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ESTROGEN RECEPTOR POLYMORPHISMS AND LATE-LIFE DEPRESSION

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Introduction: Despite a putative role for estrogen in depression, studies on the association between depression and estrogen receptor (ER) polymorphisms are surprisingly lacking.

Objectives: To determine the association between ER polymorphisms and late-life depression in 6809 men and women and to investigate factors which could modify this association.

Method: Community-dwelling elderly aged 65 years and older were recruited in France as part of the Three City Study. Depression was assessed using the Centre for Epidemiological Studies Depression Scale and the Mini-International Neuropsychiatric Interview, according to DSM-IV criteria. The association between five polymorphisms of the ER-α and ER-β with depression was determined using multi-adjusted logistic regression models.

Results: Men with the AA genotype of the ER-β rs4986938 polymorphism had an increased risk of depression, while in women, carriers of the A allele for the ER-β rs1256049 had an increased risk. Subsequent analysis indicated that the increased risk in women occurred only in those not using hormone treatment. In women the CC and GG genotypes of the ER-α PvuII and XbaI, respectively were associated with a decreased risk of depression. A significant interaction between the ER-α PvuII and ER-β rs4986938 polymorphisms suggests they may act together to modify the depression risk.

Conclusions: Sex-specific associations between ER polymorphisms and depression have been identified, with HT appearing to be beneficial for genetically vulnerable women. These findings of distinct genetic susceptibility to late-life depression may be important for designing novel hormone-based therapies that would have optimal effectiveness in sub-groups of depressed women and men.

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