General abstract
Developmental Dyslexia is among the most prevalent neurobehavioural disorders in school-aged children and is characterized by high heritability. This symposium brings together recent behavioural and molecular genetic studies on reading (dis)ability. Individuals with dyslexia are at the bottom end of the continuous distribution of variation in reading ability. Therefore, both studies taking a categorical approach (studying affected cases) and studies taking a continuous approach (studying normal variation) can inform us about dyslexia. We present a twin study, in which the relative contribution of genetic and environmental influences to individual differences in reading ability is investigated, as well as the extent to which these influences overlap with influences to other cognitive domains. In another talk a family study is presented. This study examined the role of specific environmental factors on children’s reading ability, and the resemblance of parents and children for reading ability. Furthermore, we have three presentations on the search for specific genetic variants that contribute to the susceptibility of dyslexia. Since dyslexia often co-occurs with specific language impairment (SLI), there may be common biological and genetic influences on these complex and heterogeneous disorders. Both disorders show high heritability (50-80%) and have been associated with rare and common variation in several different genes. However, many of these genetic findings await replication, and still the large majority of heritable variation is unexplained. Finally, a study focussing on the effect of one gene is presented, the PCSK6 gene. Identifying specific genetic associations can ultimately elucidate the pathways from genes to neural systems, cognitive processes and the reading disorder at the behavioural level.

The aetiological overlap of reading with cognitive abilities
Maria Tosto – University of London
Maria G. Tosto & Yulia Kovas
Twin studies suggest that the same genetic factors influence a wide range of cognitive abilities and disabilities - the phenomenon described as the Generalist Genes Hypothesis. Discrepancies among cognitive skills seem to largely arise from environmental effects. Similarly, the stability of cognitive performance seems to largely stem from genetic effects, whereas discrepancy in performance across development is largely explained by changes in environment. For example, 80-90% of the moderate correlation between reading at age 7 and at 10 is genetically mediated in the normal range and in low performing children. Molecular genetic studies have begun to identify the ‘generalist’ genetic variants, for example associated with reading ability, language, g and mathematics. This research can lead to better prediction of learning disability and to planning individualised interventions.

Elsje van Bergen – University of Oxford
Elsje van Bergen, Titia van Zuijen, & Peter F. de Jong
Dyslexia tends to run in families. This might be because affected parents pass on genetic risk factors, or because affected parents provide a less advantageous literacy environment at home. In this study we investigated familial influences on reading ability. We tested 100 children and both their parents on reading ability and examined the influence of SES and home-literacy environment (HLE) on children’s reading ability. Results showed that SES and HLE indeed predict children’s reading ability. However, children’s reading ability was more strongly related to their parents’ reading ability, and SES and HLE did not predict children’s reading over and above parental reading. These findings highlight the complex interplay between environmental and genetic influences.

Genetic contributions to oral and written language impairments.

Dianne Newbury – University of Oxford

Specific Language Impairment (SLI) is defined as a substantial deficit in oral language skills despite adequate intelligence and opportunity. This common childhood condition has a high level of comorbidity with the written language disorder, developmental dyslexia and both show evidence for the existence of strong genetic contributions. Using genetic studies of individuals with speech and language impairments, we have identified common variants and structural rearrangements which may contribute to susceptibility to SLI. We have investigated variations across SLI and dyslexia candidate genes in groups of children affected by oral or written language disorders and find evidence for the existence of complex genetic relationships between these disorders.

Genome-wide screening for DNA variants associated with dyslexia and language impairment

Alessandro Gialluisi – MPI Nijmegen

Gialluisi A, Newbury D, Wilcutt EG, Olson RK, Brandler WM, Paracchini S, Monaco AP, Francks C, Fisher SE

To help identify new genetic effects on dyslexia and Specific Language Impairment (SLI), we are performing a Genome Wide Association Study (GWAS) on affected children and their siblings. We included in the study 502 subjects from the SLI Consortium (UK), 728 subjects from the CLDRC study of dyslexia (Colorado, USA), and 958 subjects belonging to a British dyslexia dataset. All of the subjects included in the study were assessed with several reading and language-related measures and genotyped on Illumina® genome-wide SNP arrays. The datasets underwent QC, haplotype inference and SNP imputation using 1000 Genomes data. Then both univariate and multivariate GWAS on reading and language-related traits has been carried out, followed by GWAS meta-analysis. Also, to identify the contribution of structural variants to these disorders, we will perform association testing with CNVs. The results and implications of this comprehensive, hypothesis-free approach will be discussed.

Silvia Paracchini – University of St Andrews

It is firmly established that developmental dyslexia has a strong genetic basis but very few risk genes have been identified so far. Recently, we have identified an intriguing genetic association. We showed the PCSK6 gene correlates with a quantitative measure of relative hand skills. PCSK6 is known to play an important role in the NODAL pathway in determining left/right body asymmetries in the early stages of development. The association appears to be specific in individuals with dyslexia, yet there is no correlation between dyslexia and handedness. Bioinformatic analysis of the associated locus has revealed a mechanism acting on gene expression regulation. In addition, we have found an enrichment of genes involved in setting up body asymmetries in top ranking
association with this handedness measure. Understanding the molecular mechanism underlying the PCSK6 association with handedness will provide a platform to understand the complex link between neuroanatomical asymmetries, behavioural laterality and neurodevelopmental disorders.