Many thanks to all families who have helped us in the past, or are considering helping our future work. This update provides an overview of all the research that has been made possible by your contribution of a DNA sample. All of the work described below has been published in recognised journals and for each paper we have summarized the main aims and findings of the investigation. A reference is given for each paper and this should enable you to access the full article if you wish. However, if you have any problems accessing the full text, please contact me at dianne@well.ox.ac.uk and I will send a pdf.


This paper looked at DNA samples from the Guys and Cambridge families. We searched all 23 chromosomes from each DNA sample given and identified those genetic regions that were more similar in the family members affected by SLI than we would expect. This enabled us to identify 2 regions that we believe contain genes which make people prone to SLI. One region is on chromosome 16 and the second is on chromosome 19. This study was important because it allowed us to narrow the location of genes which may cause susceptibility to SLI from 23 chromosomes to 2. However, each of the identified regions is very large and contain hundreds of genes, any one of which might be causing the proposed susceptibility.


In this investigation, we looked at a specific gene on chromosome 7 called FOXP2. This gene had been shown to be important in a family affected by developmental verbal dyspraxia. This is a particularly severe, but relatively rare, kind of language delay which is caused by problems with the fine movement of the muscles required for talking. We sequenced the gene in some of the DNA samples collected from Guys but did not find any mutations that explained the language problems experienced by these families.

Several other groups also looked at this gene in autistic and language-impaired families but did not find any genetic changes. We now believe that changes in this gene cause some cases of verbal dyspraxia but are relatively rare in more general cases of SLI. However, it is known that this gene acts by switching on and off other genes in the cell. It is therefore hoped that if we can identify which gene it controls, then these may play a role in SLI.
Highly significant linkage to the SLI1 locus in an expanded sample of individuals affected by specific language impairment. The SLI consortium (SLIC). The American Journal of Human Genetics (2004) Volume No. 74, Pages 1225-1238

For this paper, we looked at the previously identified regions on chromosomes 16 and 19 in further DNA samples collected from Guys, Cambridge, Edinburgh and Aberdeen. In these samples, we again saw that parts of chromosomes 16 and 19 were more similar in the family members affected by SLI than we would expect. The process by which we initially identified these regions was based on a statistical analysis. This means that there is a slight chance that the increased sharing might just have happened by chance. The fact that we also see an increased sharing in these additional families therefore increases our confidence that genes within these regions are important for the development of SLI.


In this study we used DNA samples from Guys, Cambridge, Edinburgh and Aberdeen to look at how the shared DNA regions on chromosomes 16 and 19 affect different measures of language ability. We found that the region on chromosome 16 seemed to be particularly important for individuals who had problems with non-word repetition, spelling and reading tests indicating that it may be important in the memory processing of new words. In contrast, the region on chromosome 19 seemed to be important for ability across a wide range of language tasks but did not seem to affect performance on literacy tasks such as reading and spelling. This study also indicated that a region on chromosome 10 may also be important for understanding language (receptive language).


In this investigation, we used the DNA samples from the Manchester group and looked at the previously identified regions of chromosomes 16 and 19 to see if they were important in these families. We again found that these regions are genetically more similar in individuals affected by SLI than we would expect by chance alone, further supporting our previous findings.

In this collaborative paper, we again looked at the effects of a specific gene upon language ability. For this study we used DNA collected from families at Guys, Cambridge, Edinburgh and Manchester. The gene we looked at on this occasion was called CNTNAP2. This gene was interesting because it was found to interact with FOXP2 which has been shown to be important in a family affected by developmental verbal dyspraxia. As explained above, we had previously found that FOXP2 was not generally important to SLI. However, we still believed that other genes which interact with FOXP2 may be relevant. The researchers in the FOXP2 lab found that one of the functions of FOXP2 is to switch off another gene known as CNTNAP2. This process is thought to be important for interactions between cells in the developing brain. When we looked at variations in the CNTNAP2 gene in SLIC samples, we found that genetic variants around CNTNAP2 affect performance on the non-word repetition task. This is the first time that a specific gene has been linked to ability on language-related tasks in SLI families. Interestingly, other groups have also found that certain genetic variants in CNTNAP2 are more common in autistic patients than in the general population. These findings have led researchers to propose that genetic variants in the CNTNAP2 gene may be involved in susceptibility to SLI and autism indicating that there is a shared genetic link between these 2 highly related disorders. This is the first time anyone has demonstrated such a link.


Our most recent research has focussed upon the characterisation of the genetic sequence in a region of chromosome 16 that we believe may be important in SLI susceptibility. We have looked at thousands of common genetic variants across this region and have found clusters of variants in two genes (known as ATP2C2 and CMIP) that we think contribute to SLI susceptibility. We think that differences in the genetic sequence around ATP2C2 and CMIP may alter the way in which these genes work and, this causes a reduction in memory span making it more difficult to learn a new language. When we looked at these variants in a second sample of individuals, we found that the decrease in memory span is particularly strong in individuals with language impairment. We believe that this is because these individuals also carry additional genetic risk factors that interfere with other biological processes important for language development. The idea is that genetic variants in ATP2C2 and CMIP subtly reduce your memory span but this would not be obvious unless they are combined with additional risk factors (genetic or environmental). When combined with these other risk factors, the extra strain on your memory will be sufficient to make you prone to language impairment.
Recent Research Funding

The SLI team have recently paired up with the dyslexia team in Prof Monaco’s lab to perform a joint study investigating gene-gene and gene-environment interactions underlying speech, language and reading development. Over the last few years several genes underlying dyslexia susceptibility have been identified and as described above, we are now starting to also identify genes which make some individuals prone to language disorders. Dr Paracchini, in our lab, has just secured funding to investigate whether these genes interact with each other or with environmental factors to bring about the onset of dyslexia and SLI. This investigation requires very large numbers of samples and so Dr Paracchini will be using DNA collected from the Avon Longitudinal Study of Parents and Children (ALSPAC) for this study.

It has been an exciting couple of years for the SLI project team, culminating in the identification of genetic variants that are associated with language impairment. The technology which supports our genetic research has developed a great deal over the last year or two meaning that genetic studies that previously took decades to perform can now be completed in a relatively short time frame and this has enabled the identification of genes underlying many disorders including diabetes and heart disease. As work progresses, our understanding of how genetic variation can cause susceptibility to complex genetic disorders is expanding and our understanding of the intricate pathways underlying human development is also growing. None of the above work would have been possible without you and the donation of your time, DNA. So many, many thanks and congratulations to yourselves for allowing this exciting research to take place. We will of course keep you updated with any future progress and you can always check our website for news updates (http://www.well.ox.ac.uk/monaco/SLI.html).