

What makes us ill?

**UNI
FR**
■

UNIVERSITÉ DE FRIBOURG
UNIVERSITÄT FREIBURG

What makes us ill?

Looking for vulnerability factors for mental illness...

Prof. Dr. Chantal Martin-Soelch

In the framework of the burden of mental disorders in our society, we present here the approach of a team of specialists, based at the the Department of Psychology, at the University Fribourg in Switzerland. Our team has specialised in 1) the search for risk and vulnerability factors for mental illness, 2) the development of preventive interventions in the field of mental health and 3) the education of health professionals. We will present these three points with regard to the burden of mental health disorders and the current state of research in the field of mental disorders, with a special emphasis on brain responses to rewards.

The burden of mental health disorders

Mental health disorders are major causes of disability worldwide. According to the World Health Organisation (WHO) survey on the global burden of disease,¹ depression is expected to be the second cause of disability worldwide in 2020; and abuse of alcohol, tobacco and illegal substances belong to the 10 major risk factors for diseases worldwide.¹ The principal challenges related to mental health disorders and substance abuse consist of the development of efficient treatment and preventive interventions.¹ For both, treatment

and prevention of mental disorders, the identification of vulnerability factors is essential.

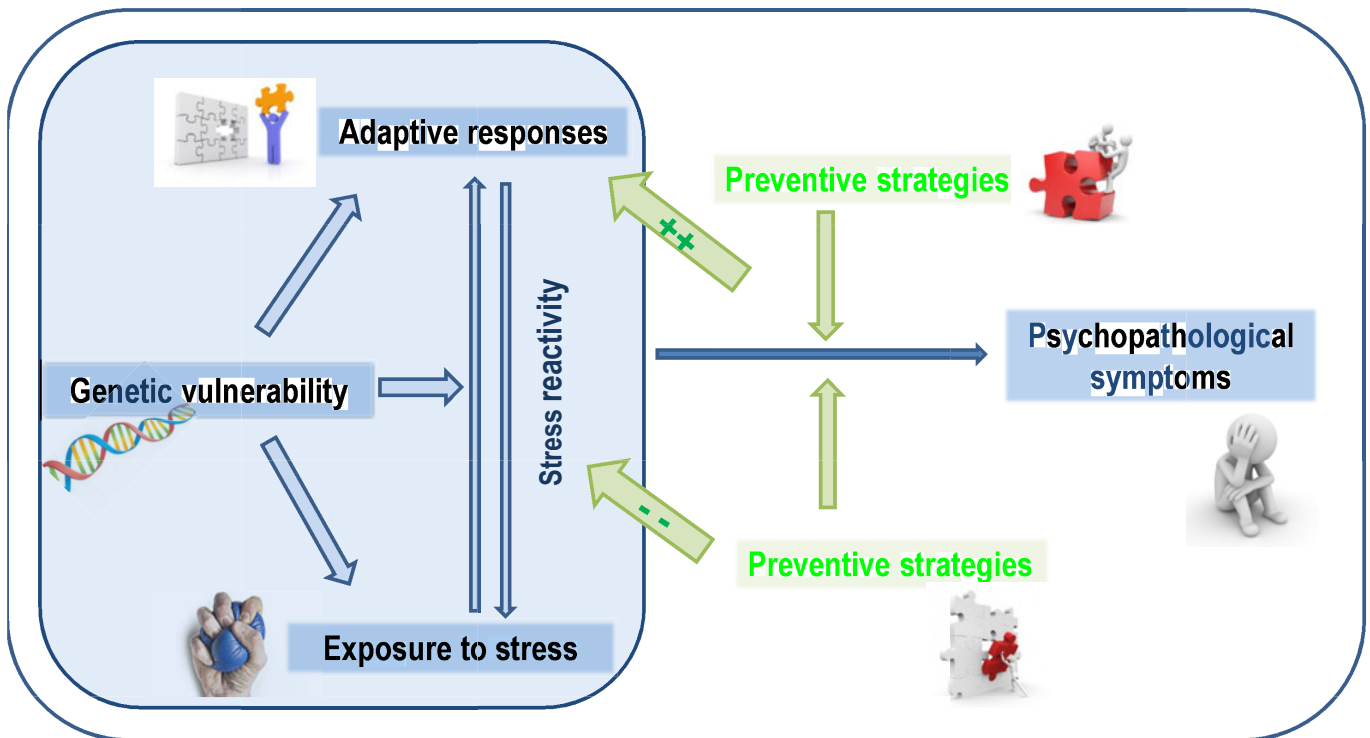
In other words it is necessary to understand what makes us ill in order to treat and to prevent the pathological conditions. Mental health disorders are, however, numerous and diverse, going from a simple phobia to complex eating or personality disorders. Risk factors are therefore also multiple. Recent models postulate a multi-causality for mental disorders, meaning that the causes for mental illnesses consist in the interaction of several factors and that there is not one identifiable cause for each pathological condition. It is currently postulated that there are risk factors that are specific for each disorder and other risk factors that are associated with a general vulnerability for mental problems.

Risk factors for developing mental health disorders: interaction between physiology and environment

Research in the last decade focused on the search for biomarkers for mental disorders, especially but not only on the search for specific genetic factors. The results obtained in this framework are nowadays integrated in a so-called biopsychosocial model that emphasises the interaction between biological elements, such as genes, with environmental factors, that can be social and/or psychological in nature.



“Mental health disorders are major causes of disability worldwide. According to the World Health Organisation (WHO) survey on the global burden of disease, depression is expected to be the second cause of disability worldwide in 2020...”



One specific environmental factor that has received much attention is the experience of stress. Stress is the response of the body and or individual to any demand that requires physical and or psychological adjustment. In this context, a stressor is a stimulus or an event that is perceived by the individual as threatening for the homeostasis and the survival of the organism.² In case of confrontation with a stressor, there is a common stress response at physiological level that mainly includes the hormonal system and the autonomic nervous system and leads to the secretion of cortisol; and chronic stress exposure results in excessive cortisol secretion.³ The central nervous system also reacts to acute stressors with the activation of a network of brain regions working together to process stressful information. A large body of evidence shows the importance of accumulated exposure to stress on physical health, especially on cardiovascular function, diabetes or chronic pain conditions as well as on the development of several psychopathological conditions, including depression, alcohol and substance abuse, eating disorders, anxiety disorders

and of course the so-called stress-related disorders, that include among others post-traumatic stress disorders and adjustment disorders.

However not stress alone, nor a specific genetic vulnerability alone can explain the development of mental health disorders. For instance, in depression, genetic influences alone seem to be too weak to explain the appearance of depressive symptoms, while the nature x nurture interaction is thought to be the strongest predictor in this disorder.⁴ More specifically, the exposure to stressful environment, in particular during development, i.e. during periods of increased plasticity of brain regions, in association with a specific sensitivity of individual's genetic inheritance represents an increased risk of developing depression. Similar results were found for other mental diseases such as alcohol or drug dependence, anxiety disorders and post-traumatic disorder. In this context, the importance of early life stress on subsequent changes of the genetic material, a process called epigenetic changes. These changes can contribute to enduring modifications in the individual responses to stress.⁵

Measures performed before and after the intervention to assess its efficacy



Clinical interview and questionnaires to assess psychological measures related to the intervention



Brain imaging: measure of brain activity related to processes targeted by the intervention



Ambulatory assessment of behavioral and physiological measures related to the intervention in every day life

Reward reactivity as a vulnerability factor?

Even if the role of the interaction between stress-exposure and specific genetic sensitivity in the etiology of mental disorders has been well-documented, other risk factors might also be involved. The responses to rewarding information at behavioral and neurobiological levels have emerged as potential risk factors recently. Rewards are involved in motivation, as individuals are more prone to perform certain behaviour, especially if not totally interesting for them, when they know that they will receive a reward afterwards. Rewards are also involved in learning processes, as a behaviour that will be followed by a reward will be showed again with higher probability. Obtaining reward is in turn associated with pleasant feelings which work as a reinforcement. Rewards can be

directly associated with the satisfaction of physiological needs – as a good meal for instance – or be of a more abstract nature, as is the case for money. In the 1950s, two researchers – Olds & Milner – evidenced specific brain reactions to rewarding stimuli in animals. This led to the major discovery of a so-called brain reward system or cerebral reward system, i.e. a specific network of brain regions that treat reward-related information. This system is thought to be responsible for exploratory behaviour and for adaptation to the environment. It is therefore not surprising that this system was also investigated in the framework of mental disorders. Our group played a pioneering role in this context with the first neuroimaging studies investigating the neural and behavioural responses to monetary rewards in addicted patients.⁶ Neuroimaging methods allow the investigation of



“In the field of mental health, preventive interventions should be able to identify individuals or population at risk and to target specific risk factors.”

neural processes in vivo in the human brain. These early studies were motivated by the fact that drugs of abuse have a direct or indirect effect on the dopamine system (one of the neurotransmitter systems in the brain) that is thought to also be associated with the brain reward system. Our results showed a reduced or even a lack of reaction to monetary rewards in the brains of opiate addicts, and even of smokers. We replicated these results in further studies also with individuals regularly consuming cannabis. In the meantime, these findings have been conceptualised as the “highjacking” of the cerebral reward system that is thought to be one of the determinants of addiction in association with the activation of the neurobiological stress systems.⁶

These first results initiated a new stream of research that has investigated the function of the brain reward system in different mental disorders. Blunted responses to rewarding information were found in depression (in association with specific genotypes as shown by our group, eating disorders, schizophrenia and post-traumatic stress disorder. This suggests that reduced reactions to rewards are not specific to drug abuse or drug addiction, but can be found in several mental disorders. However it remains unclear whether this is a consequence of being mentally ill or a vulnerability factor. Speaking for the second hypothesis are findings obtained in individuals with higher risk for mood disorders, i.e. young adults with parents suffering from depression or from bipolar disorder, that also evidenced reduced brain responses to rewards in these individuals even in the absence of any depressive symptoms. These findings suggest that the observed impairment in the function of the cerebral reward system is not a mere consequence of being ill, but could be a vulnerability factor that precedes the onset of the disorders, but might also stay after remission, increasing then the risk of relapse.

Based on this knowledge, an ongoing study by our group is now investigating in a prospective and longitudinal way predictors for the development of mental disorders or psychological distress in several populations at risk. Because the identification of vulnerability factors is crucial to develop preventive strategies, and to reduce the societal costs of mental disorders, it is important that longitudinal and prospective studies investigating biological and psychological risk factors get priority support from funding agencies.

Development of preventive interventions

In the field of mental health, preventive interventions should be able to identify individuals or populations at risk and to target specific risk factors. Preventive psychological interventions should activate the individual’s own resources and give him the necessary tools to adjust in case of adversity. According to the current state of research that we briefly summarised here, individuals are at risk of developing mental disorders or psychological distress more generally, if they have a genetic vulnerability or if they have been or will be faced with exposure to repeated or to traumatic stress. Concerning genetic vulnerability, preventive intervention should target young individuals with first-grade relatives having suffered a mental disorder. This is especially important for depression and schizophrenia, as for both disorders having close relatives with the disorder strongly increases the risk of developing this disorder. With regard to stress exposure, preventive intervention should focus on individuals in specific stressful environments due to their social or work situation. In this context, first year university students were identified as a specific population at risk as they have to face new academic challenges in a competitive environment and for many of them it is

also the first time they leave home and live alone. Psychological distress is elevated in this group and suicide or suicidal thoughts are not uncommon.

At the University of Fribourg in Switzerland we developed a first preventive intervention targeting university students that focused on stress management, on the enhancement of emotional awareness and the strengthening of feelings associated with positive experience, and that specifically work on the vulnerability factors highlighted in the previous sections. This program, called in French “Ge-De-Stress” (program for multidimensional stress management), is composed of modules that can be adapted to other populations at risk, as for instance health professionals working in emergency units or individuals that have been exposed to a traumatic event. Collaborations with other universities and hospitals are ongoing to establish and adapt these programs to other groups. Another potential application of our prevention strategy is the prevention of relapse in individuals who have had a first episode of depression or psychosis.

The development of our prevention programs is associated with research on efficiency and efficacy in parallel in order to offer evidence-based interventions. Therefore we also have the necessary competencies to evaluate intervention programs using multimodal approaches combining behavioural methods, questionnaires and clinical interviews, but also neuroimaging methods to highlight changes in the brain, and ambulatory assessments that measure the changes in everyday life.

Educating health professionals

Not only are the search for vulnerability factors and the development and evaluation of preventive interventions important to us, but also the dissemination of our knowledge and more

specifically the education of health professionals. This is the best way to achieve prevention and efficient care in the field of mental disorder on a large scale. We offer a master of advanced study in Health Psychology in collaboration with the Universities of Geneva and Lausanne in Switzerland, which combines three certificates of Advanced Studies that can be followed independently. The contents of these Certificates of Advanced Studies are 1) Psychological Counselling in the field of Health and Family; 2) Behavioral Sciences applied to Health promotion, and 3) Practice analysis in health care. The CAS are open to all health professionals and the MAS in Health Psychology is specific for psychologists. More information on these education programs can be found at <http://www.unifr.ch/psycho/mas-psychosante/fr/>.

Our team

Our team is located in the Department of Psychology at the University of Fribourg and collaborates with several universities in Switzerland, Germany, France and Norway as well with the United States. The team is headed by Professor Chantal Martin-Soelch, who is chair of the unit of Clinical and Health Psychology. Professor Martin-Soelch was previously Head Psychologist and Head of the Research Division at the Department of Psychiatry and Psychotherapy at the University Hospital Zurich and before this she was research fellow at the National Institutes of Mental Health (NIMH) in Bethesda. She previously worked in several other Swiss universities and hospitals. She is the recipient of several competitive grants and published mainly in the field of the cerebral brain system and its role in psychopathology.

More information on:

www.internationalinnovation.com/rewards-in-all-the-wrong-places/

References

- 1 Whiteford HA, Degenhardt L, Rehm J, et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *Lancet* 2013;382:1575-86.
- 2 Monat A, Lazarus RS. *Stress and Coping: An Anthology*. New York: Columbia University Press; 1991.
- 3 Tsigos C, Chrousos GP. Hypothalamic-pituitary-adrenal axis, neuroendocrine factors and stress. *Journal of psychosomatic research* 2002;53:865-7.
- 4 Heim, C. and E.B. Binder, Current research trends in early life stress and depression: Review of human studies on sensitive periods, gene–environment interactions, and epigenetics. *Experimental Neurology*, 2012. 233(1): p. 102-111.
- 5 Russo, S.J., et al., Neurobiology of resilience. *Nat Neurosci*, 2012. 15(11): p. 1475-1484.
- 6 Martin-Soelch C, Leenders KL, Chevalley A-F, Missimer, J, König G, Magyar S, Mino, A, Schultz, W. (2001). Reward mechanisms in the brain and their role in dependence: Evidence from neurophysiological and neuroimaging studies. *Brain Res Rev.*, 36(2-3):139-49.

“Because the identification of vulnerability factors is crucial to develop preventive strategies and to reduce the societal costs of mental disorders, it is important that longitudinal and prospective studies investigating biological and psychological risk factors get priority support from funding agencies.”



UNIVERSITÉ DE FRIBOURG
UNIVERSITÄT FREIBURG



UNIVERSITÉ DE FRIBOURG
UNIVERSITÄT FREIBURG

Prof. Dr. Chantal Martin Soelch
Department of Psychology
University Fribourg
Rue P-A Faucigny 2
CH-1700 Fribourg

Phone: +41 26 300 76 90 (secretary)
chantal.martinsoelch@unifr.ch
www.unifr.ch/psycho/staff/martin-soelch-chantal
www.unifr.ch/psycho/en/research/psychli