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Risk-based follow-up of neuro-cognitive outcome in survivors of pediatric ALL: Why genes matter

Maria Francesca Dalla Porta, Chiara Colliva, Monica Cellini and **Johanna MC Blom**
University of Modena and Reggio Emilia, Italy

Neurocognitive impairment occurs in a substantial number of children diagnosed with acute lymphoblastic leukemia (ALL). However, considerable inter-individual variability exists; some children are more likely than others to develop neurocognitive problems in the face of similar individual and disease related problems. Understanding genes that regulate neurotransmitter availability in the frontal cortex may help to unravel the complex neurobiological processes that underlie variability in cognitive dysfunction which are especially important with respect to the daily functioning of children with ALL.While the effects of many clinical and patient characteristics on executive function have been well documented, behavioral genetics studies in pediatric oncology are sparse and few studies have dedicated their efforts to understanding the effect of genetic variation on EF outcomes in children and adolescents survivors of ALL. This study presents preliminary evidence that suggests an association between various genes and risk of impaired EF (mental flexibility, working memory and processing speed) in survivors of ALL; in particular, the link with serotoninergic system (5-HTTLPR) and metabolic vulnerability (MTHFR) appeared significant in our sample of patients, while the dopaminergic system seemed less involved. Thus, individual genetic susceptibility emerges as a risk factor in the specific psycho-social context of each patient and family. Therefore, including genetic profiles in the comprehensive evaluation of children with ALL may help to define and detect neurodevelopmental impairment associated with chemotherapy and problems linked to disease progression in a timely manner. This then allows us to plan early interventions for those most vulnerable for impaired cognitive development.

francesca.dallaporta@gmail.com