Interesting letter commenting on a recent systematic review and meta-analysis of a possible causal link between patients with a previous diagnosis of bipolar disorder (BPD) and increases in the idiopathic likelihood of a subsequent diagnosis of idiopathic (unexplained) Parkinson’s Disease (PD).

The methods used in this study to explore possible overlapping genetics between BPD and PD involve using LINKAGE DISEQUILIBRIUM SCORE REGRESSION (LDSC) on a GENOME-WIDE ASSOCIATION STUDY (GWAS).

LDSC is an interesting statistical technique used in genetics, which examines the relationship between linkage disequilibrium scores and test statistics of the SINGLE NUCLEOTIDE POLYMORPHISMS (SNP's) from GWAS. SNP's are a way of identifying genetic variation that exists between individuals, and have been implicated in various disease states. GWAS is an important tool for identifying genetic factors underlying complex disease traits.

The LDSC analysis can be used to identify the SNP's associated with a particular trait, and succeeds where other more traditional multivariate regression models fail. This is because the number of SNP's in an association study is usually much larger than the sample size (no of observations). LDSC can be used as a VARIABLE SELECTION technique to exclude irrelevant inputs (SNP's), and hence aid dimension reduction, in a high dimension sparse data input space.

The study was a retrospective case control cohort. It was a well-designed study composed of prevalent cases of BPD and PD. The study the authors cited was sufficiently powered, the BPD group had a 1:9 ratio of cases to control, the PD group the ratio was roughly 1:1 cases to control. A ratio above 1:4 cases to control would be sufficient anything higher would be overkill.

The results concluded that there was no linkage between BPD and PD from the LDSC analysis. There was significant result for the Genetic Risk Score (GRS) for PD with PD status and GRS for BPD with BPD status, but importantly no association with GRS for BPD with PD, this confirmed the LDSC analysis.

I wonder whether any thought had been given to the prior probabilities of PD in the population compared to the sample for the study. The event rate of PD is 1% in the population and 2.7% in the sample. Did the authors adjust for oversampling in the LDSC regression analysis?

There was admission by the author that the study did not take into account that the medication used to treat acute BPD, e.g. high potency anti-psychotics like Haloperiodol, can cause drug induced PD. I thought this was an important oversight which call into question why the study was done in the first place.