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GENE-ENVIRONMENT INTERACTIONS OF CORTICOTROPIN-RELEASING HORMONE RECEPTOR 1 (CRHR1) AND STRESSFUL LIFE EVENTS IN SUICIDE ATTEMPTS

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Objectives: Suicide is a leading cause of death in young people worldwide. Risk factors for suicidal behaviors and endophenotypes are partly heritable, and include variants in genes that drive stress diathesis in addition to, or by interaction with, certain adverse environments. Hypothalamic-Pituitary-Adrenal (HPA) axis genes are candidates for association with the dysregulated cortisol response to psychosocial stress that is observed in suicidal individuals. The role of HPA axis genetic variation will be explored in the context of varying “susceptibility” to suicidality after exposure to certain stressful life events.

Methods: A family-based association test was used on a case offspring-parent “trio” sample of 672 suicide attempt cases and their parents. Single nucleotide polymorphisms (SNP's) and/or haplotypes in CRHR1 were studied for interaction with age of exposure to physical and/or sexual assault, gender, and/or lifetime exposure to other types of stressful events.

Results: Preliminary findings show interactions of certain CRHR1 SNP's with sexual and/or physical assault that are associated with suicide attempt, possibly using a violent method. Possible associations with candidate endophenotypes such as Cluster B personalities and early-onset major depression are under investigation.

Conclusions: Interactions of HPA axis genetic variants and stressful life events are consistent with a stress diathesis model of suicidal behavior, and may additionally influence the method and medical damage outcomes of suicide attempts, which may explain part of the diversity within this phenotype.