Mutations in the DJ-1 gene have recently been shown to cause autosomal recessive Parkinson’s disease. To estimate the prevalence of this mutation, an analysis was undertaken of 39 index cases of Parkinson’s disease in whom a family history suggested autosomal recessive inheritance. No DJ-1 mutations were found in these patients, indicating that this gene is unlikely to be of numerical significance in clinical practice. The hypothesis was also tested that young onset Parkinson’s disease patients in whom, despite extensive analysis, only a single heterozygous parkin mutation was found, might harbour a second mutation in the DJ-1 gene—that is, digenic inheritance. No patient was found with a single mutation in both DJ-1 and parkin genes, making this mode of inheritance unlikely. Finally it was confirmed that PARK6 and PARK7 (DJ-1), despite being phenotypically similar and mapping to the same small chromosomal region of 1p36, are caused by mutations in separate genes.

Following the recent publication of a fifth Parkinson’s disease gene, DJ-1, by Bonifati et al., there has been much interest in ascertaining its biological and clinical importance. To date, however, there have been no published data estimating DJ-1 prevalence in Parkinson’s disease.

Mutations in DJ-1 were discovered in two consanguineous families from geographically isolated regions in Europe. This brings to five the number of genes reported that are directly implicated in Mendelian Parkinson’s disease. While the function of the protein remains to be elucidated, it has been proposed that it may be involved in the cellular response to oxidative stress. The gene maps to chromosome 1p36–35 and comprises eight exons, the first of which is alternatively spliced and non-coding. Three other recessive (PARK7 locus) and comprises eight exons, the first of which is alternatively spliced and non-coding. Three other recessive parkin promoters have been described and mapping to the same chromosomal region of 1p36, are caused by mutations in separate genes.
Long range PCR for the detection of the exon 1–5 deletion described by Bonifati et al was done as previously reported.3

RESULTS
In a cohort of 39 index Parkinson’s disease patients with probable autosomal recessive inheritance, we did not find any pathogenic mutation in the DJ-1 gene.

We also did not find pathogenic DJ-1 mutations in a smaller cohort of four patients in whom, despite extensive genetic analysis, we could only determine a single heterozygous parkin gene mutation.

Finally no DJ-1 mutations were found in three PARK6 linked families.

DISCUSSION
The large cohort of autosomal recessive patients studied indicates that the frequency of pathogenic DJ-1 mutations is low in Parkinson’s disease, especially given that we excluded from analysis any known parkin gene mutations. We also screened all our samples for the 14 kbp deletion reported by Bonifati et al,1 and did not find it. This indicates that the deletion may be confined to the genetically isolated population in the Netherlands, where it was originally found.3

At present the role of DNA diagnostic testing for mutations in DJ-1 is unclear, but these data suggest that such testing will not yield numerically significant results and therefore, unlike the parkin gene, DJ-1 is unlikely to be of clinical importance in neurological practice. More work will also be needed to elucidate the possible role of large genomic rearrangements.

We were unable to prove our hypothesis of digenic inheritance between parkin and DJ-1 in Parkinson’s disease. This does not exclude other recessive genes being involved in this mode of inheritance of Parkinson’s disease. Indeed our group also has evidence of young disease onset patients with non-synonymous heterozygous DJ-1 mutations in whom a second pathogenic mutation has not been found (unpublished data). Large scale rearrangements, however, have not as yet been excluded in these patients. Further work is needed to establish the role of digenic or oligogenic inheritance in Parkinson’s disease.

Finally, we have confirmed that PARK6 and PARK7 are not allelic and that at least two recessive Parkinson’s disease loci lie within a very small chromosomal region of 1 p.

REFERENCES
DJ-1 mutations in Parkinson's disease

D G Healy, P M Abou-Sleiman, E M Valente, W P Gilks, K Bhatia, N Quinn, A J Lees and N W Wood

J Neurol Neurosurg Psychiatry 2004 75: 144-145

Updated information and services can be found at:
http://jnnp.bmj.com/content/75/1/144

These include:

References

This article cites 13 articles, 4 of which you can access for free at:
http://jnnp.bmj.com/content/75/1/144#BIBL

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/