

GENETICS OF PSYCHIATRIC DISORDERS

Jürgen Deckert

Department of Psychiatry, Psychosomatics and Psychotherapy, UK Würzburg, Germany

Psychiatric disorders are not different from other disorders in that their etiology is complex. Environmental and genetic factors contribute to their pathogenesis. Their relative contribution though differs between disorders and between individual cases. With regard to genetic factors one has to differentiate between rare familial cases with Mendelian inheritance and causative genes and the majority of sporadic cases in which the contribution of individual susceptibility genes is small. One example is dementia of Alzheimer type. While in a small group of families mutations in genes such as Presenilin 1, Presenilin 2 and Amyloid Precursor Protein are causing a dominantly inherited form of Alzheimer's disease, in the overwhelming majority of sporadic cases the major susceptibility gene ApoE is associated with a 3-4 fold increased risk for the disorder, but by itself is not able to cause it. As a consequence numerous individuals with the ApoE risk variant never will succumb to Alzheimer's disease. Also in other mental disorders such as schizophrenia, bipolar affective disorder, uni-

polar depression and anxiety disorders the situation is similar. Disease loci have been identified in linkage studies in schizophrenic and bipolar affective families some of which including the putative causative genes have been replicated in metaanalyses. Numerous candidate gene association studies to identify susceptibility genes have been performed in patient versus control cohorts mostly with ambiguous results. Recently, genome wide association studies have become possible allowing with their hypothesis free approach the identification of novel genes and pathways. While these genes like ApoE will not be of diagnostic or predictive value, they may well help to contribute to the development of novel therapeutic approaches. In fact, the first practical application of genetic findings may come in the field of pharmacogenetics. Similar to already established procedures in oncology, identification of genetic variants prior to the initiation of pharmacotherapy may contribute to a more individualized therapy in the future.