Cladistic Analysis: Its Applications in Association Studies of Complex Diseases

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Abstract

***Introduction**: With the increase in genotype data generated by high throughput typing technologies, there is currently a lack of complexity-oriented analytical methods that can maximise the information obtained from these raw data for the study of complex diseases. We introduce the cladistic analysis that is traditionally applied in evolution studies and taxonomy, to specify relevant comparisons of traits associated with each haplotype/genotype in a population sample. **Methods**: Haplotypes are determined from the genotype data and linked to each other by their evolutionary relationships to form a cladogram. This is then used to specify relevant statistical comparisons. The central assumption is that any functionally important genetic variation causing a phenotypic effect at any point in the course of evolution will be embedded in the framework of haplotypes represented by the cladogram. **Applications**: There are various applications of cladistic analysis in the study of complex diseases. Basically, it helps in the identification of haplotypes that are associated with a disease state or a significantly altered level of quantitative trait. However, its limitations are that only polymorphic sites on the same DNA strand can be analysed and that recombination events must be relatively rarer than mutational events. **Conclusions**: In the absence of methods that can recognise the complexity of the genotype organization, and given its ability to exploit evolutionary information for optimising the analytical strategy, cladistic analysis would be a method of choice for studying multi-loci effects on a quantitative trait or disease outcome.*

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