I7 Search for Association Between Suicide and Dopamine D2 Receptor Polymorphism

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The goals of this presentation are to search for the relationship of dopamine D2 polymorphism and suicidal behavior on DNA samples of completed suicides, in order to lead to insight into the mechanisms involved in suicidal behavior and eventually suicide prevention.

Suicide is an important public health problem. Despite the serious efforts to develop prevention programs little exists that can be offered in order to avoid this tragic outcome because the specific mechanisms that lead to suicide are ignored. Various genetic-epidemiologic studies have been consistently suggesting that genetic factors play an important role in the predisposition to suicide; however, the precise genetic mechanisms involved are not yet known.

Several lines of evidence indicate that dopaminergic neurotransmission is involved in the pathogenesis of suicidal behavior. Studies have shown that the density of dopamine receptors is varied in brain regions of depressed subjects. Genes that code for proteins, involved in regulating dopaminergic neurotransmission, have thus been major candidate genes for association studies of suicide and suicidal behavior.

The authors' hypothesis is that genetic factors that code for components of the dopaminergic system may account for an important part of the total genetic variability involved in suicide. Thus, the authors' goal is to identify the polymorphism of these genes. To do so, a study was conducted where completed suicide cases in Crete were studied and genetic variations in these subjects were compared to a control group.

Blood samples from 30 unrelated suicides of Cretan origin have been collected. DNA obtained from these cases as well as from 30 controls were genotyped dopamine D2 receptor polymorphism.

DNA was extracted from blood using Chellex extraction method and quantified. DNA amplification was carried out in 20 ?L reactions using approximately 100 ng of genomic DNA 50 ng of each primer and 0.5 U *Taq* DNA polymerase (5 units/µL) 250 mM of each of the four dNTPs, 2.1-2.75 mM MgCl2, and 2 mL of buffer. Thermocycling was carried out on a Perkin Elmer 490 Thermal Sequencer. Samples that had a good yield of PCR product as determined by electrophoresis, were digested with the restriction enzyme *Taq* I. Digested DNA electrophoresed in a polyacrylamide medium and visualized by silver staining. Individuals were genotyped as A1A1, A1A2 or A2A2 based on the pattern of banding. Following the direct counting of genes for the observed values the expected ones were calculated and Hardy-Weinberg equilibrium was estimated. Contingency tables and chi 2 test was carried out for the statistical interpretation.

Although slightly elevated the A1 gene frequency in the samples of suicide completers (A1=0.18) compared to the control (A1=0.11), the statistical interpretation did not show any association. These results suggest that the dopamine D2 polymorphism is unlikely to play a major role in the genetic susceptibility to suicide.

Conflicting results among the present and previous studies regarding an association between the polymorphism and suicidal behavior, suggest the possibility that there may be unidentified specific subtypes of suicidal behavior that are significantly associated with the polymorphism. Possible reasons for this may be the relatively small number of subjects studied which might not be adequate for a satisfactory statistical evaluation.

Finding genes that are involved in the predisposition to suicide will represent an important step in the genetic study of behavioral and psychiatric disorders that may lead to insight into the mechanisms involved in suicidal behavior, impulsivity and aggression. In addition, the identification of genes implicated in suicide may be useful to elucidate targets for intervention and eventually suicide prevention.

Suicide, Dopamine D2 Receptor, Polymorphism

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