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Neurobiology and treatment of adolescent female conduct disorder: FemNAT-CD consortium: a new European cooperation

In this issue, we continue our series on research projects in Europe connecting several countries. In the following, a project launched and financed by Seventh EU Framework Programme for Research (FP7) last year on conduct disorders in females will be introduced. Many European countries contribute to this cooperation by doing research in aetiology, development and treatment of this disorder, which becomes more and more important due to its increasing prevalence rates and severity.

Conduct disorder is one of the most common reasons for referral to Child and Adolescent Mental Health Services and has a highly negative impact on the affected individual as well as their families, teachers, and society [10]. It is one of the major reasons for school dropout, and affects ~15 % of all adolescents in Europe. Although the number of females exhibiting serious aggressive behaviours is growing, the majority of studies on biomarkers, neurocognitive phenotypes, and therapeutic treatment of CD have focused on male subjects only, despite strong evidence for a differential aetiology and neurobiology of female CD [3]. As a consequence, female CD remains a highly neglected research area resulting in a significant gap of knowledge on neurobiological and environmental mechanisms underlying the development of the disorder in females leading to an absence of sex-specific targets for prevention and intervention. Teenage pregnancies are common in females with CD, and the children of females with CD are also at greater risk for CD [8]. Further individual and societal problems strongly associated with female adolescent CD are difficulties in integration into the working life, teenage prostitution, chronic health problems, substance abuse, and delinquency [2]. The aim of the FemNAT-CD consortium, therefore, is to study the underlying neurobiology of female conduct disorder throughout adolescence, and implement new therapeutic strategies for the affected girls.

Over the last decades the prevalence of CD characterised by aggressive and antisocial behaviours violating the rights of others and societal rules (DSM-IV TR, ICD-10) [1, 11] has increased in the western industrialised world [5]. European and North American studies have reported a prevalence of CD of around 1–3 % in girls and 2–5 % in boys, with rates increasing during puberty [7]. Conduct problems (including subclinical symptoms) are observed in ~14 % of girls and 16 % of boys in Europe [9]. Interestingly, a strong persistence of CD has especially been observed in girls [6]. Associated costs for society are tremendous and of permanent duration [4, 10]. Major limitations of previous research are the lack of integrated genetic, epigenetic, neurobiological and neuroendocrinological studies in combination with neuropsychological, brain imaging and clinical phenotyping studies to delineate biomarkers of female CD, female-specific CD subtypes and predictors of persistence and remission. In addition, there is a lack of neuropsychological and neurobiological mechanism-based, new treatment approaches beyond parent training and neuroleptic treatment. Indeed, no female-specific therapeutic approaches have been studied in adolescents with CD despite evidence of sex-specific treatment responses with, e.g. smaller effects of parent training in females compared to males. The present proposal aims at overcoming these limitations by implementing an integrated and multidisciplinary research approach.

The specific aims of the FemNAT-CD study and consortium are therefore:

First, using a large case–control sample, we will carry out a cross-sectional study from pre-puberty to post-puberty to examine neurobiological and neurocognitive mechanisms underlying female adolescent CD. In a subgroup, we will also perform the first prospective longitudinal study across the pubertal transition.

Second, we will investigate new treatment approaches. A new psychological treatment, CD adapted group-based dialectic behaviour therapy (DBT-CD-A), will be studied in a randomised controlled trial in female adolescents. Two proof-of-concept studies will assess the effect of oxytocin and tryptophan challenge in females and males. A complementary animal model will add pre-clinical neurobiological evidence.

Third, we will disseminate knowledge on the impact of female adolescent CD on society and on the necessity of standardised clinical assessment as well as new treatment options by distributing information about the study design and results within the consortium, to collaborating youth welfare institutions, and to local as well as international medical, psychological, educational, forensic and political communities. We will develop and translate the DBT-CD-A manual. Conference talks and publications will be organised, and the development of clinical guidelines on diagnosis and treatment of CD in females will be supported.

Partners of the FemNAT-CD consortium have specific expertise and an outstanding scientific track record in genetic (Dublin, Frankfurt, Ulm), epigenetic (Munich, Ulm), phenotypic and clinical (Aachen, Amsterdam, Athens, Barcelona, Basel, Bilbao, Birmingham, Dublin, Frankfurt, Southampton, Szeged), neurocognitive (Aachen, Birmingham, Heidelberg, Frankfurt, Southampton), brain imaging (Aachen, Amsterdam, Basel, Birmingham, Heidelberg, Frankfurt, Southampton), neuroendocrinological (Aachen, Amsterdam, Basel, Heidelberg, Frankfurt, Regensburg, Southampton, Trier), and animal model (Regensburg) research, and have successfully performed randomised controlled psychotherapy trials (Aachen, Basel, Heidelberg, Frankfurt) as well as pharmacochallenge studies (Aachen, Heidelberg). In addition, monitoring of studies, online database development, and the broad range of statistical methods necessary to analyse the complex dataset will be provided by Dublin and Heidelberg in cooperation with all partners.

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