Developmental dyslexia and its complex genetic puzzle

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Developmental dyslexia (DD) is a neurodevelopmental disorder defined as a persistent failure to acquire efficient reading skills despite normal intelligence, sensory capabilities, and adequate education. DD is a heritable multifactorial disorder where genetics and environment affect the neurobiological, neuropsychological, and behavioral level of a person. Considering the complex phenotype, over the past decades several genetics studies have been done in large dyslexia-families or dyslexia-cohorts demonstrating only in a small part of them the genetics causes of DD. In the 70's, based on twins and family studies, it was suggested that some forms of dyslexia could be heritable [1,2] with estimate heritability around 70%. The first evidence arrived using linkage genetic technologies and the DYX1 locus was identified [3]. In the recent decades new 8 DYX loci (DYX2-DYX9) and other chromosome regions were associated to DD. Between the years 2003 and 2006, due to several association studies, a series of genes were candidate as possible dyslexia-risk genes: DYX1C1 (locus DYX1), KIAA0319 and DCDC2 (locus DYX2) [4-6]. Today, over 30 genes are described as causative or associated in the development of DD. Unfortunately, animal model studies demonstrating a clear biological contribution (as errors in neural migration and/or axon guidance) were performed only for few of them [7]. Summarizing, the genetics results collected so far suggest that DD is an additive or interactive effect of multiple genetic and environmental risk factors. Therefore, due to the heterogenic phenotype and the complex genetics, more powerful studies should be done, using large cohorts of several thousand samples and adopting a different approach based on the integration between clinical, developmental, and cognitive methods on one side and molecular genetics techniques on the other. In the 2014 we created an interdisciplinary collaboration between the University of Trieste and the Institute for Maternal and Child Health IRCCS "Burlo Garofolo" of Trieste, with the main aim to perform a genetic study in Italian families with dyslexia. Our work is divided in 2 parts. The first one is focused on validating the most replicated dyslexia-risk genes and those proposed by Poelmans et al. (2011) [8] using the chip-array technology (several hundred of thousand of SNPs - Illumina) and Next Generation Sequencing (Ion Torrent PGM– Life Technologies). The second one is targeted to discover new candidate DD risk-genes by using linkage analysis and Exome Sequencing in selected families negative to the first step.

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