

Evidence for Linkage and Association with Reading Disability, on 6p21.3-22

Kaplan, D.E., Gayan, J., Ahn, K., Won, T.W., Pauls, D., Olson, R.K., DeFries, J.C., Wood, F., Pennington, B.F., **Page, G.P.**, Smith, S.D., Gruen, J.R. (2002). Evidence for linkage and association with reading disability, on 6p21.3-22. *American Journal of Human Genetics*, 70 (5):1287-1298.



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This is the first of my papers to study the genetics of reading disability. In this paper we described the steps we took to transition from coarse grain localization, using family-based linkage analysis, to much finer resolution, using association analysis.

Reading disability (RD), or dyslexia, is a very common disorder with a large genetic component. As a result, it has been extensively studied for a number of years. A number of studies used a family-based approach called linkage analysis to roughly identify the position in the genome of genes whose variation predisposes people to RD. At the time we initiated our study, several groups had identified significant linkage on chromosome 6p21.3-22. Unlike previous studies that used linkage, we proposed to use an alternative method called association analysis for fine localization of the reading gene. Linkage works well to scan the entire genome with a few hundred markers. To cover the entire genome with association requires about 1,000,000 markers. At the time, this was not possible; thus, association could only be used once linkage had reduced the region of interest to a small interval.

We used a number of molecular genetic techniques to develop markers across this region for association studies. We then genotyped these markers in a population we developed and had assessed for a number of different aspects of reading competence. We found that the marker JA04 was significantly associated with orthographic choice ($\chi^2=9.48$; empirical $P=.0033$) as well as several other reading-related traits. This study laid the foundation for our future studies, one of which is also an RTI Author Award-winning paper, which localized the first reading disability gene very close to the JA04 marker.

Link: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC447603/>