

# The ACTION Newsletter



Aggression in Children:  
unraveling gene-environment  
interplay to inform Treatment  
and Intervention strategies



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## Looking beyond the child

Over the past few years, transforming child mental health care has become a prominent issue in the Netherlands. Child mental health care is considered to be too child-focused and to neglect the heterogeneity of the child's problems. Therefore, recent efforts have been striving for a personalised approach, accompanied by a plea for an increased involvement of the child's environment within the therapeutic process.

The work done by ACTION supports this fully. In this newsletter, one can read that clinicians across Europe see a relationship between parental problems and treatment effectiveness. Furthermore, the importance of including parents is demonstrated in an empirical study (in preparation) using data from Sweden and a literature review. Clinical consequences are substantial. At present, we treat children, and involve parents predominantly for addressing the child's problems. In order to help children adequately, we need to equally focus on the problems of the parents, both during diagnostic assessment and treatment. As mental health problems are closely related to socio-economic status, it comes as no surprise that the literature review introduced in this newsletter calls for attention to this last aspect as well.

The heterogeneity observed amongst risk and protective factors is another issue that is being emphasized by ACTION work. Both the literature review and clinicians' evaluations show that diversity is substantial. Tailor-made treatment is a necessity. However, this can be challenging within the context of using clinical practice guidelines. Although many endorse the development of European guidelines for treating severe behavioural problems in children, they also call for a personalized focus. While this seems contradictory, it does not need to be so. Many argue that guidelines should not adopt a static cookbook format, but rather a dynamic decision-tree design. Ultimately, this is what ACTION strives for.

Over the coming years, ACTION will uniquely enrich our insight into factors that contribute to a child's development when SBPs jeopardise their future. Particularly when being able to enrich diagnostic assessment with insights from (epi)genetics and metabolomics, we will be a step further towards a personalised approach, and a better future for children and their families.



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## Inventory of mental health professionals' current practices and perceived critical needs for managing SBPs in children across Europe

Audri Lamers and Raluca Gatej, Curium-LUMC

### The inventory

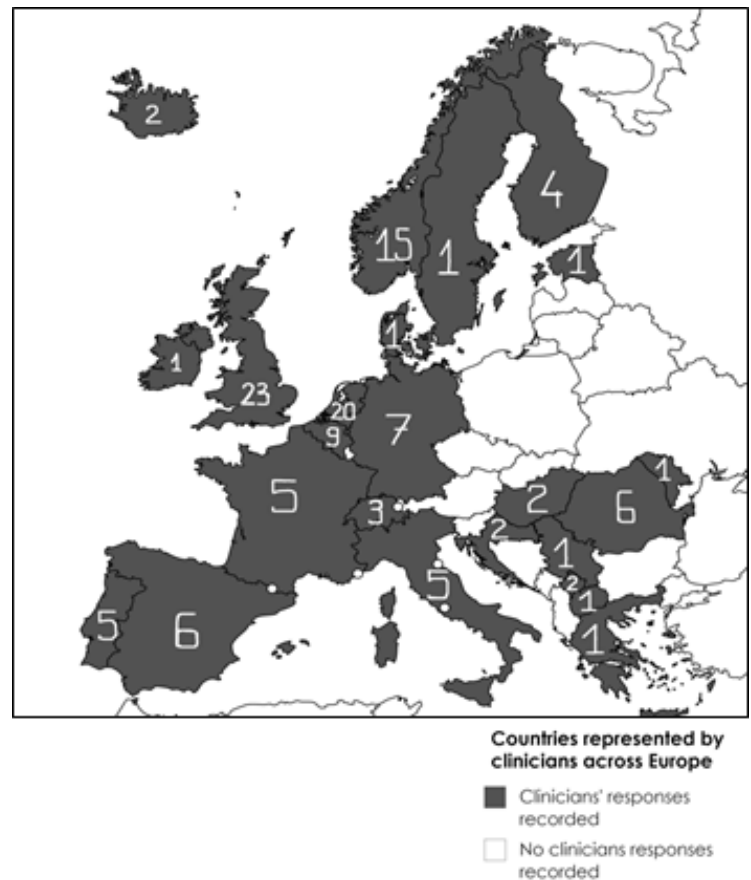
SBPs, including aggression, are one of the most common complaints in youth mental health. Although treatment supported as efficacious exists, many concerns emerged that it does not reach these children. Our project aimed to tackle these concerns by gathering clinicians' views on the challenges, diagnostic, and treatment practices for SBPs in children. 124 clinicians with a psychology/psychiatry background filled in a semi-structured interview.

**Diagnosis.** A majority of clinicians reported using a combination of categorical, descriptive, and dimensional diagnoses. Most often, they use diagnostic tools such as taking a developmental history and clinical interviews with the parents/child/teachers. To a lesser extent parent rating scales, questionnaires and tests are also employed.

**Risk indicators.** Clinicians perceived high severity of symptoms (e.g., risk to self/others) as influencing most their decision to indicate SBPs specialized treatment. Comorbidity (e.g., ADHD, depression), poor daily functioning, and deficient family environment followed. Clinicians also indicated that hospitalization may be necessary for children with severe symptoms, comorbid disorders and coming from a disorganized family.

**Treatment.** Clinicians reported using behavioral and cognitive-behavioral-based programs (CBT) in a systemic fashion to treat SBPs. Over 98% of clinicians reportedly used at least one evidenced-based method (EBM), with CBT and pharmacotherapy (>65% of clinicians) and behavioral therapy (41%) predominating. Clinicians may also use specific interventions such as problem-solving skills training (34%), the Incredible Years (34%), Anger Coping Program (28%), Video-feedback (22%), PMTO (20%), and Triple P – level 4 or 5 (20%). Although not ideal, when needed, hospitalization is generally short (i.e., up to 1 month).

**Treatment elements.** Clinicians believed that what maximizes treatment success is using positive/differential reinforcement principles and parent programs, focusing on positive



behaviors, and building parent-child and client-therapist relationships, all within a multi-disciplinary approach. On the contrary, they rated poor therapeutic alliance, low motivation, parents' psychopathology, working with the child only, and mismatch with the therapist as warning predictors of poor response to treatment.

*Challenges and critical needs.* The most common challenges experienced in practice included poor collaboration with schools/social services, stigma, poor financial and EBM resources/guidelines, and a lack of response from society towards SBPs in general. With regards to the latter, clinicians emphasized that childrens' mental health is not a priority across services, government, and the larger society, as evidenced by children with SBPs being passed back and forth between schools, psychiatric, social and legal services. Consequently, clinicians stressed the need for multidisciplinary coordination, developing alternative (community) resources for long-term support, better training/ resources in education and social services, and a sensibilisation campaign to increase awareness of the need for early intervention for SBPs.

### **Conclusions and directions**

Although the European clinicians in our study revealed using evidence-based interventions for SBPs, challenges such as poor collaboration with the systems surrounding the child, stigma, and lack of financial resources appear to affect early identification and intervention. Clinicians directed the next efforts towards improving support for parents, schools and social services, delivering interventions from both specialist and non-specialist community services, reinforcing cross-discipline collaboration, creating guidelines to include elements perceived as successful in practice, and increasing public awareness of SBPs overall.



Dr. Audri Lamers is a Clinical Psychologist and Senior Researcher at Curium-LUMC, Centre for Child and Youth Psychiatry. For the ACTION consortium, she is responsible for the Inventory of European Practices, under the supervision of Professor Robert Vermeiren. In 2016, Audri successfully defended her PhD thesis on the parent-team therapeutic alliance in child psychiatry. Currently she continues combining clinical work and scientific research with a special interest in the application of scientific research results to improve the quality of clinical work.

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Alexandra-Raluca Gatej started working as a student research assistant at Curium-LUMC, Centre for Child and Youth Psychiatry in November 2015. She completed the MSc Child & Adolescent Psychology program, at Leiden University in August 2016, and has since been continuing her collaboration with Curium-LUMC as a PhD student. Raluca conducted literature reviews, data collection and analysis, scientific write-ups and dissemination of the project, under the supervision of Dr. Audri Lamers.

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## Long-term outcomes of children with oppositional defiant disorder and conduct disorder-like problems

Peter Roetman, Curium-LUMC

The inventory conducted by the ACTION consortium (the previous article in this newsletter) amongst European clinicians treating children with aggression/SBPs concluded that parental mental disorders are a major risk factor for a negative treatment outcome. This notion converges with a considerable amount of research showing that parental mental disorders and childhood behavioral problems are both associated with negative outcomes in adolescence and adulthood. Yet, longitudinal research on children with behavioral problems and parents with mental disorders is lacking. The cooperation with the Child and Adolescent Twin Study in Sweden (CATSS) enabled us to test whether, similarly to clinicians' opinions in the previous article, children with behavioral problems and parents with a mental disorder are worse off than their counterparts without parents with a mental disorder.

Nine-year-old children with/without parent-reported Oppositional Defiant Disorder-like (ODD) and Conduct Disorder-like (CD) problems and parent(s) with/without a mental disorder were compared on outcomes at ages 15 years (N = 6319) and 18 years (N = 3068). The Swedish National Patient Register was used to access parental diagnoses (N = 596 at age 15, N = 270 at age 18) made by clinical psychologists and psychiatrists, covering a variety of mental disorders (e.g., anxiety, developmental, substance abuse). Outcomes at age 15 and 18 years consisted of indices of psychosocial functioning (e.g., school performance, peer problems) and psychopathology. Correction was performed for gender and social economic status.

The preliminary results indicate that ODD and CD-like problems at age nine are associated with all negative outcome measures at age 15 and 18 years, stressing the pervasiveness and long-term impact of behavioral problems. Surprisingly, the direct effects of parental mental disorders were mainly resulting from the father's, while previous research has focused primarily on the mother's. These findings suggest an important role of paternal mental disorders on long-term outcomes, with paternal mental disorder showing positive associations not only with antisocial behavior (e.g., violent/nonviolent crime, aggression, and conduct problems), but also with school performance and hyperactivity problems. Maternal diagnoses were positively associated with peer problems and negatively associated with hyperactivity problems.

The interactions between parental mental disorders and ODD/CD-like problems at nine years and outcomes at age 15 and 18 showed mixed results. The interaction of maternal mental disorder and ODD/CD-like problems at age 9 years was associated with low prosocial behavior in adolescence, while the interaction of paternal mental disorder and ODD/CD-like problems was associated with increased truancy. Surprisingly, paternal mental disorder in combination with ODD/CD-like problems had a protective effect on outcomes characterizing aggressive behavior (e.g., proactive/reactive aggression, violent crime). This suggests that the presence of any

mental disorder in parents in combination with child behavioral problems isn't automatically a predictor of negative long-term outcomes.



THE AUTHOR

Peter Roetman has been working as a PhD student at Curium-LUMC since April 2015. His main task is to collect the clinical cases with behavioral problems for the biomarker study at Curium-LUMC, a Centre for Child and Adolescent Psychiatry, under the supervision of Prof. Robert Vermeiren and Dr. O. Colins.

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## Identifying risk and treatment opportunities for aggression

Anne Hendriks, VU University Amsterdam

### Synthesis of meta-analyses and systematic reviews on treatment effectiveness for childhood aggression

This study provided a synthesis of 64 meta-analyses and systematic reviews on treatments for childhood aggression. For universal and selective prevention, effects were mostly absent or small; for indicated prevention and interventions, effects were mostly small or medium. For most moderators, effects were absent or mixed. Moderators with a positive effect on treatment effectiveness for childhood aggression were pre-test levels of aggression, individual implementation, and parental involvement.

The results of this synthesis yielded two underlying patterns. First, indicated prevention and interventions targeting aggression use similar treatment programs, and yield comparable outcomes, whereas universal prevention and selective prevention mostly target general factors associated with the risk of developing childhood aggression, use similar treatment programs, and yield comparable outcomes. Second, although treatments may benefit from more knowledge on the causes of individual differences, these were seldom studied as moderators. These findings suggest that future research distinguishing between targets of the treatment (i.e., factors associated with future childhood aggression vs. present aggressive behaviors) and a stronger emphasis on individual differences in treatment effectiveness for childhood aggression would be particularly promising.

### The next project

Treatments might benefit from more insight into whether the contribution of genetic and environmental factors is moderated by factors associated with the risk to develop aggression. One factor that has consistently been associated with an increased risk for aggression - either proximally, through factors such as parenting practices, or distally, through factors such as neighborhood characteristics - is socioeconomic status. Our next study aims to investigate whether the contribution of genetic factors, shared environmental factors, and unique environmental factors to individual differences in aggression is different across socioeconomic status strata. The sample consists of ~24.000 seven-year-old twins of the Netherlands Twin Register. With this study we hope to further the knowledge on risk factors for aggression and opportunities for treatments.



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## Assessing psychopathic traits in early childhood

Olivier Colins, Curium-LUMC

### The Childhood Problematic Traits Inventory (CPTI)

Adult psychopathic personality is commonly described as a multifaceted personality disorder comprising of a constellation of co-occurring interpersonal, callous–unemotional, and behavioral/lifestyle traits. Research shows that psychopathic traits can already be measured in (early) childhood and adolescence, and are related to severe conduct problems, delinquency, and aggression. To bolster what is known about the developmental pathways towards adult psychopathy, the Child Problematic Traits Inventory (CPTI; Colins et al., 2014) has been developed. This research tool assesses interpersonal, callous–unemotional, and behavioral/lifestyle traits in 3- to 12-year-old children. Its psychometric qualities have been supported amongst 3- to 12-year-olds in Sweden, the Netherlands, Italy, Spain, and China.

The CPTI is administered to the clinic-referred, aggressive 6- to 12-year-olds who are included in the ACTION epigenetic and biomarker study (1) to test if the psychometric properties of the CPTI can be replicated in this population; (2) to evaluate if the CPTI can identify a subgroup of children with the highest levels of aggression; and – on the long run – (3) to explore if epigenetic mechanisms are involved in the deficits that may hallmark children with high levels of psychopathic traits (e.g., lack of emotional resonance).



THE AUTHOR

Olivier F. Colins, Ph.D., is a senior researcher at the Leiden University Medical Center, Department of Child & Adolescent Psychiatry). His main research focusses on conduct problems, aggression, criminality, psychopathy and psychopathology in various settings (forensic, clinical, community), age-groups (pre-school, childhood, adolescence, adulthood), and contexts (clinical protocol versus research projects). For the ACTION Research Program, he was involved in designing the study, in co-supervising the biomarker and epigenetics study, and will co-author scientific papers.

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## Early Career Scientists Workshop, Nijmegen, The Netherlands

Anne Hendriks and Jenny van Dongen, Ph.D., VU University Amsterdam

### Aim of the meeting

On October 31st and November 1st, forty early career aggression scientists from 9 different countries (Finland, Germany, Hungary, Italy, The Netherlands, Switzerland, Spain, UK, and the US) gathered in Nijmegen, The Netherlands, to attend the first Early Career Scientists (ECS) Workshop on Aggression! The event was organized following joint efforts from 4 European projects: ACTION, [Aggressotype](#), [Matrics](#), and [FemNAT-CD](#), and was attended by PhD students and postdoc researchers from the four projects. It was a great opportunity for the ECS researchers to get to know each other and about each other's work, to talk about collaborations between the 4 consortia, and to learn more about aggression and state-of-the-art research from world class speakers.



Lecture by Robert Vermeiren

### The first day

The first day started with an introduction of the consortia by ECS representatives of each consortium. Anne and Jenny introduced the ACTION consortium and all ACTION researchers who were present briefly introduced themselves. Next, the lectures were kicked off by Prof. Jan Buitelaar and Prof. Robert Vermeiren (ACTION partner 2, Curium-LUMC, Dept. child and adolescent psychiatry), who taught and discussed with the ECS researchers about the clinical characterization of aggression, sub-classifications and their development, and the various neural, cognitive and behavioural aspects of aggression. The lectures were followed by ECS



Jenny and Anne work at the department of Biological Psychology at the VU University Amsterdam. Both were involved in organizing the ECS workshop

researchers' poster and laptop presentations. The afternoon was dedicated to basic and state-of-art lectures about genetics and MRI. Dr. Michel Nivard (ACTION partner 1, VU Amsterdam) explained all the basics of genetics. In a parallel session, Dr. Christian Beckmann explained the basics of MRI research. The formal part of the day was closed by Prof. Barbara Franke and Dr. Stephane De Brito who gave talks about the current state of the field of genetics, and MRI, respectively,

of aggression phenotypes. The first day was closed by a cooking class and dinner, which gave the ECS researchers the opportunity to get to know each other better in a relaxing atmosphere.

### The second day

The second day kicked off with an interactive lecture by Dr. Susan Young about treatments for aggression. Next, Prof. Jeffrey Glennon presented animal models of aggression. After that, in smaller groups, the ECS researchers brainstormed various opportunities for continuing collaboration between the consortia and for dissemination of research findings. The brainstorming session ended with a plenary discussion on the groups' ideas and other possible opportunities for collaboration. Next, Prof. Richard Tremblay gave a lecture via Skype on the role of the environment in aggression, followed by a lecture by Dr. Jenny van Dongen on epigenetics as a possible biological mediator of environmental influences on (aggressive) behaviour. The day finished with a closing discussion between the consortia leaders and the ECS researchers on how we can continue collaboration efforts between the consortia.



Group picture of the attendees



Since August 2015, Anne has been working for ACTION as a PhD student at the VU University Amsterdam tutored by Prof. Catrin Finkenauer and Prof. Meike Bartels. Before this, she studied Child Development and Education at the University of Amsterdam.

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Jenny works as a postdoc on the analysis of DNA methylation data in combination with phenotypic and genetic data from twins and families.

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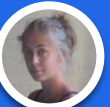



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