THE ROLE OF SNPs ANALYSIS IN NEUROCOGNITIVE ASSESSMENT OF CHILDREN WITH CHRONIC OR SEVERE DISEASES SUCH AS EPILEPSY, ASTHMA OR ACUTE LYMPHOBLASTIC LEUKEMIA

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Chronic or severe diseases often display compromised executive functioning (EF) which significantly affect the course of development and quality of life. One of the most critical problems is why some children are more likely than others to develop neurocognitive and behavioral problems in the face of similar patient specific profiles (e.g. age, gender, treatment, pathology and social context). At the moment we do not know what factors are responsible for this variability, but we do know that some genetic factors may render the developing brain more susceptible to damage or traumatic experiences than others. Some polymorphisms are firmly liked to treatment toxicity (like MTHFR), others reduce the capacity for neuronal repair (for example polymorphisms in BDNF) or neurotransmitter availability, activity ,and function like dopamine and serotonin (polymorphisms in COMT and 5-HTT). Separate or together, these polymorphisms may directly influence individual cognitive and emotional capacity and depend on the brain areas that are developing, reorganizing or declining at the time of the exposure.

The aim of this study is test the hypothesis that some specific polymorphisms linked to neurodevelopment and neurotoxicity may constitute a risk factor and compromise cognitive function in children with chronic or severe diseases, and subsequently use the data to plan comprehensive assessment and early interventions of the children found most vulnerable. Eighty-nine patients diagnosed with epilepsy (41), asthma (35) and Acute Lymphoblastic Leukemia (LLA) (13) were enrolled from the Pediatric Unit of the University Hospital of Modena. Besides the presence of these diseases, a subgroup of patients had difficulty in the language domain (ex: Specific Language Disorder and/or Dyslexia). DNA was collected by buccal swab and extracted for the analysis of various polymorphisms. Patients underwent a short battery of direct and indirect neurocognitive tests composed by the Brief Rating Inventory of Executive Function Test (BRIEF/BRIEF-P) and Children Color Trail Test 1 and 2 (CCTT). We found that children with epilepsy or LLA had a higher prevalence of deficits in executive functioning especially on working memory and planning skills with respect to asthma patients that overall seem to be less compromised in these skills. The MTHFR C677T polymorphism seems to play an important role concerning the responsiveness to anti-epileptic and chemotherapy. More surprisingly this polymorphism displayed a correlation with the specific profile of deficits related to executive functions observed in our patient population. In epileptic patients, heterozygous for MTHFR C677T and COMT, executive function was markedly worse, which indicates an additive effect for these polymorphisms. ALL patients did worse in the presence of 5HTT heterozygosity. With respect to asthma, specific polymorphisms seem not to correlate with EF in a major way. In conclusion: genetic vulnerability expressed as polygenic risk should be considered as part of behavioral and cognitive risk assessment, especially with respect to executive functioning which includes both cognitive ads well as emotional skills. The analysis of SNPs adds an important additional parameter

and renders the assessment more complete because it provides specific information on the individual's responsiveness and functioning in relation to both the treatment and the environment where different chronic or severe diseases display differential risk factor profiles. Thus, multidisciplinary domain relevant and context specific longitudinal risk assessment will help to capture the functional domains most compromised in time and allow for early intervention. In this way we may avoid the detrimental effects of long-term behavior, emotional and pharmacological toxicity.