jon Stone, Professor Simon Wessely

15.50–16.00 Closing remarks
Tom Pettersson
Professor
Former Board member
Signe and Ane Gyllenberg Foundation

THEME 1

Welcome and introduction

Welcome

Professor Per-Henrik Groop

Honoured symposium speakers and guests,

As the chairman of Signe and Ane Gyllenberg Foundation, it is a great honour to welcome you to Hanaholmen for our 75th Anniversary Symposium on Psychosomatic Medicine Revisited.

Seventy-five years is a long time, and much has happened during these years. Although I have not personally known Ane or Signe, I am convinced they would be grateful and pleased with what the foundation has achieved. Establishing a foundation with a specific purpose like researching Psychosomatic Medicine is challenging, but Ane and Signe's vision has proven to be ahead of its time. They understood the need to support medical research that considers both the soma and the psyche.

Ane Gyllenberg was born on Christmas Eve 1891 and was deeply influenced by his family's values of truth and spirituality. In 1919, he married Signe Säfström, and they had twin daughters. Ane made his first career as a banker and became one of Finland's most respected bankers. His difficult entrepreneurial years in the 1920s shaped his thinking for life.

During the 1930s, Ane embraced anthroposophic medicine. This interest was driven by the limitations of conventional medicine at the time. Ane understood that medicine involves both the soma and the psyche, leading to his vision of a foundation supporting psychosomatic research.

Over the past 75 years, psychosomatic medicine has evolved significantly, with advancements in understanding the complex interactions between the mind and body. Research now includes neuroendocrinology, psychodermatology, and neuroimmunology, highlighting the importance of a holistic approach to healthcare.

This year, we celebrate the 75th anniversary of Signe and Ane Gyllenberg Foundation, culminating in this symposium. I extend my heartfelt thanks to the organizing committee and the lecturers for their dedication and hard work.

The symposium aims to foster engaging discussions and collaborative exchanges among experts in the field. We anticipate thought-provoking presentations and lively debates that will advance our understanding of psychosomatic medicine. This event provides a unique opportunity to learn from each other, share experiences, and explore new research avenues.

A warm welcome to all!

KEYNOTE LECTURE

Mentalization, Resilience and Psychosomatic Symptoms

Professor Peter Fonagy

Peter Fonagy, Professor of Contemporary Psychoanalysis and Developmental Science at University College London, set the tone and scope of the symposium in his wide-ranging presentation on mentalization, resilience and psychosomatic symptoms.

First, he introduced us to the importance of a rupture in an attachment relationship. A rupture which is repeatedly experienced and healed becomes the basis for secure attachment, whereas a rupture repeatedly left unrepaired can lead to two different outcomes.

One is the “attachment hypoactivating pattern” where a patient suppresses emotions that could activate attachment needs, and the second is a “hyperactivating pattern”, where the attachment needs become exaggerated, leading to a clingy and needy phenotype. Both outcomes increase the risk of psychosomatic symptoms (via a disrupted stress system) because the emotions are not recognized properly. In a hypoactivating pattern they are barely recognized at all, whereas in a hyperactivating pattern they are misinterpreted and inflated.

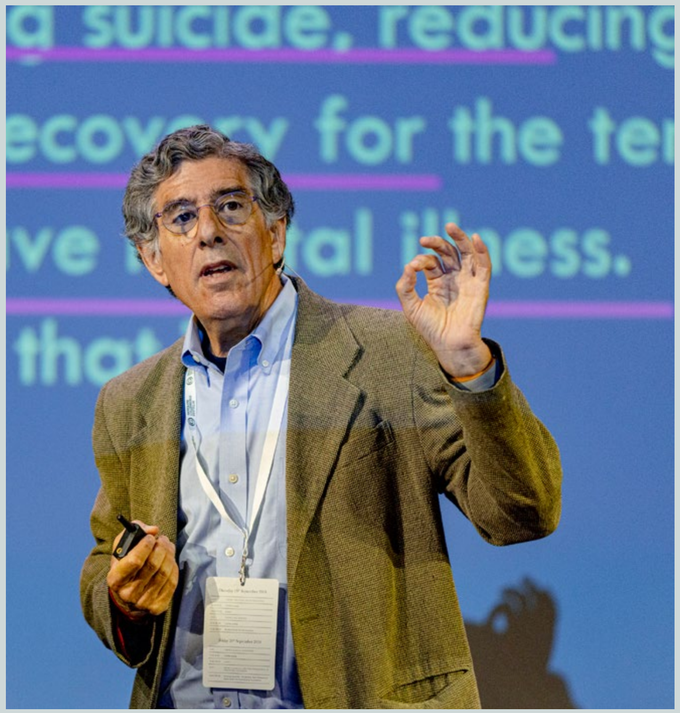
Resilience, however, can be strengthened through mentalization. According to Fonagy, that is the ability to “have someone’s mind in your own mind” based on self-knowledge that starts to form in the early attachment relationship. Mentalization is a more complex concept than empathy. Whereas empathy is the ability to feel what others are feeling, mentalization is the capacity to understand actions—one’s own and others—in terms of the thoughts and feelings that drive these actions. Because of the deficiencies in self-knowledge, i.e. a mismatch in recognizing one’s own emotions or motivations, people with hypo- or hyperactive patterns usually have problems with mentalization, which makes them vulnerable to psychosomatic symptoms, such as feeling social emotions as bodily ailments. Psychotherapy can be helpful in improving mentalization and thus increasing resilience.

Resilience, however, can be strengthened through mentalization.

KEYNOTE LECTURE

Mind, Brain and Body in the Cultivation of Well-being as a Skill

Professor Richard Davidson



From the depths of mentalization, Professor Richard Davidson from the University of Wisconsin Madison took us on a tour of his groundbreaking research on well-being and meditation. He started with a quote from philosopher William James, who wrote that "...the faculty of voluntarily bringing back a wandering attention over and over again, is the very root of judgment, character and will." But the true inspiration for his research came from no lesser a figure than the Dalai-Lama who visited his laboratory in 2001 and suggested to Davidson that the mind can be trained to be healthy.

It is from this insight that Davidson has produced an impressive body of work that addresses the effects of meditation on health and well-being. For example, studies with Tibetan monks—who have participated with the permission of the Dalai Lama—have shown that experienced meditators have the rare ability to sustain attention for long periods at a time; have different perception of pain than novices; and recover more rapidly from negative experiences. In other words, they are more resilient. Furthermore, other studies have shown that meditation may influence immune function, which may go some way to explaining why meditation can alleviate symptoms in asthma and other inflammatory conditions.

Based on his research, Davidson has developed the Healthy Mind Program application that is freely available for download. It is a step-by-step guide to increase the skills needed for a healthy mind and to decrease psychological stress.

Other studies have shown that meditation may influence immune function, which may go some way to explaining why meditation can alleviate symptoms in asthma and other inflammatory conditions.

KEYNOTE LECTURE

Current Understanding and Management of Functional Somatic Symptoms

Professor Peter Henningsen

Peter Henningsen, Professor of Psychosomatic Medicine and Psychotherapy at the Technical University of Munich, was the first speaker to address the predictive processing model as the mechanism underlying functional and psychosomatic symptoms. In this model the brain is not a passive organ that only processes sensory information, but an active one that filters all sensory information through prior experience.

Prior experience creates predictions (e.g. 'this is painful') and these predictions can become a sort of nocebo, whereby sensory information is amplified making sensory stimuli painful. In this perspective, psychosomatic symptoms are prediction errors which serve to protect us from harm. This helps to explain why many psychosomatic symptoms develop after an organic disease such as infection; prior negative experiences during infection will color the symptoms experienced afterwards.

This model has many implications for understanding patients with functional diseases. First, the effects of prior experience can be extended to early attachment relationships, because caregiver behavior may have modulated a patient's expectations of pain, relief, pleasure and bodily satisfaction. There are also social implications, such as a patient's expectations about how much social support they can expect to have in any given situation, which may modulate interpretation of prediction errors. Cultural expectations will also impact interpretation. Looking from this point of view, trying to locate the "cause" of psychosomatic symptoms from a specific organ or brain or environment becomes an exercise in futility. On the contrary, functional diseases may become, over time, part of self-image and identity, shaped by social and cultural factors and personal history. The implication for management is to focus more on "priors" that shape and color the symptoms and less on symptoms themselves.

In this perspective, psychosomatic symptoms are prediction errors which serve to protect us from harm.

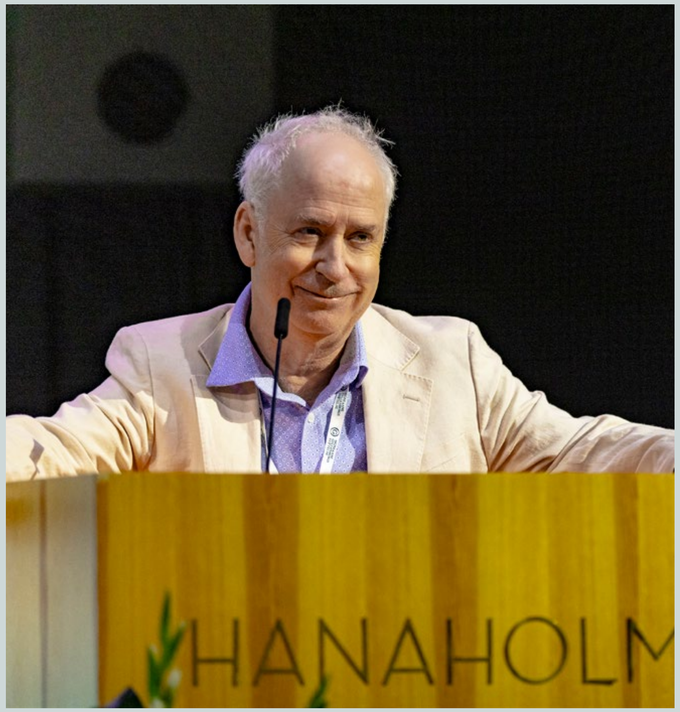
THEME 2

Mechanisms

KEYNOTE LECTURE

Can Science Speak for Itself?

Professor Sir Simon Wessely



Professor Sir Simon Wessely, Regius chair of psychiatry at the Institute of Psychiatry, Psychology and Neuroscience in London focused his talk on a key question for current times when science is increasingly politicised and polarised; "can science speak for itself?".

Wessely introduced us to his career in the 1980s, when he was working as one of the few psychiatrists at the National Hospital of Neurology and Neurosurgery at Queen Square. It was just at a time when the hospital, which prided itself as being the home of neurology, started to get referrals concerning a new and mysterious illness, myalgic encephalomyelitis (ME). The neurologists swiftly found no evidence for encephalomyelitis, or any other neurological disorder, despite severe symptoms and disability. This contributed to the increasing preference for the term Chronic Fatigue Syndrome (CFS). It was a frustrating situation which was often resolved by referrals to psychiatrists, who as Wessely showed were often seen by their colleagues as the person you saw when there was "nothing wrong with you". Some sufferers responded to this by describing psychiatry as "the dustbin of the medical profession".

Wessely walked us through the complex history of CFS focusing on media representations, namely the repeated dichotomy between CFS on the one hand being a "real disease" or on the other "all in your head," "made up" or "unreal", showing how easy it was to conflate psychological processes with feigning. In 1987 the Sunday Times set the tone with the headline that "Virus research doctors prove shirkers really are sick". Right from the start, research into CFS would be introduced with comments to the effect that this new work proves CFS is real and not psychiatric.

Sir Simon showed how time after time "proper research" which usually means the strictly biomedical is welcomed. In contrast any research focusing on psychological processes is "improper" and considered contemptuously disrespectful to the reality of the patients' symptoms, disability and distress. This tragically continues to this day. In 2022, 35 years on, we read in an Australian newspaper that "new research" proves "the disease isn't imagined or illegitimate". The following year under a headline "serious research begins on chronic fatigue syndrome", a Canadian newspaper tells us the illness "had long been dismissed as a psychological illness". And this year (2024) the Daily Mail uses new biomedical research to remind us that prior to this - "chronic fatigue syndrome has been dismissed as all in mind".

Sir Simon emphasised that he had no problem at all with the statement that CFS is a real illness, which he considers is a statement of fact. What he found depressing was that during all this time the media felt it necessary to follow an uncontroversial affirmation that CFS was real, with an unnecessary and offensive assumption that psychological or psychiatric disorders are not. All too often this slips into assumptions of feigned illness. He has yet to meet any colleague in this field who thinks this is so. But the result is that any research that might suggest a role for psychological, social or rehabilitative approaches in helping patients must be flawed, because otherwise it would mean that CFS is not real. Wessely said that the campaign to discredit moderately effective and safe rehabilitative approaches such as graded exercise therapy and CBT was doubly disappointing. First, because in his view it was good science, and second, because now sufferers from CFS, at least in the UK, had been left with very little if any treatment.

On the surface this is surprising because there are plenty of conditions, such as rheumatoid arthritis, diabetes, cancer, heart disease and so on in which patients actively lobby for holistic or rehabilitative approaches, which may include psychosocial. But there is a difference between these conditions and CFS. Sufferers from those disorders do not doubt that their doctors believe their conditions "real" and so it is safe to explore more holistic approaches without any feeling of denigration. But CFS, despite 40

years of effort to prove otherwise, still remains unexplained and controversial. And despite 40 years of media reports to the contrary no biomedical aetiology has been established. Patients can be left in a state of constant unease. Does my doctor really believe me? Sadly, the conflation of psychological with not being real or even feigned still persists in some professionals as well as the subeditors who write the ongoing headlines which perpetuate the confusion. Ironically it is you in this audience who run services for patients trapped in this limbo who know we are dealing with a real and devastating illness.

Wessely said this impasse is set to continue, until the "virus research doctors" he first encountered 40 year ago, or anyone else, find clear biomarkers and more effective treatments. Perhaps then we will see the back of those headlines that contrast the "real" world of CFS with the "unreal" world in which people imagine that we toil. And then professionals will be able to offer, and sufferers accept, those, admittedly modestly, effective interventions and to do so in an atmosphere free from controversy or rancour.

Wessely ended by saying that early in his career, in the days before e-mails and internet, he gradually became aware of hostility from some quarters to some of his published research (and that of many others). He asked for advice from his seniors, and was told not to worry, because the work was good, and "the science would speak for itself". The science, he concluded, remained good, but the advice was terrible. The truth is that science still needs all the help it can get.

But CFS, despite 40 years of effort to prove otherwise, still remains unexplained and controversial.

Stress, Fatigue, and Illness Behaviour

Professor Mats Lekander

Professor Mats Lekander from the University of Stockholm and Karolinska Institutet provided an interesting view on sickness behavior and the implications for functional disorders. In Lekander's lab, volunteers are injected with a bacterial component, LPS, which temporarily causes all the hallmarks of disease symptoms without causing the disease itself. It allows researchers to test volunteers' responses under sickness behavior.

Lekander's work has shown that activation of sickness machinery, even in the absence of pathogens, has a clear influence on mood; most importantly increasing fatigue and anxiety, decreasing pain threshold and often leading to general anhedonia. Another aspect of sickness behavior is avoidance, which has two sides: one for the patient, who usually avoids unnecessary social interaction while sick; and another for the non-sick, who can usually tell even from very weak cues if a person is sick and may thus avoid the person to safeguard against infection.

These findings may help us to understand functional somatic disorders, since there is remarkable overlap of core symptoms and the brain's alarm system—anxiety, pain and especially fatigue. In Sweden, the most common cause of sick leave is "exhaustion disorder". In studies, the feeling of sickness in exhaustion disorder is comparable to the feeling of sickness in chronic fatigue syndrome and chronic pain.

In Sweden, the most common cause of sick leave is "exhaustion disorder".

Structural and Functional Autonomic Disorders are on a Different PAGe

Professor Thomas Chelimsky

Professor Thomas Chelimsky, a world-renowned specialist in autonomic disorders from Virginia Commonwealth University in Richmond, started his speech by introducing us to two related, but distinct disorders: orthostatic hypertension (OH) and postural tachycardia syndrome (POTS). The interest for the symposium lies in the fact that OH is a structural (hardware) problem, whereas POTS is regarded as a functional (software) disorder.

First, he walked us through the early observations that led researchers to suspect that POTS might be a functional disease: POTS usually develops after a major "insult", such as infection or injury and in contrast to OH, is accompanied by other overlapping functional conditions such as chronic fatigue syndrome, IBS and fibromyalgia. Moreover, POTS patients have many more symptoms than OH patients, who are, astonishingly, often unaware of their condition even in the face of profound hypotension. Earlier research about autonomic disorders had helped Chelimsky and colleagues suspect that many of the features of POTS originated in the periaqueductal gray area (PAG) of the brain. The PAG is involved in numerous important functions such as sexual behavior, food and water intake and prosocial behavior. However, more specifically, different areas in PAG control behavior under threat, generating emergency fight, flight or freeze responses. Activation of the freeze response generates hypotension, paralysis and endogenous opioid-mediated analgesia.

Chelimsky speculates that POTS and its associated chronic pain co-morbidities emerge when the PAG fails to reset properly after a freeze response to a life-threatening event (which can be physical such as Covid, or a sexual assault, or psychological, such as emotional abuse). When "stuck" in emergency mode, persistent baroreflex impairment generates POTS and persistent attempted opioid-mediated analgesia generates the associated pain syndromes. Demonstrated by a video of an impala surviving a leopard attack in the wild unscathed, the freeze mode requires a motor reset, which has the appearance of a functional neurologic non-epileptic event. Dr Chelimsky also speculated that these non-epileptic events in humans constitute repeated attempts to properly reset the PAG to its normal mode, which is why they are often seen in patients who have POTS. The most effective management emphasizes rehabilitative methods and trauma-informed cognitive behavior strategies that focus on turning off the false alarm.

The most effective management emphasizes rehabilitative methods and trauma-informed cognitive behavior strategies that focus on turning off the false alarm.

Placebo and Nocebo

Professor Luana Colloca

How does one squeeze more than twenty years of placebo research into a half-hour lecture? That was the challenge for Luana Colloca, Professor and specialist in placebo and nocebo studies at the University of Maryland. Her lecture contained very little talk of sugar pills or inert substances, since most of Colloca's research uses verbal suggestions and social cues as placebo or nocebo.

A method she often uses is to pair painful stimuli with color cues (red = intense pain; green = low pain) and to modulate the experience by placing electrodes on volunteers' fingers. A volunteer is told it will alleviate or increase the pain, but in reality it does nothing. Numerous experiments have revealed, for example, that part of the placebo effect in pain modulation comes from the activation of endocannabinoid system; so the placebo response is a genuine biological response. There are also interesting sex-dependent differences in that vasopressin boosts the analgesic placebo effect in women but not in men.

Another interesting line of research is how an observation of someone else's placebo or nocebo effect is enough to bring about the same effect in the observer. In a rarer study, where analgesic placebos were investigated using patients suffering from chronic pain, the placebo was linked not to patients' expectations but to prior experiences. Other research also shows that when people's expectations are "muddled" (i.e. intense pain when not expecting it or vice versa) this has a strong effect on pain experience.

In more recent research, Colloca and colleagues have tried to figure out why some people are sensitive to placebo, whereas others are less so. The results so far indicate that negative emotional states, such as pain-related fear, catastrophizing and emotional distress, reduce the placebo effect. An important and often neglected factor that also reduces placebo effect is insomnia.

Another interesting line of research is how an observation of someone else's placebo or nocebo effect is enough to bring about the same effect in the observer.

Placebos and Placebo Effects: Making Sense of the Conceptual Confusion

Professor Pekka Louhiala

In his lecture, physician-philosopher Professor Pekka Louhiala explored the confusion related to the concepts of placebo and placebo effect in medicine. In particular, he criticized three common myths that are prevalent both in the scientific literature and in the media. These myths are: 1. Placebos work. 2. Placebos are commonly described. 3. Open placebos work.

Louhiala demonstrated that behind these myths there are many ways to understand the basic concepts and that the different meanings are often disregarded, leading to misunderstandings and confusing statements. First, placebos are inert substances and do not work; it is the context, expectations and conditioning that create the effect. Placebos as such have little to do with so-called placebo effects. The second myth is also based on a conceptual misunderstanding. Inert substances are not commonly prescribed and the concept of impure placebo is not at all helpful here. Physicians may prescribe ineffective medication or too small doses of effective drugs, but these should not be called placebos. The third myth is of more recent origin and refers to numerous studies, according to which openly delivered placebos seem to be helpful in many conditions. Again, it is not the (open) placebos that are helpful, but the context and the message delivered with them.

Louhiala concluded that despite these conceptual problems research on placebos and so-called placebo effects has greatly increased our understanding of the importance of context and caring relationships in medicine.

Placebos as such have little to do with so-called placebo effects.

From Mechanisms to Clinical Practice

Adjunct Professor Helena Liira

In the final talk on Thursday, Chief Physician Adjunct Professor Helena Liira told us about her experiences at Finland's first clinic for functional disorders, founded in 2019. Since then, two cohorts have started: one for functional diseases in general (Sympa) and one for so-called long COVID (post COVID-19). The latter received a grant from the EU's Horizon program. Additional data is gathered through the Helsinki University Hospital Data Lake and from international cohorts.

So far, the comparison with cohorts indicates that they are symptomatically very close to each other with just minor variations. On the other hand, analysis with the post COVID-19 cohort shows that female sex, comorbidities, BMI and mental health-related variables predicted the highest symptom burden. Recovery seems to be a bit better in the post COVID-19 cohort than in the Sympa cohort, but Liira emphasized that defining recovery in a patient population that keenly observes its symptoms is challenging. She also talked about how political commentators and the media can cause nocebo effects, just as happened in Finland during the COVID-19 pandemic, when the expert panel from the Ministry of Social Affairs and Health predicted that half of the adult population and one in fifty minors could develop long COVID.

The most important objectives in the near term are educating primary care practitioners to recognize and manage patients with functional symptoms and disorders, and to educate patients about the mechanisms that may result in the brain's alarm system going awry.

She also talked about how political commentators and the media can cause nocebo effects, just as happened in Finland during the COVID-19 pandemic.

THEME 3

Clinical syndromes

Functional Neurological Disorders – Past, Present and Future

Professor Jon Stone

Jon Stone, Professor of Neurology at the University of Edinburgh, and Secretary of the FND society (fndsociety.org), presented an overview of functional neurological disorder (FND) from past to present. From a historical perspective, FND used to be called hysteria. There was widespread interest and fascination about hysteria even before Freud's time, and this fascination continued with Freud's definition of conversion disorder.

Different definitions from this early era serve to remind us that doctors were on the right track in their understanding of "hysteria". This can be seen from Sir Benjamin Brodie's citation: "It is not the muscles which do not obey the will, it is the will itself which does not enter into the action." The idea of conversion disorder, Stone said, may still sometimes be useful to consider as a mechanism in some cases of FND, but it is much too narrow a concept to describe all people with these symptoms. Interest in FND declined and reached a low point in the second half of the last century, when FND was considered imaginary or even malingering by many neurologists. Only in the last few decades has renewed interest in FND emerged. We now know that it is common and debilitating, and its prognosis is comparable to other neurological conditions like multiple sclerosis.

Stone also presented us with fascinating patient cases of functional leg weakness, seizures, facial spasms and ankle dystonia showing how to recognize them using 'rule in' clinical features, and not as a diagnosis of exclusion. As to what disposes people to FND, instead of simple unifactorial models, we now have multifactorial models similar to those in conditions like stroke with predisposing, precipitating and perpetuating factors. Precipitating factors are often novel physical experiences, such as pain, infection or a panic attack, which may become persistent through aberrant predictive brain processing. Stone provided an interesting comparison between phantom limb syndrome and functional leg weakness, both being based on prediction errors—albeit differently—whereby the brain does not update the sensory information properly.

He has also completed a website and app with the latest information on functional neurological disorders, which is also available in Finnish (neurosymptoms.org/fi). Stone finally described the current evidence for multidisciplinary treatment using physiotherapy and psychological therapy as well as several promising lines of novel treatment including electrical stimulation and virtual reality therapy.

Precipitating factors are often novel physical experiences, such as pain, infection or a panic attack, which may become persistent through aberrant predictive brain processing.

Environmental Intolerance

Adjunct Professor Markku Sainio

A few years ago, Finland was in the grips of sick building syndrome (SBS), where molds in indoor air were suspected of causing serious symptoms. SBS grew to become a national epidemic out of proportion. Adjunct Professor Markku Sainio from the University of Helsinki introduced us to the history of the epidemic and lessons learned. An interesting point he made was how characteristically "Finnish" this epidemic was. Compared to other environmental intolerances, Denmark had much greater prevalence of multiple chemical sensitivity (MCS), while Southern Europe was struggling with electromagnetic field sensitivity.

To describe the discussion around sick building syndrome in Finland as an epidemic is not an exaggeration, since numerous surveys conducted at the time clearly showed that a large fraction of the population believed that bad indoor air could lead to serious illness. The mystery started to crack through the research conducted with other environmental intolerances, which clearly showed that there was a thin connection between exposure and symptoms. Other important observations were that: a) there was low correlation between symptoms and the buildings most in need of renovation; b) symptom surveys intensified the symptoms because subjects subsequently paid more attention to them; and c) parents' worries about indoor air in schools was contagious and affected children's symptoms (which led to widespread debate on school indoor air).

An important "lightning bolt moment" occurred when doctors started to characterize the patient population and found that patients with the most severe symptoms were suffering from functional disorders. Since, the "there is no fire, so turn off the alarm" approach worked, and the epidemic has since waned. Patients suffering from SBS have almost disappeared from clinics and hopefully SBS will not be replaced with other environmental intolerances. The new cases are, however, less pronounced than the ones with SBS.

An important "lightning bolt moment" occurred when doctors started to characterize the patient population and found that patients with the most severe symptoms were suffering from functional disorders.

Why Does Pain Persist?

Professor Eija Kalso

Eija Kalso, Professor in Pain Medicine at the University of Helsinki, reviewed in her lecture the current knowledge of pain as a biopsychosocial entity. Nociception refers to the physiological mechanisms whereby pain, a sensory signal, reaches the brain. Nociception becomes pain once it has been analyzed in the brain, put into context with the past, present and future, and given a meaning.

Pain is always a personal emotional experience affected by social and psychological factors. These factors have an essential role in the trajectory where nociceptive signals may become self-perpetuating, leading to chronic pain as the descending inhibitory controls of pain are disrupted, e.g. due to anxiety, fear, and uncertainty. Anxiety is closely associated with pain, as its evolutionary value is to protect us from harm.

Two important examples of factors promoting persistent pain include sleep and childhood adversities. Good deep sleep (non-REM sleep) enhances the function of the glymphatic system, leading to better clearance of pro-inflammatory waste products from the brain. Lack of REM sleep can lead to emotional dysregulation. Lack of sleep increases pain and pain disrupts sleep. This leads to a vicious circle, where poor sleep and pain aggravate each other. Adverse childhood experiences disrupt the stress system and can lead to anxiety and depression—both risk factors for chronicity. Adequate prevention and management of pain necessitate timely targeting all these biopsychosocial factors.

Adverse childhood experiences disrupt the stress system and can lead to anxiety and depression—both risk factors for chronicity.

What is the Legacy of ‘Getting It Right’ for People with Functional Symptoms

Professor Mark J. Edwards

What can people with functional symptoms tell us about how our health system works—and especially of its failings? A lot, said Mark J. Edwards, Professor of Neurology and Interface Disorders at King’s College London. Edwards started his speech with an idea from philosopher John Rawls: If you knew nothing about what your place in life would be, how would a rational person design the health care system? An obvious answer is a system where every patient is met as a whole person; not divided into parts where different divisions take care of different parts of you and never the whole.

This kind of integrated system is, in fact, what everybody—including doctors, nurses, patients and the public—wants. Even hospital management wants it, at least judged by mission statements that promise every patient will be met with compassion and patient-centered care. Scientific evidence speaks for the integrated system too: patients suffer when they don’t get integrated treatment—such as when your heart gets treatment, but your depression does not—and patients benefit when their mental health is treated at the same time as their chronic illness.

In Edwards’ talk, patients with functional symptoms can lead the way when trying to imagine better health care. They refuse to play the role of the good patient, and their diagnoses refuse to be located only in the body or only in the mind. This is the psychosomatic interface that lies between the disease and lived experience, and taking it seriously could help us design health care that is genuinely integrated.

Patients with functional symptoms can lead the way when trying to imagine better health care.

The Neurobiology of Stress-Mediated Gastrointestinal Dysfunction in Disorders of Gut-Brain Interaction

Professor Qasim Aziz

The brain and gut are engaged in constant bidirectional signaling mediated by hormones, the immune system and microbiota, and changes in any one of these may have consequences for the others. How these changes can lead to chronic gut pain was the subject for Qasim Aziz, Professor of neurogastroenterology at Queen Mary University of London.

The importance of microbiota for brain-gut signaling is illuminated by studies in germ-free mice. Without gut bacteria, mice not only become hypersensitive to gut pain, but their immune system becomes overactive too. Gut bacteria also has an effect on brain development since in germ-free mice the anterior cingulate cortex grows larger, and the periaqueductal gray area shrinks compared to controls. Being germ-free, of course, is not a natural condition, but early adverse experiences—such as too early separation from the mother—produce changes in the microbiome like those seen in germ-free mice.

New research into IBS has revealed that even though the gut may look perfectly healthy, cytokines in the gut cells are high and cytokine levels correlate with pain intensity. The immune reaction seems to be aggravated by hyper-activation of mast cells, so, unsurprisingly, IBS pain can be alleviated with antihistamines. Interestingly, after bacterial infection, the immune system may develop antibodies against dietary antigens, also mediated by histamines, causing aberrant pain.

Aziz concluded the lecture by introducing us to the research on the effect of personality types in experiencing pain. From this perspective, the extroverted personality type has a higher pain threshold and responds to threat with a fight or flight response, while the neurotic type is more sensitive to pain and responds to threat with the freeze response.

Without gut bacteria, mice not only become hypersensitive to gut pain, but their immune system becomes overactive too.

The Non-pharmacological Management of Disorders of Gut-Brain Interaction (DGBI)

Professor Gisela Chelimsky

How do non-pharmacological interventions work with functional gastrointestinal disorders? This was the subject for Professor Gisela Chelimsky from Virginia Commonwealth University in Richmond, who presented several lines of evidence that interventions targeting the brain or nervous system can be helpful.

The first evidence is from so-called FODMAP diet, where all fermentable oligo-, di-, and monosaccharides and polyols are removed from the diet and then reintroduced one by one. These studies have shown that removing FODMAP sugars from the diet improves not only gastrointestinal symptoms, but also improves mood by decreasing anxiety and depression. Furthermore, a remarkable study from 2022 showed that the sugars which most aggravate GI symptoms are fructans and mannitol, and, astonishingly, IBS patients' brains respond differently to fructans than do those of healthy controls. This shows that the brain is involved in producing IBS symptoms.

The other non-pharmacological interventions studied are exercise, different forms of psychotherapy and vagal modulation. Exercise and psychotherapy have turned out to improve GI symptoms together with psychological well-being. In vagal stimulation (usually through the conchae or tragus), improvements in GI symptoms such as pain and distress have been observed, but there has been no observable effect on mental health. Studies with electrical stimulation of the ear have shown improvements in GI symptoms and general well-being, enhanced vagal activity and, maybe somewhat surprisingly, a decrease in serotonin and proinflammatory cytokines.

This shows that the brain is involved in producing IBS symptoms.

Long COVID and Chronic Fatigue Syndrome

Professor Markku Partinen

Professor Markku Partinen, neurologist and renowned sleep researcher in Finland, explored the mysteries of fatigue syndromes in his lecture on long COVID and ME/CFS. He reminded us that fatigue syndromes are not new phenomena. In 1871, Jacob Mendes da Costa described a disease called soldier's heart—now known as Da Costa's syndrome—which had many of the hallmarks of chronic fatigue syndrome, including postural tachycardia. In 1917, the world witnessed another fatigue syndrome called von Economo's disease, also known as encephalitis lethargica, which probably developed in the aftermath of the Spanish flu.

Fatigue syndromes are not new phenomena.

Since then, numerous postviral fatigue syndromes with fatigue as the core symptom have been described all over the world. From this perspective, an increase in fatigue-related symptoms after the COVID-19 pandemic shouldn't come as a surprise. The surprise, however, is the huge variation between countries in reported fatigue-related symptoms after the COVID-19 pandemic. There was a lot of variation in diagnoses of ME/CFS to begin with—for example, ME/CFS diagnoses were 45 times more common in Norway than in Finland—but this variation changed substantially after the COVID-19 pandemic. For example, the occurrence of ME/CFS increased remarkably in Finland but hardly changed at all in the USA. This variation suggests that in addition to biological factors, sociocultural and psychological factors are also at play with long COVID.

Furthermore, careful comparison of the symptoms of long COVID and ME/CFS and POTS has helped Partinen and colleagues to divide long COVID into four different subtypes. In the long-lasting type, the core symptoms are fatigue, sleepiness and cognitive problems; in POTS-type, postural tachycardia and palpitations; in headache-type, headache and urinary problems; and in abdominal type, nausea and abdominal pain. The prognosis of long COVID is better than ME/CFS, and the persistent low quality of life in ME/CFS patients should be addressed.

THEME 4

Clinical care and management of functional disorders

Frida's Pain: a Biopsychosocial Perspective

Professor Judith Rosmalen

Judith Rosmalen, Professor of Psychosomatic Medicine at the University Medical Center Groningen, introduced us to the TRAILS study. TRAILS (Tracking Adolescents' Individual Lives Survey) is a multi-disciplinary study that has been ongoing since 2001. It includes more than 2,200 participants who have been enrolled since they were ten or eleven years of age. Since the study began, some of them have become parents and more than 500 participants from this second generation have also enrolled.

The longitudinal nature of the research has allowed researchers to identify several factors that increase the odds of functional somatic symptoms, which they have divided into three categories: predisposing, precipitating and perpetuating. Among predisposing factors, Rosmalen mentioned sexual abuse, low IQ—especially in the face of high parental expectations—and personality traits such as perfectionism. Precipitating factors mentioned were parental divorce, a parent's death and negative life experiences. Important perpetuating factors identified are parental overprotection, school absence and—not surprisingly—an inactive lifestyle.

In the FEEL-IT study, Rosmalen and her colleagues studied how childhood experiences of TRAILS participants are transferred to the next generation, following the second generation from birth onwards. They delved into the social origins of functional somatic somatic symptoms by concentrating on children's perception of illness and child–parent interaction. This research involved puppet interviews of small children and researchers' observations of parents' behavior when small children were vaccinated. They have also analyzed how illness is described in books for small children.

Throughout her lecture, Rosmalen reminded us of the story of artist Frida Kahlo, who had more than a fair share of pain in her life. There was an obvious reason for pain—her spine was broken in an accident—but at the same time she was exposed to many of the factors that were associated with pain as identified in the TRAILS study.

Important perpetuating factors identified are parental overprotection, school absence and —not surprisingly— an inactive lifestyle.

A Novel, Concentrated Treatment Approach for Chronic Health Challenges

Professor Gerd Kvale

In the concluding lecture, Professor Gerd Kvale from the University of Bergen gave us an inspiring talk on the so-called 4-day treatment developed in Norway. The treatment was originally intended for patients with obsessive-compulsive disorder (OCD) but was later extended to other chronic health challenges—with remarkable results.

First, Kvale introduced us to her early work on anticipatory nausea in cancer treatment and a fascinating case where a patient going through chemotherapy had developed a peculiar syndrome: he would vomit every time he saw a certain hue of red. This was, of course, a classic case of conditioning, but for Kvale, it amounted to a great insight: cues we become conditioned to are meant to protect us from danger and disease, and this would reflect in our behavior. Conditioning was adaptive, and in Kvale's research those at greatest risk of conditioning were also the fastest learners.

Conditioning could become debilitating after the danger was over, but turning it off was the real challenge. It could not be switched off by insight to the causes of conditioning any more than one can switch off salivating when smelling something delicious. However, it could be retrained, and this has become the basis for the 4-day treatment. In the approach, the treatment of OCD focuses not on what patients are thinking, but in their behavior, the goal being to weaken behavioral rituals by doing something that is incompatible with the "command". The rule of thumb is not to obey the alarm.

Kvale and colleagues have shown that this approach is useful also in many other chronic health challenges such as COPD, type 2 diabetes and depression. The idea here is that whenever people are faced with serious illness, they will develop what are called sickness behaviors. These behaviors are supposed to protect the person from illness, but in the long run many of them will become perpetuating factors that will only make the illness worse. These behaviors can be targeted just the same as the rituals in OCD and the wonderful results speak for themselves.

The idea here is that whenever people are faced with serious illness, they will develop what are called sickness behaviors.

Closing remarks

Professor Tom Pettersson

Dear friends and colleagues,

We have enjoyed two days of outstanding presentations by experts in psychosomatic or functional disorders. We have gained an up-to-date clinical overview, explored underlying mechanisms, and discussed management and treatment. We have learned about the importance of mentalization, resilience, and trust in other people for preventing functional disorders. A memorable sentence is “When the I becomes a we, illness becomes wellness”. We are now aware of the four pillars of a healthy mind: awareness, connection, insight, and purpose. Other central topics have been the interactions between the immune system and the brain, the gut-brain-axis, the mechanisms of pain, placebo and nocebo, and the functional symptoms persisting after COVID-19 in some individuals.

We have become more knowledgeable and wiser, but also humbler in relation to the issues we have dealt with and the problems that are still unresolved. We realize the importance of a multidisciplinary approach to functional disorders and the need for different professional groups to work together in patient care.

We have come a long way since 1949, when diseases like peptic ulcer, essential hypertension, and bronchial asthma were regarded as prototypes of psychosomatic disorders. Over the past 75 years, our understanding of functional somatic symptoms has improved substantially, and we have learned to know that functional disorders are common and complex phenomena encountered in almost every medical specialty.

Our warmest thanks go to our speakers, who were truly hand-picked by the Foundation and its scientific committee. It has been a privilege and a pleasure to listen to your presentations. We at the Gyllenberg Foundation wish you every success in your future research. Special thanks to the chairmen of the sessions, the participants in the discussions, and the audience, whose presence and commitment were crucial for this successful symposium.

Special thanks go to our scientific committee, consisting of Risto Vataja, Markku Partinen, and Markku Sainio. Your expertise and broad international network of contacts have been vital for the success of our conference. A big thank you to our chairman Per-Henrik Groop and the entire acting medical board.

It is with admiration that I have watched the hard work and dedication of the organizers of our anniversary symposium. A heartfelt thank you to Jannica Fagerholm, Antonia Laszlo, and Gabriella Tjeder-Kajander.

We remember our donors Ane and Signe Gyllenberg with the deepest gratitude for their foresight in forming a foundation that supports research, the significance of which will only increase in the years to come.

In conclusion, thank you all for contributing to the vibrant and intellectually stimulating atmosphere of our event. I wish you a safe and secure journey home.

Tom Pettersson,
MD, Professor h.c.

Feedback

I got several new viewpoints to discuss with my patients. Also new interesting research ideas arose from presentations and discussions.

—

I work with these patients daily in my clinic, so it affected a lot. I learned a lot of new things and now understand Even better The mechanisms, which makes the patient education easier and more effective. I Will definitely take a lot of this Into My everyday practice.

—

The symposium gave me a lot of inspiration and increased my enthusiasm to do more multidisciplinary work. It also made me more conscious about my own biases that affect the way I see health problems, and which I should remember to consider when doing my own research/ future work with patients.

—

I will try to take every given information to the care of the patients, when considering their treatment or when evaluating their situation.

Uutta tutkimustietoa. Hyvin relevantteja kliiniseen työhön.

—

It gave me new ways to communicate about these symptoms in patients.

—

One of the best conferences I have attended!

—

Kiitos, tämä oli yksi parhaimpia ellei paras yhden substanssin koulutus koko urani (30v) ajalta.

—

Thank you for the amazing symposium, this kind of events are super important for initiating cross-disciplinary discussion and providing new perspectives on such an important topic!

—

Thank you for an exquisite symposium. Nourished body and soul in a fantastic setting.

Organizing committee

ORGANIZING COMMITTEE

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