

Neuroimaging epistasis in Alzheimer disease

Tricia A. Thornton-Wells

Vanderbilt Kennedy Center for Research on Human Development, USA

Biological epistasis is pervasive but challenging to detect statistically, especially in genetically and clinically heterogeneous disorders, such as Alzheimer disease. Leveraging the wealth of genome-wide data requires intelligent variable selection and hypothesis-driven modeling approaches. Furthermore, the probability of over-fitting sparse data necessitates replication of interactive effects in independent datasets. By utilizing continually updated databases of biological knowledge, we are mining the rich phenotypic data available from the Alzheimer's Disease Neuroimaging Initiative cohorts to derive new knowledge and hypotheses about this disorder. We present biological knowledge-based gene-gene interactions that explain variability in Alzheimer disease pathology beyond known main effects using quantitative neuroimaging and cerebrospinal fluid biomarkers.