

# Imprinting and Linkage Analyses Based on Case-Parents Trios

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## Abstract

The recombination rates in meioses of females and males are often different. Some genes that affect development and behavior in mammals are known to be imprinted, and more than 1% of all mammalian genes are believed to be imprinted. When the gene is imprinted and the recombination fractions are sex-specific, the conventional transmission disequilibrium test (TDT) is shown to be still valid for testing for linkage. The power function of the TDT is derived, and the effect of the degree of imprinting on the power of the TDT is investigated. A simple statistic for testing for imprinting effects is also developed. The proposed parent-of-origin effects test statistic (POET) is shown to be normally distributed and can be employed to test for imprinting in situations where the marker locus need not be a disease susceptibility locus and where the female and male recombination fractions are sex-specific. Based on the POET, a novel statistic ITDT for testing for linkage is proposed, which is shown to be more powerful than the TDT in the presence of imprinting. The validity of the POET, TDT and ITDT are assessed by simulation. The power approximation formulae for the POET, TDT and ITDT are derived and the simulation results show that they are accurate. The simulation study on power comparison shows that the ITDT outperforms the TDT for imprinted genes. The improvement can be substantial in the case of complete paternal/maternal imprinting.