Genetic Aspects of Opiate Addiction

By Arthur Falek, Ph.D.

What is known about the genetic aspects of opiate addiction? Opiates such as heroin and dilaudid are drugs which have long been known to relieve or depress pain but increased consumption frequently result in uncontrolled drug use and addiction. These properties of opiates led to the discovery that there are specific opiate receptors in the brain and that the central nervous system itself produces substances with opiate-like activities. More recent observations are that the opiates circulate as well in other parts of the body as well as the central nervous system and elicit responses from various nonneuronal tissues including the white cells of the immune system. In our laboratory we studied the effects of opiates on human white cells, lymphocytes, and in particular T-lymphocytes, and have found that opiates result in a reduction in the genetic functions of these cells as a consequence of chromosome damage and deficient DNA repair capacity. What appears to be evident from our studies is that opiates directly effect the individual’s immune system by altering the functions of the body’s T-cell lymphocytes which results in genetic damage at the time of DNA replication.

One well known method to explore the genetic aspects of a trait is to investigate the occurrence of the trait in both members of identical (monozygotic) twin pairs as compared with its occurrence in both members of fraternal (dizygotic) twin pairs. If genes are significant in the occurrence of opiate addiction then if one member of an identical twin pair, who share the same genes, is affected then most frequently the second member of the twin pair will be similarly affected, that is the twin pair will be concordant.
for opiate addiction. On the other hand, fraternal twins who have approximately half of their genes in common will be less concordant and there will be increased numbers of pairs who are discordant for opiate addiction. By comparing the frequency of concordance in monozygotic as compared with that found in dizygotic pairs of twins, researchers are then able to determine the extent to which genes influence vulnerability to opiate addiction. A large scale data based study of monozygotic and dizygotic male twins recruited from the Vietnam Era Twin Registry found evidence which indicates that genetic influences contribute to a common vulnerability for abusing addictive substances but vary from one addictive substance to another. According to the Director of the study, the genetic influence for addictive drugs was greatest for heroin than for any other addictive drug. In a smaller twin sample using addictive drugs, researchers found that the influences for abuse, dependence or both were greater for males than for females. While these investigators found no evidence of genetic influences for opiate abuse or dependence in females, in males genetic influences were consistently larger than environmental influences. As was noted, while the above studies cannot tell us anything about the risk of addictive behaviors for a particular individual, these studies are of value in defining variations in drug use vulnerability in the population. As there are very few two or more generation families affected by opiate abuse, family studies have not been informative about the genetic aspects of opiate abuse.

The multiple genetic findings reported above do suggest that opiate addiction, like of other substances of abuse, need to be investigated at the molecular genetic level as a complex genetic disorder. Because of the environmental issues surrounding its
occurrence this requires not only a search among offspring of an affected parent(s) for evidence of the trait in question, but also detailed investigation of other similarities in these family members for other possible trait affecting components which may more clearly define those most likely to be affected among those at high risk. This aspect is particularly important in the continuing search for evidence of a possible molecular genetic component to the occurrence of this disorder in families. Current studies are exploring variabilities in the psychological adjustments of high risk offspring of an affected parent(s) as well as parental psychopathologies which may more precisely identify potential homogeneous phenotypic subtypes for molecular biological investigations. In addition to studies searching for evidence of a genetic basis for those individuals and family members who have an increased vulnerability to opiate addiction are studies aimed at identifying the impact of opiates in altering the expression of specific genes in the human genome.

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