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Alan Fisch, MD

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Families of Alcoholics: New Findings

First some definitions: "Co-morbid" refers to two or more disorders existing together in one person. "Aggregation" refers to conditions clustering in a subset of families. Co-morbidity may result from secondary effects of one disorder on another while co-aggregation in families likely represents a shared genetic pool. Family studies usually focus on environmental effects, genetic-environmental interactions and genetic effects.

All studies of alcohol dependence show that alcohol dependence tends to aggregate within certain families. In a recent study in the December, 2004 issue of Archives of General Psychiatry, it was found that the lifetime risk of alcohol dependency is 28.8% in the relatives of alcoholics and 14.4% in controls, a twofold increase. Also, the rates of specific substance dependence were markedly increased in relatives of alcoholics for cocaine, marijuana, opiates, sedatives, stimulants, and tobacco. Co-aggregation was also found to exist for anti-social personality disorder, panic disorder, obsessive-compulsive disorder, post-traumatic stress disorder, and major depression. The aggregation of anti-social personality disorder, drug/alcohol dependence, anxiety disorders, and mood disorders in certain families suggests common mechanisms for these disorders and alcohol dependence within some families.

This study attempted to identify disorders aggregating in relatives of persons with alcohol dependence and thus specifies areas of possible shared genetic vulnerability. There was observed the previously noted excess of aggregated anti-social personality disorder diagnoses and modest excess of major depression. However, anxiety disorders were found to be significantly aggregated with special reference to obsessive-compulsive disorder, panic disorder and post-traumatic stress disorder. The conclusion of this study was to take note of patterns of anxiety disorder in the families of alcohol dependents as pointing to a genetic phenotype to be studied further and treated in the effort to reduce alcohol dependence.

Number two: A recent issue of Psychiatric News has an article "Brain-Receptor Abnormality Linked to Alcoholism Risk." The article focuses on brain, neurotransmitter, and receptor information as it relates to alcohol dependence. Earlier work has found the CNS endogenous opioid system to be involved in alcoholism, and when an alcoholic views pictures of alcoholic beverages, the prefrontal cortex and thalamus "light up" on scans.

In the brain, certain glutamate receptors are known to be among the main targets of the chemical molecule ethanol. Then theoretically, specific glutamate receptors (called NMDA) may contain an inherited

abnormality. When challenged with Ketamine that mimics alcohol and specifically "turns off" the NMDA receptors, there was a marked difference in response between healthy young adults with and without a positive family history of alcohol dependence. The group with a family history of alcohol dependency incurred significantly less dysphoria – i.e., anxiety, depression, somatic concern, and guilt feelings and many fewer negative symptoms such as emotional withdrawal and psychomotor retardation. Many prior studies have shown that a reduced sensitivity to the dysphoric effects of alcohol is the strongest predictor of the subsequent development of alcoholism.

Therefore, do you see a linkage between article number one and number two? Is the glutamate receptor, NMDA, malformed or dysfunctional and an important factor in the pathophysiology of alcoholism and a potential target for further research and treatments? Let us know what you think.

--please address questions, comments, feedback to: Alan Fisch, MD, co-chair, Continuing Education, National Library of Addictions, Inc. 617-264-9767

Brain Anomaly may hold key to Addictions

Alan Fisch MD Co-Chair, Continuing Education
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Cocaine-addicted patients show a specific and consistent brain anomaly which may be relevant for all addictive disorders. A recent study at MGH using advanced imaging techniques has demonstrated a surprising finding: The Amygdala has long been known as an important center involved in drug craving, primarily because of its association with motivation and reward; it has a fundamental role in addiction. During adolescence, the right side of the Amygdala normally becomes larger than the left. However, in this study, the Amygdalas of cocaine addicts were found to be smaller than the normal controls and consistently failed to show the normal asymmetry. Additionally, there was no difference in the configuration, whether the drug use was for decades or one year, which argues against the role of an unfolding degenerative process. Also, there was noted a correlation between the smallest Amygdalas and the highest levels of drug craving throughout the day. What is being postulated is a neuronal dysfunction or the action of specific genes which lead to the abnormal growth pattern of the Amygdala; this in turn leads to a deficiency or inability to **regulate** pleasure or reward signals.

This is a different and more complex concept than the simple notion of reward substitution or self-medication, as causal forces in the development of addiction in certain individuals. These new findings hold enormous implications for the treatment of addictions and for further research in the areas of genomics and psychopharmacology.