



Communications of the European Society for Child and Adolescent Psychiatry

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With this contribution we want to continue our series on research projects in Europe where several countries, most of them also represented in ESCAP, cooperate intensively. Beate Herpertz-Dahlmann, ESCAP-Editor.

European Multicenter Tics in Children Studies (EMTICS): exploring the onset and course of tic disorders

Veit Roessner · Pieter J. Hoekstra

Tic disorders are neuropsychiatric disorders that start in childhood and adolescence. They are characterized by involuntary, rapid, recurrent, non-rhythmic motor movements or vocal utterances that are of sudden onset and do not serve an apparent purpose. Despite a growing body of research on tic disorders their causes and pathophysiology are still insufficiently understood. EMTICS will undertake pre-clinical and cohort studies that address susceptibility factors for pediatric and adolescent tic disorders combining clinical, epidemiological, genetic, microbiological and immunological aspects.

EMTICS is funded by the European Union 7th Framework Health Program and combines 27 partners from 11 different countries (Belgium, Denmark, Germany, Greece, Hungary, Israel, Italy, The Netherlands, Spain, Switzerland, and the UK). Coordinated by the University Medical Center Groningen, this study started in 01/12/2011 for the duration of 66 months. It will involve affected patients ($n = 700$) and at-risk but as yet unaffected first-degree relatives ($n = 500$) within an integrated, multidisciplinary research strategy.

The main hypothesis is that the onset and exacerbation of tic disorders are dependent on identifiable genetic factors interacting with identifiable environmental factors. It is specifically hypothesized that the likelihood of an onset or exacerbation of tics is increased after recent exposure to pharyngeal Group A Streptococcus (GAS) in the form of either carriage or infection. The onset or exacerbation of tics is supposed to be mediated by identifiable immunological mechanisms in at least a subsample of children, involving both the innate and adaptive immune system. Furthermore it is assumed that the onset or exacerbations of tics are associated with consistent patterns of gene expression, in which identifiable environmental factors are involved, most notably GAS carriage or exposure to psychosocial stress. Finally, the hypothesis that treatment with antibiotics in children with a tic disorder who exhibited a positive GAS throat culture will lead to reduction in symptom severity will be evaluated.

Within EMTICS stand two large-scale multicenter longitudinal cohort studies, entitled ONSET and COURSE. ONSET is a 3 year longitudinal observational study using clinical and laboratory assessments in a high-risk sample of 500 children between 4 and 10 years of age. They are all first-degree relatives (siblings or offspring) of patients with a chronic tic disorder, but have not manifested tics or obsessive-compulsive symptoms at the time of study enrolment. Exposure to pharyngeal GAS carriage or infection and information on other environmental factors will be collected. COURSE is a 1 year longitudinal observational study of a pediatric and adolescent population (700 children at the age from 5 to 16 years) with an already diagnosed chronic tic disorder, in which the course of symptom severity and occurrence of exacerbations will

be linked to environmental adversities (exposure to pharyngeal GAS carriage or infection and psychosocial stressors).

In both studies the patients will be in contact with the study center every 2 months, alternating between a telephone interview and a clinical visit. During the telephone interview an evaluation of a possible tic onset/exacerbation will take place and a stress questionnaire will be filled in. During the study visit in the clinical center the parents and the child will fill in different questionnaires including tic symptoms, obsessive–compulsive behavior, ADHD symptoms, stress, and quality of life. Furthermore different biological samples will be taken: throat swabs (identifying a possible GAS carriage), hair specimens (analyzing chronic stress level by the stress hormone cortisol), and blood samples (DNA, RNA, immune measures, cellular immune response). Currently the first study centers have started to recruit children and adolescents.

Although the main focus of EMTICS is on human studies, there is also a separate animal model Work Package that involves the development of a mouse test

battery aimed at mimicking behavioral (stereotypical, compulsive and perseverative patterns), immune and brain abnormalities isomorphic to clinical symptoms of tic disorders, as a function of induced autoimmunities. Different mouse strains will be exposed to passive transfer of streptococcus-induced antibodies, characterized by neuronal cross-reactivity (from both humans and animals).

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