THE ETIOLOGY OF MENTAL DISORDERS

Concise, Clear and Synoptical

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INTRODUCTION

A mental disorder usually occurs in one third of the population during the course of life. Mental disorders are mostly chronic and frequently life-long. On the whole, psychiatric disorders do not usually result in the patient's death, but may significantly deteriorate their quality of life. Their negative impact on the economy is also not negligible. Regardless of medical breakthroughs, contemporary treatment of mental disorders is far from satisfactory. We are able to treat; however, a complete and successful cure is still rare. One of the reasons is that we do not fully recognize the exact causes of mental disorders. That is why the treatment is normally symptomatic, rather than causal. Based on the ever-growing knowledge on the etiology of mental disorders, it will be possible to significantly improve therapeutic and preventive measures in the future, and thus mitigate the patients' suffering.

The aim of this textbook is to acquaint the readers with the most recent findings related to complex causes of mental illnesses. While preparing the text, we were amazed at how similar the etiology of individual mental disorders generally is to each other, regardless of strikingly different clinical presentations, e.g. dementia in contrast to schizophrenia or even anxiety disorders. In every case, some genetic background is challenged by specific environmental factors, and this gene-environment (GxE) interplay is represented by epigenetic changes. Individual mental disorders are only different from each other in the extent and specificity of particular etiological factors.

We wish you pleasant reading,

The authors

BASIC FACTORS RELATED TO ETIOLOGY OF MENTAL DISORDERS

The aim of this textbook is not and cannot be to explain in detail genetics, the molecular biology of the brain or statistics beyond the scope of clinical psychiatry. Nevertheless, in order to facilitate understanding of the text, we present a brief explanation of related basic professional and scientific terminology.

SINGLE-NUCLEOTIDE POLYMORPHISMS

A single-nucleotide polymorphism (SNP; pronounced "snip") is a difference in base pair that affects a single base pair. This term is used when referring to a variation that has a population frequency of 1% or greater. Single-nucleotide polymorphisms may be positioned within coding sequences of genes, non-coding regions of genes, or in the intergenic regions. The term "variant" with a qualifier about pathogenicity is preferred in clinical diagnostic testing over "mutation", although use is inconsistent in literature. However, strictly speaking in human genetics a mutation is a genetic variant of low population frequency in contrast to a polymorphism with an allele frequency of 1% or more. In contrast to mutations, which occur less frequently and generally have a negative impact on protein function, SNPs are not clearly detrimental.

In etiology of mental disorders, both common SNPs with small effect (a minor allele frequency of 0.05 or greater; a typical odds ratio of 1.05–1.15) as well as rare SNPs with large effect (a minor allele frequency 0.01–0.05) play a significant role.

Coding variant: A genetic variation in the protein encoding region of a gene. Coding variants are divided into non-synonymous and synonymous types, depending on whether the amino acid composition of the resulting protein is affected or not, respectively. Non-synonymous variants are further divided into missense and nonsense variants. In a missense variant, the amino acid sequence is altered but the protein is functional. However, in a nonsense variant the amino acid sequence is changed by the introduction of a premature stop codon and the resulting protein is non-functional. In a synonymous variant, the amino acid sequence of the protein is not affected.

Noncoding variant: A genetic variation that is not in the protein encoding region of a gene. However, these variants can be functional if they reside in and disrupt functional elements, for instance noncoding RNA sequences or regulatory sites (e.g. promoters, enhancers, suppressors, or splice-sites).