Aggression and Antisocial Behavior in Underserved Populations – Towards a Comprehensive Treatment Approach

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Content

Abstract

Antisocial behaviors are highly prevalent among children and adolescents as well as adults. When these behaviors reach clinical significance they place a high burden on the individual, his or her immediate surrounding and society in general. Better insight into the correlates of antisocial behavior is needed in order to develop adequate prevention and intervention strategies matched to an individual's personal risk to engage in antisocial behavior and experience associated risk factors. To date, studies have indicated a strong relationship between community violence exposure and antisocial behavior. However, most studies have investigated samples with a mixed composition of healthy children and adolescents as well as those with a clinical diagnosis. Little is known about the specific associations between community violence exposure and antisocial behaviors in healthy controls compared to children and adolescents with existing, clinically significant behavioral problems (i.e., a diagnosis of conduct disorder). Furthermore, little is known about the effectiveness of intervention programs targeting antisocial behaviors in underserved settings with a high prevalence of aggressive behavior disorders, such as correctional institutions or residential youth settings.

This dissertation aims to further the understanding of the correlates of antisocial behaviors as well as the treatment of youths and adults exhibiting these behaviors in restrictive settings. First, the specific association between community violence exposure and antisocial behaviors in a healthy child and adolescent sample as well as a clinical sample with a diagnosis of conduct disorder was examined. Second, the effectiveness of an evidence-informed skills training designed to target antisocial behaviors of offenders within correctional settings was evaluated. Third, a comprehensive, randomized-controlled treatment evaluation plan for a skills training adapted to the needs of female adolescents with conduct disorder residing in residential youth settings is introduced.

The research presented in this dissertation expands current knowledge on the relationship between community violence exposure and antisocial behaviors. It is shown that there are no clear differences between the association of witnessing community violence and antisocial behavior between healthy controls and those with a diagnosis of conduct disorder. Thus, any potential confound with regard to studies that have used mixed samples can be ruled out. Furthermore, this work provides evidence for the effectiveness of a skills training targeting behavioral problems in inmates. The more sessions are completed the fewer disciplinary infractions are received. Finally, a treatment evaluation protocol

adhering to the rigorous standards of the CONSORT guidelines is introduced. The protocol introduces a comprehensive implementation and evaluation guide to evaluate the effectiveness of a skills training designed for antisocial, aggressive female adolescents within residential youth settings. The results of this work encourage future studies to further investigate the association between community violence exposure and antisocial behaviors in healthy youths compared to those with a diagnosis of CD in a longitudinal approach. Design and evaluation of interventions for antisocial youths who are exposed to violence are called for, especially in settings with high prevalence rates of aggressive behavior disorders. In addition, treatment evaluation studies should use rigorous standards for scientific evaluation as exemplified in the final study to provide instructive implications and increase the clinical gain.

Chapter 1 – General Introduction

1.1 Antisocial Behavior –Clinical Presentation and Course

1.1.1 Antisocial Behavior – Clinical Presentation

Antisocial behaviors such as lying, stealing, rule violations or fighting are highly prevalent and can be observed in most children and adolescents throughout the course of their development (Connor, 2012). However, antisocial behavior may become clinically significant, once this behavior becomes increasingly frequent, intense or chronic and causes significant impairment in an individual's family, school, job and/or peer environment (Frick & Dickens, 2006; Matthys & Lochman, 2017). When a child's or adolescent's antisocial behavior is judged to be of clinical relevance, one of two diagnoses may be considered. Conduct disorder (CD) is one diagnosis categorized in the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM–5; (American Psychiatric Association, 2013)) and the International Classification of Mental and Behavioral Disorders (ICD-10; (World Health Organization, 1992)) under the umbrella term disruptive behavior disorders (DBD). The second diagnosis subsumed within the DBD classification is oppositional defiant disorder (ODD), and is often considered to be a precursor of CD (Moffitt et al., 2008). A third disorder within the DBD category focuses less on antisocial behavior and more on impulsivity, inattention and/or hyperactivity, i.e., attention-deficit (hyperactivity) disorder (Connor, Steeber, & McBurnett, 2010), and will not be the focus of the present manuscript for reasons of limited scope. Children and adolescents with diagnosable levels of antisocial behavior represent a heterogeneous group (Frick, 2016). They may not only differ in kind and extent of symptoms but also in their expression of comorbid symptoms/disorders. While ODD is mostly characterized by negativistic, irritable, and angry mood, as well as defiant, disobedient, and hostile behavior, CD is represented by more severe patterns of antisocial behavior (American Psychiatric Association, 2013). More specifically, CD is defined by aggressive and rule-breaking behaviors that violate the rights of others. Aggression is directed towards other people, animals, or objects, i.e., destruction of property. In addition, deceitfulness, theft, and serious rule violation comprise further key symptoms of CD.

If antisocial behavior patterns persist into adulthood a diagnosis of antisocial personality disorder (ASPD; according to DSM-5) or dissocial personality disorder (according to ICD-10) may be given. ASPD is a pervasive pattern of disregard for the needs and rights of others usually beginning in childhood or early adolescence (Black, 2015). As such, its associated features are similar to those of CD and include impairments in self-functioning (e.g., ego-centrism, goal-setting based on personal gratification) and interpersonal functioning (e.g., lack of concern, lack of remorse, exploitation, coercion) (American Psychiatric Association, 2013). In addition, pathological personality traits in the

domains of antagonism (e.g., manipulativeness, deceitfulness, callousness, hostility) and disinhibition (e.g., irresponsibility, impulsivity, risk taking) comprise DSM-5 criteria for ASPD (American Psychiatric Association, 2013). Psychopathy or sociopathy are further terms associated with adult antisocial behavior. Psychopathy, while not recognized in the diagnostic criteria of the DSM 5 or ICD-10, includes a variety of affective, interpersonal and behavioral characteristics, such as grandiosity, superficial charm, impulsiveness, fearlessness, deceitfulness or aggression (Hare & Neumann, 2008; Patrick & Brislin, 2015). When examining symptom criteria, psychopathy seems similar to ASPD and there has been ongoing debate about whether the two disorders differ substantially (Derefinko & Widiger, 2016; Glenn, Johnson, & Raine, 2013). However, many have argued psychopathy to be a non-isomorphic (Poythress et al., 2010) more severe form of clinical impairment with many individuals diagnosed with psychopathy also meeting the criteria for ASPD but not the other way around (Hare, Hart, & Harpur, 1991; Ogloff, Campbell, & Shepherd, 2016) while also displaying pronounced differences with regard to personality (Derefinko & Widiger, 2016) and neurobiological aspects (Blair, 2008).

1.1.2 Antisocial Behavior – Course and Impact

Children and youth with antisocial behavior constitute a problem not only for the individual and his/her immediate social surrounding but also for society in general (Blair, Leibenluft, & Pine, 2014; Frick, 2016). CD is one of the most frequent reasons for referral to child and adolescent psychiatric services (Baker, 2013; Costello & Janiszewski, 1990; Kazdin, 1995). Children and adolescents with CD frequently cause family conflict and pose a problem for schools that are trying to manage their problem behavior, while at the same time trying to protect the needs and safety of other students and teachers (Matthys & Lochman, 2017). Victimization by adolescents with CD tends to have serious physical and/or emotional implications (Frick & Dickens, 2006). Furthermore, CD has a poor long-term prognosis with many affected individuals recycling through various social services (e.g., special school programs, mental health services, residential care, juvenile justice institutions) resulting in huge amounts of costs associated with their treatment (Bardone et al., 1998; Pedersen & Mastekaasa, 2011; Scott, Knapp, Henderson, & Maughan, 2001). Especially early symptoms (i.e., before the age of 10) of aggressive behavior tend to be associated with a high persistence of symptoms and a negative course (Bevilacqua, Hale, Barker, & Viner, 2017; Frick, 2016). Furthermore, a greater number of symptoms, co-morbid disorders and the presence of callous-unemotional traits have a poorer outcome prognosis (Berkout, Young, & Gross, 2011; Blair et al., 2014; Frick, 2016). More precisely, CD in childhood is known to predict impaired mental health (e.g., substance use, depression), involvement with the criminal justice system (e.g., greater risk for arrest, court convictions), economic hardships (e.g., low SES, homelessness), poor academic/occupational

functioning (e.g., poor academic/job performance or school drop-out), social problems (e.g., poor interpersonal competence) and poor physical health (e.g., greater risk for sexually transmitted diseases, respiratory problems) in late adolescence and adulthood (Frick, 2012; Odgers et al., 2008). For females, CD has been associated with teenage pregnancy and abortion (Pedersen & Mastekaasa, 2011). With an additional increased risk for developing antisocial personality disorder (ASP) as an adult (Matthys & Lochman, 2017; Storm-Mathisen & Vaglum, 1994), youth with CD place a significant financial and safety burden on the state and community resources available (Baker, 2013). A recent longitudinal study examining the outcome of a Belgian population-based sample with conduct problems followed participants from childhood into young adulthood (Sentse, Kretschmer, de Haan, & Prinzie, 2017). Four trajectories were identified with life-course persistent young adults being least favorably adjusted followed by an adolescent-onset group. A childhood-limited group was found to display more internalizing symptoms when compared with a low conduct problems (control) group. Within this sample, the life-course persistent group comprised 25 percent of the overall sample (Sentse et al., 2017). Moreover, a longitudinal study investigating the types of childhood psychiatric disorders preceding young adult crime indicated that about half (51.4% males, 43.6% females) of young adult criminal offenders had a history of a child psychiatric disorder (Copeland, Miller-Johnson, Keeler, Angold, & Costello, 2007). Severe/violent offender status of the young adult sample was predicted by either the presence of CD with comorbid internalizing disorders or substance use with additional internalizing disorders.

Similar to child and adolescent antisocial behavior disorders, ASPD and psychopathy inflict significant costs to the criminal justice system, health and social service agencies as well (Black, 2013). ASPD is often associated with various comorbid disorders and a chronic and pervasive course (Glenn et al., 2013). A study investigating the psychiatric comorbidity of ASPD in offenders found a higher suicide risk, higher rates of mood, anxiety, psychotic, substance use, somatoform disorders, borderline personality disorder, and ADHD to be associated with ASPD. In addition, inmates with ASPD tended to be younger, reported less quality of life and presented with a greater recidivism risk (Black, Gunter, Loveless, Allen, & Sieleni, 2010). Similarly, elevated levels of psychopathic traits have been associated with younger age at first manifestation, being male, suicidal behaviors, violent behaviors, incarceration, homelessness, substance abuse, histrionic, borderline and ASPD as well as panic and obsessive compulsive disorders (Coid, Yang, Ullrich, Roberts, & Hare, 2009). Particularly the presence of comorbid disorders such as substance use and schizophrenia has a strong negative impact on the course, prognosis and outcome of ASPD and psychopathy (Martens, 2000; Walter, Wiesbeck, Dittmann, & Graf, 2011). A longitudinal study on 45 men admitted to a psychiatric hospital with a fulfilled diagnosis of ASPD outlines the chronic and pervasive course of the disorder (Black,

Baumgard, & Bell, 1995). With an average follow-up period of 29 years 42.2 percent of the sample was unimproved, while 26.6 percent was in full remission. Most frequent comorbid disorders found related to substance use, generalized anxiety disorder and depression (Black et al., 1995). With regard to psychopathy a stable and chronic course has been found as well. A meta-analysis of 53 studies indicates that psychopathy is moderately associated with delinquency, general and violent recidivism in the transition between middle childhood to adolescence (Asscher et al., 2011). Likewise, inspecting the transition between adolescence and young adulthood results from the Pittsburgh Youth Study examining the stability of psychopathy in adolescents aged 13 with a follow-up at age 24 indicated a moderately stable relationship (Lynam, Caspi, Moffitt, Loeber, & Stouthamer-Loeber, 2007). Furthermore, data from an adult community sample demonstrate similar associations between psychopathy, violent behavior and substance use to those found in forensic samples with moderate to strong associations (Neumann & Hare, 2008).

1.2 Risk Factors for Antisocial Behavior

1.2.1 Biological and Individual Risk Factors for Antisocial Behavior

Several risk factors (i.e., variables predicting an increased probability to engage in antisocial behavior) have been identified in the past. The development of early and persistent antisocial behavior is commonly thought to be related to a combination of adverse biological and environmental factors (Byrd & Manuck, 2014; Li, 2017; Tuvblad & Beaver, 2013). A growing body of research, for instance, indicates that biological risk factors increase an individual's risk for developing antisocial behavior. Correspondingly, specific genes have been linked to antisocial behavior and behavioral genetics research has determined that large amounts of variance can be explained through genetic influences (Tielbeek et al., 2017). Furthermore, subtle deficits, such as deficient empathy, heightened threat sensitivity or deficient decision making, contribute to emotion regulation problems, deficient impulse-control and interpersonal difficulties (Fairchild, Van Goozen, Calder, Stollery, & Goodyer, 2009; Gilmour, Hill, Place, & Skuse, 2004; Moffitt, 2006). Additional individual level factors, such as callous-unemotional traits, lack of guilt and low school motivation/achievement (Jolliffe, Farrington, Piquero, Loeber, & Hill, 2017) as well as low self-control (Vazsonyi, Mikuška, & Kelley, 2017) may further steer an individual towards engaging in antisocial behaviors.

Autonomic nervous system (ANS) functioning has recently been studied in relation to adolescent antisocial behavior (Fanti, 2016). Psychophysiological research has provided evidence suggesting that decreased autonomic baseline arousal, e.g., low resting heart rate or low resting electrodermal activity as well as reactivity measures to aversive cues are associated with aggressive and antisocial

behavior in children and adolescents (for a review see (Ortiz & Raine, 2004; Portnoy & Farrington, 2015)). However, there are contradicting results with regard to the significance of basal ANS measures in the prediction of antisocial behavior. A recent meta-analysis has indicated a trend towards weaker associations between low resting heart rate and antisocial behavior with increasing publication year (Portnoy & Farrington, 2015). Some of the contradictions may be a result of small sample sizes (Portnoy & Farrington, 2015), no separation between sexes (Koenig et al., 2014), use of single ANS markers, and failure to control for lifestyle factors that are likely to exert influence (Hu, Lamers, de Geus, & Penninx, 2017; Pagani, Lévesque-Seck, Archambault, & Janosz, 2017; Portnoy & Farrington, 2015). A recent investigation that took all of the above-mentioned limitations into account found only weak associations between baseline ANS measures and antisocial behavior (see Appendix 1).

1.2.2 Environmental Risk Factors for Antisocial Behavior

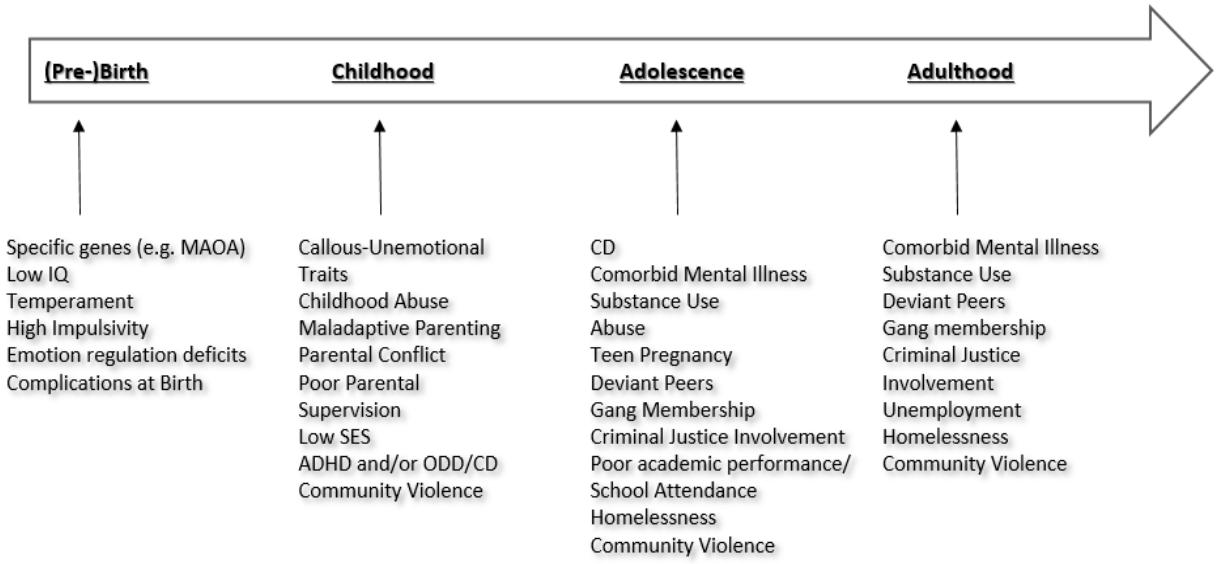
Moreover, contextual factors, such as family disruption and low parental supervision (Jolliffe et al., 2017), parental criminal behavior (Besemer, Ahmad, Hinshaw, & Farrington, 2017), abuse, neglect or maladaptive parenting (Lereya, Samara, & Wolke, 2013; Pinquart, 2017), low socioeconomic status (Piotrowska, Stride, Croft, & Rowe, 2015), neighborhood violence (Fowler, Tompsett, Braciszewski, Jacques-Tiura, & Baltes, 2009) and affiliation with deviant peers (Carlo et al., 2014; Gillies, Boden, Friesen, Macfarlane, & Fergusson, 2017) have all been associated with antisocial behavior in the past. There has been mounting evidence that poverty and neighborhood violence are crucial determinants for psychopathology in general, including antisocial behavior disorders (Costello, Compton, Keeler, & Angold, 2003; Emerson, Einfeld, & Stancliffe, 2011; Fowler et al., 2009; Holz et al., 2015). Indeed, an individual's neighborhood has gained increased attention within the study of child and adolescent antisocial behavior. More specifically, the degree to which an individual is (currently or in the past) exposed to violence within his or her community has been consistently linked to conduct problems or conduct disorder and delinquency (Fowler et al., 2009; Hong, Huang, Golden, Upton Patton, & Washington, 2014). Community violence exposure (CVE) is defined as either the witnessing of violent events within one's neighborhood or the direct victimization by others from the community (Schwab-Stone et al., 1995). A comprehensive meta-analysis conducted by Fowler et al. (2009) found strong effect sizes for the relationship between CVE and externalizing behaviors (.72 for witnessing; .78 for victimization) in adolescents. Next to the empirical support, various theories outlining reasons for the relationship between CVE and antisocial behavior exist. Social learning theory, for instance, implies that children may exhibit greater antisocial behavior after frequent CVE due to role modeling (Bandura, 1978; Forster, Grigsby, Unger, & Sussman, 2015). That is, a high rate of exposure may lead children to view violence as legitimate and normative. According to general strain theory, youth

residing in violent communities may have limited opportunities to achieve individual life goals through legitimate means (Agnew, 1992). In addition, social control theorists postulate that a lack of institutions and organizations that foster law-abiding behaviors in violent communities may be an additional reason for an increased likelihood to engage in antisocial behaviors (Hirschi, 2002). Given CVE's strong association with antisocial behavior in adolescence as well as its high prevalence, particularly in urban settings, CVE has become the focus of many researchers (Buka, Stichick, Birdthistle, & Earls, 2001; Finkelhor, Turner, Shattuck, & Hamby, 2015; Stein, Jaycox, Kataoka, Rhodes, & Vestal, 2003). While European adolescents tend to report less CVE compared to U.S. youth, rates are nevertheless substantial (Hillis, Mercy, Amobi, & Kress, 2016; Mercy, Krug, Dahlberg, & Zwi, 2003). Correspondingly, CVE is now considered an important risk factor that should be assessed early on and addressed in the treatment of children and adolescents with severe conduct problems (Javdani, Abdul-Adil, Suarez, Nichols, & Farmer, 2014).

While an increased exposure to violence may make children and adolescents more likely to display antisocial behavior, the presence of CD also increases the likelihood for youngsters to experience CVE (e.g., through affiliating with deviant peers or provoking instances of violence; (Halliday-Boykins & Graham, 2001; Mrug & Windle, 2009). Therefore, one might argue that the strong association between CVE and conduct problems found within adolescent samples might reflect a biased finding due to the fact that violent adolescents are also more likely to live in violent neighborhoods. Indeed, when examining the literature on CVE and mental health problems in children and adolescents, the majority of articles report on disadvantaged community sample (i.e., adolescents from urban, low-income households residing in deprived, high-crime neighborhoods with high rates of immigrants/ethnic minorities; (Copeland-Linder, Lambert, & Ialongo, 2010; Dempsey, Stacy, & Moely, 2000; Frey, Ruchkin, Martin, & Schwab-Stone, 2009; Goldner, Gross, Richards, & Ragsdale, 2015; Gorman-Smith, Henry, & Tolan, 2004). Hence, these studies likely include a mixture of healthy and clinically impaired children and adolescents. Such mixed samples might obscure findings through producing a stronger association than might be given if one separated healthy groups from psychologically impaired. In addition, little is known about the specific strength of association between recent CVE and antisocial behavior in children and adolescents with a diagnosis of CD. Thus, the question remains whether the magnitude of previously reported associations between CVE and antisocial behavior might merely be due to the fact that more violent adolescents are also the ones stemming from more violent neighborhoods. Investigating this question is important for establishing targeted prevention and intervention strategies for at-risk youth residing in neighborhoods characterized by high crime rates, gang violence and/or poverty (Hong et al., 2014).

Whereas biological factors, such as genetics or temperament, play a major role for the development of disruptive behavior in early childhood, social factors seem to become more important with increasing age (please refer to figure 1 for a graphic overview (H. Steiner, Daniels, Stadler, & Kelly, 2017)). More specifically, neurological impairments in combination with environmental risk factors that increase the risk for failing to acquire social norms play a causal role in the early development of ODD and CD (Odgers et al., 2008). In contrast, the development of CD in adolescence seems to be less associated with biological predispositions or the preceding diagnoses of ADHD and/or ODD (Moffitt, 2006; Odgers et al., 2008). Instead a desire to rebel against social norms in combination with poor parental supervision and affiliation with deviant peers plays a key role (Odgers et al., 2008). To better understand the interplay between biological and environmental risk factors on adolescent and adult pathways of antisocial behaviors large scale, multidisciplinary approaches like the FemNAT-CD study "Neurobiology and Treatment of Adolescent Female Conduct Disorder: The Central Role of Emotion Processing " (www.femNAT.CD-eu) are promising. The aim of the FemNAT-CD project is to explore the underlying mechanisms of conduct disorder, assessing genetic factors, changes in brain structure and function, endocrinological correlates, the function of the autonomous nervous system and various environmental risk factors such as maltreatment, neglect, harsh parenting or community violence.

Figure 1: Selected Risk Factors for the Development of Antisocial and Aggressive Behavior from Birth to Adulthood



As the number of risk factors increase for a given individual, the risk to develop persistent antisocial behavior patterns increases alongside due to the interplay of risk factors with each other (Jolliffe et al., 2017). For instance, a child with a difficult temperament may be at increased risk to evoke harsh or punitive parenting (T. G. O'connor, Deater-Deckard, Fulker, Rutter, & Plomin, 1998). This form of parenting, in turn, may facilitate the child's anger or irritability even further and increase their display

of antisocial behavior (Drabick, Gadow, & Sprafkin, 2006). Likewise, children growing up in a violent, disadvantaged community may be more likely to affiliate with antisocial peers (Chung & Steinberg, 2006; Haynie, Silver, & Teasdale, 2006). These friendships, in turn, may further increase the time spent in such violent neighborhoods as well as the antisocial activities performed by the child (Chung & Steinberg, 2006; Haynie et al., 2006). Ultimately, these factors affect the mental processes of an individual through, e.g., normalizing violent behaviors (Gaylord-Harden, So, Bai, Henry, & Tolan, 2017), increasing an individual's aggressive-impulsive response access, or enhancing the presence of hostile-attribution bias (Lösel, Bliesener, & Bender, 2007). While there is an abundance of studies investigating the impact of early risk factors on the development and/or maintenance of antisocial behavior disorders (Murray & Farrington, 2010), less attention has been dedicated to the impact of recent risk factors. The transition between adolescence and young adulthood marks a critical time period with regard to the potential persistence of antisocial behavior, as emerging adulthood is considered a high-risk period for the incidence of mental illness (Hamdi & Iacono, 2014). Correspondingly, prevalence rates of CD peak among the oldest adolescents (Merikangas et al., 2010). Therefore, more research is needed focusing on risk factors that may heighten the chance of (continued) antisocial behavior patterns during this transition period.

1.3 Prevalence of Antisocial Behavior

1.3.1 Prevalence of Antisocial Behavior

Conduct problems (including ODD or subclinical symptoms) are observed in approximately 14% of girls and 16% of boys in Europe (Ravens-Sieberer et al., 2008). Lifetime prevalence rates for ODD are estimated at 12.6 percent while for CD rates are around 6.8 percent in a nationally representative sample of US adolescents (Merikangas et al., 2010). Another study, specifically examining the prevalence of life course persistent versus adolescent limited CD reports rates of 0.5 and 4.6 percent respectively for females, while for males rates of 1.9 and 5.1% respectively were found (A. A. Moore, Silberg, Roberson-Nay, & Mezuk, 2017). Although the delinquency case rate for male adolescents is much higher compared to females, research suggests rising rates for female youth. A recent report from the Juvenile Court Statistics indicates a rising trend of 31 percent for delinquency cases involving females between the years of 1985 to 2013, while the caseload for males is reported to have decreased (Hockenberry & Puzzanchera, 2015).

ASPD is estimated to occur in approximately 3.8 percent of the general public (Trull, Jahng, Tomko, Wood, & Sher, 2010). When looking at sex separately, ASPD is found in 5.7 percent of males and 1.9 percent of females (Trull et al., 2010). Psychopathy is estimated to occur in less than 1 percent of the general population (Coid, Yang, Ullrich, Roberts, Moran, et al., 2009; Dolan & Doyle, 2007; Hare et al.,

1991). A two-phase household survey study of over 600 individuals within England, Wales and Scotland, for instance, demonstrated very low rates of psychopathy. Of the few individuals within the sample that did display elevated levels of psychopathic traits, the majority exhibited significant co-occurring problems similar to those found in forensic or psychiatric populations (Coid, Yang, Ullrich, Roberts, Moran, et al., 2009). Little is known about sex-specific differences in prevalence of psychopathy in the general population (Dolan & Doyle, 2007; Logan & Weizmann-Henelius, 2012).

1.3.2 Settings with a high Prevalence of Antisocial Behavior

There are settings with a disproportionately high number of children and adolescents with ODD and/or CD. A typical setting in which a great number of adolescents with antisocial behavior are found is the youth welfare sector (Bronsard et al., 2016; Connor et al., 2010; Dunleavy & Leon, 2011; Jozefiak et al., 2016; Schmid, Goldbeck, Nuetzel, & Fegert, 2008). For instance, a study examining the prevalence of psychopathology in roughly 400 adolescents admitted to a residential treatment center, reported disruptive behavior disorders as the primary diagnoses found within the sample with a prevalence of 49 percent (Connor, Doerfler, Toscano, Volungis, & Steingard, 2004). Furthermore, they reported a high presence of co-morbidity with 39 percent of adolescents exhibiting more than one diagnosis. In addition, girls were identified to have higher levels of psychopathology compared to boys. The study further underlined a high rate of transfers (with an associated high rate of relationship cut-offs) with 84 percent of the sample reporting at least two out-of-home placements prior to the current one. Again girls were more likely than boys to report a greater number of prior out-of-home placements (65% vs. 40%). With regard to abuse, girls were also more likely than boys to have experienced physical abuse (60% vs. 40%), sexual abuse (64% vs. 27%), or a combination of both (46% vs. 18%; (Connor et al., 2004). In Germany an investigation of 689 children and adolescents from 20 residential care institutions revealed a substantial rate of approximately 60 percent fulfilling a clinical diagnosis according to ICD-10 (Schmid et al., 2008). The majority of the clinically significant sample exhibited disruptive behavior disorders and showed high comorbidity. Similar findings have been reported by other studies investigating the (mental) health of children and adolescents placed in youth welfare settings (Neely-Barnes & Whitted, 2011); for review see (Bronsard et al., 2016; Keil & Price, 2006).

Another setting with disproportionately high rates of CD and ODD is the juvenile justice system (Colins et al., 2010; Fischer, Barkley, Smallish, & Fletcher, 2002; Sourander et al., 2007; Wasserman, McReynolds, Schwalbe, Keating, & Jones, 2010). The National Center for Mental Health and Juvenile Justice in collaboration with the Council of Juvenile Correctional Administrators conducted a comprehensive mental health prevalence study in three juvenile justice settings, including community-based programs, detention centers and secure residential facilities (Shufelt & Cocozza,

2006). Of the overall sample (1,400 youth), 70.4 percent met criteria for at least one mental health disorder with the majority (46.5%) presenting with disruptive behavior disorders. A Dutch study investigating the prevalence of psychiatric disorders in a male sample of incarcerated adolescents found very high rates of 90 percent reporting at least some type of disorder and 75 percent reporting a disruptive behavior disorder (Vreugdenhil, Doreleijers, Vermeiren, Wouters, & Van Den Brink, 2004). A recent literature review on the prevalence of psychiatric disorders in detained male adolescents indicates substantial rates as well, with 46.4 percent of the sample presenting with CD and 19.8 percent fulfilling criteria for ODD (Colins et al., 2010). Likewise, incarcerated females have been found to display high rates of disruptive behavior disorders as well ranging between 32-73 % (Teplin, Abram, McClelland, Dulcan, & Mericle, 2002).While the prevalence of disruptive behavior disorders in juveniles is high, it is a risk factor for adult criminality and incarceration as well (Copeland et al., 2007).

Correspondingly, the setting containing the greatest number of adults diagnosed with or meeting the criteria for ASPD and/or psychopathy is the criminal justice system (Bebbington et al., 2017; Beryl, Chou, & Völlm, 2014; Graf & Dittmann, 2007; Habermeyer, Passow, & Vohs, 2010). According to a study conducted by Black and Larsen (2000) almost 80 percent of men and 65 percent of women in U.S. correctional institutions meet the criteria for ASPD. Another study focusing on newly incarcerated offenders only found a prevalence of 35.3 percent with no significant gender differences (Black et al., 2010). In general, it is estimated that prisoners are 73 times more likely to have ASPD compared to the general population (Bebbington et al., 2017). A study on the prevalence of psychopathy in prisoners from England and Wales found rates of 7.7 percent for males and 1.9 percent for female inmates (Coid, Yang, Ullrich, Roberts, Moran, et al., 2009). A German study specifically investigating the prevalence rate of psychopathy in incarcerated females (using a modified cut-off score of 25 instead of 30) reported a prevalence of 17 percent (Lehmann & Ittel, 2012). Likewise, a rate of 16.4 percent was found in Finnish male prisoners (Jüriloo et al., 2014).

1.4 Aggression and Misconduct in Youth Welfare and Criminal Justice Settings

Due to substantial rates of antisocial behavior in youth welfare settings and correctional institutions it is not surprising that aggression and institutional misconduct are a major concern (B. Steiner, Butler, & Ellison, 2014; Walters & Crawford, 2014). In general, misconduct in youth residential settings and correctional institutions can pertain to (but is not limited to) violence, drug use, escapes, property or security-related offenses, or violations of other rules (e.g., failure to follow instructions, not being on time, dress code violation) (Camp, Gaes, Langan, & Saylor, 2003; Quinn & Shera, 2009). The environment in which individuals reside has been reported to exert additional influence on

misconduct through factors such as criminogenic effects (through increased exposure to delinquent peers), social climate, staff-resident/inmate relationships or institutional management (Camp et al., 2003). A survey study on the prevalence of violence towards residential or group care social workers indicated a substantial rate of 81 percent of social workers reporting to have experienced some form of violence within the course of one year (Alink, Euser, Bakermans-Kranenburg, & van IJzendoorn, 2014). While the majority reported verbal threats, about half of the social workers stated to have experienced incidents of physical violence. Furthermore, prevalence of institutional misconduct was investigated in a study using a sample of delinquent females from a youth correctional institution who had committed serious and violent offenses prior to their incarceration (Blackburn & Trulson, 2010). Nearly one third of the sample engaged in major misconduct by committing violent offenses, such as staff or ward assaults. A large-scale study examining the prevalence of adult inmate misconduct in samples of a correctional institution, reported a prevalence of 44.83 percent of behavioral infractions within the stock population of which 10.47 percent were judged as potentially violent (Sorensen & Cunningham, 2010). A rate of 50.34 percent for rule violations was found for newly admitted inmates including 12.34 percent of potentially violent infractions (Sorensen & Cunningham, 2010). While rates of infractions in the general prison population are moderate to high, many studies indicate that inmates with mental illness show higher rates of misconduct (Houser, Belenko, & Brennan, 2012; D. J. James & Glaze, 2006; O'keefe & Schnell, 2007; B. Steiner & Wooldredge, 2009; Wright, Salisbury, & Van Voorhis, 2007). A meta-analysis on 90 studies investigating prison misconduct found a greater number of antisocial traits, high aggressiveness and high impulsivity to be among the strongest predictors for institutional misconduct (Gonçalves, Gonçalves, Martins, & Dirkzwager, 2014). Besides the physical and psychological consequences associated with behavioral infractions, the associated financial implications cause further distress. Accumulation of and the commission of major rule infractions tends to result in higher custody placements or controlling supervision in the case of residential settings (Bastiaanssen, Delsing, Kroes, Engels, & Veerman, 2014; Browne, Cambier, & Agha, 2011). Placements, such as administrative segregation, are costly: for instance, costs associated with housing a supermax prisoner within an Ohio State Prison in 2003 amounted to $149 per day compared to $63 per day for an average general population prisoner (Browne et al., 2011). The majority of the increase in costs is due to greater staff numbers, as one corrections officer is required for every 1.7 prisoners (Browne et al., 2011). Correspondingly, an analysis of the costs associated with behavioral infractions at a medium-security prison yielded an estimate of $970 on average per documented misconduct (Lovell & Jemelka, 1996). Unfortunately, consequences (e.g., solitary confinement) to institutional misconduct tend to further limit individuals' opportunity to engage in rehabilitative services as well as educative, recreational and peer activities (Trupin, Stewart, Beach, & Boesky, 2002). Considering the physical, psychological

and financial expenses associated with institutional misconduct successful treatment of antisocial individuals seems indispensable.

1.5 Lack of Effective Intervention in Settings with a high Prevalence of Antisocial Behavior

A substantial amount of children and adolescents in youth residential settings exhibit antisocial behavior. Even higher rates can be found in juvenile and adult correctional settings (Bebbington et al., 2017). Both populations present with poorer mental health, social functioning, substantial psychiatric comorbidity, greater risk for suicide, economical problems and extensive histories of criminal activity (Black et al., 2010). Furthermore, there is evidence that inmates with mental health disorders, particularly those with high levels of behavioral dyscontrol, commit more institutional violations, serve longer sentences and report greater rates of victimization compared to inmates with no psychological impairments (F. W. O'Connor, Lovell, & Brown, 2002). As such, these individuals require intensive mental health treatment and pose considerable management problems (Connor et al., 2004; Fazel, Hayes, Bartellas, Clerici, & Trestman, 2016; Heflinger, Simpkins, & Combs-Orme, 2000). Appropriate treatment of antisocial adolescents within residential settings and criminal justice-involved youth and adults is critical for reasons of safety, successful community-reintegration and a reduction of recidivism (Bebbington et al., 2017; Berzins & Trestman, 2004; Fazel et al., 2016). Although a range of mental health interventions has been used with antisocial adolescents and adults within youth welfare and correctional settings, evidence regarding their effectiveness is limited (Quinn & Shera, 2009).

1.5.1 Mental Health Services for Children and Adolescents within Youth Welfare Institutions

Despite the alarmingly high prevalence of mental health problems in general, and ODD and CD in particular, only a small proportion of adolescents involved with child welfare receive mental health treatment (Burns et al., 2004; González-García et al., 2017). Data of a U.S. nationally representative sample of children and adolescents who were investigated by child welfare agencies due to reports of maltreatment and consisted of a large proportion of individuals with mental health problems (one half of the sample) indicated that only one-fourth of the sample received any specialty mental health treatment within the past year (Burns et al., 2004). A sample of 113 foster youth between the ages of 16.5 to 17.5 years were found to be nearly 10 times more likely to use mental health services compared to adolescents within the community (Shin, 2005). However, the most frequent services used within the sample were diagnostic interviews making up 50 percent of documented mental health services. While diagnostic assessments are important and useful first steps in the treatment of psychologically impaired youth, they are not to be mistaken with actual therapy (Shin, 2005). Likewise, investigation of psychotherapeutic services received by a German sample of 689 children

and adolescents within residential care revealed low rates of treatment (Nützel, Schmid, Goldbeck, & Fegert, 2005). While more than half of the sample fulfilled a clinical diagnosis, only half of the clinically impaired youths received mental health treatment. In Spain four out of ten children in residential care do not receive mental health services despite presenting with a need (González-García et al., 2017).

With regard to the kind of treatment needed, a meta-analysis of 27 controlled studies by De Swart et al. (2012) analyzed youth residential care within the past thirty years and concluded that treatment provided within the institution was as effective as treatment provided outside of the institution. Evidence-based treatments, however, were significantly more effective compared to treatment as usual (De Swart et al., 2012). In general, treatment approaches including cognitive behavioral therapy, milieu therapy and family treatment have been found to be most promising in treating children and adolescents within youth residential settings (for review see (Grietens et al., 2014)). There is, however, still room for improvement as existing treatment approaches do not seem to strongly appeal to adolescents in moments of crisis. A recent investigation of the attitudes of adolescents within residential care reveals that although social workers are perceived as supportive, adolescents do not seek them out for help when experiencing personal problems (Harder, Knorth, & Kalverboer, 2017). Hence, more evaluations of treatment effectiveness and responsivity for children and adolescents within youth welfare are needed as contextual factors of the setting itself impact the implementation, facilitation and achievable gains of a program (S. James, Alemi, & Zepeda, 2013; Leve et al., 2012).

1.5.2 Mental Health Services for Adolescents and Adults within Corrections

Once having entered the correctional system as an adult evidence-based mental health treatments targeting the specific needs of inmates with emotional instability and conduct problems are limited (Epperson et al., 2011). Research suggests that the time clinical staff may spend treating inmates with mental disorders is inversely correlated to their education and training (Human Rights Watch, 2003). Limited staff, low salaries and large caseloads result in limited treatment groups and, thus, not all inmates in need receive mental health care (Human Rights Watch, 2003). Furthermore, of the existing therapy programs, most do not account for co-occurring substance use disorders, which are prevalent in approximately three quarters of inmates with mental health disorders and often found in individuals with ASPD and/or psychopathy (D. J. James & Glaze, 2006; O'keefe & Schnell, 2007). A study examining the extent of evidence-based programs specifically for drug-involved offenders within correctional facilities and community-based treatment programs indicated that most programs offered fewer than 60 percent of evidence-based practices (Friedmann, Taxman, & Henderson, 2007).

Of the evidence-based programs that do exist, cognitive-behavioral approaches have been applied more frequently within correctional systems and have produced some encouraging results (Brazão et al., 2015; Golden, 2002; Milkman & Wanberg, 2007; Smith, Gendreau, & Swartz, 2009; Wilson, Bouffard, & MacKenzie, 2005; Zajac, 2015). A meta-analysis of the effectiveness of CBT programs with adult and juvenile offender populations found reductions in reoffending rates ranging between 25-50 percent (Landenberger & Lipsey, 2005). Interestingly, serious, high-risk offenders seem to benefit significantly from CBT interventions, contradicting any presumption that these types of offenders may be less suited for treatment (Smith et al., 2009). Furthermore, larger effects tend to be observed when the treatments include elements of anger control and interpersonal problem solving (Lipsey, Landenberger, & Wilson, 2007). CBT approaches that combine the three aforementioned therapy techniques and are specifically used within correctional settings include Moral Reconation Therapy (MRT; (Little & Robinson, 1988)), Thinking for Change (T4C; (Golden, 2002)), and Reasoning and Rehabilitation (R&R; (Ross, Fabiano, & Ewles, 1988)). More recently, also dialectical behavior programs (K. E. Moore et al., 2016), acceptance commitment therapy (Lanza, Garcia, Lamelas, & González-Menéndez, 2014) and mindfulness-based approaches (Auty, Cope, & Liebling, 2017) have been evaluated for use with co

rrectional populations. A recent meta-analysis on the effectiveness of treatments for offenders with mental health problems reveals an overall medium effect size (0.50) for treatments offered within correctional facilities, with studies using an active control design reporting lower effect sizes (0.21) (Yoon, Slade, & Fazel, 2017). No differences between individual and group formats were found and no sustained improvements at follow-up, three and six months post intervention, could be identified. The authors conclude, along with previous evaluations, that no particular approach has demonstrated clear superiority and room for improvement and further clarification of the effectiveness of currently applied interventions still exists (Aos, Miller, & Drake, 2006; Bartlett et al., 2015; Epperson et al., 2011; Fazel et al., 2016; Landenberger & Lipsey, 2005; Yoon et al., 2017).

1.6 Methodological Criteria for Conducting Treatment Evaluation Studies

While there is an urgent need to provide effective treatment to incarcerated antisocial adults with and without a history of ODD and CD, it seems even more pressing to intervene at an earlier stage to prevent incarceration altogether or at the very least reduce the risk for an early and long criminal career. Unfortunately, there is a lack of high-quality treatment evaluation studies within youth welfare settings providing information on the effectiveness of interventions (Grietens et al., 2014; Leve et al., 2012). Without thoroughly conducted trial research, the evidence-base for any given intervention is lacking its scientific foundation and is of limited utility.

It is stated within the Declaration of Helsinki that authors are required to publicize the results of their study and to ensure their accuracy and completeness (World Medical Association, 2013). The gold standard and most rigorous method of treatment evaluation is to conduct a randomized-controlled trial (Cipriani & Geddes, 2015). Participants are allocated randomly to receive one or more interventions. Thereby, it is ensured that no systematic differences between groups exist that might affect the outcome. Additional features, such as blinding or allocation concealment, comprise further methods to prevent an overestimation of effects. As randomized-controlled trials provide evidence of causality, they represent one of the most powerful tools in research (Cipriani & Geddes, 2015). However, several studies that have investigated the quality of past randomized-controlled trials have identified a range of issues. Boutron and colleagues (2010), for instance, systematically investigated RCTs published within the year of 2006 and found that 40 percent of all studies presented distorted information in at least two sections of their main text (Boutron, Dutton, Ravaud, & Altman, 2010). Other issues identified with published RCTs refer to a lack of or insufficient discussion of limitations (Ioannidis, 2007), an association between financial ties and favorable conclusions (Als-Nielsen, Chen, Gluud, & Kjaergard, 2003; Rattinger & Bero, 2009) and embellished conclusions that do not portray the reported results within industry-supported studies (Jørgensen, Hilden, & Gøtzsche, 2006; Yank, Rennie, & Bero, 2007). This finding is a problem as it prevents readers from being able to accurately assess the quality and impact of a given trial (Schulz, Altman, & Moher, 2010).In addition, Zajac (2015) stressed the importance of monitoring fidelity and to conduct regular process and fidelity evaluations during program implementation.

Several recent reviews of treatment evaluation studies specifically conducted within youth residential care have identified further common limitations of past studies. Leve et al. (2012) criticized that few studies have presented long-term follow-up results informing about the sustained effects of treatment approaches. Furthermore, they noted that few studies applied a fully blinded data collection process, thereby risking biased data estimates. A failure to report effect sizes comprised another point of contention as it left authors at a loss with regard to how substantive the reported effects were (Leve et al., 2012). Finally, collecting data from more than one source was advised to improve the quality and accuracy of the data. Grietens et al. (2014) have described further content-related problems in the implementation of treatment evaluation studies within youth residential care. The authors contended that many programs lack a specific description as well as necessary information on professional and organizational aspects, such as the type and number of adolescents required for a group or the skills required to attain and preserve a positive group climate.

As a result, a group of international researchers from various disciplines has formed to continually monitor the trial literature and establish a set of guidelines to help researchers improve their reporting of RCTs. The proposed guidelines have been based on a review of more than 700 RCTs and more than 400 journals worldwide have endorsed the Consolidated Standards Of Reporting Trials (CONSORT; (Schulz et al., 2010)). Treatment evaluations of interventions for antisocial youth within residential care settings complying with these standards are urgently needed to provide insight into the utility, evidence-base, and feasibility of a given program.

1.7 Knowledge Gaps

The effects of CVE on adolescent antisocial behavior have been extensively investigated within the past decades. However, most studies have examined mixed, disadvantaged community samples, thereby combining healthy individuals with clinically impaired adolescents. Therefore, the presence of an ecological fallacy due to aggregated groups cannot be rejected. Our aim was to study the association between CVE and conduct problems separately in a healthy versus a clinical (i.e., conduct disordered) child and adolescent sample in order to provide a definitive answer to the question whether an ecological fallacy effect can be out ruled. In addition, we examined the specific effects of proactive and reactive aggression as mediators on the association between CVE and conduct problems to get further insight into the mechanism behind the association of the two variables.

Many children and adolescents diagnosed with CD show adverse long-term outcomes with a high proportion becoming involved with the criminal justice system and becoming incarcerated as adults. Unfortunately, only limited evidence-based treatments are available to correctional populations with a need for the design and evaluation of improved interventions. Therefore, our aim was to conduct a treatment evaluation study of a newly developed skills training specifically designed for aggressive and impulsive inmates.

Finally, despite the urgent need to intervene early little is known about the effective treatment of antisocial girls residing within youth welfare settings. Past literature has shown that rates of female delinquency are rising. Furthermore, girls with antisocial and aggressive behavior tendencies are at increased risk for physical diseases, teenage pregnancies, persisting symptoms and higher levels of psychopathology, a greater number of out-of-home placements and a greater likelihood to experience abuse compared to their male counterparts. Of the treatment evaluation studies that do exist many present with methodological limitations providing limited insight into the effectiveness, significance and sustainability of the respective intervention. Therefore, our next aim was to adapt an evidence-informed skills training designed for offenders within correctional systems to the specific needs of girls with ODD and/or CD within youth residential settings and evaluate the intervention

adhering to the latest scientific standards of cluster-randomized controlled trials. This treatment evaluation study should provide clinicians and social workers with a comprehensive evidence base and guide their future choice of treatment when confronted with girls who display diagnosable levels of aggression and antisocial behavior.

1.8 Aims

(1) Examine the association between CVE and conduct problems separately in a big European sample of male and female adolescents with CD versus healthy controls
    i. Report on strength of association between CVE and conduct problems within a strictly clinical versus healthy population to investigate the presence of an ecological fallacy
    ii. Parse out effect of proactive and reactive aggression and examine their impact as potential mediators in the relationship between CVE and conduct problems in adolescents with CD and healthy controls

(2) Evaluate the effectiveness of a skills training developed within a correctional setting for inmates with emotion regulation deficits
    i. Investigate the effectiveness of the intervention through examining the effect of attendance on the number of post-program disciplinary infractions
    ii. Examine what inmates benefit most from the program through including security risk score and type of psychiatric diagnosis as additional predictors

(3) Design a randomized-controlled trial to evaluate the effectiveness of an evidence-based intervention for girls with ODD and/or CD placed in youth welfare institutions
    i. Adapt an evidence-informed skills training to the needs of the respective population (i.e., female adolescents with ODD/CD) and the requirements of the setting in which it takes place
    ii. Design a comprehensive and feasible plan to evaluate the effectiveness of the adapted skills training on a behavioral, neurobiological and neuropsychological level

Chapter 2 – Community Violence Exposure and Conduct Problems in Children and Adolescents with Conduct Disorder and Healthy Controls

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Abstract

Exposure to community violence through witnessing or being directly victimized has been associated with conduct problems in a range of studies. However, the relationship between community violence exposure (CVE) and conduct problems has never been studied separately in healthy individuals and individuals with conduct disorder (CD). Therefore, it is not clear whether the association between CVE and conduct problems is due to confounding factors, because those with high conduct problems also tend to live in more violent neighborhoods, i.e., an ecological fallacy. Hence, the aim of the present study was: (1) to investigate whether the association between recent CVE and current conduct problems holds true for healthy controls as well as adolescents with a diagnosis of CD; (2) to examine whether the association is stable in both groups when including effects of aggression subtypes (proactive/reactive aggression), age, gender, site and socioeconomic status (SES); and (3) to test whether proactive or reactive aggression mediate the link between CVE and conduct problems. Data from 1178 children and adolescents (62% female; 44% CD) aged between 9 years and 18 years from seven European countries were analyzed. Conduct problems were assessed using the Kiddie-Schedule of Affective Disorders and Schizophrenia diagnostic interview. Information about CVE and aggression subtypes was obtained using self-report questionnaires (Social and Health Assessment and Reactive-Proactive aggression Questionnaire (RPQ), respectively). The association between witnessing community violence and conduct problems was significant in both groups (adolescents with CD and healthy controls). The association was also stable after examining the mediating effects of aggression subtypes while including moderating effects of age, gender and SES and controlling for effects of site in both groups. There were no clear differences between the groups in the strength of the association between witnessing violence and conduct problems. However, we found evidence for a ceiling effect, i.e., individuals with very high levels of conduct problems could not show a further increase if exposed to CVE and vice versa. Results indicate that there was no evidence for an ecological fallacy being the primary cause of the association, i.e., CVE must be considered a valid risk factor in the etiology of CD.

Keywords: community violence exposure, conduct disorder, reactive aggression, proactive aggression, adolescence, antisocial behavior

INTRODUCTION

Community violence exposure (CVE) is defined as the witnessing of violence within a community, falling victim to violent acts oneself, or being subjected to a combination of both experiences (Schwab-Stone et al., 1995). CVE is a common and persistent public health issue in many inner city neighborhoods (Buka et al., 2001; Stein et al., 2003). Although the prevalence of CVE has been reported to be lower in many European countries compared to the US (Mercy et al., 2003; Hillis et al., 2016), it has nevertheless been recognized as a global public health problem by the World Health Organization (2002). A comprehensive meta-analysis of 114 studies on the effects of CVE on adolescent mental health by Fowler et al. (2009) found that the effects of CVE were strongest on the subsequent development of post-traumatic stress disorder, followed closely by externalizing problems. Specifically, effect sizes for the relationship between CVE and externalizing problems were 0.72–0.78 for witnessing violence and victimization, respectively. Fowler et al. (2009) found that relationship between exposure to CVE and externalizing behaviors was stronger in adolescents compared to children. Further factors that have been shown to influence the effects of CVE on mental health outcomes are gender and socioeconomic status (SES). Namely, being male (Javdani et al., 2014), and coming from lower SES strata (Anderson et al., 2001) have been found to increase the strength of the association between CVE and conduct problems.

Overall, research evidence to date suggests that the association of CVE and conduct problems is reciprocal, enhancing the chances of a negative spiral of increasing conduct problems and greater violence exposure. For instance, a bi-directional relationship between CVE and externalizing problems has been reported by Mrug and Windle (2009). The authors found that CVE was linked to the development of later conduct problems and delinquency. Likewise, baseline delinquency predicted higher rates of later CVE. Although there is much evidence indicating that violence exposure in early childhood is a major risk factor for the development of Conduct Disorder (CD; for a review see Burke et al., 2002), to date it is not known whether there are similarly strong associations between recent CVE and current conduct problems in adolescents with CD. If a reciprocal relationship between CVE and conduct problems exists, strong associations between recent CVE and current conduct problems would be expected.

Children and adolescents with CD constitute a group that is *particularly* prone to experiencing violence exposure due to the nature of their diagnosis. CD is defined as a repetitive and persistent pattern of violent and antisocial behavior (American Psychiatric Association, 2013). For children and adolescents with CD, it is difficult to separate CVE as a form of unintended environmental exposure from self-provoked situations that reflect part of the adolescent's symptomatology (Halliday-Boykins

and Graham, 2001; Lynch, 2003). Children and adolescents with CD may encounter violent situations in ways other than as innocent bystanders, e.g., as a result of being present when a friend initiates a fight or robs a person or indeed as the perpetrator themselves. Much of the CVE literature focuses on community samples derived from urban, low socio-economic backgrounds, representing ethnic minorities and living in neighborhoods with high crime rates (Dempsey et al., 2000; Gorman-Smith et al., 2004; Frey et al., 2009; Copeland-Linder et al., 2010; Goldner et al., 2015). As such, these studies have likely included a mixture of healthy and clinically impaired youth. According to epidemiological research around 22.2% of adolescents within a national representative US sample reported a history of a psychiatric disorder that was accompanied by severe impairment or distress, of which 9.6% comprise behavioral disorders, such as CD or attention-deficit/hyperactivity disorder (Merikangas et al., 2010). For European countries specifically, it is estimated that around 38.2% of the general population of the European Union (EU) exhibit a mental disorder each year, with 5% of that proportion relating to externalizing behavior (Wittchen et al., 2011). Generally, adolescents from low-income neighborhoods exhibit greater mental health problems than those living in higher-income neighborhoods (Aneshensel and Sucoff, 1996). Although past CVE studies have offered unique insights into the debilitating effects of CVE on adolescents' psychosocial adjustment, the effects of CVE remain to be disentangled among a sample in which healthy and clinically-impaired individuals can be distinguished. Investigating these two groups separately allows precluding the presence of an ecological fallacy, i.e., the finding of stronger associations between CVE and conduct problems than is actually the case, due to the aggregation of healthy and clinically impaired adolescents. Specifically, insight into the associations between recent CVE and current conduct problems in an adolescent sample with CD and a healthy control sample will answer the following questions: does recent CVE continue to be of relevance in terms of determining current conduct problems in healthy adolescents as well as in those who have developed diagnosable levels of conduct problems, i.e., those with a CD diagnosis? Can we exclude an ecological fallacy that may have developed due to a lack of studies investigating the effects of CVE and conduct problems in an exclusive group of healthy adolescents vs. adolescents with CD?

Studies have shown that effects of CVE on later conduct problems persisted even when controlling for an individual's initial aggression level (e.g., Schwab-Stone et al., 1995; Farrell and Bruce, 1997; Miller et al., 1999; McCabe et al., 2005; Weaver et al., 2008). However, aggression is heterogeneous and may take different forms. Two key forms of aggression that are commonly distinguished are reactive and proactive aggression (for overview, see Kempes et al., 2005). Reactive aggression refers to impulsive forms of aggression, usually evoked by high arousal levels and strong emotions such as anger or fear. In contrast, proactive aggression is an instrumental, often pre-meditated form of

aggression, characterized as callous and goal-oriented behavior and thought to be associated with low levels of arousal. Reactive aggression may be explained through the frustration-anger model (Dollard et al., 1939), explaining why this form of aggression is commonly linked to provocations or threats. Proactive aggression, on the other hand, is better understood through social learning theory (Bandura, 1973). This theory outlines why proactive aggression is often motivated by reward-orientation and is reinforced by positive outcomes following aggressive behavior. There have been more recent theories proposed since then which have set out hypotheses regarding the distinct neurobiological bases of these two aggression subtypes. For instance, reactive aggression has been linked to orbitofrontal cortex dysfunction and impaired emotion regulation (Bechara et al., 2000; Blair and Cipolotti, 2000) while proactive aggression is thought to be associated with amygdala dysfunction and a diminished response to distress cues (Blair, 1995, 2005). Research has shown that proactive but not reactive aggression may be predictive of later delinquency, conduct problems and violent offending in mid-adolescence as well as criminal behavior later in life (Pulkkinen, 1996; Vitaro et al., 1998; Raine et al., 2006). Conversely, reactive aggression was found to predict impulsivity and hostility (Raine et al., 2006).

Thus, when investigating the association between CVE and conduct problems, it is not only necessary to parse out effects of aggression but also to examine the role of each of these aggression subtypes separately. To date, it remains to be investigated how the relationship between recent CVE and current conduct problems may differ according to aggression subtypes. One possibility is that greater violence exposure is associated with more proactive aggression, perhaps because such exposure normalizes violence or leads to a desensitization to the effects of violence. More proactively aggressive children and adolescents, in turn, may intentionally choose to enter violent situations. Another possibility is that greater violence exposure is associated with more reactive aggression, possibly due to its effects on sensitivity to threat or even the neural circuits implicated in reactive aggression. Individuals with high levels of reactive aggression may, in turn, act out aggressively in response to CVE.

In summary, many studies have shown that there is a strong association between CVE and conduct problems. However, to date no study has investigated this association separately in children and adolescents with a diagnosis of CD and a sample exclusively made up of healthy controls to examine the deleterious effects of CVE separately in high and low-risk groups. Finally, the literature has not differentiated between reactive and proactive forms of aggression in terms of possible mediators of the association between CVE and conduct problems. We know that the relationship between CVE and aggression still holds when controlling for levels of prior aggression. Understanding how

different types of aggression (i.e., reactive vs. proactive) may explain the link between CVE and conduct problems within healthy controls vs. children and adolescents with CD might be important for further specifying etiological models.

We had the following hypotheses:

1. We expected to observe a strong association between recent CVE and current conduct problems in children and adolescents with CD as well as in healthy controls.
2. This relationship between CVE and current conduct problems was expected to hold, even when accounting for effects of aggression subtypes.
3. We tested (exploratively) whether the association between CVE and conduct problems is primarily mediated by proactive or reactive aggression in children and adolescents with CD and healthy controls.
4. We expected increased age, lower SES and male gender to be linked to greater rates of CVE as well as conduct problems in both groups.

MATERIALS AND METHODS

This study was conducted within the framework of the ongoing European multi-disciplinary FP7 (i.e., European Commission's 7th Framework Health program) project ''Neurobiology and Treatment of Adolescent Female Conduct Disorder: The Central Role of Emotion Processing'' (FemNAT-CD). A detailed outline of the methodological aspects of the project is available on the official website (www.femnat-cd.eu). Assessments were conducted at clinical sites from seven European countries: Germany, Greece, Hungary, Netherlands, Spain, Switzerland and the UK.

Participants

Child and adolescent participants between the ages of 9 and 18 years were recruited through various means, including distribution of study information in schools, sports and leisure clubs, through street promotion and contacts with psychiatric clinics, youth offending services, or youth welfare institutions.

The inclusion criterion for the CD sample was a current diagnosis of CD according to DSM-IV-TR criteria (American Psychiatric Association, 2000). Exclusion criteria for both CD and control groups were a history and/or current diagnosis of autism spectrum disorder, schizophrenia, bipolar disorder or mania, fetal alcohol syndrome (all according to DSM-IV-TR), any known monogenetic disorders, chronic or acute neurological disorders, severe medical conditions or valid indications of an IQ < 70 (measured with the vocabulary and block design subtests of the Wechsler Intelligence Scale for

Children (WISC) or vocabulary and matrix reasoning subtests of the Wechsler Adult Intelligence Scale (WAIS; Wechsler, 2008) depending on the participant's age; at UK sites, the Wechsler Abbreviated Scale of Intelligence was used for all ages (Wechsler, 1999). Additional exclusion criteria for healthy controls included any other current disorder according to DSM-IV-TR criteria as well as a past history of Attention-Deficit/Hyperactivity Disorder, Oppositional Defiant Disorder or CD.

From the current study sample, 1178 children and adolescents had complete data on all key measures and thus were included in the present analysis. Consistent with the aim of the study to over-recruit female participants, there were more females than males (62 vs. 38%) and slightly more than half of the overall sample was healthy controls (56%). The number of male children and adolescents was spread evenly across CD and control subjects (50% each). With regard to females, there were slightly more controls than CD subjects (60 vs. 40%). Comparison of the CD and control groups suggested that children and adolescents with CD were significantly older than controls (*M* age CD = 14.4, *SD* = 2.3 vs. *M* age controls = 13.9, *SD* = 2.6, $t = 3.63$, $p < 0.001$) and were characterized by significantly lower SES (*M* SES CD = 0.3, *SD* = 0.9 vs. *M* SES controls = 0.3, *SD* = 1.0, $t = 9.36$, $p < 0.001$).

Procedure

Participants and their legal guardians received detailed study information via telephone, mail or email prior to the day of assessment. On the first assessment day, participants were given the opportunity to ask questions and it was assured that both parent/legal guardian and children knew that participation could be declined or stopped at any point during the course of the study. Written informed consent was obtained from the participants and their legal guardians. If consent of the legal guardian was unavailable, participants were included only if considered old enough according to the ethical requirements of the respective country (i.e., 16 in Switzerland and UK, 18 all else). Research was carried out in compliance with the fundamental ethical principles as stated by the Declaration of Helsinki and its later amendments as well as with the ethical standards of the institutional and/or national research committee. All subjects and legal guardians gave written informed consent in accordance with the Declaration of Helsinki. If it was not possible to obtain consent from the legal guardian, participants were included only if considered old enough to provide informed consent according to the ethical requirements of the respective country (i.e., <=16 years in Switzerland and the UK, <=18 years in all other countries). Ethical approval was obtained from all local ethics committees (Basel—Ethikkommission Nordwest- und Zentralschweiz, Frankfurt—Ethik-Kommission Fachbereich Medizin Klinikum der Johann Wolfgang Goethe-Universität, Aachen—Ethik-Kommission an der medizinischen Fakultät der rheinisch-westfälischen technischen Hochschule Aachen, Amsterdam—Medisch Ethische Toetsingscommissie Vrije Universiteit Medisch Centrum,

Birmingham and Southampton—NHS Research Ethics Committee, Bilbao—Comite Etico de Investigacion Hospital Universitario Basurto, Barcelona—Comite Etico de Investigacion Clinica Parc de Salut Mar, Szeged—Human Reproduction Committee, Athens—Ethics Committee of Aiginiteio University Hospital of Athens).

In order to obtain information on mental health problems, semi-structured interviews were conducted with the children/adolescents and, if available, with their legal guardian in separate rooms/consecutively by trained, postgraduate-level investigators. Information obtained from both interviews was then combined to obtain a final summary judgment. Questionnaires assessing CVE were handed to the participant subsequent to the interview. Investigators were available to provide help to participants and clarify the meaning of items if requested. In line with the ethics committees' decision for the respective universities, participants were compensated with a gift card or a small monetary payment.

Measures

Community Violence Exposure. Initially developed by Richters and Saltzman (1990), and modified by Schwab-Stone et al. (1995, 1999) and Ruchkin et al. (2004), two scales of the Social And Health Assessment (Weissberg et al., 1991) assessing direct victimization as well as the witnessing of violence in the community, served as the measure of CVE. For the victimization scale, seven items assessed how often in the past year participants had been: (1) beaten up or mugged; (2) threatened with serious physical harm by someone; (3) threatened because of their race/ethnicity; (4) shot or shot at with a gun; (5) attacked or stabbed with a knife; (6) chased by gangs or individuals; or (7) seriously wounded in an incident of violence. Participants reported their answer on a 5-point Likert scale from 0 (never), 1 (1–2 times), 2 (3–5 times), 3 (6–9 times) to 4 (10 times or more). The witnessing scale included seven items asking the respondents how frequently they had seen someone else being exposed to the same violent acts in their community within the past year on the same 5-point Likert scale as described above. The two scales were found to have good psychometric properties in a sample of American inner-city youth (Richters and Martinez, 1993). With respect to our sample, the witnessing subscale produced a Cronbach's alpha of 0.89 for cases and 0.77 for controls, i.e., good/satisfactory internal consistency respectively. The victimization subscale resulted in an alpha of 0.81 for cases and 0.67 for controls indicating good/questionable internal validity (Bland and Altman, 1997).

Conduct Problems. The Kiddie Schedule for Affective Disorders and Schizophrenia—Present and Lifetime (K-SADS-PL; Kaufman et al., 1997) is a semi-structured diagnostic interview used to screen

for the current presence or lifetime history of a broad range of disorders ranging from affective disorders (i.e., depression, bipolar disorder), schizophrenia and substance use disorders through to externalizing disorders (i.e., CD, ADHD). The K-SADS-PL is administered independently to the adolescent as well as their caretaker to assess the presence of DSM-IV-TR psychiatric disorders (for this study, the CD present section was used). Summary ratings are derived from clinical judgment using both interview sources as well as other information available on file. The items of the instrument are scored on a scale from 0 to 3. A rating of 0 indicates no (insufficient) information, a score of 1 indicates a given symptom is not present, 2 indicates a subclinical expression, while a score of 3 is given when a symptom is present and clinically significant. Scores were recoded, so that a clinical rating of ''not present'' is represented by 0, a subclinical rating by a score of 1, and a clinically significant rating by a score of 2. Unknown ratings were recoded into missing data. For the purpose of the current study, mean item scores were calculated for CD based on the current summary ratings. That is, a mean score was calculated across all CD symptoms for each individual. This procedure allowed inspection of current conduct problems at the *symptom-level* and therefore represented a more comprehensive estimation of problematic behavior symptoms with regard to the healthy control group. In other words, conduct problems were assessed on a dimensional level including subclinical expressions to assess the association between CVE and conduct problems. Inter-rater reliability for the K-SADS-PL section used was based on 75 CD individuals and found to be almost perfect with a percentage agreement of 94.67 and Cohen's k of 0.907 (95% *CI*: 0.819–0.995; Landis and Koch, 1977).

Aggression Subtypes. Developed by Raine et al. (2006), the Reactive-Proactive aggression Questionnaire (RPQ) measures self-reported reactive (11 items, e.g., ''I have damaged things because I felt mad'', ''I have gotten angry when frustrated'', ''I have had temper tantrums'') and proactive (12 items, e.g., ''I have had fights to show that I was on top'', ''I have vandalized something for fun'', ''I have gotten others to gang up on someone'') aggression. Each item is answered on a 3-point Likert scale (0 = never, 1 = sometimes, 2 = often). The two scales were found to have good internal validity (0.84 for reactive, 0.86 for proactive aggression) in its original evaluation study comprising a sample of American school boys (Raine et al., 2006). Further validation studies in several countries have subsequently confirmed reliability and validity across the genders and various populations (e.g., different age groups, non-offender vs. criminal samples; Fossati et al., 2009; Fung et al., 2009; Cima et al., 2013). With regard to the present sample, Cronbach's alpha was 0.84 for adolescents with CD and 0.79 for controls for the reactive aggression subscale indicating good to satisfactory internal consistency. The proactive subscale yielded estimates of 0.85 for adolescents with CD and 0.67 for controls indicating good/questionable internal consistency (Bland and Altman, 1997).

Socioeconomic Status. SES was calculated based on parental income, education as well as occupational status. Classifications were made using the International Classification of Education (UNESCO Institute for Statistics, 2015) and the International Standard Classification of Occupations (International Labour Organization, 2012). Human rater and computer-based ratings were combined into a standardized factor (M = 0, SD = 1) score using Principal Component Analysis. Internal consistency of the composite SES score was acceptable (a = 0.74). Due to potential economic variation on the country level, SES was centered and scaled within each country, in order to obtain an indicator of relative socioeconomic position.

Data Analysis

The data were analyzed using the Statistical Package for Social Sciences (SPSS-23; IBM Corp, 2016, Armonk, NY, USA), Analysis of Moment Structures (AMOS-23; Arbuckle, 2014) and R (R Core Team, 2013) with the packages ''plot3D'', ''ggplot2'' and ''localgauss''. For descriptive results sample mean scores were calculated for witnessing, victimization, conduct problems, reactive and proactive aggression measures to characterize the two groups. Furthermore, Mann-Whitney-U tests and two-sample sample *t*-tests were calculated to gain more insight into group differences. Local Gaussian correlations and 2-D plots were computed to approximate density functions and obtain further insight into the distribution of CVE and conduct problems within the two groups. Structural equation modeling (SEM) was used for analyzing the primary models since it allowed us to compare the model fit of successively nested models with each other. In all SEM models age, gender, site and SES were used as control variables. For the final model age, gender and SES were inspected as moderating variables, while site served as a control variable.

Analyses were conducted on two different CVE constructs: (1) witnessing violence was examined as a latent variable by parceling the seven items comprising this scale into three indicators; (2) using the same procedure, victimization was inspected separately as well. Through the use of latent variables, we were able to reduce measurement errors and improve the accuracy of the findings (Little et al., 1999). The method of parceling was chosen in order to overcome low communality and reliability frequently encountered with the use of individual items and to decrease the likelihood for distributional violations (Little et al., 1999, 2002). Items were grouped into parcels based on item-total correlations (Little et al., 1999, 2002). Items with highest and lowest item-total correlations were grouped together, resulting in two groups with two items and one group with three items (see Table 1 for detailed list of parcel composition). The parceled indicators loaded well on their respective factors with loadings ranging between 0.59 and 0.88 (see Table 1).

TABLE 1 | Parcel composition and standardized loadings of parceled indicators by group.

	Witnessing items	Victimization items	Witnessing loading (CD/Control)	Victimization loading (CD/Control)
Parcel 1	Beat up Gun shot Discrimination	Beat up Gun shot Discrimination	0.88/0.65	0.85/0.68
Parcel 2	Chasing Threats	Chasing Knife attack	0.84/0.88	0.75/0.63
Parcel 3	Knife attack Serious wound	Threats Serious wound	0.85/0.87	0.81/0.59

Chi-square, the Root Mean Square Error of Approximation (RMSEA; Browne and Cudeck, 1993) and the Comparative Fit Index (CFI; Bentler, 1990) were used as indicators of goodness of fit. While for the commonly employed Chi-Square test greater (insignificant) *p*-values generally indicate better fit, the RMSEA requires values of 0.05 or less and CFI values of 0.95 or greater to consider a model to be of acceptable fit (Bentler, 1990; Browne and Cudeck, 1993).

To test the mediation hypotheses, change in model fit when direct paths from CVE to conduct problems were removed was assessed controlling for site and moderating effects of age, SES and gender (Holmbeck, 1997). Additionally, the magnitude of the indirect effects of CVE on conduct problems via reactive or proactive aggression was estimated (Holmbeck, 1997). For the group comparison, a series of up to four models were examined for cases and controls separately, including comparisons between an exploratory model in which all paths between the variables were free to vary for each group. This model served to pinpoint the variables of interest for each group. Then, a fully constrained model was examined, in which all primary paths were set as equal for both groups. Consequently, the second model hypothesized no group differences for all associations/paths. If this model was true, constraining the paths to the same value should not significantly decrease the overall model fit (as compared to the first model). If indicated (i.e., if second model significantly decreased model fit) a third model, in which some selected paths were non-constrained, was inspected. These selected paths were identified by re-examining the paths of the first model and selecting potentially different associations between patients and controls. The selected paths were unconstrained and allowed to differ by group. If the model fit significantly improved compared to the second model (and was not worse than that for the first model), it would suggest the presence of group differences in the model. A final select model would then be produced in which all insignificant paths are deleted and again compared against the model fit of the previous model.

RESULTS

Descriptive Analyses

Children and adolescents with CD reported significantly greater CVE within the past year than healthy controls for both witnessing violence, $U = 88840$, $p < 0.001$ (*M* witnessing CD = 0.62, *SD* = 0.75 vs. *M* witnessing controls = 0.13, *SD* = 0.29) and victimization, $U = 97557$, $p < 0.001$ (*M* victimization CD = 0.28, *SD* = 0.46 vs. *M* victimization controls = 0.03, *SD* = 0.11; see **Figure 1**). As healthy controls rarely reported victimization events within the past year, only the witnessing violence subscale of the SAHA was included in all further analyses. In both groups the distribution of CVE was skewed as many individuals reported zero to low frequency of exposure within the past year. **Table 2** presents the means and prevalence rates (i.e., the percentage of individuals having experienced the respective item at least once within the past year) of each witnessing item by group and shows that children and adolescents with CD experienced all of the listed events to a much greater extent than their healthy counterparts. Supplementary Table S1 (presented in Supplementary Material) shows the exact percentage of endorsed frequencies within the past year by group. In both groups, ''threats with physical harm'' was the most frequently endorsed form of violence exposure (49.5% vs. 16.0%), while ''getting shot'' was the least frequently encountered event (12.2% vs. 0.9%) by children and adolescents with CD and healthy controls, respectively. In addition, means and standard deviations for reactive and proactive aggression are presented in Table 2.

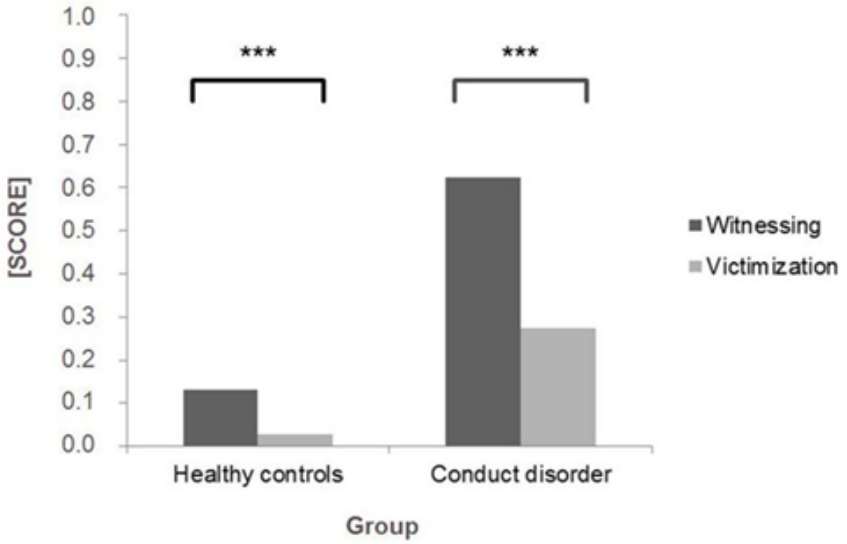

FIGURE 1 | Mean scores (with a possible range of 0–4) for SAHA witnessing violence and victimization subscales within the past year reported by healthy controls (n = 662) and children and adolescents with conduct disorder (CD; n = 516). $p < 0.001$.

TABLE 2 | SAHA witnessing subscale items and reactive and proactive aggression questionnaire mean scores by group.

Witnessing item	*CD* (*N* = 516) Mean (% endorsed yes)	*Controls* (*N* = 662) Mean (% endorsed yes)
In the past year, have you seen someone else: : :		
1. Being chased by gangs/individuals	0.73 (45.0)	0.16 (12.6)
2. Get threatened with serious physical harm	0.99 (55.1)	0.21 (16.4)
3. Getting beaten up/mugged	0.84 (47.4)	0.18 (14.0)
4. Being attacked/stabbed with a knife	0.43 (28.6)	0.05 (4.4)
5. Seriously wounded after an incident of violence	0.60 (38.0)	0.12 (9.6)
6. Getting shot/shot at with a gun	0.18 (13.6)	0.02 (0.9)
7. Getting threatened/harmed for their race/ethnicity	0.61 (34.3)	0.16 (12.5)
Reactive aggression	1.07 (0.46[1])	0.50 (0.33[1])
Proactive aggression	0.38 (0.38[1])	0.10 (0.13[1])

[1]Values represent corresponding standard deviations.

Figures 2A,C shows a broader range of witnessed violence for adolescents with CD than for healthy controls, although high values for witnessing are rare amongst both groups. For controls, recent witnessing and current conduct problems have a highly left-skewed distribution, since most individuals have low current conduct problems and low frequency of recent exposure to witnessed violence. For adolescents with CD, current conduct problems are more normally distributed (Figure 2C). Figure 2B shows that for both adolescents with CD and healthy controls a positive linear trend (green line) between recent witnessing and current conduct problems can be observed. Testing the significance of the association of CVE and conduct problems between groups in a SEM model, while controlling for site effects as well as the moderating effects of age, gender and SES indeed revealed significant associations for both groups (CD: beta = 0.36, $p < 0.001$; and controls: beta = 0.20, $p < 0.001$). A Loess fitting function (red line) shows that the fit line flattens or even becomes slightly negative in the higher range of current conduct problems or witnessing violence. This finding can be corroborated assessing local Gaussian parameters (Figure 2D): Local Gaussian parameters show a positive trend across the whole spectrum of current conduct problems/witnessing violence, whereas in the higher range of both variables, the association becomes neutral (white) or even negative (purple). These findings indicate a ‘‘ceiling’’ effect, i.e., that beyond a high level of current conduct problems, witnessing violence is not able to increase the level of symptoms, and vice versa.

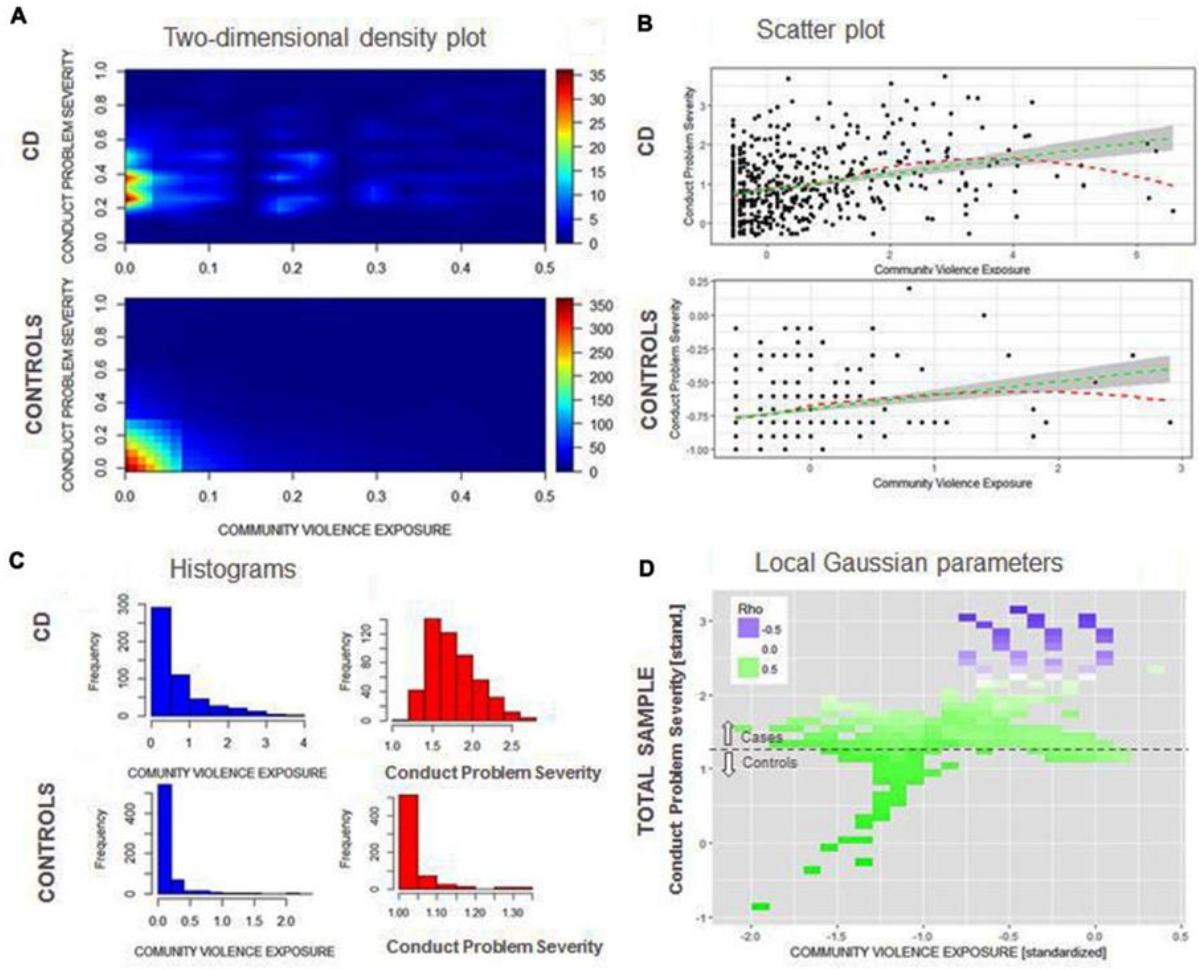

FIGURE 2 | (A) Two-dimensional density plot for community violence exposure (CVE; x-axis) and current conduct problems (y-axis) for adolescents with CD (top) and healthy controls (bottom) using plot3D. **(B)** Scatterplot and linear (green) and loess (red) regression line for CVE (x-axis) and conduct problems (y-axis) for adolescents with CD (top) and controls (bottom) ggplot2. **(C)** Histograms for both CVE and current conduct problems for adolescents with CD and controls. **(D)** Stability of the correlation between CVE and current conduct problems along the range of both variables (high correlations = green; low correlations = purple) using {localgauss}.

Mediation Analysis of Reactive and Proactive Aggression in the Overall Sample

Reactive and proactive aggression partially mediated the relationship between witnessing community violence and conduct problems. Mediation was tested by a 1 *df* Chi-Square change test of the model with and without estimating direct paths from witnessing community violence to conduct problems (also refer to Table 3, ''Introduction'' section). The model fit changed significantly after deleting the respective path: χ^2 (19) = 152.21, $p < 0.001$; RMSEA = 0.075, CI = 0.064 - 0.086; CFI = 0.969; change in χ^2 (1) = 64.46, $p < 0.001$, suggesting that reactive and proactive aggression were not acting as full mediators. In order to assess partial mediation further, the path between witnessing community violence and conduct problems was constrained to the regression weight of a direct

effects model. A significant change in model fit (χ^2 (19) = 241.75; RMSEA = 0.097, CI = 0.086 - 0.108; CFI = 0.948; change in χ^2 (1) = 154.00; p < 0.001) supported partial mediation. The association between witnessing community violence and conduct problems (i.e., the path coefficient) still remained highly significant (beta = 0.25, p < 0.001) even when accounting for the indirect effects of proactive and reactive aggression.

TABLE 3 | Fit statistics for all models.

Measure/Model	χ^2 (df)	RMSEA	CFI
1. Mediation			
All paths free			
Overall sample			
1.1 No direct path[3]	152.21 (19)	0.075 (0.064; 0.086)	0.969
1.2 Total effects[4]	87.75 (18)	0.056 (0.044; 0.067)	0.984
Change in fit 1.1–1.2	130.81 (1), p < 0.001		
2. Mediation			
Multilevel Analysis[1]			
All paths free			
2.1 No direct path[3]	156.08 (38)	0.051 (0.043; 0.060)	0.953
2.2 Total effects[4]	129.88 (36)	0.047 (0.038; 0.056)	0.963
Change in fit 2.1–2.2	26.2 (12), p < 0.001		
All primary paths equated across group[2]			
2.3 Total effects[4]	188.07 (41)	0.054 (0.046; 0.061)	0.942
Change in fit 2.3–2.2	58.19 (5), p < 0.001		
Selected paths free			
2.4 Total effects[4]	130.78 (37)	0.045 (0.037; 0.053)	0.963
Change in fit 2.4–2.2	0.9 (1), n.s.		
Selected paths free, insignificant paths deleted			
2.5 Total effects[4]	146.25 (51)	0.039 (0.031; 0.046)	0.962
Change in fit 2.5–2.4	15.47 (14), n.s.		

[1]Refers to the two-group analysis, i.e., CD and controls analyzed separately; [2]assumption of no group differences; [3]full mediation model; [4]partial mediation model.

Proactive and reactive aggression as mediators between CVE and conduct problems in adolescents with conduct disorder and healthy controls

A multilevel analysis examining the mediating effects of reactive and proactive aggression on the association between witnessing community violence and conduct problems separately within children and adolescents with CD and healthy controls, and controlling for site and moderating effects of SES, age and gender revealed partly differential effects of aggression subtypes between groups.

When examining the impact of witnessing violence, we followed a series of models to determine the best explanatory model (see Method section above). A first unconstrained model fit the data well (see Table 3, Section 2). A constrained model significantly decreased model fit, indicating that there

were at least some differences in the model paths between adolescents with CD and controls (χ^2 (41) = 188.07, p < 0.001; RMSEA = 0.054, CI = 0.046 - 0.061; CFI = 0.942; change in χ^2 (5) = 58.19, p < 0.001). Re-examination of the first model and chi-square change tests confirmed significant increases in model fit when compared to the constrained model for all primary paths except for the path between reactive aggression and witnessing violence (1. path between witnessing violence and conduct problems: χ^2 (40) = 174.27, p < 0.001; RMSEA = 0.052, CI = 0.044 - 0.060; CFI = 0.947; change in χ^2 (1) = 13.80, *p* < 0.001; 2. path between reactive aggression and conduct problems: X^2(40) = 165.06, p < 0.001; RMSEA = 0.050, CI = 0.042 - 0.058; CFI = 0.951; change in χ^2 (1) = 23.01, *p* < 0.001; 3. path between proactive aggression and conduct problems: χ^2 (40) = 150.99, p < 0.001; RMSEA = 0.047, CI = 0.039 - 0.055; CFI = 0.956; change in χ^2 (1) = 37.08, *p* < 0.001; 4. path between proactive aggression and witnessing violence: χ^2 (40) = 184.18, p < 0.001; RMSEA = 0.054, CI = 0.046 - 0.062; CFI = 0.943; change in χ^2 (1) = 3.89, *p* < 0.05). Therefore, all other paths were unconstrained in a selected-paths-free model. This select model fit the data significantly better than the constrained model (χ^2 (37) = 130.78, p < 0.001; RMSEA = 0.045, CI = 0.037 - .053; CFI = 0.963; change in χ^2 (4) = 57.29, p < 0.001). Further, the select model did not significantly decrease model fit compared to the unconstrained model (change in χ^2 (1) = 0.9, *n.s.*). In a final step, all non-significant paths were deleted. The fit of this final model was not significantly worse than that of the select model (change in χ^2 (14) = 15.47, *n.s.*). Therefore, Figure 3 contains the standardized path coefficients from the final, most parsimonious model.

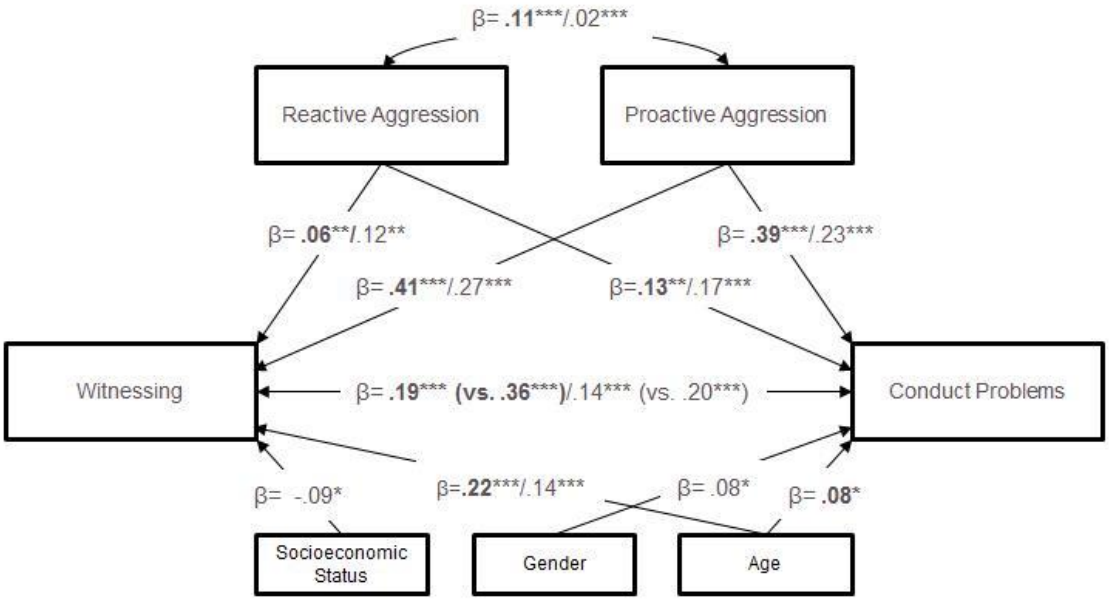

FIGURE 3 | Standardized path coefficients of mediation analysis by group. Note: results for CD group are displayed in bold, with those for the control group presented in normal font; coefficients in brackets represent the direct path model (analyses were controlled for site); only significant coefficients are displayed. p < 0.001; p < 0.01; p < 0.05.

Across groups, the coefficients demonstrate a partial mediation effect. Further, in both groups both aggression subtypes had a significant impact on the association between witnessing violence and conduct problems, however, proactive aggression showed a stronger effect. Between groups, children and adolescents with CD showed a significantly stronger link between witnessing violence, proactive aggression and conduct problems compared to controls.

Furthermore, moderating effects of age, gender and SES were considered. Across groups, age played a significantly moderating role with regard to witnessing violence, such that older individuals tended to witness more violent events (CD: beta = 0.22, $p < 0.001$; controls: beta = 0.14, $p < 0.001$). In addition, older children and adolescents with CD showed significantly more conduct problems compared to their younger counterparts (beta = 0.08, $p < 0.05$). With regard to gender, male controls witnessed significantly more violence than female controls (beta = 0.08, $p < 0.05$). Finally, controls with a lower SES tended to show significantly more conduct problems than control subjects with a higher SES background (beta = -0.09, $p < 0.05$).

DISCUSSION

The present study demonstrated that recent witnessing of community violence is strongly positively associated with levels of current conduct problems in both children and adolescents with CD as well as healthy controls. Furthermore, the association between witnessing community violence and conduct problems remained significant in both groups even when including aggression subtypes (i.e., reactive/proactive aggression) as mediators in the model while controlling for the moderating effects of SES, gender and age and accounting for site effects. Proactive aggression had a stronger impact on the association between witnessing community violence and conduct problems than reactive aggression in both children and adolescents with CD and controls. When comparing the two groups, proactive aggression accounted for a greater proportion of the relationship between witnessing violence and conduct problems in children and adolescents with CD. Increased age was associated with greater rates of witnessing violence in both groups, while it was additionally associated with greater conduct problems in adolescents with CD. For controls, a lower SES was associated with greater conduct problems and being male was associated with greater exposure to witnessed violence. As such, the results of the present study are in line with findings on the well-established link between CVE and conduct problems, and extend the existing literature by demonstrating that: (1) the association between recent witnessing and current conduct problems is strongly detectable even in a group with a formal diagnosis of CD as well as a group with no clinical impairments; (2) the

associations between recent witnessing of violence and current conduct problems persist even when accounting for reactive/proactive aggression across adolescents with CD and healthy controls; (3) the association between recent witnessing of violence and current conduct problems is primarily explained by proactive aggression across the two groups. Thus, the present study highlights the importance of not only taking into account early childhood risk factors known to predict the development of conduct problems and CD (Loeber et al., 2009; Bernhard et al., 2016), but also focusing on current factors in the young person's life, such as witnessing community violence, that are likely to maintain or exacerbate conduct problems.

The present study indicates that a strong association between recent witnessing of violence and current conduct problems exists even in groups characterized by the absence of any clinically significant impairment or the presence of CD. Past studies have never investigated the relationship between CVE and conduct problems in an exclusively healthy population nor in an adolescent sample with CD. The fact that current findings indicate a robust positive association in both groups allows us to reject the possibility of an ecological fallacy due to potential confounding effects within community samples comprising a mixture of healthy and clinically impaired adolescents.

Furthermore, the present finding that recent witnessing of community violence has a strong impact on current conduct problems in children and adolescents with CD as well extends the results of studies suggesting that greater levels of violence exposure and high levels of conduct problems tend to co-occur (Sanchez et al., 2013; Cecil et al., 2014; Voisin et al., 2016). Results of a longitudinal study indicated bi-directional effects between CVE and conduct problems, suggesting a downward spiral (Mrug and Windle, 2009). The present finding of a strong association for children and adolescents with CD might point to a similar pattern. However, findings also underline that in the presence of a high rate of CVE as well as severe levels of conduct problems, eventually a ceiling effect sets in, where the strength of association between the two variables is reduced or even becomes negative. Gaylord-Harden et al. (2017) specifically investigated the cumulative impact of CVE on psychopathology in a male adolescent community sample. CVE was found to show a curvilinear relationship with internalizing problems and a positive linear relationship with violent behavior. Present findings suggest that in the case of an extremely violent group with high levels of CVE at baseline, effects of CVE on subsequent violent behavior may be much smaller due to ceiling effects.

Self-reported proactive and reactive aggression subtypes did not fully explain the link between recent witnessing of community violence and current conduct problems for children and adolescents with CD as well as for healthy controls. As such, the present findings are in line with studies indicating

persisting effects of CVE on conduct problems when controlling for baseline levels of aggression (Schwab-Stone et al., 1995; Farrell and Bruce, 1997; Miller et al., 1999; McCabe et al., 2005; Weaver et al., 2008). Specifically, the finding that the association between witnessing violence and conduct problems remains when controlling for aggression subtypes suggests that it is not just the CD individual's own level of reactive/proactive aggression that explains the link between witnessing community violence and conduct problems.

Furthermore, results of the present study showed that, for both groups, proactive aggression had a stronger mediational effect on the link between witnessing violence and conduct problems than reactive aggression. This finding aligns with studies on chronic CVE and associated desensitization processes (i.e., emotional numbing and use of aggression increasingly being seen as acceptable) resulting in higher levels of externalizing behavior (Ng-Mak et al., 2004; Boxer et al., 2008; Mrug et al., 2016; Gaylord-Harden et al., 2017). Translating these findings to the present study, one might expect that those children and adolescents witnessing more violence in their neighborhoods may have also undergone desensitization processes that have led them to become more proactively aggressive. In turn, these desensitized children and adolescents might also more readily seek out situations where violence is likely to occur or commit acts of violence which they also ''witness''.

Reactive aggression, on the other hand, explained less of the association between witnessing violence and conduct problems than proactive aggression. In addition, the mediating effects of reactive aggression on the relationship between witnessing violence and conduct problems were similar in children and adolescents with CD and healthy controls. This result is surprising in the context of studies that have identified impulsivity as a correlate and predictor of CVE (Lambert et al., 2010) as well as of studies that have identified impulsivity as a relevant moderator of the effects of CVE on adolescent deviant behavior (Low and Espelage, 2014). However, Monahan et al. (2015) previously suggested that declines in impulse-control happen only in response to *increases* in CVE rates independent of an individual's baseline rate (Monahan et al., 2015). While we have not directly investigated this, the impact of differences in CVE exposure rates over time (e.g., a change that might occur if one moves from a high to a low violence neighborhood) is something that should be considered in future studies. Furthermore, the current findings could partly be explained by the *type* of CVE assessed. Studies have shown that as the proximity of the exposure increases, the effects on emotional distress and internalizing symptoms increase as well (Fowler et al., 2009). Compared to direct victimization, witnessing community violence might evoke less emotional arousal and thus less of a response due to the more distal nature of the exposure. Individuals might feel less personally involved and are thereby less likely to act out in response.

Finally, consistent with the literature (Fowler et al., 2009), older adolescents in both groups tended to witness more violent events compared to their younger counterparts. In addition, older adolescents with CD showed more conduct problems than children. This finding aligns with studies identifying adolescence as the peak time for the majority of referrals to child and adolescent psychiatric clinics (Loeber et al., 2000) and studies that show that self-reported rates of violent offending are highest at age 16–17 years (Elliott, 1994). For controls, being male was linked to greater exposure to violence, while coming from a lower SES background was associated with greater conduct problems. Both findings have been demonstrated previously (Anderson et al., 2001; Buka et al., 2001; Javdani et al., 2014). The fact that gender and SES exerted no influence on levels of CVE and conduct problems for children and adolescents with CD might be based on the fact that the group represents a homogenous group. That is, children and adolescents with CD came from lower than average SES strata and the females within this group exhibited clinically significant levels of conduct problems. Furthermore, all children and adolescents with CD were exposed to some level of CVE and displayed some level of conduct problems by definition. As such, gender and SES would be expected to have less impact in this population compared to a more representative sample.

Strengths and Limitations

While this study adds to our understanding of the specific associations and mediation effects regarding the link between CVE and conduct problems, it remains a snapshot of the sample's situation at the time of assessment, i.e., a cross-sectional investigation. Hence, it is limited when it comes to exploring pathways of CVE to conduct problems as well as the long-term or cumulative effects of CVE. Consequently, it cannot shed light on whether CVE and/or reactive/proactive aggression precede the development of conduct problems or emerge as a consequence of conduct problems. Future studies using longitudinal designs will be able to shed more light on the consequences and persistence of such effects. Furthermore, it has been shown that cross-sectional approaches to mediation may result in misleading estimates (Maxwell et al., 2011). Again, it would be more valid to apply the present mediation models to data collected as part of a longitudinal study with repeated measurements of CVE, conduct problems and aggression subtypes.

Due to very low victimization rates in healthy children and adolescents, here we only focused on witnessing community violence. Fowler et al. (2009) concluded that witnessing and victimization were equally predictive of externalizing behaviors. Nevertheless, it would have been interesting to

see whether reactive aggression might play a greater role in mediating the association between direct victimization and conduct problems.

In the present study, only age, gender and SES were considered as additional moderators. Aside from these variables, some additional important factors identified in previous research have been family structure, school characteristics and peer relationships (Buka et al., 2001; Chen et al., 2016). These variables present further risk or protective factors in the relationship between CVE and psychopathology but were unavailable to the authors. Future studies should therefore take these moderators into account when analyzing differences between children and adolescents with CD and healthy controls.

Finally, information obtained with regard to CVE and aggression subtypes relied on self-report data and may have been subject to social desirability effects (e.g., respondents exaggerating the extent of community violence in their neighborhoods to sound tough). Particularly with regard to CVE, past studies have found differences between informants, with parents reporting lower CVE rates for their offspring than the adolescents themselves (Kuo et al., 2000). As the present sample was mostly comprised of adolescents, it seemed safer to rely on self-report data in order to avoid potential under-reporting.

Despite these limitations, the present study is the first to systematically investigate and disentangle the effects of witnessing community violence and conduct problems in a clinical population (i.e., children and adolescents with CD) and a healthy population. As such, it is the first study to demonstrate that recent witnessing is related to current conduct problems in an exclusively healthy sample as well as in children and adolescents with CD even when taking their levels of reactive/proactive aggression into account. Further, this study is the first to illustrate that *recent* CVE is associated with the level of current conduct problems and therefore may play a role in the development or maintenance of conduct problems even for those with pre-existing externalizing behavior.

Implications

An important implication for etiological models of the development of conduct problems is that neighborhood violence might be an important contributing factor, for healthy youths and particularly for children and adolescents with CD. From a clinical perspective, the strong association between witnessing community violence and conduct problems highlights the need for prevention and/or

intervention strategies, as the relationship between the two variables is likely to intensify over time. The present results emphasize the need to consider recent CVE in addition to early risk factors. Correspondingly, it has been demonstrated that multimodal intervention programs with an additional focus on the adolescent's environment (e.g., Multi-systemic Therapy, Multidimensional Family Therapy) are more effective in reducing conduct problems as opposed to programs that do not take an individual's environment into account (Weisz and Kazdin, 2010; National Collaborating Centre for Mental Health, Social Care Institute for Excellence, 2013).

An important direction for future research will be to test for relationships between CVE and conduct problems in young people with CD and controls using a longitudinal design. Based on the findings of Fowler et al. (2009), we know that the strongest relationships hold between lifetime measures of externalizing behavior and lifetime CVE illustrating the cumulative impact of CVE on conduct problems over time (Fowler et al., 2009).

CONCLUSION

Witnessing community violence is a highly prevalent experience for children and adolescents in Europe, and is strongly associated with the individual's level of current conduct problems, in healthy controls as well as in children and adolescents with CD. As such, the present study is able to show a robust relationship between recent CVE and conduct problems not only in a clinically impaired sample but also in a healthy group, thereby reducing the possibility that previously reported associations between these variables were explained by an ecological fallacy. Furthermore, the present study demonstrates a strong association between recent CVE and current conduct problems, which is primarily mediated by proactive aggression. The challenge for the future lies in breaking the dangerous cycle of young people being exposed to community violence, and going on to perpetrate violence against others as a result.

AUTHOR CONTRIBUTIONS

CMF coordinates the FemNAT-CD FP7 research project. DD, AH, AF-R, SADB, KK, BH-D, GF, CMF, AP, MK and CS designed the study and took over site-specific coordination of the FemNAT-CD FP7 research project. LK, MP, HO, RV, LJ, KA, AB, AM, KG-M, IP, AW, JCR, RC, RHB, LG, SB, MG, GK, MAG-T, ES-P, RD, HL, ZK, ABG, AS and RS recruited subjects and collected data. LK drafted the manuscript together with CS, NV and MS. NMR, MP, SADB, KK, GF, CMF, AP and MK helped in manuscript preparation and critically reviewed the article.

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SUPPLEMENTARY MATERIAL

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Chapter 3 - Evaluating START NOW: A Skills-Based Psychotherapy for Inmates of Correctional Systems

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Abstract

Objective: This study investigated whether higher attendance in a skills-based group therapy program designed for inmates was associated with fewer rule infractions as reflected in the number of disciplinary reports received in a state correctional system.

Methods: Administrative data were provided by the Connecticut Department of Correction and Correctional Managed Health Care at UConn Health, the system's health care organization. This was a retrospective cohort analysis of START NOW program participation events from 2010 through 2013 (N=946). Participants were adult male and female inmates, both sentenced and unsentenced, with and without recorded psychiatric diagnoses. The number of disciplinary reports was documented for up to six months after program participation. Incident rate ratios are pre-sentenced from zero-inflated negative binomial regression models. Predictive margins examined variation in the effect of sessions attended on disciplinary reports in the post-program period across security risk groups and primary psychiatric diagnosis groups.

Results: For each additional session of START NOW completed, a 5% reduction was noted in the incident rate of disciplinary reports. The effect of program participation was robust to all model considerations. Inmates with higher overall security scores appear to benefit most from program participation. The program was also found to be effective across primary psychiatric diagnosis classifications.

Conclusions: START NOW was shown to be an effective treatment option for reducing disciplinary infractions by inmates.

INTRODUCTION

The prevalence of impulse dysregulation and mental illness is high in correctional systems, with estimated rates of symptoms as high as 50% among U.S. detainees (1–3). In Connecticut, more than two in three newly incarcerated inmates meet criteria for at least one lifetime psychiatric illness (3). Emotional instability and episodes of aggression by inmates raise safety and adjustment concerns, including population management issues and increased recidivism risk (4). Personality, psychotic, and substance use disorders are prevalent among prisoners (5); these disorders are often linked to impulsivity and institutional violence (6–10). The presence of co-occurring mental and substance use disorders has been linked to future violence (11). In addition, many inmates who may not meet criteria for a psychiatric disorder may nevertheless lack adequate impulse and affect regulation and interpersonal skills requisite for adequate functioning, either in the community or in a correctional environment (4). This suggests that efforts designed to improve behavioral outcomes may need to include inmates irrespective of diagnosis or perceived need for mental health treatment. Evidence-based mental health treatments targeting the specific needs of incarcerated populations are currently very limited (12), and alternatives to current options could be of value to providers and custody staff alike.

Generally, there is support for cognitive-behavioral therapy (CBT) in the treatment of offenders (13, 14). CBT has been found to reduce recidivism rates (15). Dialectical behavior therapy is associated with positive outcomes, but it has not found broad correctional use because of its cost and care intensity (16–18). Other CBT approaches in correctional systems, such as Moral Reconation Therapy, Thinking for a Change, and Reasoning and Rehabilitation, have shown encouraging results (19–22). However, no therapy shows particular superiority over others, with clear room left for improvement (23, 24). Here we introduce a new option.

START NOW is an evidence-informed coping skills therapy designed for incarcerated individuals (25–27). A group therapy format is employed to optimize cost-effectiveness and offer participants a chance to provide feedback and support. A formative evaluation of START NOW in two prisons indicated high satisfaction rates among participants and reduced psychiatric hospitalization (25). An unpublished quasi-experimental study of an adaptation of START NOW in a residential community treatment program reported a dose-response effect for START NOW; attendance at each program session resulted in a 2% reduction in the odds of re-arrest and re-incarceration (26). The study reported here further investigated START NOW's effectiveness by examining whether greater

program participation was associated with fewer disciplinary reports in a large sample of incarcerated adults.

METHODS

Design and Data Sources

We conducted a retrospective cohort analysis of participants who entered the START NOW program from 2010 through 2013. Inclusion criteria were age 18 or older at program initiation and incarceration for at least one month after program participation. The number of disciplinary reports was measured up to six months after participation.

Data were collected from electronic administrative records maintained by the Connecticut Department of Correction (CDOC) and Correctional Managed Health Care at UConn Health. Data were linked by a common identifier, de-identified, and delivered to the study team. The study was approved by CDOC and by UConn Health's Institutional Review Board Panel 2, which maintains expertise on human subject protections for corrections populations.

Intervention

START NOW consists of 32 sessions in four units (foundational, emotion management, interpersonal, and future-focused skills) in a CBT framework as detailed elsewhere (25–27). Motivational interviewing and collaborative therapy engagement are theorized to enhance treatment adherence and effectiveness (26). A facilitator manual provides detailed instructions for each session. All participant material is written at a fifth-grade reading level or below. Jargon is avoided, and iconic visual imagery, along with repetition, is used throughout (26). START NOW was implemented in seven correctional facilities (one housing only female prisoners) and facilitated by formally trained master's- and doctorate-level clinicians with ongoing clinical supervision and fidelity monitoring. Fidelity monitoring was conducted by both the facilitator and the supervisor with structured instruments (26).

Population

The study population was all inmates (at least 18 years of age, of either sex, and of any race or ethnicity) who participated in START NOW between 2010 and 2013. Because an inmate could participate more than once, the unit of analysis was participation events, rather than individuals. Both sentenced and unsentenced inmates participated (Connecticut is one of six states currently with an integrated jail and prison system). Participation was not limited to inmates with a recorded

psychiatric diagnosis. Our analysis excluded participants with a CDOC-assigned overall security risk or mental health care need score of 5 (highest risk or highest need), because these inmates constituted a group too small to analyze as a distinct group and because they resided in inpatient psychiatric units and would not be permitted to participate in the group format. Inmates were referred by a mental health professional, case worker, or correctional officer, or they were self-referred. No restrictions on primary psychiatric diagnosis or history of infractions were placed on participation beyond exclusion of inmates in segregation. Initially, the data contained 1,112 records. After data cleaning, there were 946 participation events, representing 846 unique inmates.

Measurements

Number of disciplinary reports. The dependent variable was the count of disciplinary reports received up to six months after program participation. The CDOC sanctions inmates who commit offenses while in custody by issuing three classes of disciplinary reports ranging from A to C; A class offenses are the most serious (28). This study combined A and B class offenses and omitted petty offenses (C class) from analysis because petty offenses are unreliably recorded.

Time at risk after participation (that is, time during which disciplinary reports were subject to being counted) was restricted to no less than one month and up to six months. Setting boundaries in the post-period and allowing variation in time at risk were required to first ensure that there was a reasonable minimal time span to observe disciplinary infractions after participation and because inmates varied in time in custody after participation. As described below, our multivariate analysis accommodated variation in time at risk.

Number of sessions completed. The focal independent variable was a simple count of number of sessions completed.

Overall risk score. At admission, CDOC assigns inmates an overall risk score ranging from 1 to 5, which is periodically updated. CDOC classification staff assign a risk level through an evaluation of seven scoring criteria: escape profile, severity or violence of the current offense, history of violence, length of sentence, pending charges or detainers, discipline history, and gang membership (27). We tested whether the overall risk score reduced the effect of the number of sessions attended on the number of disciplinary reports and whether risk score groups varied in the effect of number of sessions attended.

Psychiatric diagnosis and comorbidity. The treating clinician enters psychiatric diagnoses (primary and co-occurring) into an electronic database. In this study, an inmate's primary diagnosis was classified into one of six groups: no diagnosis; personality disorder; substance use disorder; psychotic disorder; mood disorder; or anxiety, posttraumatic stress dis-order, or other diagnosis. We also evaluated the effect of the number of co-occurring diagnoses, a count that included the primary diagnosis. We investigated whether diagnosis and comorbidity attenuated the relationship between sessions attended and offense reports and whether primary diagnosis groups varied in the effect of the number of sessions attended.

Control variables. We adjusted estimates for the effects of sociodemographic factors. Race-ethnicity was a set of mutually exclusive dummy variables, including black, white, Hispanic and other, as recorded by the CDOC. Education was measured in years of school completed. Sex was a dummy variable (male=1). Age was measured in years at the time of program initiation.

Modeling variables. Number of days after program participation was a count of time at risk of receiving a disciplinary report in the post-program period and was used to adjust estimates in multivariate analyses. Number of CDOC admissions was a simple count of prior intakes, including the current admission. Number of admissions was used as a predictor to model excess zeros in the logistic portion of the two-part zero-inflated negative binomial (ZINB) model, with the reasoning that those with fewer admissions would have greater impulse control than those with more admissions and would thus be less likely to receive any disciplinary reports.

Data Analysis

In descriptive analyses, we calculated the range, mean, and standard deviation for age and all count variables as well as number and percentage for all categorical variables. Multivariate analysis employed ZINB models. Most observations (N=801 of 946) involved no disciplinary reports. ZINB is a two-part model that separately accounts for zero-inflation via logistic regression and main effects via a negative binomial regression. These models are appropriate for overdispersed count data. Following the methods of the UCLA Institute for Digital Research and Education (29), we found that the ZINB model was preferred to the zero-inflated Poisson model (like-lihood ratio test=17.30, $p < 0.001$) for our data. Furthermore, a Vuong test indicated that zero-inflated models were superior to standard negative binomial models ($z=1.60$, $p < 0.05$); however, adjustments for variation in exposure time or for clustering within the individual were not possible while running the Vuong test. Multivariate analysis presents incident rate ratios from ZINB models, with standard errors adjusted for clustering within the individual. Stata's cluster(var) option for ZINB (30) was used. Estimates also

adjusted for variation in post-program exposure time by using Stata's exp(var) option (30). Our primary analysis tested whether number of sessions had a negative effect on the count of disciplinary reports and whether this effect was robust to other study variables hypothesized to also predict number of disciplinary reports. We used number of CDOC admissions in the prediction of zeros in the logistic part of the two-part model. Because interaction coefficients are difficult to interpret in nonlinear models (31), we investigated variation in the effect of the number of sessions attended across security risk groups and primary diagnosis groups via Stata's margins commands and plotted the results (30).

RESULTS

Table 1 presents descriptive statistics from 946 participation events. The unadjusted mean number of disciplinary reports in the post-program period was 0.30 (range=0–8). The mean number of sessions attended was 14.34 (range=1–32). Participants were fairly equally distributed across four security risk groups, each representing about 20%-30% of the sample. Half of the sample (50%) had no recorded psychiatric diagnosis. Mood disorder was the most common primary diagnosis classification (20%), followed by psychotic disorder (10%) and substance use disorder (7%). The mean number of comorbid psychiatric disorders was 1.17 (range=0–9). The great majority of the sample was male (92%). The mean age at program initiation was 35.68 (range=18–72). The racial-ethnic breakdown of the sample was as follows: white, 43%; black or African American, 36%; Hispanic, 20%; and other race-ethnicity, 1%. The mean number of years of school completed was 11.54 (range=1–18). The mean number of days observed in the post-program period was 165.70 (range=30–180 by study design). Finally, the mean number of CDOC admissions was 6.5266.40 (range=1–43).

TABLE 1. Characteristics of START NOW participants, 2010–2013
(N=946 participation events)

Variable	Range	N	%
N of disciplinary reports (M±SD)	0 – 8	0.30 ± 0.93	
N of sessions (M±SD)	1 – 32	14.34 ± 10.21	
Overall security score[a]			
Group 1		213	23
Group 2		182	19
Group 3		265	28
Group 4		286	30
Diagnosis group			
No diagnosis		477	50
Personality disorder		54	6
Substance use disorder		69	7
Psychotic disorder		90	10
Mood disorder		185	20
Anxiety, PTSD or other disorder		60	6
N of psychiatric diagnoses (M±SD)[b]	0 – 9	1.17 ± 1.51	
Male		873	92
Age (M±SD)	18 – 72	35.68 ± 11.06	
Race-ethnicity[c]			
White		405	43
Black or African American		336	36
Hispanic		192	20
Other		13	1
Education (M±SD years)	1 –18	11.54 ± 1.78	
Days after program participation (M±SD)[d]	30 –180	165.70 ± 35.57	

[a] Group 1 is the lowest risk.

[b] The number of comorbid psychiatric diagnoses includes primary diagnosis, if any.

[c] Mutually exclusive categories

[d] By design, the period during which disciplinary reports were subject to being counted was limited to 30–180 days after program participation.

Table 2 presents incident rate ratios and robust standard errors for six ZINB models of number of post-program disciplinary reports regressed on number of program sessions attended and combinations of other study variables to elucidate specific effects. Model 1 indicates that more program sessions attended was associated with fewer disciplinary reports received in the post-program period ($p < 0.001$). More specifically, there was a 5% decrease in the incident rate of disciplinary reports for every additional session attended. Model 2 adds the security risk group to the number of sessions. Compared with the incident rate of disciplinary reports for the lowest security risk group (security group 1), the rates for security groups 3 and 4, respectively, were 4.64 ($p < 0.001$) and 11.23 ($p < 0.001$) times as high.

Model 3 adds psychiatric diagnosis classification to number of sessions. Compared with the incident rate for the group lacking a psychiatric diagnosis, each of the diagnostic classifications had significantly greater rates, ranging from 3.77 times (substance use disorder diagnosis, $p < 0.001$) to

8.80 times (mood disorder diagnosis, p < 0.001). Model 4 adds number of comorbid psychiatric diagnoses to the predictors in model 3. There was a 17% increase in the incident rate of disciplinary reports for each additional diagnosis (p < 0.05). Although the independent effects of psychiatric diagnosis classification remained in model 4, the sizes of these relationships were slightly reduced when comorbidity was considered in the model. Model 5 includes number of sessions, security risk group, and psychiatric considerations. All significant relationships between the variables and the number of disciplinary reports that were observed in the other models remained significant. Model 6 adds socio-demographic controls to all other study variables and serves as the full, final model. Age was independently predictive of number of disciplinary reports (p < 0.001). A 4% decrease was noted in the incident rate of disciplinary reports for every additional year of age. Gender and race-ethnicity were not predictive factors. Across all models, number of program sessions attended appeared to be a particularly robust independent predictor of number of disciplinary reports.

TABLE 2. Incident rate ratios (IRRs) from zero-inflated negative binomial models of number of disciplinary reports received regressed on number of sessions attended (N=946 participation events)[a]

	Model 1		Model 2		Model 3		Model 4		Model 5		Model 6	
Variable	**IRR**	**SE**	**IRR**	**SE**	**IRR**	**SE**	**IRR**	**SE**	**IRR**	**SE**	**IRR**	**SE**
N of sessions	.95***	.01	.95***	.01	.94***	.01	.94***	.01	.95***	.01	.95***	.01
Security group 2			2.05	1.07					2.24	1.08	2.33	1.05
Security group 3			4.64***	2.16					2.97*	1.33	3.15**	1.30
Security group 4			11.23***	5.14					5.93***	2.52	5.73***	2.26
Personality disorder					8.74***	3.09	6.12***	2.16	3.96***	1.23	4.42***	1.46
Substance use disorder					3.77***	1.36	2.54*	1.02	2.20*	.85	2.14*	.79
Psychotic disorder					7.68***	2.47	4.71***	1.62	3.03***	.99	3.22***	1.08
Mood disorder					8.80***	2.27	6.05***	1.89	4.24***	1.26	4.23***	1.27
Anxiety, PTSD, or other disorder					8.65***	2.89	6.48***	2.34	5.40***	2.15	4.95***	1.75
N of diagnoses[b]							1.17*	.08	1.13*	.07	1.13*	.07
Male											1.05	.32
Age (years)											.96***	.01
Black or African American[c]											.97	.19
Hispanic[c]											.89	.25
Other race-ethnicity[c]											1.79	.80
Education (years)											1.01	.05
Constant	.37***	.95	.00***	.00	.00***	.00	.00***	.00	.00***	.00	.00***	.00

[a] Reference categories: security group 1, no diagnosis, female, and white. The analyses controlled for overall security score, psychiatric diagnoses, comorbidity, and sociodemographic factors. Estimates are adjusted for clustering within the individual. Variation in post-program exposure time was adjusted with the exp(var) option in Stata 13.

[b] The number of comorbid psychiatric diagnoses includes primary diagnosis, if any.

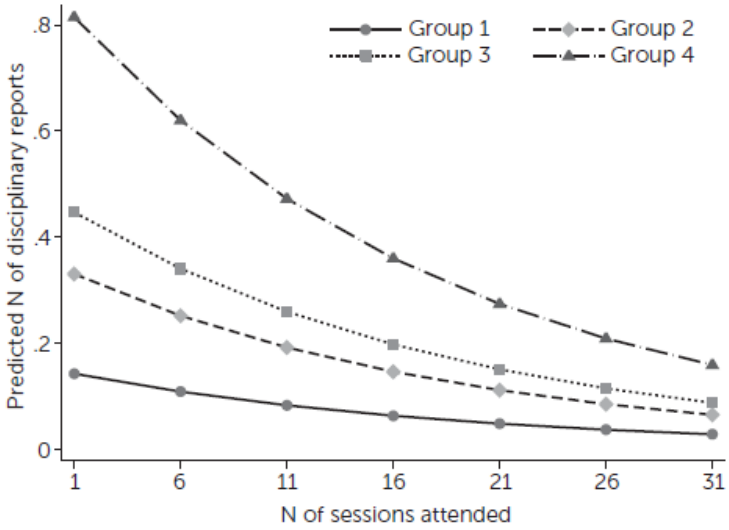
[c] Race-ethnicity categories were mutually exclusive.

* p< 0.05, **p< 0.01, ***p< 0.001

To further investigate the effect of number of program sessions attended on disciplinary reports by security risk groups and primary diagnosis groups, Stata's margins post-estimation command was utilized and plotted (30). Figure 1 depicts the predictive margins of security risk group predicting number of disciplinary reports by number of sessions attended. Generally speaking, all security risk

groups benefited from more sessions attended. However, the higher the overall security risk score, the greater the reduction in number of disciplinary reports with more sessions attended.

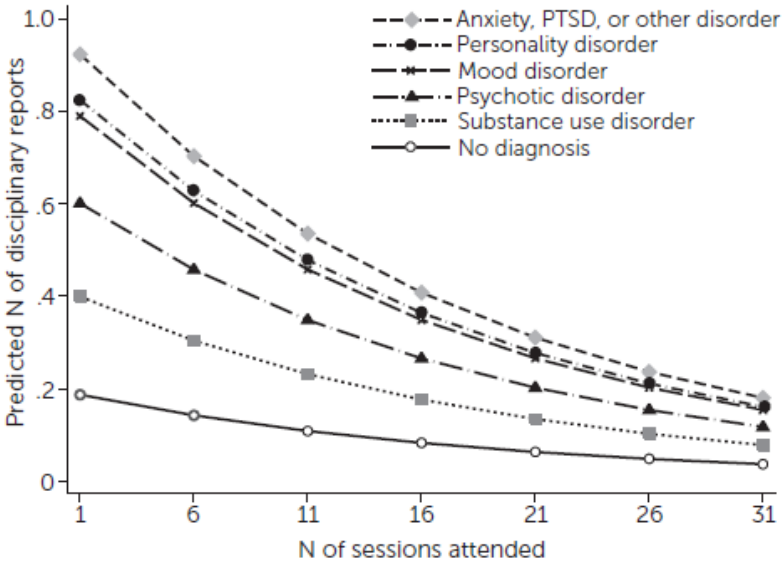
FIGURE 1. Predictive margins of security risk groups predicting number of disciplinary reports by number of sessions attended[a]



[a] Group1 is the lowest risk.

The same procedures followed for Figure 1 were followed for Figure 2 to plot the predicted margins of psychiatric diagnosis classifications. All diagnostic groups appear to have benefited from more sessions attended, and groups with the highest predicted number of infractions with few sessions attended benefited more with increasingly higher levels of participation.

FIGURE 2. Predictive margins of diagnosis categories predicting number of disciplinary reports by number of sessions attended



DISCUSSION

This study examined whether higher attendance in a group therapy program designed for inmates was associated with fewer disciplinary reports received in a state correctional system. Results indicate a significant reduction in the receipt of disciplinary reports in the post-program period with a greater number of sessions attended. Generally, it has been found that longer treatment interventions produce more significant changes (32, 33). A 5% decrease in the incident rate of disciplinary reports was found for every session attended. Despite the structural constraints present in correctional settings, such as frequent movement across facilities, this finding suggests that every effort should be made to retain participants in the program.

The study also examined whether security risk groups and primary psychiatric diagnosis classification groups varied in the relationship between sessions attended and disciplinary reports received. Results indicate that higher risk groups benefited most from more program participation. This suggests that when there is a waiting list of potential program participants, priority should be given to members of the groups with higher security risk. We also found that all diagnostic groups appeared to benefit from greater participation, although some groups more than others. In particular, inmates with anxiety, personality, and psychotic disorders had the steepest downward predicted number of disciplinary reports with more sessions attended. This finding may also suggest groups to target for participation and retention.

This study was not without limitations. The sample was limited to adults, and most were male offenders. Future studies should include youths and women in sufficient numbers to examine separately. Furthermore, this study did not include a control group. Future studies should seek to employ a prospective randomized comparative effectiveness design to further elucidate and compare the unique contributions of START NOW with alternative therapy options. Because of a very small sample and the distinct treatment context of offenders with the most restrictive security and care need scores, these participants were omitted from analyses. In addition, the relationship between number of sessions attended and number of reports received may not be entirely conclusive, because some inmates who engaged in behavioral infractions may have voluntarily or involuntarily discontinued participation sooner. Other inmates with high levels of impulse control may have self-selected into longer program participation. Finally, this study did not control for an inmate's status (sentenced versus unsentenced) or participation in other (concurrent) treatment programs that may have had an impact on behavioral infractions. However, it must be acknowledged

that the robust finding that number of sessions attended was associated with fewer reports strongly suggests a program effect.

Despite these limitations, this study adds evidence of the effectiveness of START NOW beyond that previously published (27) and extends the knowledge base about the program's effectiveness to the wider state correctional context. Future research will investigate the program's impact on clinical outcomes in addition to behavioral outcomes. Additional outcomes to consider include the level and nature of offenses and ultimately, recidivism and hospitalization.

CONCLUSIONS

This study provides evidence that START NOW is effective in reducing the number of disciplinary reports received by inmates in correctional settings. The program is relatively inexpensive and flexible and is effective for a variety of inmate subpopulations. START NOW participation demonstrably reduced behavioral infractions and thereby eliminated the costs associated with disciplinary hearings that would have taken place. Of greater potential significance is the benefit to participants and the people with whom they interact, whether during incarceration or subsequent to release. Further work is needed to determine the extent of any such benefits.

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Chapter 4 - START NOW - a comprehensive skill training programme for female adolescents with oppositional defiant and conduct disorders: study protocol for a cluster-randomised controlled trial

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ABSTRACT

Background: In Europe, the number of females exhibiting oppositional defiant disorder (ODD) and conduct disorder (CD) is growing. Many of these females live in youth welfare institutions. Consequently, there is a great need for evidence-based interventions within youth welfare settings. A recently developed approach targeting the specific needs of girls with ODD and CD in residential care is START NOW. The aim of this group-based behavioural skills training programme is to specifically enhance emotional regulation capacities to enable females with CD or ODD to appropriately deal with daily-life demands. It is intended to enhance psychosocial adjustment and well-being as well as reduce oppositional and aggressive behaviour. We present the study protocol (version 4.1; 10 February 2016) of the FemNAT-CD intervention trial titled 'Group-Based Treatment of Adolescent Female Conduct Disorders: The Central Role of Emotion Regulation'.

Methods/design: The study is a prospective, confirmatory, cluster-randomised, parallel-group, multi-centre, randomised controlled trial with 128 institutionalised female adolescents who fulfil the diagnostic criteria of ODD and/or CD. Institutions/wards will be randomised either to provide the 12-week skills training as an add-on intervention or to provide treatment as usual. Once the first cycle is completed, each institution will run a second cycle with the opposite condition. Primary endpoints are the pre-post change in number of CD/ODD symptoms as assessed by a standardised, semi-structured psychiatric interview (Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime, CD/ODD section) between baseline and the end of intervention, as well as between baseline and a 3-month follow-up point. Secondary objectives include pre-post change in CD/ODD-related outcome measures, most notably emotional regulation on a behavioural and neurobiological level after completion of START NOW compared with treatment as usual.

Discussion: To our knowledge, this study is the first to date to systematically investigate the effectiveness of an adapted integrative psychosocial intervention designed for female adolescents with ODD and CD in youth welfare settings.

Trial registration: German Clinical Trials Register (DRKS) identifier: DRKS00007524. Registered on 18 December 2015 and with the World Health Organisation International Clinical Trials Registry Platform.

Keywords: Randomised controlled trial, Treatment, Adolescents, Females, Residential care, Conduct disorder, Oppositional defiant disorder, Skills training, Emotion regulation

BACKGROUND

Across European countries, an increase in mental health problems, along with a growing rate of violence and aggression in youths, can be observed [1]. Children and adolescents with conduct problems, including aggression, represent a highly heterogeneous group. From a diagnostic perspective, aggressive and oppositional behaviour has been subsumed under the diagnoses conduct disorder (CD) and oppositional defiant disorder (ODD) [2]. The heterogeneity is reflected not only by a great variety of symptoms ranging from impulsive, hot- tempered quarrels or stealing to acts of cruelty to animals or people but also by the extent of co-morbidity (e.g., attention-deficit disorder, depression, anxiety disorders, learning difficulties, posttraumatic stress disorder). Furthermore, research indicates that especially children and adolescents with ODD and CD bear a high risk for maladjustment and the persistence of aggressive and antisocial behaviour symptoms into adulthood [3–6]. In that sense, youth with ODD or CD represent a highly vulnerable group with a significant risk and cost, not only to themselves but also to their immediate surroundings and ultimately to society as a whole.

Although especially CD has long been considered a male-typical disorder (with male-to-female prevalence ratio estimates ranging from 2:1 to 8:1 [7]), recent re- search suggests rising and rather high prevalence rates of about 1–3% among girls and female adolescents [8– 10]. Conduct problems (including ODD or sub-clinical symptoms) are observed in approximately 14% of girls and 16% of boys in Europe [11]. Not surprisingly, prevalence rates of specific populations, such as incarcerated females, are considerably higher, ranging between 32% and 73% [12]. Although the number of females exhibiting ODD and CD is growing, the majority of studies on therapeutic treatment options for CD have been focused primarily on male subjects, despite strong evidence that the course and overall psychosocial adjustment problems associated with CD are often more severe in females than in males [7, 13]. Sequelae such as school failure, substance abuse, delinquency, child prostitution, and early pregnancy (often associated with poor parenting skills) pose serious problems on an individual as well as a societal level.

The development of ODD and CD is generally seen to be caused by an interplay between adverse psychosocial and neurobiological factors that can ultimately result in severely impaired emotional regulation capacities [14]. Patients with ODD and patients with CD are characterised predominantly by impulsive-aggressive behaviour that is often associated with high emotional vulnerability exemplified by hypervigilant behaviour in response to neutral stimuli. In addition, patterns of

thought that include automatic appraisals and distortions of attribution are often found. On top of that, adolescents with conduct problems frequently experience interpersonal difficulties, which are oftentimes associated with high levels of psychological distress. For these youth, a therapeutic approach focused on stress tolerance, mindful- ness, emotional regulation, interpersonal skills and adequate handling of emotions is well-suited and directly tailored to their needs [15]. As for a specific sub-group of adolescents with CD that can be best described as callous-unemotional with associated features, such as a lack of emotional responsivity, lack of empathy, extreme patterns of thought (e.g., black-and-white thinking), and interpersonal difficulties without any associated psychological distress, different kinds of therapeutic strategies seem to be needed. Here, interventions focused on enhancing empathic capacities, moral reasoning and perspective-taking are required [15]. So far, research indicates that, next to individual skills training, adolescents with ODD/CD benefit immensely from therapeutic approaches that involve their direct environment [16, 17]. More specifically, children with disruptive behaviours primarily benefit from parent-focused interventions, whereas adolescents with externalising behaviours respond very well to multi-modal approaches [16].

The intervention

One specific approach that has accumulated support for use with forensic patient populations and appears very suitable for the treatment of female adolescents with ODD/CD is START NOW [18]. Developed at the Department of Correctional Managed Health Care, University of Connecticut, USA, the skills programme was evaluated at multiple correctional facilities through- out the State of Connecticut [18]. In its original format, START NOW is a manualised, group-based skills training programme designed for use within correctional institutions. The focus of the intervention is on (1) increasing self-control over impulses, (2) enhancing emotion recognition and regulation, (3) making judgements and decisions on the basis of consequences and (4) improving stress management and coping skills [19]. START NOW is an integrative evidence- informed intervention based on several therapeutic approaches. These therapeutic elements were chosen because of research findings as well as suitability for the target population (i.e., patients with behaviour disorders) and for integration with other aspects of the planned treatment. More specifically, the programme combines aspects of cognitive behavioural therapy (CBT), motivational interviewing (MI), dialectical behaviour therapy (DBT) and trauma- sensitive care. The subsequent sections outline the different elements

that comprise START NOW in more detail and elaborate on their relevance with regard to the target population.

Cognitive behavioural therapy

CBT represents the theoretical underpinning of the intervention. The programme integrates functional analysis to help group members break down behaviour patterns and understand their own behaviour in the context of its antecedents and consequences. In addition, CBT serves to help patients understand how their own conceptualisation of events is connected to their mood and behaviour. Understanding these cognitive processes increases patients' control and understanding of their behaviour. Furthermore, it facilitates recognition and coping with potential triggers, the modification of cognitions and attitudes, as well as the replacement of problematic behaviours with alternate conduct. Within the CBT framework, new skills are being taught and practiced within as well as between sessions (including role-playing, problem-solving, group discussions or practice exercises) to facilitate transfer [20].

A meta-analysis of outcomes from 26 research articles addressing the effectiveness of group therapy with adult offenders [21] revealed positive effects of CBT, including improved interpersonal functioning, improved self- esteem and anger management, as well as a decrease in feelings of anxiety and in disciplinary sanctions. There is also long-standing support for using CBT-based approaches with adolescents who exhibit externalising problem behaviours [22–25]. Furthermore, evidence suggests that a therapeutic group approach incorporating practical issues in daily-life situations is well-accepted in adolescents and may show high effectiveness even in severely aggressive youth [26]. In addition, CBT has been shown to be feasible for use with counsellors: A training programme using treatment manuals resulted in highly skilled implementations, high levels of counsellors' self- reported confidence to use the intervention effectively, and high satisfaction ratings [27].

Motivational interviewing

MI forms an additional part of the START NOW programme. It is seen as a useful complement to CBT because it represents a client-centred approach that directly addresses a patient's ambivalence and facilitates motivation for change [28]. In this sense, MI helps to provide the basis for the patient's willingness to engage in the intervention [29, 30], whereas CBT provides the specific tools and strategies to change problematic behaviours. Adolescents with ODD or CD do not tend to show much

insight into the degree of inadequacy of their misconduct and as a result do not present with a great motivation for change. Therefore, a therapeutic stance that is marked with validation and empathy on the one hand, and the exploration of dysfunctional behaviours and their associated negative consequences on the other hand, is a feasible treatment strategy also for the treatment of adolescents with disruptive behaviour disorders [31]. START NOW uses several MI aspects, such as the view that ambivalence toward change is common and normal. Furthermore, discussions and exercises stimulating change talk and designed to over- come potential ambivalence are provided. Finally, self-efficacy and positive behaviours are evoked and reinforced throughout the whole intervention [32].

In the past, there have been other effective interventions that have combined the two approaches [33, 34]. The literature reveals positive indications for the use of MI with adolescents: Effects have been found in the areas of substance use [35, 36], weight-related problems [37, 38] and diabetes [39]. In a cluster-randomised trial investigating the effectiveness of single-session MI intended to reduce adolescent substance use behaviour, for instance, researchers found moderate to large effect sizes [36]. Furthermore, MI has been linked to better treatment retention rates mostly in adult populations in various settings [40–42].

Cognitive modifications

Because the original format was designed for use with correctional populations, the developers decided to include cognitive modifications of the regular clinical approach in response to studies indicating that high numbers of incarcerated individuals have sustained traumatic brain injuries (TBIs) [43], as well as studies revealing low effectiveness of interventions that do not take such impairments into account [44]. Regarding the presence of TBI in adolescents exhibiting disruptive behaviour disorders, research has shown high prevalence rates [45]. In a study of the incidence of TBI among 720 delinquent adolescents in youth services institutions throughout the State of Missouri, USA, investigators found incidence rates of self-reported lifetime TBI as high as 18.3%, meaning nearly one in five adolescents reported having sustained a TBI at some point in their lives [45]. Because TBI has been linked to reduced verbal capacities, school problems and concentration problems [46], START NOW was designed to address such limitations by using participant workbooks written at a fifth- grade reading level, with little jargon, using many pictures and repetitions of key concepts and integrating a lot of practice exercises and group discussions to enhance understanding and recollection.

Dialectical behaviour therapy

START NOW further includes some principles that are compatible with DBT. The therapy, which was originally developed for patients with borderline personality disorder [47], has been increasingly applied to forensic sample populations living in residential care settings or correctional facilities [48, 49]. Fundamental to the development of DBT is a biosocial theory that conceptualises a patient's emotional dysregulation as the result of a biological tendency toward emotional vulnerability in conjunction with an invalidating rearing environment [50]. Within START NOW, two key concepts of DBT are found: (1) emphasis on dialectics and (2) mindfulness. The balance between validation and confrontation mainly represents the so-called dialectical relationship work that can also affect the degree of motivation for change as well as the willingness to explore new behaviour patterns [51]. Mindfulness stemming from Eastern spiritual practices was first and innovatively combined with CBT strategies within DBT [52]. Within START NOW, a subset of mindfulness exercises is offered, ranging from interactive exercises to inner mindfulness practices that involve paying close attention to one's own body. Adolescents are encouraged throughout the programme to try each type of exercise and decide for themselves what kind of mindfulness practice best works for them.

Applying DBT strategies to settings where there is a high prevalence of ODD and CD is highly reasonable because this target population shows many of the same risk factors for the development of emotion dysregulation as do borderline patients [49, 53]. The first evidence that DBT is likely to be effective in females with CD symptoms has already been shown [54–56]. Nelson- Gray and colleagues [54], for instance, found significant reductions in externalising and internalising symptoms in an outpatient sample of youth with ODD. With regard to mindfulness specifically, a randomized-controlled trial with 228 non-clinical first- to third-grade students showed significant improvements in terms of text anxiety, social skills and selective attention [57]. The use of mindfulness techniques with adolescents with externalising problems has also been investigated in a handful of studies, and to date the results are encouraging, with small to medium effect sizes, with regard to aggressive, non-compliant acts; social behaviour; attention; and subjective happiness [58–60].

Trauma-sensitive care

START NOW integrates aspects of trauma-sensitive care. This approach includes the central idea that dysfunctional behaviour can emerge as a result of an individual's adjustment to adverse, highly stressful life circumstances. In this sense, many kinds of currently problematic behaviours may be

understood as initially adaptive coping strategies in response to negative situations. In the long term, however, those adaptive strategies may become associated with a preponderance of negative consequences. START NOW specifically uses some concepts of Trauma Affect Regulation: Guide for Education and Therapy [61], including focusing exercises as well as self-monitoring. Research indicates that adolescents in residential care settings represent a population with a high incidence of trauma histories and trauma symptoms. In one study of different types of maltreatment experiences over and above the incidence of conduct problems in female adolescents in out-of-home care, researchers identified a large proportion of the sample reporting severe to extreme maltreatment experiences, ranging from 20% for sexual abuse to 33% for emotional abuse [62]. Furthermore, these maltreatment experiences were shown to be connected to trauma-related symptoms in emerging adulthood. These findings speak to the relevance of using trauma-sensitive interventions for maltreated adolescents to help them connect their current symptoms with traumatic past experiences.

The context

From the perspective of the social worker, adolescents' behavioural dysregulation and persistent tendency to test boundaries, along with their lack of insight into their problematic situation, trigger anger, disappointment and helplessness [53]. It is therefore necessary to introduce a multi-modal concept that integrates all involved professions and parties to enhance communication, transparency and support and to decrease stress levels that originate from the challenges of dealing with adolescents with ODD/CD [53]. Because of the decreased chance of generalisation of the taught skills, in vivo coaching seems most adequate to help ensure that youth with ODD and CD will practice newly introduced strategies consistently in daily-life situations [15]. Unfortunately, to date, there is no study in which researchers have specifically investigated the effectiveness of a skills training programme combining the above-listed therapeutic elements for the treatment of institutionalised female adolescents with ODD or CD.

Effectiveness of START NOW

A treatment evaluation study of the original START NOW intervention in the United States showed that this approach is effective for difficult-to-manage, impulsive and aggressive detainees [63]. Analyses of a mixed-gender sample of inmates (*n* = 946 participation events) indicated that START NOW was effective in reducing the number of disciplinary reports received. More specifically, a dose-response relationship was found: Zero-inflated negative binomial regression analyses indicated that

each additional session was associated with a 5% reduction in the incidence rate of disciplinary infractions. Furthermore, participation in the skills training yielded high satisfaction rates and reduced psychiatric hospitalisation days [19, 64]. It was therefore concluded that the intervention programme represents a viable treatment option for reducing problem behaviour in incarcerated populations.

The present study

Within the framework of the FP7 project Neurobiology and Treatment of Adolescent Female Conduct Disorder: The Central Role of Emotion Processing (FemNAT-CD; see http://www.femnat-cd.eu/ for more information), a European multi-disciplinary study, the aim of the present study is to evaluate the effects of an adapted, gender- specific START NOW intervention for females with ODD/CD living in youth welfare institutions. To our knowledge, no prior study has evaluated the effects of such a CBT-based intervention combining aspects of multiple other therapeutic approaches for this specific population in the youth welfare sector. The adaptation of the original START NOW intervention still employs the same underlying principal components of the skills training, but it uses a slightly modified framework (i.e., individual sessions on top of group sessions to enhance personal understanding and relevance of content; shortened length of the programme due to frequent temporary, time- constrained placements) and adjusted content (i.e., illustrations and theme stories tailored to teenage girls' interests). Furthermore, the intervention will be conducted by staff members of the respective youth welfare institution. Intensive pre-training and supervision, including fidelity monitoring, will be provided. The intervention comprises weekly group sessions (14 sessions, 90 minutes each) and individual sessions (45 minutes each). The aim of the individual sessions is to ensure the transfer of the content of the group training into the personal, daily routines of the participants. Girls are encouraged to practice the skills introduced during the START NOW training between sessions in their daily social interactions with the aid of the responsible social worker. In addition, parents will be sent information on START NOW and information regarding efficient parenting strategies and communication skills with adolescents. In essence, key aspects of the START NOW skills training have remained the same within the adapted version and are well-suited for the target population that can, similarly to the target population of the original format, be described by emotional regulation deficits, many invalidating and traumatic relationship experiences, high impulsivity and a low motivation for change.

Hypotheses

On the basis of the literature, it is hypothesised that female adolescents participating in the add-on START NOW programme will show a greater reduction of aggressive symptoms and co-morbid psychopathology as well as enhanced emotional regulation as compared with adolescents undergoing treatment as usual (TAU). The primary outcome measure refers to the change in number of ODD/CD symptoms endorsed over time as assessed using a semi-structured psychiatric interview (Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime [K-SADS-PL], sections ODD/CD) with the female adolescent and her respective social worker.

Regarding secondary outcomes, it is hypothesised that START NOW will result in a reduction of co-morbid psychopathology and an enhancement of life satisfaction and emotional regulation skills compared with TAU alone. The predictive value of psychosocial and neuro- biological as well as specific personality variables will be investigated. The question of who benefits most from intervention programmes (and who does not) is of major interest to offer effective and tailored intervention strategies. There is accumulating evidence that patients with CD with elevated callous-unemotional traits profit less from current interventions [14, 65]. This might be due to a biologically determined hypo-responsiveness to distress cues that might interfere with social learning [66]. We thus hypothesise that reduced emotional responsiveness/elevated callousness is predictive of low intervention success in females with CD/ODD. Accordingly, we will focus on change in heart rate variability (HRV) because HRV has been identified as an important correlate of emotional regulation difficulties and treatment response [67]. In addition, in a sub-sample, we will evaluate change in neural functional correlates using a functional paradigm specifically assessing emotional regulation capacities under emotionally distressing conditions [68–71]. Further, we expect that the intervention comprising staff training and regular supervision will re- duce self-reported stress and symptoms of burn-out in involved social workers.

Methods/design

The present study is a prospective, confirmatory, cluster-randomised, multi-centre, international phase III trial with two parallel groups (intervention vs. TAU) and three trial phases (baseline assessment, 12 weeks of treatment, 12 [±1] weeks of follow-up observation). The intervention condition is incorporated into the usual standard care within residential care (START NOW + TAU) vs. TAU. A randomised controlled AB-BA design will be used. Institutions will be randomised to start

either with the intervention group (A) or with the control group (B) (TAU). After having conducted A or B, each institution will run the other condition: Institutions starting with TAU receive START NOW, and institutions that finished START NOW and the follow-up assessment conduct a new group with TAU, whereby strict rules are defined to eliminate the risk of carry-over effects.

Study centres

The study will take place at youth welfare institutions located in proximity to four clinical trial centres. Study centres include the departments of child and adolescent psychiatry at the university hospitals in Basel, Switzerland (CS, principal investigator); Frankfurt, Germany (CMF); Aachen, Germany (BHD); and Amsterdam, The Netherlands (AP). Data management as well as biometric and statistical support are provided by the Institute of Medical Biometry and Informatics (IMBI), University of Heidelberg, Germany. The Coordination Centre for Clinical Trials (Koordinierungszentrum für Klinische Studien [KKS]) at the University of Heidelberg is in charge of study monitoring.

Participants

Several youth welfare institutions will be asked to partici- pate. If they agree, female adolescents in the institutions who are aged 12–20 years and their legal guardians will be asked if they want to participate. Diagnostic assessment will be standardised according to criteria of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR) or the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5). Diagnostic information is obtained via a semi- structured clinical interview (K-SADS-PL). Inclusion and exclusion criteria are listed in Table 1.

Criteria for withdrawal

Participants may withdraw from the study (1) at their own request or the request of their parents/legal representatives; (2) if, according to the investigator's opinion, participation in the trial would be harmful for the participant's well-being; or (3) if the participant's behaviour significantly disturbs and impedes group sessions due to, for example, aggressive behaviour directed toward other group members or herself.

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Female adolescents aged 12–20 years
	Diagnosis of current CD (DSM code 312.8) and/or ODD (DSM code 313.81)
	Sufficient writing and reading skills (in German or Dutch)
Exclusion criteria	History or current clinical diagnosis of autism spectrum disorder according to ICD-10, DSM-IV-TR or DSM-5 (autism, Asperger syndrome, pervasive developmental disorder-not otherwise specified, atypical autism, autism spectrum disorder)
	History of or current clinical diagnosis of schizophrenia according to ICD-10, DSM-IV-TR or DSM-5
	Current clinical diagnosis of bipolar disorder or mania according to ICD-10, DSM-IV-TR or DSM-5 (History of bipolar disorder or mania is not an exclusion criterion for individuals with CD.)
	Fetal alcohol syndrome according to ICD-10, DSM-IV-TR or DSM-5
	Known monogenetic disorder, genetic syndrome (e.g., fragile X syndrome, Down syndrome, Prader-Willi syndrome)
	Any chronic or acute neurological disorder (e.g., cerebral palsy, motor problems due to motor or metabolic disorder, current treatment for epilepsy, history of severe traumatic brain injury) (Mild traumatic head injury without loss of consciousness is not an exclusion criterion.)
	Any valid indication of IQ <70 (e.g., special education, previous test results)
	Severe medical condition interfering with the intervention, including suicidal ideation
	Concurrent group-based psychotherapeutic treatment such as START NOW, DBT-A or similar interventions

Abbreviations: CD Conduct disorder, *DBT-A* Dialectical behaviour therapy for adolescents, *DSM-IV-TR Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, DSM-5 Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, ICD-10* International Classification of Diseases, Tenth Revision, *IQ* Intelligence quotient, *ODD* Oppositional defiant disorder

Concomitant treatment

Additional treatments administered to the participants on entry into the trial or at any time during the study are documented as concomitant treatments on the respective pages of the case report form (CRF). Concomitant treatments are allowed in the intervention group as well as the control group as long as they do not represent a group-based psychotherapeutic approach.

Examples of concomitant treatments include individual psychotherapy or external support activities that serve to strengthen social-emotional, cognitive or physical competencies (e.g., drama club, chess club, soccer). Medication and changes in dosage will also be documented through- out the study.

Measurement time points

Assessments will be conducted at baseline (T1), 6 weeks after the start of the intervention (mid-treatment [T2]), 3 months after the start of the intervention (end of treatment [T3]) and 3 months after the end of the intervention (T4). The flow of participants from recruitment through the end of the study is shown in Fig. 1. To promote participant retention, regular contact with participants through telephone calls, on-site visits and information letters is provided. Furthermore, participants who discontinue the intervention but are still interested in taking part in the data assessments are

nevertheless assessed. Because the number of sessions attended is a control variable in the analysis, continuing data collection with participants who are drop-outs is not a problem.

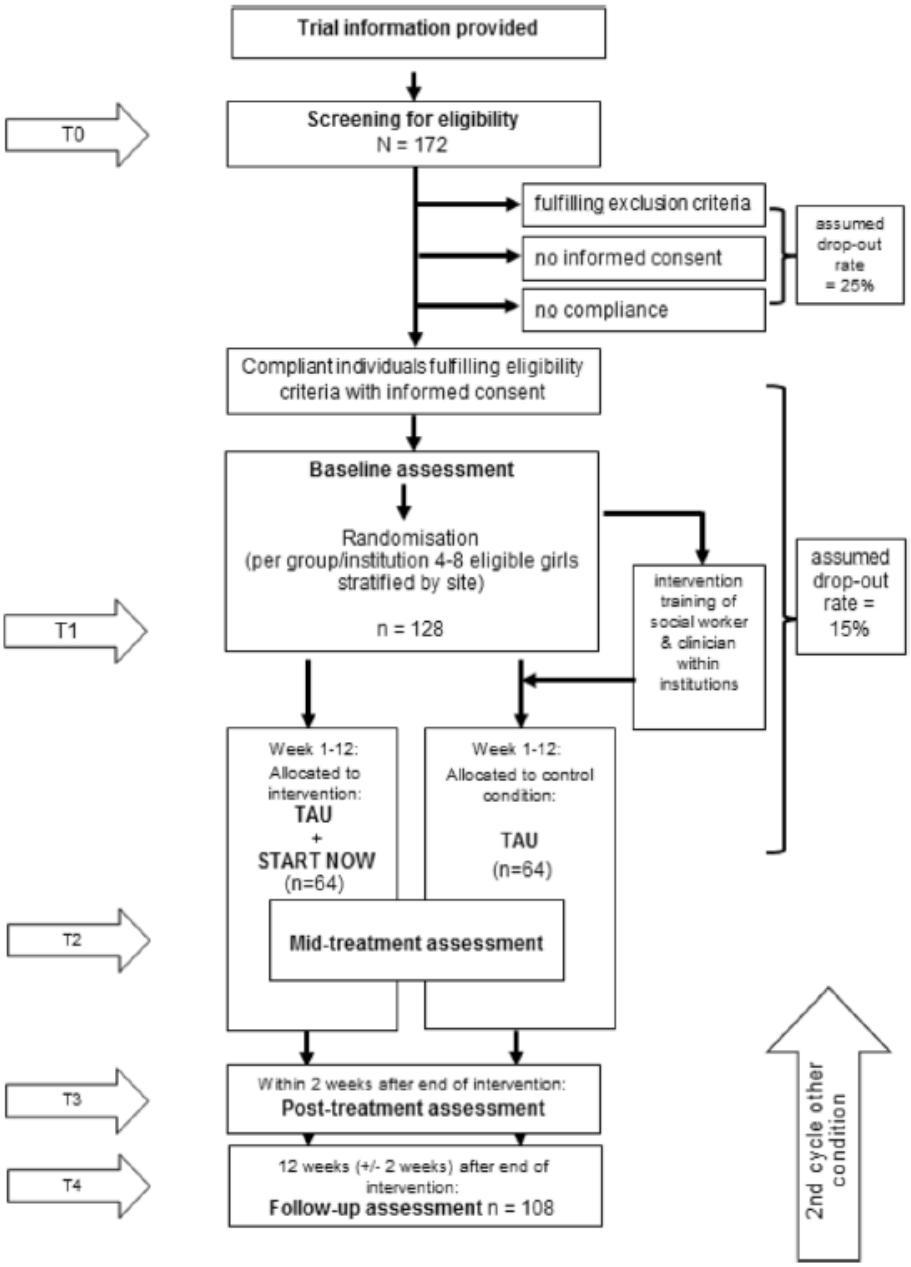

Fig. 1 Trial flowchart. *TAU* Treatment as usual

Primary outcome measure

The primary outcome variable is defined as change in number of fulfilled CD/ODD diagnostic criteria as assessed by a standardised, semi-structured clinical interview between baseline and post-treatment and between baseline and follow-up. The K-SADS-PL will be used [72, 73]. Interviewers will

be trained by an experienced clinician, and regular consensus meetings will be held. The K-SADS-PL is a widely used and validated semi-structured diagnostic interview designed to assess current and past episodes of psychopathology in children and adolescents according to DSM-IV-TR/DSM-5 criteria. Interviews are conducted with the adolescent as well as with a social worker from the participant's respective youth welfare institution who is not involved in the intervention. Symptom measures, diagnoses and severity ratings derived from the interview are based on the obtained information combined with clinical judgement. Thus, summary ratings are achieved by including all sources of information.

Secondary outcome variables

Further objectives of the present trial are to assess pre- post changes in different aggression phenotypes and CD/ODD-related outcome measures in girls participating in the START NOW training compared with those receiving TAU. In adolescents, the Reactive-Proactive Aggression Questionnaire [74], used to distinguish be- tween reactive and proactive/instrumental forms of aggression, and the Relational Aggression Questionnaire [75], which assesses relational aggression strategies such as excluding members of the peer group or spreading gossip, will be used. The Child Behaviour Checklist [76] is used to assess various externalising (attention problems, aggression, delinquency) and internalising (e.g., anxiety/depression) symptoms in adolescents via self- and parent-report. The Affective Reactivity Index (as self-rating form and as caretaker rating) [77] is used to capture general irritability. To assess psychopathic traits, the Youth Psychopathic Traits Inventory [78] will be used. Next to this self-rating questionnaire, the Inventory of Callous-Unemotional Traits, Parent Report [79], will be obtained from parents to capture change in parent-reported callous-unemotional traits. Social workers will rate aggression symptoms in daily-life situations with the modified Overt Aggression Scale originally developed by Yudolfsky et al. [80]. In adolescents also, a time-sampling short assessment procedure (eco- logical momentary assessment) will be used with measures collected twice daily (after lunch and after supper on 4 consecutive days; pre-, mid- and post-assessment) to capture current emotions and regulation capacities while minimising retrospection effects and interference with the daily routine. To assess change in deliberate emotional regulation strategies, the Difficulties in Emotion Regulation Scale [81] will be used.

Each female adolescent will define individual goals, and their attainment will be investigated on the basis of Goal Attainment Scaling [82]. In addition, general life satisfaction of the adolescents [83] will be assessed with the Brief Multidimensional Students' Life Satisfaction Scale. Caretakers' self-

efficacy, burn-out symptoms and job satisfaction will be assessed with the Burnout Screening Scale, a composite instrument comprising different questionnaires [84–88]. In the intervention group, the clients' and trainers' satisfaction with the programme will be assessed (Client Satisfaction Questionnaire/ Training Satisfaction Questionnaire) [19].

Moderators of outcome measures

Several potential moderators of the outcome variables will be assessed. The Massachusetts Youth Screening Instrument version 2 [89] is a self-report questionnaire that screens for a multitude of behaviour problems and potential emotional distress. The Pubertal Development Scale [90] is used to assess pubertal stage using words, rather than pictures, in those participants aged 12 years and above. The Social and Health Assessment scales [91]— specifically the subscales that relate to peers and neighbourhood environment, but also those that assess alcohol and drug use, bullying and future outlook—are used in the present study. To assess intelligence quotient (IQ), two sub-tests of the Wechsler Intelligence Scale for Children, Fourth Edition [92], or the Wechsler Adult Intelligence Scale, Fourth Edition, are performed with the adolescents: vocabulary as a measure of verbal comprehension and matrix reasoning to examine perceptual reasoning capacity. The Diagnostic Interview for DSM-IV Personality Disorders (Axis II [93]) is a semi-structured diagnostic interview done to assess the ten DSM-IV personality disorders. In the present study, a sub-section is used to assess borderline personality disorder symptoms. The quality of the youth welfare institution is systematically assessed through use of the Institutional Quality Index (IQI). The Treatment as Usual Questionnaire (TAU-Q) is distributed to assess the youth welfare institution's standard care. Both the IQI and TAU-Q were developed specifically for the purpose of the present study. The Childhood Experience of Care and Abuse Questionnaire [94] is a self-report questionnaire that was developed to mirror an existing validated interview measure: the childhood experience of care and abuse. The questionnaire assesses lack of parental care (neglect and antipathy), parental physical abuse, and sexual abuse from any adult before age 17 years. Information regarding pre-natal and perinatal risk factors for antisocial behaviour, such as maternal smoking in pregnancy, post-natal depression and negative living conditions in early life, as well as the socio-economic status, is additionally assessed during a standardised interview with primary caregivers. For a detailed overview on measurement time points/trial schedule, please refer to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist shown in Fig. 2. For a detailed overview on information given within this protocol please consult (Additional file 2).

TRIAL SCHEDULE

Informant: A – adolescent C – caretaker P - parent	**A**	**C/P**	**A**	**C/P**	**A**	**C**	**A**	**C/P**	**A**	**C/P**
Timepoint:	**T0 Screening**		**T1 Baseline assessment**		**T2 Mid-treatment assessment**		**T3 Post assessment**		**T4 Follow-up**	
			≤ 4 (+2)weeks before start of intervention				≤ 2 weeks after end of intervention		12 weeks (+/- 2 weeks) after end of intervention	
Enrolment:										
Check Inclusion Exclusion-criteria	●	●								
Written informed consent	●	●								
Allocation post T1			●	●						
Interventions:										
START NOW			◆—	—	—	—	—	—◆		
TAU										
Assessments:										
Baseline Variables:										
Medical history[2]				●						
IQ: WISC-IV/ WAIS-IV[3] vocabulary and matrix reasoning	●									
Outcome Variables:										
Kiddie-SADS-PL[1]			●	●						
Kiddie-SADS-P(L) sections CD/ODD	●	●		●			●	●	●	●
DIPD-IV			●							
Additional Variables:										
CECA-Q			●							
CBCL/YSR[4]			●	●			●	●	●	●
DERS			●		●		●		●	
YPI			●				●			

ICU				●				●		●

Informant: A – adolescent C – caretaker P - parent	**A**	**C/P**	**A**	**C/P**	**A**	**C**	**A**	**C/P**	**A**	**C/P**
Measures:	**T0 Screening**		**T1 Baseline assessment**		**T2 Mid-treatment assessment**		**T3 Post assessment**		**T4 Follow-up**	
BMSLSS			●		●		●		●	
GAS-S, GAS-P			●	●			●	●	●	●
ARI-S, ARI-P			●	●			●	●		
M-OAS[5]				●		●		●		
I-EMA[5]			●		●		●			
BSQ				●				●		
Neuropsychological, neurophysiological measures and real life data:										
Neuro-psychol. test battery[6]			●				●			
Neuro-physiol. test battery[7]			●		●		●			
Optional measures (additional consent required):										
Saliva sample (genetic)[8]			●							
fMRI[9]			●				●			
Concomitant Intervention and satisfaction measures:										
QAF[10]						●				
CSQ/TSQ					●		●	●		
IQI				●						
TAU-Q[11]				●		●		●		●

[1] full interview at T1 (with parents if available), sections CD and ODD (present) only at T0, T2-T4
[2] obtained in a semi-structured clinical interview, the “Medical History Questionnaire”, in addition though inspection of records
[3] if not possible to assess at T0 assessed at T1; WISC-IV for adolescents < 17 years, WAIS-IV for >= 17 years.
[4] CBCL will be assessed by parents
[5] modified-overt aggression and I-EMA questionnaire will be assessed pre, mid and post training on 4 consecutive days
[6] Emotional Go/Nogo Task, Passive Avoidance Learning Test
[7] basal and reactivity ANS measures (HR/HRV/RSA, SCL, SCRs), at T2 only basal ANS measures
[8] saliva probes for genetic Analyses (Genetic laboratory Frankfurt) (can be collected also at later visits)
[9] post-assessment only in Basel
[10] Quality Assurance Form (QAF) will be assessed during two START NOW sessions (one in unit 1/one in unit 2)
[11] TAU-Q will be assessed at baseline regarding the last 6 weeks before start of intervention.

Fig. 2 (See figure on previous page.) Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist for the trial. *ANS* Autonomic nervous system, *ARI* Affective Reactivity Index, *BMSLSS* Brief Multidimensional Students' Life Satisfaction Scale, *BSQ* Burnout Screening Scale, *CBCL* Child Behaviour Checklist, *CD* Conduct disorder, *CECA-Q* Childhood Experience of Care and Abuse Questionnaire, *CSQ* Client Satisfaction Questionnaire, *DERS* Difficulties in Emotion Regulation Scale, *DIPD-IV* Diagnostic Interview for DSM-IV Personality Disorders, *EMA* Ecological momentary assessment, *fMRI* Functional magnetic resonance imaging, *GAS* Goal Attainment Scaling, *HR* Heart rate, *HRV* Heart rate variability, *ICU* Inventory ofCallous-Unemotional Traits, *IQ* Intelligence quotient, *IQI* Institutional Quality Index, *K-SADS-PL* Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime, *MOAS* Modified Overt Aggression Scale, *ODD* Oppositional defiant disorder, *QAF* Quality Assurance Form, *RSA* Respiratory sinus arrhythmia, *SCL* Skin conductance level, *SCR* Skin conductance response, *T1, T2, T3, T4* Time points 1, 2, 3 and 4, *TAU* Treatment as usual, *TAU-Q* Treatment as Usual Questionnaire, *TSQ* Training Satisfaction Questionnaire, *WAIS* Wechsler Adult Intelligence Scale, *WISC-IV* Wechsler Intelligence Scale for Children, Fourth Edition, *YPI* Youth Psychopathic Traits Inventory, *YSR* Youth Self-Report

Neurobiological measures of emotion processing

Neuropsychological correlates

The emotional go/no go task [95] will be used to examine regulation under multiple emotional conditions, including positive, negative and neutral facial expressions. With the Passive Avoidance Learning Test, we intend to assess stimulus-reinforcement learning (adapted from [96]).

Autonomous correlates

Autonomous correlates will be measured as part of a neuropsychological test battery. Basal autonomic nervous system (ANS) parameters will be measured during a 5-minute resting protocol [97]. ANS reactivity will be measured during a countdown task [98] and while watching emotion-evoking film clips [99]. Especially HRV seems to be a promising indicator of treatment success [67, 100].

Neural correlates

Neural correlates will be studied using functional and structural magnetic resonance imaging at baseline. Changes in these neural correlates will be investigated (in a sub-sample post-intervention in Basel and Aachen only) as mechanisms underlying the brain's adaptation to treatments likely related to both structural plasticity and functional response alterations [101].

Genetic functional variants

Genetic functional variants in saliva (serotonergic, noradrenergic, dopaminergic, neuropeptide) will be investigated to test the hypothesis that specific functional genetic variants are predictive of low intervention success.

Sample size calculation and statistical analysis

The sample size calculation is based on the primary efficacy endpoint 'pre-post treatment change in number of fulfilled CD/ODD diagnostic criteria' after the 12-week group-based START NOW training programme for female adolescents (as add-on therapy to TAU) com- pared with TAU only within youth welfare institutions. On the basis of results reported by Nelson-Gray et al. [54], pre-post changes in the treatment group of $\mu = 3$ and in the control group of $\mu = 1$, as well as a conservative common standard deviation of 3.5 for both groups, are expected. Because the Nelson-Gray et al. study intervention comprised only 1 DBT training module and only 16 sessions instead of 14 group sessions + 12 individual sessions as in our study, compared with the change of 2.24 in the Nelson-Gray study, we expect at least $\mu = 3$. In addition, it has to be assumed that TAU in youth welfare settings will also result in reduction of ODD/CD symptoms. Owing to the group therapy and the respective appropriate randomisation procedure, we will have a correlated data structure. To account for that, a design effect of 1.08 to adjust for intra-group correlation of 0.02 is assumed. To achieve a power of 80% ($\alpha = 5\%$, two-sided; two-sample *t* test), a total of 108 patients is required for the analysis. Therefore, 172 patients will be assessed for eligibility to obtain 128 patients to be randomised (assuming that 25% of screened patients are not eligible). A drop-out rate of 15% is expected (including major protocol violations and loss to follow-up). The problem of missing values is partly resolved in the confirmatory analysis by application of an imputation strategy. Nevertheless, another 15% of patients will be randomised to compensate for the loss of information caused by drop-outs and loss to follow-up. The sample size calculation was done using nQuery Advisor 7.0 soft-ware (Statistical Solutions, Cork, Ireland).

Statistical methods

The full analysis of the primary outcome measure will be conducted on the basis of the intention-to-treat (full analysis set) population, including all randomised patients. To account for the data structure, a linear mixed model with the primary endpoint (change in ODD/CD score between baseline and end of intervention) as the response variable, including baseline CD/ODD symptoms, group, age, site and IQ as fixed factors and the respective cluster as a random factor, will be applied.

The random intercept, as well as the residuals, will be assumed to be normally distributed. The correlation structure can be referred to as compound symmetry [102], which is a common assumption in cluster-randomised trials [103]. The results will be presented as the mean between-group difference with the corresponding two-sided 95% confidence interval. The associated Hedges' effect size *g* [104] will be calculated, in addition to the practice-related intra-cluster correlation coefficient. To fit the primary model, the restricted maximum likelihood approach will be used. The overall type I error rate is set at $\alpha = 5\%$ (two- sided) and will be controlled by applying the multiple test procedure for hierarchically ordered hypotheses. The first null hypothesis states that the change in ODD/ CD score between baseline and end of intervention is equal for both the intervention and control groups (H_{0I}: $\mu_{1I} = \mu_{2I}$). This hypothesis will be tested at a two-sided level of significance of 5% against the alternative hypothesis (H_{1I}: $\mu_{1I} \neq \mu_{2I}$). Only if the first hypothesis can be rejected will the second null hypothesis, which states that the change between baseline and follow-up (12 weeks after end of intervention) will be equal in both groups (H_{0II}: $\mu_{1II} = \mu_{2II}$), be tested in the same way. This second hypothesis can then be tested also at a two-sided level of significance of 5% against the alternative hypothesis (H_{0II}: $\mu_{1II} \neq \mu_{2II}$). Application of this multiple test procedure for hierarchically ordered hypotheses assures control of the overall type I error rate of 5%. Both null hypotheses will be tested by applying a random effects model that includes baseline CD/ODD symptoms, group, age, institution and IQ as fixed factors and cluster as a random factor. This statistical analysis plan was specified before the opening of the database.

Methods against bias

Eligibility assessment, obtaining informed consent and enrolling the participants in the trials are performed at each trial site by one of the local investigators. Institutions will be randomised to start with either the intervention group or the TAU control group. The institutions will be randomised in fully eligible groups (group size of four to eight participants), stratified by site using a centralised web- based tool (http://www.randomizer.at [14 Jan 2013], Medical University of Graz, IMBI, Statistics and Documentation, c/o Prof. Andrea Berghold). The randomisation tool is supervised by the IMBI at the University of Heidelberg, Germany.

Screening and baseline assessment are performed before the randomisation procedure, so that data obtained at intake are blinded with regard to group membership. Furthermore, all interviews will be conducted with someone who is not involved in the training.

To ensure that START NOW is implemented in all residential institutions in a comparable way, all staff trainers are trained before the beginning of the study and have to pass a practical and written test. The 2-day- long pre-training will be conducted after randomisation and before the start of the intervention. To increase treatment adherence, a facilitator manual with a detailed session-by-session outline will be used next to the work- book for adolescents. The application of the modularised sessions is strictly monitored. In addition, trainers are supervised by START NOW facilitators every other week during the intervention period. To assess adherence and competence, two training sessions of the programme (one in unit 1, one in unit 2) will be either directly attended by one START NOW supervisor or videotaped. The quality check (Quality Assurance Form [QAF] [19]) will be focused on adherence to the content of the programme and basic trainer competencies (use of motivation interviewing, rolling with resistance, validation).

With regard to the trial design, institutions that were randomised to start with the intervention condition first and subsequently provide a second cycle of TAU have to fulfil two conditions to eliminate potential carry-over effects:

1. Only social workers are involved who have not been previously trained and an exchange on START NOW content between girls is unlikely because of rare opportunity.

2. In case girls who participated in START NOW remain in the institution in the same living group after the whole cycle has ended, the time interval between the end of an intervention group and a second cycle of TAU is longer than 6 months.

Data quality is continuously monitored by the data management team (IMBI), University of Heidelberg, and the KKS). Data will be entered electronically at each local study centre site. Range checks for data values are done to promote data quality. Clinical monitors inspect subject-related data during on-site visits to ensure that all data are correct, complete and gathered according to data protection laws.

The original study forms will be kept at the trial site. Participants' files are stored in locked cabinets, and access to the study data will be restricted. Data will be collected, processed and stored according to the data protection laws.

Safety and ethical issues

Research activities within the FemNAT-CD START NOW project will be carried out in compliance with the fundamental ethical principles stated in the Declaration of Helsinki. The KKS, an institution that is independent from other trial staff and experienced in monitoring psychotherapy trials, will monitor the study, adapted to good clinical practice guidelines as stated by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, and KKS has approved the standard operating procedures. The trial (protocol version 4.1) has received approval from the local ethics committees at the University of Basel (reference EKNZ 2014/075), the University of Frankfurt (445/13 – version 5), the University of Aachen (EK 037/15) and the University of Amsterdam (2014.581-NL52038.029.14).

Any modification to the protocol will require a formal amendment and approval by each local research ethics committee. The protocol must be agreed upon by the trial steering committee (principal investigators at the Department of Child and Adolescent Psychiatry, University of Basel, and local investigators at the University of Frankfurt, University of Aachen and University of Amsterdam) and the data management team (KKS and IMBI) at the University of Heidelberg.

Participants will be enrolled only after they have received comprehensive information from the responsible investigator. Participants and their parents/legal representatives will also receive information sheets and will have the opportunity to discuss the trial with the investigator. Written informed consent for the study will be obtained by the investigator from all participants and their parents/legal representatives who are willing to participate in the trial. An example consent form is pro- vided (see Additional file 1). All participants will be informed that they can stop participating in the study at any time without having to give justification. Participants are provided with the right to have their information re- moved from the database at any time. Because TAU is allowed for both the intervention the control groups, and because the control group will subsequently undergo the intervention condition, participants in either group do not experience any disadvantage with regard to group allocation in relation to clinical intervention. Control subjects who leave the institution before the start of the intervention condition are given the opportunity to participate in an outpatient START NOW group. Results will be published regardless of the magnitude or direction of the effect and will follow Consolidated Standards of Reporting Trials (CONSORT) and its extension 5 to cluster-randomised trials.

An independent data and safety monitoring board (DSMB) including three independent clinical experts and one biometrician is established to monitor the progress of the trial and ensure adherence to protocol. Safety parameters include that all serious adverse events (SAEs) or adverse events reported by the subject or detected by the local investigator that occur during the trial and all noticeable problems must be documented in the CRF. In case of an SAE, the ethics committee will be informed within 7 days after the SAE has been reported. In addition, the DSMB will also be regularly informed. In case of a significant preponderance of SAEs that might causally be associated with the trial, the DSMB will terminate the trial. Patients who are enrolled in the study are covered by indemnity for negligent harm by study insurance policies.

To guarantee confidentiality and anonymity, all participants are allocated consecutive participant identification (ID) numbers. The local principal investigator of each study site will maintain a subject ID list (participant ID codes with the corresponding participants' names) to enable records to be identified. Authorised persons may inspect the subject-related data collected during the trial, ensuring compliance with the data protection law (inspectors, monitors, auditors). Only encoded data will be stored (centre code and consecutive ID number). Saliva samples will be stored for 30 years. Data identifying a person will be available only at the local sites. All data collected in the online database will be managed in a safe and secure environment. The system used for data management is validated and is compliant with U.S. Food and Drug Administration regulations (21 CFR part 11). All data transmission is encrypted with Secure Sockets Layer (SSL) technology. All changes to data are logged with computerised timestamps in an audit trail which includes the name of the author/editor, the date/ time of the change, a reason for the change and the new information. The IMBI Heidelberg database server with the stored data is located in a secure data centre of the university and is protected by a firewall. The system pro- vides an infrastructure to support user roles and rights. Only authorised users are able to enter or edit data, and access is restricted to data of the subjects in the respective centre.

DISCUSSION

This study protocol presents a randomised controlled trial testing the effectiveness of an adapted version of a cognitive behavioural skills training programme, START NOW, in institutionalised females with a diagnosis of ODD and/or CD. To date, to our knowledge, the study represents the only randomised controlled trial of the efficacy of the START NOW intervention specifically designed for female adolescents with disruptive behaviour problems within youth welfare institutions. There is an

internationally recognised lack of randomised controlled studies investigating the efficacy of integrative therapeutic approaches [48, 49]. Consequently, the present study gives profound consideration to the repeatedly formulated necessity to develop integrative intervention approaches deriving from sound theoretical rationales, addressing core deficits of patients with ODD and patients with CD, and applying gender-specific strategies and materials. On the basis of convincing evidence that emotion processing is severely affected in ODD and CD, the presented approach, focused on enhancing emotional regulation and interpersonal capacities, is well- suited for this target group.

There is a specific need to implement and evaluate intervention approaches in settings where most of the affected adolescents live, most notably in residential care settings [105, 106], because residential treatment by itself seems not sufficiently effective in reducing externalising symptoms [107]. Effective treatment of severely aggressive, rule-breaking and unit-destructive behaviour is crucial to the safe operation of the residential environment [53]. This is of major relevance for staff workers dealing with adolescents who experience severe behavioural and emotional dysregulation. Thus, the implementation of evidence-based intervention approaches within youth welfare institutions is needed to strengthen the chance of continuous care and to avoid repeated relationship break-offs in severely affected adolescents living in these settings [107]. As such, the results of the present study shall be of high relevance for residential care settings and shall evoke further debates over, if not directly enhance, the standard of care provided within the youth welfare sector.

Essential methodological issues will be considered to manage threats to internal validity on the outcome of the present randomised controlled trial [108]. START NOW is manualised, and all facilitators receive 2 days of rigorous, standardised training. Beyond an in-depth preparation, START NOW's implementation will be checked via regular fidelity monitoring assessed by the respective supervisor through use of a standard QAF. The study is large enough to determine the presence of clinically important effects, and mediators and moderators of response will be investigated. Our primary outcome measure is based on a clinical interview conducted by independent observers with both the adolescent and a (non-involved) social worker. In doing so, we gather comprehensive information that does not rely on a sole source and combines interview information, file information and clinical judgement to reach a final conclusion. Furthermore, the fact that we continuously collect neurobiological and neurophysiological data presents a major advantage because we will subsequently be able to combine and compare these objective indicators with the clinical data

collected. Procedurally, the randomized AB-BA design is a further benefit because it will enable us to assess within-institution effects. This point is of particular importance, because youth welfare institutions vary extremely with regard to size, type of population served, organisational and structural aspects, financial resources, and professional training opportunities. The automated online randomization procedure is clearly defined and reflects the study design. The statistical analysis takes the different study centres and institutions into account. Furthermore, a strong advantage of the rpesent study is the 3-month follow-up period to investigate long-term effects of the intervention.

Limitations

A limitation of this study lies in the fact that a blind assessment can be realised only during baseline assessment. At post-assessment and follow-up, participants and other informants included in the assessments (social workers and adolescents) are aware of the condition they are in, and thus their evaluation may be biased. How- ever, to overcome potential bias with regard to the primary outcome measure, the interview assessing CD/ ODD symptoms will be conducted with social workers who are not involved in the training. In addition, to assess main secondary measures of emotion processing, objective neurobiological indicators are used which are not influenced by expectation effects.

Trial status

In January 2015, the first group was randomised. Recruitment is expected to be finished by January 2017.

Additional files

Additional file 1: Example informed consent form used at the Basel site. (PDF 194 kb)

Additional file 2: SPIRIT 2013 Checklist. (DOC 121 kb)

Abbreviations

ANS: Autonomic nervous system; ARI: Affective Reactivity Index; BMSLSS: Brief Multidimensional Students' Life Satisfaction Scale; BSQ: Burnout Screening Scale; CBCL: Child Behaviour Checklist; CBT: Cognitive behavioural therapy; CD: Conduct disorder; CECA-Q: Childhood Experience of Care and Abuse Questionnaire; CONSORT: Consolidated Standards of Reporting Trials; CRF: Case report form; CSQ: Client Satisfaction Questionnaire; DBT: Dialectical behaviour therapy; DBT-A: Dialectical behaviour therapy for adolescents; DERS: Difficulties in Emotion Regulation Scale; DIPD-IV: Diagnostic Interview for DSM-IV Personality Disorders; DSMB: Data and safety monitoring board; DSM-IV-TR: *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*; DSM-5: *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*; EMA: Ecological

momentary assessment; FemNAT-CD: Neurobiology and Treatment of Adolescent Female Conduct Disorder; fMRI: Functional magnetic resonance imaging; GAS: Goal Attainment Scaling; HR: Heart rate; HRV: Heart rate variability; ICD-10: International Classification of Diseases, Tenth Revision; ICU: Inventory of Callous-Unemotional Traits; ID: Identification; IMBI: Institute of Medical Biometry and Informatics; IQ: Intelligence quotient; IQI: Institutional Quality Index; KKS: Coordination Centre for Clinical Trials (Koordinierungszentrum für Klinische Studien); K-SADS-PL: Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime; MI: Motivational interviewing; MOAS: Modified Overt Aggression Scale;
ODD: Oppositional defiant disorder; QAF: Quality Assurance Form; RSA: Respiratory sinus arrhythmia; SAE: Serious adverse event; SCL: Skin conductance level; SCR: Skin conductance response; SPIRIT: Standard
Protocol Items: Recommendations for Interventional Trials; SSL: Secure Sockets Layer; T1: T2, T3, T4, Time points 1, 2, 3 and 4; TARGET: Trauma Affect Regulation: Guide for Education and Therapy; TAU: Treatment as usual; TAU-Q: Treatment as Usual Questionnaire; TBI: Traumatic brain injury; TSQ: Training Satisfaction Questionnaire; WAIS: Wechsler Adult Intelligence Scale; WISC-IV: Wechsler Intelligence Scale for Children, Fourth Edition; YPI: Youth Psychopathic Traits Inventory; YSR: Youth Self-Report

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Availability of data and materials

The study protocol is officially registered with the German Clinical Trials Register (DRKS) (DRKS00007524; date of registration 18 December 2015) and the World Health Organisation International Clinical Trials Registry Platform, and thus the data and materials are publicly available.

Authors' contributions

CF coordinates the FemNAT-CD FP7 research project. CS and LK drafted the manuscript. CS designed the trial with the help of DS, CMF, AP, BHD and RLT. CS and LK supervised the implementation of the study. DS contributed to calculating statistical power for the primary outcome variable and writing of the statistical and

data analytical plan. LK, MP, SM, GK, KA and HO collected the data. KK contributed to the safety and ethical part of the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Ethics approval and consent to participate

The trial (protocol version 4.1) has received approval from the local ethics committees at the University of Basel (reference EKNZ 2014/075), the University of Frankfurt (445/13 – Version 5), the University of Aachen (EK 037/

15) and the University of Amsterdam (2014.581- NL52038.029.14). Written informed consent and legal guardian consent (for participants <18 years old or in accordance with legal requirements of the respective country) must be provided before enrolment in the trial.

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Chapter 5 - General Discussion

This dissertation was dedicated to increasing knowledge about the risk factors and treatment of aggression and antisocial behavior in underserved populations. First, we examined the association of CVE and conduct problems in specific groups of children and adolescents. Second, this work examined the effectiveness of a treatment intervention for offenders with aggressive behavior tendencies in correctional settings. Finally, this dissertation presents a treatment evaluation plan for a newly adapted intervention designed for antisocial females within youth residential settings, where violence and aggression are frequently encountered and treatment resources are limited. Our study "Resting Autonomic Nervous System Activity Is Unrelated to Antisocial Behavior Dimensions in Adolescents: Cross-Sectional Findings from a European Multi-Centre Study" offers some additional insights with regard to the association between resting heart rate and antisocial behavior (see appendix 1).

Violence Exposure, Aggression and Antisocial Behavior

Novel findings with regard to the specific association between recent CVE and current conduct problems in a child and adolescent sample with conduct disorder and a healthy sample with no clinical impairments are presented in Chapter 2. As such, it provides evidence that CVE and antisocial behavior are strongly interrelated and that this finding holds across a variety of individuals (healthy young people and those with CD) stemming from a variety of contexts (different communities across different countries). Thereby, Chapter 2 extends previous literature demonstrating a co-occurrence of greater levels of violence exposure and high levels of conduct problems (Cecil, Viding, Barker, Guiney, & McCrory, 2014; Sanchez, Lambert, & Cooley-Strickland, 2013; Voisin, Patel, Hong, Takahashi, & Gaylord-Harden, 2016) as well as studies reporting on bi-directional effects (Mrug & Windle, 2009).

In addition, Chapter 2 shows that findings within both groups persisted even when accounting for the mediating effects of aggression subtypes. In line with this result, previous literature has shown that effects of CVE on conduct problems remain when controlling for baseline levels of aggression (McCabe, Hough, Yeh, Lucchini, & Hazen, 2005; Weaver, Borkowski, & Whitman, 2008). Proactive aggression had a stronger mediational effect on the association between recent CVE and current conduct problems than reactive aggression for both groups. This result aligns with studies suggesting emotional numbing and favorable attitudes towards violence (i.e., desensitization) in individuals

chronically exposed to community violence resulting in higher levels of externalizing behavior (Boxer et al., 2008; Gaylord-Harden et al., 2017; Mrug, Madan, & Windle, 2016).

Despite long called upon increases in prevention and intervention (Fowler et al., 2009), high rates of witnessed and experienced community violence within relatively affluent (e.g., Switzerland, UK) as well as relatively poor European countries (e.g., Hungary, Greece) were demonstrated. Highest rates were detected in antisocial young people (i.e., those with a diagnosis of CD). Chapter 2 thereby extends the large body of research that has investigated the impact of early risk factors on current antisocial behaviors (Murray & Farrington, 2010a), through systematically investigating and disentangling the effects of witnessing community violence and conduct problems in a clinical population (i.e., children and adolescents with CD) and a healthy population. As such, it is the first study to provide evidence for a strong association between recent witnessing and current conduct problems in an exclusively healthy sample as well as in young people with CD, even when taking their levels of reactive/proactive aggression into account.

Chapter 2 shows that community violence is a serious problem for many children and adolescents across Europe. Given the urgency of this public health issue, efforts to try to reduce community violence and offer support for young people who have experienced community violence in the past need to be undertaken. To date, numerous prevention programs have been developed and evaluated (Abt, 2017). Frameworks of these programs tend to target either family, school, treatment and community factors (Matjasko et al., 2012) or use conceptualizations based on place, people and behavior (Abt, 2017). Family-based programs typically involve parent training. School-based programs occur within the school setting and target individual children, groups of children or peers. People-based prevention includes both family as well as school centered prevention strategies. Treatment-specific or behavior-based prevention strategies typically include social skills interventions, drug treatment, drug courts and cognitive-behavioral approaches. Community-based or place-based prevention programs involve strategies like mentoring programs or making changes in the environment to reduce risk (e.g., the Washington DC subway was designed to reduce crime by not building toilets, lockers or excess seating space to discourage lingering (Matjasko et al., 2012)).

Due to the plethora of prevention programs that are available, some research has been dedicated to finding out “what works best” in terms of prevention strategies (see (Abt, 2017; Matjasko et al., 2012) for comprehensive overview). This area of research is highly important, especially with regard to policy makers or practitioners who are able to implement prevention programs. Large effects have been found for family-based strategies (parent training). Peer mediation and other school-based interventions have also produced strong effects. Cognitive-behavioral therapy has been shown to be

effective as well, particularly multi-modal approaches such as multi-systemic therapy. Less research has focused on community-based prevention approaches, but the small number of studies in this area have suggested that environmental crime prevention strategies can have positive (albeit modest) effects (Abt, 2017; Matjasko et al., 2012). It makes intuitive sense that the greatest impact would be achieved by implementing prevention strategies in all three areas (family, school, community) to break the vicious circle of violence exposure and perpetration. Furthermore, greater effects have been found for those individuals who are at high risk of experiencing community violence as well as those who have already been exposed. This means that priority should be given to implementing programs in communities and neighborhoods with higher rates of violence as opposed to implementing programs at a universal level targeting all children and communities regardless of risk (Abt, 2017; Matjasko et al., 2012). Correctional institutions and residential youth settings contain a great number of antisocial individuals that are likely to act out and cause and/or witness violence within the settings they reside. Knowing the significant relationship between CVE and antisocial behavior, effective interventions addressing the two concepts within these violence-prone settings are urgently needed.

Implementation and Evaluation of Interventions within Corrections and Residential Youth Care

A successful implementation of evidence-based care in correctional facilities with a high risk of antisocial and aggressive behavior might reduce the risk of deviant learning or even the risk for being exposed to violence from aggressive peers (Boduszek, Hyland, Pedziszczak, & Kielkiewicz, 2012; G Bronsard et al., 2011). As Chapter 2 demonstrated that violence exposure in the community setting is positively correlated with antisocial behavior, both in healthy and particularly in aggressive adolescents, effective mental health services in corrections are essential. Responding to the insights gained in Chapter 2 (i.e., call for intervention), Chapter 3 provides evidence for the effectiveness of a skills training specifically developed and tailored to the needs of offenders with behavioral disorders within correctional settings, where a high prevalence of violence exposure is found (Walters & Crawford, 2014). Chapter 3 shows that higher attendance in a group intervention was associated with fewer disciplinary reports received by inmates in a state correctional system. Specifically, a significant reduction in the number of disciplinary reports post-program was detected for inmates with a greater number of sessions attended (i.e., a dose-response relationship). This finding is in line with previous studies that have reported more beneficial outcomes for longer treatment interventions and fewer rates of treatment attrition (Henwood, Chou, & Browne, 2015; Lipsey et al., 2007; Olver, Stockdale, & Wormith, 2011). Primary outcome variable of Chapter 3 (i.e., number of disciplinary reports received) represented an objective measure of behavioral change, as these data were collected as part of a standard process underlying the Department of Correction's (DOC) rules

of conduct and procedures (Code of Penal Discipline). Thus, count of disciplinary infractions can be regarded a reliable source of information on inmate behavior as the conditions that justify an allocation ("write up") of a "disciplinary ticket" are predetermined and entered into the DOC database immediately. Hence, count of disciplinary infractions is not subject to memory loss or memory distortion.

Furthermore, Chapter 3 illustrates that inmates with higher security risk scores benefitted most from more program participation. This finding corresponds with the literature on cognitive-behavioral programs within correctional settings that indicates greater effects for higher risk offenders (Smith et al., 2009). The intervention was further found to be effective across primary psychiatric diagnosis classifications, with greatest benefits for inmates with anxiety, personality, and psychotic disorders. Resultantly, priority of treatment should be given to offenders with high security risk scores as well as those presenting with anxiety, personality or psychotic disorders. Nonetheless, effects persisted across a broad inmate population. As such, Chapter 3 fills an important void, because effective, evidence-based treatments for mentally ill inmates that are pragmatic, well-suited for a diverse group of inmates and responsive to the structural and financial limitations of correctional settings are urgently needed (Epperson et al., 2011; Fazel et al., 2016).

Moreover, a growing body of literature has suggested that more research, specifically more rigorously conducted treatment evaluation studies, be conducted within the correctional and residential youth care system (Thompson, Duppong Hurley, Trout, Huefner, & Daly, 2017). Although there are first studies indicating that, for example, DBT-oriented programs are promising (Stadler, Manetsch, & Vriends, 2016), there is still a lack of RCT studies in the two fields and mostly low sample sizes have been investigated so far (Thompson et al., 2017). In Chapter 4 we present an opportunity to investigate the effectiveness of a newly adapted skills intervention for females with clinically significant levels of antisocial behavior residing in residential youth care in a cluster-randomized controlled trial. It is thereby intended to extend the evidence-base of the intervention presented in Chapter 3 to a different population and context, and to address weaknesses of formerly conducted treatment evaluation studies in residential youth care.

As emotion regulation and interpersonal functioning has been shown to be impaired in youth with ODD and CD, the treatment approach is particularly focused on enhancing these capacities. Structural data will be gathered to gain more information on the specific set-up of the participating institutions. The design introduced in Chapter 4 enables to examine within-institution effects. This method is of particular importance as residential settings may vary considerably. In addition, burden of staff will be assessed to gain better insight with regard to the environmental conditions, the staff's

baseline levels of functioning, and to inform policy makers on any potentially needed improvements to enhance residential youth care. Burden of staff will be assessed across time to investigate the effect of the intervention in possibly decreasing levels of stress through offering social workers a greater number of strategies and techniques to work with and improving the overall atmosphere within a given institution. In order to enhance understanding on "what works for whom" mediator and moderator analyses will be conducted to enable further refinement of the targeted intervention approach. As such, Chapter 4 gives profound consideration to the frequently called upon need to develop integrative intervention approaches based on sound theoretical rationales, addressing central deficits of antisocial behavior disorders, and applying gender- and context-specific strategies and materials (Bebbington et al., 2017; Fazel et al., 2016).

Both, Chapters 3 and 4, represent studies that were/are to be conducted in restrictive settings, where less research, particularly only few randomized-controlled trials (Schmucker & Lösel, 2015; Yoon et al., 2017), has been conducted due to the nature of the settings. Past studies examining the specific barriers to research within correctional and residential youth settings are scarce but those that do exist have identified a number of barriers: Frequent losses to follow-up caused by releases, rapid turn-overs, short durations of stay and difficulty of providing continuity of care have been identified in the past as factors that impede the implementation of treatment evaluation studies (S. James, Thompson, & Ringle, 2017; Yoon et al., 2017). In addition, institutional constraints have been reported based on scheduling conflicts, "lock-downs" or crisis interventions, high attrition rates and individual misconduct that resulted in restricted enrolment. Furthermore, institutional constraints affected the implementation of study targets due to policies prohibiting certain study materials, such as biological markers or video recordings (Yoon et al., 2017). As such, Chapters 3 and 4 respond to the specific need to implement and evaluate intervention approaches where affected individuals are living and spend most of their time: in the prison/residential youth setting (Fazel et al., 2016; Grietens et al., 2014; Leve et al., 2012). Thereby, they represent a valuable addition to the fields of corrections and youth welfare systems.

5.1 Limitations

This dissertation is aimed at providing important, informative and instructive contributions to the treatment of underserved populations with antisocial behavior. Despite the above mentioned strengths, this work is not without limitations that should be considered. While Chapter 2 has increased the knowledge base on the specific associations and mediation effects regarding the link between CVE and conduct problems in different groups of children and adolescents, it employed a cross-sectional approach. Therefore, findings are limited with regard to exploring the pathways of

CVE to conduct problems, any long-term or cumulative effects of CVE. Based on the current conceptualization we cannot make any statements concerning the temporal precedence of CVE, aggression subtypes and conduct problems nor can we make definite conclusions with regard to the mediation estimates.

Chapter 3 evaluated the effectiveness of a skills training in an adult, mostly male offender sample only. Thus, findings cannot be generalized to other populations. No control group was included which limits the value of the finding on effective behavioral change. Furthermore, although the number of sessions attended was robustly associated with fewer disciplinary reports, a definite answer on program effect may not be given without controlling for concurrent treatments received. Due to a small sample size and distinct treatment context of offenders with the most restrictive security classification score, these participants were not included in the analyses. In addition, the relationship between number of START NOW sessions attended and number of disciplinary reports may not be entirely conclusive, as few actually received a ticket and some inmates who engaged in behavioral infractions may have voluntarily or involuntarily discontinued treatment participation sooner. Inmates with better impulse-control and emotion regulation capacities may have participated in more sessions.

While conducting the RCT study from Chapter 4, one concern that arose quickly was the high number of participant drop out. Although many efforts to retain participants were made (e.g., presentations, regular contact hours, reminders, letters of appreciation) a considerable proportion of participants did not attend the post-treatment assessments. Several reasons for the drop outs were noted similar to constraints other studies have reported (S. James et al., 2017; Yoon et al., 2017): crisis interventions, transfers to other institutions, unexcused leaves, non-compliance. Accordingly, we have a drop out rate of 26 percent for the pre-post treatment comparison. Furthermore, it was difficult to receive questionnaire data from staff workers. Again, several reasons were noted for the missing data: time constraints, lack of motivation, vacation/sick days, lack of communication between staff. Of the institutions that have already completed the trial, the majority indicated that participating in the research project was very time-consuming and placed a significant burden on the social workers' daily routines. Resultantly, many said they would not participate again. The feedback from the institutions and the experiences I made myself during the coordination of the RCT project raise a debate on attempting the balancing act between highest scientific standards versus pragmatic implementation of an intervention study that is realizable and of practical utility for the setting in which it is evaluated.

5.2 Future Prospects

This dissertation furthers the knowledge about the correlates and treatment of antisocial behavior in underserved populations through studying different populations and addressing several settings in which a majority of antisocial individuals reside. A better understanding of the correlates of antisocial behavior could further improve the design of treatments for antisocial populations, while information about the effectiveness of therapeutic interventions advances mental health services for antisocial individuals living within restrictive settings characterized by a high proportion of people with mental illness and only limited treatment resources. Ultimately, results of this work may serve to reduce costs associated with antisocial individuals residing in correctional and residential youth settings through decreasing institutional misconduct and its associated consequences, shortening the length of stays, lowering the risk to recidivate or preventing a high number of transitions.

Implications for future research

Several recommendations can be made for future studies based on the current work. Future studies on the association between recent CVE and current mental health problems should employ a longitudinal approach to be able to make concrete statements about the directionality and persistence of effects. Furthermore, it would be interesting to document the association between CVE and rates of victimization in addition to witnessed community violence. More moderator variables known to impact the link between CVE and conduct problems should be investigated, such as family structure or gang membership. Specific examination of CVE and its relationship with conduct problems in antisocial and aggressive individuals residing in correctional or residential youth settings shall be of interest, as rates of violence are reported to be substantive.

Chapter 3 introduced a treatment evaluation study that did not include a control group. Future studies should seek to evaluate the effectiveness using a control group as reference and controlling for an inmate's concurrent participation in additional treatment programs. Furthermore, the results of Chapter 3 should be examined in a female and juvenile population to investigate the program's utility for other target groups. Likewise, Chapter 4 has focused on the implementation and scientific evaluation of a treatment program for antisocial females within residential youth care only. Future studies should develop a male version and evaluate its effectiveness for male adolescents within residential youth care. In addition, other community sectors should be examined aside from correctional institutions and residential youth settings, such as halfway houses or drug rehabilitation centers to ensure continuity of care. Recent research suggests that continuity of care is not ensured for individuals with mental illness who have come into contact with the youth welfare and/or legal system and that this lack contributes to adverse outcomes, such as increased rates of re-

institutionalization and re-incarceration (C. James, Stams, Asscher, De Roo, & van der Laan, 2013; Tyler, Trout, Epstein, & Thompson, 2014; Weinstein & Perlin, 2017).

Relatively few studies have investigated the existing barriers to conducting research and implementing evidence-based practices that have prevented a high number of studies. Moreover, very limited research to date exists on how to tackle these barriers. In order for successful, methodologically advanced and clinically/scientifically valuable studies to be performed, more research needs to address 1) institutional constraints (e.g., limited resources such as rooms, exclusion of staff from training and delivery of evidence-based practices), 2) organizational constraints (e.g., regulatory policies and procedures, state of emergencies), 3) staff constraints (e.g., limited number of personnel, lack of understanding/interest for research activities, high rates of burn-out, low program fidelity) and 4) population constraints (e.g., high turnover rates, limited lengths of stay, high attrition rates) (S. James et al., 2017; Steinlin et al., 2017; Yoon et al., 2017). In response to findings on the barriers, researchers should collaborate with the institutions of interest to raise awareness on existing constraints and develop ideas about how to address some of the identified issues to make research more easily realizable (Thompson et al., 2017; Yoon et al., 2017). In addition, it would be beneficial to pursue an even more client centered approach by asking the target population what kinds of interventions are needed and attractive from their perspective. To date, very little research has focused on what youths in residential care actually view as helpful and how existing interventions could be improved from their point of view to be more responsive to current trends, needs and ways of communication (Calheiros & Patrício, 2014; Harder et al., 2017; Swerts et al., 2017).

On a clinical and policy level prevention strategies should be implemented in family, school, treatment and community sectors to achieve greatest success in breaking the cycle of individuals experiencing violence and going on to perpetrate violence themselves. These prevention/intervention efforts should directly target populations at-risk of experiencing high levels of violence, such as children and adolescents in residential youth care or offenders in correctional settings. Continuity of care should be ensured through offering effective, evidence-based interventions in affiliated or adjacent settings so that individuals who transfer from a group home to an assisted living facility or an offender who transfers from prison to a halfway house are able to receive continued mental health services.

5.3 Conclusion

Several conclusive remarks can be made based on the studies presented in this dissertation. It was clearly demonstrated that community violence is a highly prevalent experience for children and

adolescents in Europe. A robust relationship between recent CVE and current conduct problems was found in different groups of children and adolescents eliminating the possibility of ecological fallacy effects in previously published works. Thus, CVE might be an important contributing factor for the development of antisocial behavior, for healthy youths and particularly for children and adolescents with a diagnosis of CD. Proactive aggression was shown to be a primary mediator of the link between CVE and conduct problems. Findings stress the importance of establishing adequate prevention and intervention strategies to break the cycle of violence exposure and violence perpetration. Consequently, approaches should be multimodal and take an individual's environment into account (National Collaborating Centre for Mental Health, 2013).

One such intervention is introduced in Chapters 3 and 4 and first evidence on the effectiveness of the proposed intervention is provided through demonstrating significant effects on behavioral problems. In addition, the first treatment evaluation showed that the intervention was effective for a broad variety of inmate subpopulations. The program has demonstrably reduced behavioral infractions and has thereby reduced costs associated with institutional misconduct. Further work is needed to extend the knowledge base about the intervention's effectiveness to other populations, settings and target outcomes.

All in all, the works summarized in this dissertation underline the need for continued research investigating effects of current risk factors likely to maintain or exacerbate mental health and behavioral problems in antisocial populations from underserved sectors. Interventions offered in the individual's direct living environment must be implemented and rigorously evaluated. Barriers to research and treatment implementation need to be identified and addressed. Continuity of care should be ensured to prevent endless cycles of re-institutionalizations or re-incarcerations.

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SEPTEMBER 2009 -JULY 2012	**University of Groningen** Groningen, *The Netherlands* BACHELOR OF SCIENCE Emphasis on: Psychology Minor: Psychology and Health
SEPTEMBER 1999 -JUNE 2008	**Willibrord Gymnasium** Emmerich am Rhein, *Germany* University Entrance Diploma
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FEBRUAR/APRIL 2016	2 modules schema therapy for children and adolescents with Dr. C. Loose (ISST approved)
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PUBLICATIONS

Oldenhof, H., Praetzlich, M., Steppan, M., Ackermann, K., Baker, R.H., Batchelor, M., Baumann, S., Bernhard, A., Clanton, R., Dikeos, D., Dochnal, R., Fehlbaum, L.V., Fernández-Rivas, A., González de Artaza-Lavesa, M., Gonzalez-Madruga, K., Guijarro, S., Gundlach, M., Herpertz-Dahlmann, B., Hervás, A., Jansen, L., Kerexeta-Lizeaga, I., Kersten, L., Kirchner, M., Kohls, G., Konsta, A., Lazaratou, H., Martinelli, A., Menks, W.M., Puzzo, I., Raschle, N.M., Rogers, J., Siklósi, R., Smaragdi, A., Vriends, N., Konrad, K., De Brito, S.A., Fairchild, G., Kieser, M., Freitag, C.M., Popma, A. & Stadler, C. (2017). Baseline Autonomic Nervous System activity in Female Children and Adolescents with Conduct Disorder: Psychophysiological findings from a European Multi-Centre Study. *Manuscript submitted for publication.*

Praetzlich, M., Oldenhof, H., Steppan, M., Ackermann, K., Baker, R.H., Batchelor, M., Baumann, S., Bernhard, A., Clanton, R., Dikeos, D., Dochnal, R., Fehlbaum, L.V., Fernández-Rivas, A.,

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Vriends, N., Kersten, L. .... & Stadler, C. (2017). Understanding the associations between community violence, peer victimization and conduct disorder in the context of cross-national differences in seven European countries. *Manuscript in preparation.*

SELECTED CONFERENCE ABSTRACTS/POSTERS

1. Kersten, L., Steppan, M., Vriends, N., Stadler, C. & the FemNAT-CD consortium (2017). Urbane Gewalterfahrung in Europa: Welche Auswirkungen auf die psychische Gesundheit sind zu beobachten? Deutsche Gesellschaft für Kinder- und Jugendpsychiatrie, Psychosomatik und Psychotherapie e.V. (DGKJP) Congress, Ulm, Germany; 03/2017.
2. Kersten, L. & Stadler, C. (2017). Slow down, Take a distance, Accept, Respect, Take action - START NOW: ein kognitiv-behaviorales Gruppentraining zur Verbesserung der Emotionsregulation. Deutsche Gesellschaft für Kinder- und Jugendpsychiatrie, Psychosomatik und Psychotherapie e.V. (DGKJP) Congress, Ulm, Germany; 03/2017.
3. Kersten, L., Steppan, M., Prätzlich, M., Mannstadt, S., Menks, W.M., Fehlbaum, L.V., Raschle, N.M., Stadler, C. & the FemNAT-CD consortium (2016). Prevalence of Community Violence Exposure and Its Effects on Mental Health Problems in European Adolescents. American Academy of Child and Adolescent Psychiatry (AACAP) 63rd Annual Meeting, New York City, NY; 10/2016.
4. Kersten, L., Dietrich, C., Fehlbaum, L.V., Mannstadt, S., Menks, W.M., Prätzlich, M., Raschle, N.M., Steppan, M., Stadler, C. & the FemNAT-CD consortium (2016). The Impact of Community Violence in Adolescents with Conduct Disorder. 5th edition of the EFCAP congress, Porto, Portugal; 05/2016.
5. Prätzlich, M., Raschle, N.M., Fehlbaum, L.V., Menks, W.M., Kersten, L., Mannstadt, S., Dietrich, C., Stadler, C., & the FemNAT-CD consortium (2016). Linking heart rate variability to psychological health and brain structure in female youths with conduct disorder. 5th edition of the EFCAP congress, Porto, Portugal; 05/2016.

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7. Kersten, L. & Stadler, C. (2015). Ein kognitiv-behaviorales Gruppentraining zur Verbesserung der Emotionsregulation für forensische Settings und stationäre Einrichtungen der Jugendhilfe. Deutsche Gesellschaft für Kinder- und Jugendpsychiatrie, Psychosomatik und Psychotherapie e.V. (DGKJP) Congress, Munich, Germany; 03/2015.

8. Cislo, A M., Trestman, R.L., Kersten, L., Sampl, S., Le, H. & Shea, K. (2014). Evaluating Start Now: An Evidence-Informed Group Therapy for Inmates with Behavioral Disorders. Presented at the the 7th Academic and Health Policy Conference on Correctional Health, Houston, TX; 03/2014.

Declaration by Candidate and Publication List

I hereby declare that this dissertation was prepared independently. The three research articles have been published to peer-reviewed journals and were written in collaboration with the listed co-authors. All citations are specified and only the mentioned sources were used in this dissertation.

The following articles are included:

Article 1

Kersten, L., Vriends, N., Steppan, M., Raschle, N.M., Praetzlich, M., Oldenhof, H., Vermeiren, R., Jansen, L., Ackermann, A., Bernhard, A., Martinelli, A., Gonzalez-Madruga, K., Puzzo, I., Wells, A., Rogers, J.C., Clanton, R., Baker, R.H., Grisley, L., Baumann, S., Gundlach, M., Kohls, G., Gonzalez-Torres, M.A., Sesma-Pardo, E., Dochnal, R., Lazaratou, H., Kalogerakis, Z., Bigorra-Gualba, A., Smaragdi, A., Siklósi, R., Dikeos, D., Hervás, A., Fernández-Rivas, A., De Brito, S.A., Konrad, K., Herpertz-Dahlmann, B., Fairchild, G., Freitag, C.M., Popma, A., Kieser, M. & Stadler, C. **(2017)**. Community Violence Exposure and Conduct Problems in Children and Adolescents with Conduct Disorder and Healthy Controls. *Frontiers in behavioral neuroscience, 11,* 219.

Data acquisition, data analysis, interpretation of the data, drafting and writing article.

Article 2

Kersten, L., Cislo, A. M., Lynch, M., Shea, K., & Trestman, R. L. **(2015)**. Evaluating START NOW: a skills-based psychotherapy for inmates of correctional systems. *Psychiatric Services*, *67*(1), 37-42.

Data analysis, interpretation of the data, drafting and co-writing the article.

Article 3

Kersten, L., Praetzlich, M., Mannstadt, S., Ackermann, K., Kohls, G., Oldenhof, H., Saure, D., Krieger, K., Herpertz-Dahlmann, B., Popma, A., Freitag, C. M., Trestman, R.L. & Stadler, C. **(2016)**. START NOW-a comprehensive skills training programme for female adolescents with oppositional defiant and conduct disorders: study protocol for a cluster-randomised controlled trial. *Trials*, *17*(1), 568.

Multi-site supervision and facilitation of the project, data acquisition, facilitation of START NOW trainings, participation in establishing questionnaires and setting up electronic database, formulating SOPs, drafting and writing the protocol.

Appendix Paper 1

Praetzlich, M., Oldenhof, H., Steppan, M., Ackermann, K., Baker, R.H., Batchelor, M., Baumann, S., Bernhard, A., Clanton, R., Dikeos, D., Dochnal, R., Fehlbaum, L.V., Fernández-Rivas, A., González de Artaza-Lavesa, M., Gonzalez-Madruga, K., Guijarro, S., Gundlach, M., Herpertz-Dahlmann, B., Hervás, A., Jansen, L., Kerexeta-Lizeaga, I., Kersten, L., Kirchner, M., Kohls, G., Konsta, A., Lazaratou, H., Martinelli, A., Menks, W.M., Puzzo, I., Raschle, N.M., Rogers, J., Siklósi, R., Smaragdi, A., Vriends, N., Konrad, K., De Brito, S.A., Fairchild, G., Kieser, M., Freitag, C.M., Popma, A. & Stadler, C. (2017). Resting Autonomic Nervous System Activity Is Unrelated to Antisocial Behavior Dimensions in Adolescents: Cross-Sectional Findings from a European Multi-Centre Study. **Manuscript submitted for publication.**

Data acquisition and critical revision of the article.

Appendix Paper 2

Stadler, C., Kersten, L. & Praetzlich, M. **(2015)** Störung des Sozialverhaltens mit fehlenden prosozialen Emotionen. *PSYCH up2date*, *9*(04), 225-235.

Drafting, formatting and co-writing the article.

Appendix 1 – Additional Co-Author Paper

Resting Autonomic Nervous System Activity Is Unrelated to Antisocial Behavior Dimensions in Adolescents: Cross-Sectional Findings from a European Multi-Centre Study

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Abstract

Purpose: Autonomic nervous system (ANS) functioning has long been studied in relation to antisocial behaviour, but relevant measures (heart rate, heart rate variability, pre-ejection period, respiration rate) have rarely been considered together. This study investigated the relationship between these measures and antisocial behaviour.

Methods: Using a sample of 1,010 youths with (47.8%) and without conduct disorder (52.2%) aged between 9-18 years (659 females, 351 males, mean age=14.2 years, SD=2.4), principal component analysis (PCA) was applied to various measures of psychopathology and antisocial behavior. Structural equation modelling was performed in order to test whether the ANS measures predicted PCA-dimensions. Cluster analysis was used in order to classify patterns of ANS activity. Analyses were performed separately for males/females and controlled for body-mass-index, age, caffeine use, cigarette smoking, sports, socioeconomic status, medication, cardiac problems.

Results: The PCA yielded three components: antisocial behaviour/comorbid psychopathology, narcissistic traits, and callous-unemotional traits. ANS measures were only weakly correlated with these components. Cluster analysis yielded high and low arousal clusters in both sexes. When controlling for covariates, all associations disappeared.

Conclusion: Our findings suggest that resting ANS measures are only weakly related to antisocial behaviour and indicate that smoking should be considered as an important covariate in future psychophysiological studies.

Keywords: autonomic nervous system, antisocial behaviour, callous-unemotional traits, smoking, cluster analysis, sex

1. Introduction

Autonomic nervous system and antisocial behavior

Autonomic nervous system (ANS) functioning has long been studied in relation to antisocial behaviour (see Portnoy et al., 2014). Antisocial behaviour can be characterized by conduct problems, aggression, psychopathic tendencies, and also comprises delinquent behaviour. Together these represent major public health and societal concerns (Portnoy & Farrington, 2015). Conduct disorder is one clinical manifestation of severe antisocial behaviour and its diagnostic criteria include aggressive (e.g., fighting, bullying, vandalism) and rule-breaking behaviour in children and adolescents (e.g., lying, theft, truancy; (American Psychiatric Association, 2013)). Due to the heterogeneity of antisocial behaviour and conduct disorder, a number of attempts have been made to characterize various subtypes or phenotypes, e.g., proactive/reactive aggression, conduct disorder with elevated psychopathic/callous-unemotional traits or in combination with internalizing symptoms or previous traumatic experiences (H. Steiner et al., 2017). Callous-unemotional traits comprising a lack of empathy, reduced guilt or reduced affective responding have been identified as important subtyping characteristics of children and adolescents with antisocial behaviour, although callous-unemotional traits can also occur in typically-developing children and adolescents (Fanti, Demetriou, & Kimonis, 2013; Herpers, Rommelse, Bons, Buitelaar, & Scheepers, 2012; Raschle et al., 2017). On a physiological level, different ANS measures have been used to identify ANS deficits in antisocial populations, and linked to some of the neurocognitive difficulties that they show, such as impairments in emotion regulation or reward processing (Fanti, 2016; Matthys, Vanderschuren, & Schutter, 2013). However, most of the studies have used just a single measure of ANS functioning, such as heart rate (Portnoy & Farrington, 2015), whereas multiple measures are needed to provide a more comprehensive assessment of ANS profiles associated with antisocial behavior. Therefore, this study aims to investigate simultaneously four cardiorespiratory ANS markers, in order to shed more light on the links between the ANS and antisocial behavior. Furthermore, the measurement of multiple ANS parameters allows for a clustering of ANS measures which might reconcile inconsistencies caused by differences in assessment of psychopathological phenotypes (Fanti, 2016). In contrast to investigating categorically defined diagnoses, we will use a comprehensive assessment approach considering a broad spectrum of antisocial behavior and adopting a dimensional approach. For a categorical approach on this dataset, please see Oldenhof et al. (this volume).

Cardiorespiratory ANS measures and antisocial behaviour

Four cardiorespiratory ANS markers measuring sympathetic (SNS) and/or parasympathetic nervous system (PNS) activity have previously been related to antisocial behavior: (1) heart rate (SNS

and PNS activity), (2) heart rate variability (PNS activity), (3) pre-ejection period (SNS activity), and (4) respiration rate (SNS and PNS activity). Several meta-analyses have confirmed low resting heart rate as a robust physiological correlate of antisocial behaviour including, e.g., aggression, psychopathy and conduct and oppositional defiant disorders (Ortiz & Raine, 2004; Portnoy & Farrington, 2015). Heart rate variability, in particular respiratory sinus arrhythmia, can be an indicator of cardiac PNS activity and is commonly quantified by spectral or time-domain analytic approaches (Grossman & Taylor, 2007). These approaches can also be used to derive many other parameters of heart rate variability (Allen, Chambers, & Towers, 2007). Reduced resting heart rate variability has been linked to externalizing and antisocial behaviour (Beauchaine, Gatzke-Kopp, & Mead, 2007; Graziano & Derefinko, 2013) and seems to be linked to lower emotion regulation abilities (Thayer, Ahs, Fredrikson, Sollers, & Wager, 2012; Williams et al., 2015). Pre-ejection period has previously been associated with reward processing which is affected in conduct and oppositional defiant disorders (Matthys et al., 2013; Sidlauskaite et al., 2017). Thereby, a lengthened resting pre-ejection period - indicating less sympathetic activity - was found in relation to conduct problems and aggression in children (Beauchaine et al., 2013). Finally, research has increasingly recognized the importance of respiration in relation to cognitive and emotional processing (Zelano et al., 2016), which are impacted in antisocial youth (Raschle, Menks, Fehlbaum, Tshomba, & Stadler, 2015). A higher respiration rate has been associated with severity of internalizing problems in girls (Blom, Serlachius, Chesney, & Olsson, 2014) and respiration rate has been linked to emotions such as anger, disgust and anxiety (Kreibig, 2010). While an association between aggressive behaviour and respiration rate has been found in animals (Carnevali, Nalivaiko, & Sgoifo, 2014), respiration rate has not yet been investigated as a correlate of aggressive or antisocial behaviour in humans. The Polyvagal Theory has been used to explain the link between the ANS and antisocial behaviour (Beauchaine et al., 2007). Despite its highly regarded, explanatory role for reasearch findings of psychopathology and emotion dysregulation (Beauchaine et al., 2007), its biological validity has been questioned, and the basic assumptions of the theory appear to have been falsified (Farmer, Dutschmann, Paton, Pickering, & McAllen, 2016; Gourine, Machhada, Trapp, & Spyer, 2016; Grossman, 2016; Grossman & Taylor, 2007).

Biological mechanisms

Neuroimaging studies have revealed biological mechanisms behind the autonomic arousal and antisocial behaviour relationship: Brain regions involved in autonomic control and emotion regulation partly overlap (Thayer et al., 2012; Thayer & Lane, 2000) and exhibit structural and functional alterations in youths with aggression (Raschle et al., 2015) and conduct problems (Rogers & De Brito, 2016). Aggression can be considered as deficient emotion regulation which reflects

abnormalities in the underlying emotion regulation network of the brain (Davidson, Putnam, & Larson, 2000). The neuro-visceral integration model elaborates on the role of one of the affected regions, the prefrontal cortex, for emotional, cognitive and autonomic regulation (Thayer & Lane, 2009). Thus, the overlap of emotion and autonomic regulation warrants the use of ANS measures for the study of aggressive behaviour.

Gaps in the literature

Overall, it can be concluded that there is substantial evidence linking ANS markers with different aspects of antisocial behaviour. However, the four ANS markers have rarely been included together in the same study. Further, many previous studies had small sample sizes. In addition, numerous studies have highlighted the importance of including sex in the description of antisocial behavior dimensions and ANS activity (e.g., Koenig & Thayer, 2016; Lehto-Salo, Närhi, Ahonen, & Marttunen, 2009), but this has rarely been done. The majority of studies on ANS activity and antisocial behaviour have not systematically controlled for lifestyle factors that may differ between typically-developing and antisocial groups (Portnoy & Farrington, 2015), even though smoking, sports, caffeine use, body mass index (BMI), medication use, and socio-economic status have all been shown to influence ANS functioning and/or psychopathology (Alvares, Quintana, Hickie, & Guastella, 2016; Hu et al., 2017; Koenig et al., 2014; Martin et al., 2008; Piotrowska et al., 2015). In particular, the influence of smoking has only been examined in a few studies (Jennings, Piquero, & Farrington, 2013; Murray et al., 2016), despite evidence indicating that smoking constitutes a risk factor for the development of antisocial behaviour and impacts brain and ANS functioning (Hu et al., 2017; Pagani et al., 2017).

Research aims

We aimed to disentangle the role of different ANS parameters in antisocial behaviour using data collected as part of a European multi-centre study (FemNAT-CD), with a specific focus on gender differences. We hereby aim to overcome several limitations of the previous literature by: (I) including two mixed measures capturing both SNS and PNS activity (i.e. heart rate and respiration rate) and two measures capturing PNS (i.e. heart rate variability) and SNS (i.e. pre-ejection period) activity separately. This approach allows us (II) to identify distinct physiological phenotypes and relate them to antisocial behaviour. As respiration rate has only been investigated in animal research, we also studied the link between respiration rate and antisocial behavior (III). Moreover, we consider (IV) the influence of covariates such as smoking, sports, caffeine, BMI, medication, cardiac problems and socio-economic status. We set out to investigate our research aims in a sample including individuals with and without conduct disorder. In line with previous literature, we hypothesized that we would

observe negative correlations between heart rate and respiratory sinus arrhythmia and antisocial behaviour, whereas we predicted that pre-ejection period and respiration rate would be positively correlated with antisocial behaviour. Further, we hypothesized that different ANS clusters would be associated with measures of antisocial behaviour.

2. Methods

2.1 Recruitment and participants

1010 adolescents (659 females, 351 males; 47.8% with conduct disorder and/or oppositional defiant disorder) aged between 9-18 years (mean = 14.2, SD = 2.4) were included in the study as part of an ongoing European multi-centre study investigating female conduct disorder (FemNAT-CD). The distribution of comorbidity patterns was as follows: conduct and oppositional defiant disorder (64.5%), conduct disorder only (23.7%), oppositional defiant disorder only (11.8%). A more detailed description of the sample characteristics (including ANS values) is provided in the article by Oldenhof et al. (this volume). The participants were recruited through schools, clinics, and youth welfare institutions in seven European countries (Germany, Greece, Hungary, Netherlands, Spain, Switzerland, and United Kingdom). All participants underwent standardized clinical interviews, filled out questionnaires and took part in an ANS measurement session. All individuals had to have an IQ >= 70 (see Fig. 1 for inclusion and exclusion criteria). Patients were diagnosed with conduct disorder based on a semi-structured clinical interview (please see section 2.2.2 below for details of the assessment). Written informed consent was obtained from the participants and their caretakers. The study was conducted in accordance with the Declaration of Helsinki and approved by all local ethics committees.

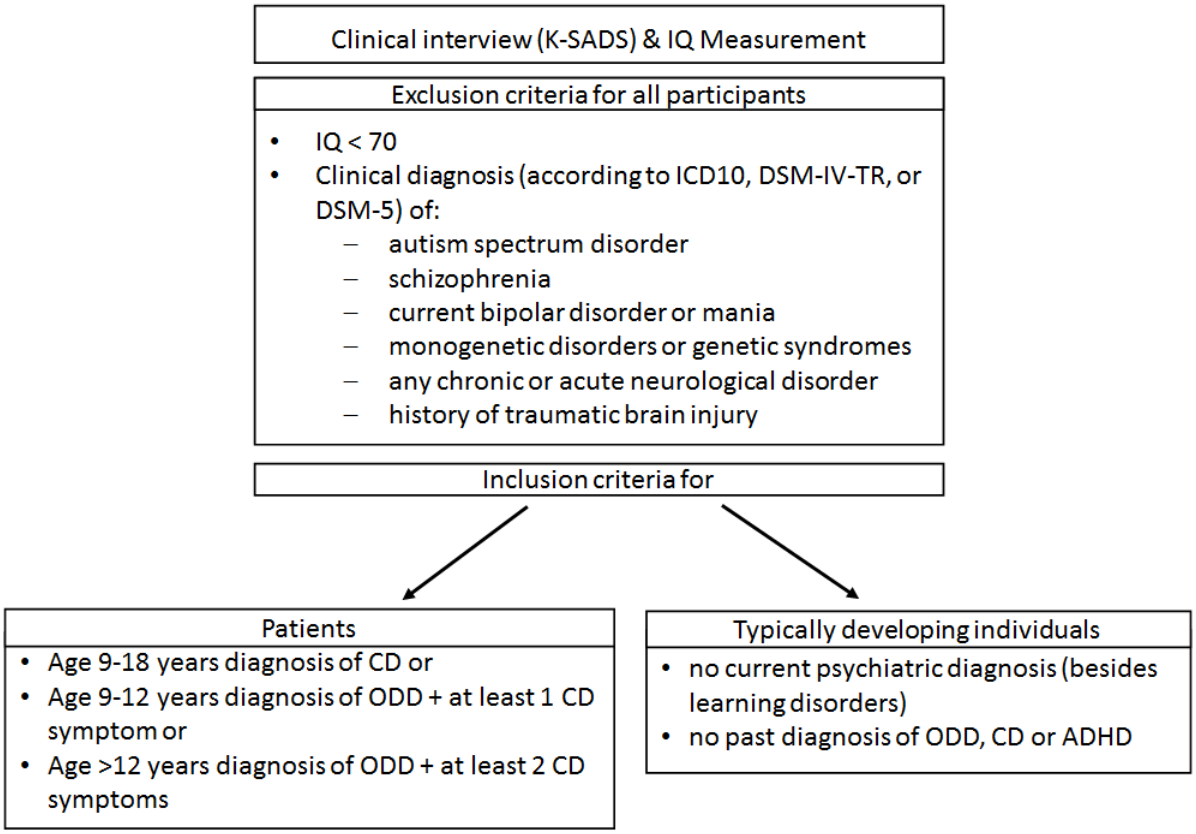

Figure 1. Inclusion and exclusion criteria in the study. CD=conduct disorder; ODD=oppositional defiant disorder; ADHD=attention deficit hyperactivity disorder.

2.2 Materials

2.2.1 ANS measures

ANS measures were assessed using electrocardiography (ECG) and impedance cardiography (ICG) registration by the VU-AMS device (Vrije Universiteit Ambulatory Monitoring System) (de Geus, Willemsen, Klaver, & van Doornen, 1995). H98SG, ECG Micropore electrodes (Covidien, Germany) were used and applied to the skin which was cleaned with alcohol beforehand. ECG data were derived from the R-peak registration, which was scored by an algorithm within the VU-DAMS software package version 3.9 and checked manually for missed or incorrect R-wave peaks and abnormalities in the registration. Abnormalities defined as premature ventricular contractions (PVCs), premature atrial contractions (PACs) or low quality ECG signal fragments were removed from the data. Ensemble averaged ICG complexes were derived from all valid heartbeats. The B-point and dZ/dt-min peak were identified in each averaged ICG complex using an algorithm within the VU-DAMS software package with a low-pass filter of -0.12 – 60 Hz. All complexes were again checked manually. Data on respiration rate was derived from the dZ-signal (thorax impedance), and identified as 'irregular respiration' when the duration of consecutive breaths reached a threshold. Whenever

more than 50% of the respiration data was identified as 'irregular', respiration rate data was set as missing. Data checking and scoring were performed by trained researchers and students and additional consensus meetings took place in order to discuss complex data.

Heart rate measurements were derived from the scored ECG signal and respiration rate was derived from the thorax impedance signal. To investigate heart rate variability, as a measure of PNS activity, respiratory sinus arrhythmia was assessed. Respiratory sinus arrhythmia was calculated using the peak-valley method (Grossman, Beek, & Wientjes, 1990) by subtracting the shortest heart period during inspiration minus the longest heart period during expiration; this was computed on a breath-to-breath basis. When no difference in shortest and longest beats could be detected, respiratory sinus arrhythmia was set to be zero for that particular breath. Respiratory sinus arrhythmia values were set as missing when more than 50% of the breaths could not be detected or were identified as 'irregular'.

Cardiac SNS activity was measured by the pre-ejection period (in msec). This is currently the most reliable non-invasive indicator of SNS functioning (van Lien, Schutte, Meijer, & de Geus, 2013) and can be derived from combined ICG and ECG recording. Pre-ejection period is defined as the time period between the onset of the left ventricular depolarization and the opening of the aortic valve. These events are marked respectively by the Q-wave onset in the ECG and the B-point in the ICG.

Baseline measurement – After the ECG/ICG electrodes were applied to the participant's body, they were given 10 minutes to habituate to the procedure. This enabled the participant to get accustomed to the setting in order to minimize the effect of stress induced by the experimental setting. Thereafter, a 5-minute excerpt from an aquatic video (Coral Sea Dreaming, Small World Music Inc.) was presented to obtain baseline ANS measures, which was proven effective in a previous study (Piferi, Kline, Younger, & Lawler, 2000). The video was presented on a DELL Latitude E5550 Laptop and Sennheiser HD 201 earphones were used.

Prior to the physiological assessment, participants were asked whether they had smoked in the past hour or consumed alcohol or used drugs in the past 24 hours. If they answered positively to any of these questions, the assessment was postponed.

2.2.2 Behavioural measures

Conduct disorder. Diagnostic information was obtained through the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997). The K-SADS-PL is a standardized, semi-structured clinical interview assessing current and past episodes of psychopathology in children and adolescents according to DSM-IV-

TR/DSM-5 criteria (American Psychiatric Association, 2000, 2013). Interviews were conducted with the participant and their parent or caretaker separately. Additionally, information from medical files was used in some cases. Summary ratings are derived from the clinical judgment of the interviewer using all available sources.

IQ. In case of missing IQ measurements, the IQ was estimated using two subtests of the Wechsler Intelligence Scale for Children: vocabulary and block design, or for participants from the age 17 on the Wechsler Adult Intelligence Scale (Petermann & Wechsler, 2008): vocabulary and matrix reasoning. At UK sites, the Wechsler Abbreviated Scale of Intelligence (WASI) was used for all ages (Wechsler, 1999).

Psychopathic traits. We used the self-report version of the Youth Psychopathic traits Inventory (YPI) (Andershed, Kerr, Stattin, & Levander, 2002) to assess psychopathy. This questionnaire consists of 50 items scored on a 4-point Likert scale from 1 to 4, ranging from "Does not apply at all" to "Applies very well". The YPI comprises the following ten subscales: dishonest charm, grandiosity, lying, manipulation, remorselessness, unemotionality, callousness, thrill seeking, impulsiveness, irresponsibility. In our study, the subscales dishonest charm (α=.80) and manipulation (α=.81) showed good, the subscales lying (α=.77), remorselessness (α=.72), impulsiveness (α=.72) and irresponsibility (α=.75) acceptable, the subscales grandiosity (α=.68), unemotionality (α=.60) and thrill seeking (α=.66) questionable and the scale callousness (α=.57) poor internal consistency.

Comorbid psychopathology. We used the Massachusetts Youth Screening Instrument Version 2 (MAYSI-2) (Grisso & Barnum, 2006) to screen for a variety of comorbid psychopathological symptoms. The MAYSI-2 is a self-report tool developed to facilitate identification of youths with mental health issues within juvenile-justice facilities. The version we used in our study consists of 48 ‘yes’ or ‘no’ questions regarding the past 2-3 months. The instrument contains seven scales: ‘alcohol/drug use’ (ADU), ‘angry-irritable’ (AI), ‘depressed-anxious’ (DA), ‘somatic complaints’ (SC), ‘suicide ideation’ (SI), ‘thought disturbance’ (TD), and ‘traumatic experiences’ (TE). The scales ADU (α=0.89), AI (α=.85), DA (α=.79), SC (α=.75), SI (α=.89) showed good, the TD scale (α=.64) sufficient and the TE scale showed poor (α=.52) internal consistencies in our study, possibly due to the use of a shortened version of this scale containing only 2 items instead of 5.

Aggression. We used the Reactive-Proactive aggression Questionnaire (RPQ) (Raine et al., 2006) to distinguish between these types of aggression. The questionnaire consists of 23 items on a 3-point Likert scale from 0-2, ranging from “never” to “often”. The proactive and reactive scales are sum scores of the respective items. The reactive (α=.88) and proactive (α=.86) scales showed good internal consistency in our study.

2.2.3 Covariates

Body mass index. Weight and height were measured on the day of the physiological assessment for the calculation of participants' body mass index (BMI).

Caffeine. We assessed caffeine use on the day of the physiological assessment by asking the participants: "How many caffeine-containing drinks (e.g., coffee, tea, coke, energy drinks) have you consumed in the past 24 hours?".

Smoking. We assessed smoking on the day of the physiological assessment by asking the participants: "How many cigarettes do you smoke on an average day?" (cigarettes/day).

Sports. We asked the participants on the day of the physiological assessment "How many hours a week do you practice sports?" (hours/week).

Socioeconomic status. Socioeconomic status (SES) was estimated based on parental income, education and occupation. Assessments were based on the International Standard Classification of Occupations (International Labour Organization, 2012) and the International Classification of Education (UNESCO Institute for Statistics, 2015). Human rater and computer-based ratings were combined into a factor score using Principal Component Analysis (PCA). Reliability (internal consistency) of the composite SES score was acceptable (α =.74).

Medication. We assessed psychotropic medication by asking the participant, caretaker, therapist or parent. For the analysis, we integrated the information as a dichotomous variable (0 = no medication and 1 = medication).

Cardiac problems. We assessed cardiac problems as a dichotomous variable (yes/no) by asking the participant: "Have you had any heart problems in the past?" (e.g., cardiac arrhythmia/heart surgery).

2.3 Statistical analyses

2.3.1 ANS measures – data cleaning and preparation.

Statistical analyses were performed using SPSS Version 24/AMOS Version 24 and R Version 3.4.2. Before analysis, data cleaning was applied to all ANS measures. We log-transformed respiratory sinus arrhythmia (lgRSA) due to a right-skewed distribution which became closer to a normal distribution after transformation. Values higher or lower than 3 SD of the sample means were classified as outliers and excluded. For respiration rate we identified 5 outliers, for heart rate 1 missing value and 7 outliers, for pre-ejection period there were 50 missing values and 1 outlier, and for the respiratory sinus arrhythmia data 8 outliers. Additionally, for respiration rate we excluded all values which contained more than 50% of irregular respiration (identified by the VU-DAMS

programme) in the 5 min baseline which was the case for 6 values. The respective respiratory sinus arrhythmia values were excluded as well. Subsequently, we checked whether the number of missing values and outliers differ in a systematic way between groups (gender and patient status). Summing up the number of missing values and outliers for all four ANS measures per individual, ANOVA was performed to identify group (gender and patient status) biases. No differences were observed between the groups. The values were excluded on a single value basis, id est, if for example the pre-ejection period value was excluded, the other ANS values of this participant were still included for analysis. Several analyses were conducted to identify potential site effects on ANS measures, e.g., due to differences in use of technical devices, climate or other local circumstances. Using a saturated model Analysis of Variance (ANOVA) on ANS measures (as dependent), patient status and gender (as fixed factors), site (as random factor) and age and testing time (as covariates), site did neither emerge as a significant main effect, nor within a significant interaction term, suggesting no bias caused by site effects.

2.3.2 Main statistical analyses

Principal Component Analysis (PCA) was performed separately for each sex, extracting orthogonal (uncorrelated) components with an Eigenvalue > 1 (Kaiser-Guttmann criterion). Standardized scores on PCA components for each individual were saved based on Bartlett-Regression. Bivariate correlations were conducted between the ANS measures, principal components and covariates. In a second step, partial correlations were used to control for the influence of covariates. Structural Equation Modelling (SEM) was performed using AMOS, with ANS measures, age and smoking as predictors and PCA components as outcome variables. Sex was included based on a two-group approach, allowing varying beta-coefficients for all paths and one common model fit for both sexes. Cluster Analysis was performed using R. At first, the R package “Mclust” (Fraley, Raftery, Murphy, & Scrucca, 2012) was used to identify the number of clusters using Bayesian Information Criterion (BIC) as a goodness-of-fit index. In a second step, k-means clustering (R package “stats”) was used to assess cluster membership for each individual based on the number of identified clusters in the first step. Cluster analysis was performed only on (standardized) ANS measures as continuous input variables, no questionnaires or other psychometric variables were included for cluster identification. Analyses of Variance (ANOVA) were applied in order to test whether clusters differed on questionnaires and subscales included in the study, as well as on covariates and principal components obtained from PCA. The results obtained using cluster analysis were cross-validated with findings from Latent Class Analysis (LCA) using Mplus, based on the number of identified clusters in the first step. Phi coefficients are reported to show the agreement of the two methods.

3. Results

3.1 Dimensions of antisocial behaviour

Table 1 illustrates the results of the PCA performed separately for both sexes using measures from the antisocial behaviour spectrum, comprising conduct disorder, reactive/proactive aggression, psychopathic traits (YPI), and comorbid psychopathology (drug and alcohol use, internalizing symptoms, traumatic experiences, MAYSI). For males and females, the Kaiser-Gutmann-criterion suggested a three-component solution. For both sexes highly similar factors emerged, considering that factor loadings for each component showed a high correspondence across the sexes (r1=.89; r2=.99; r3=.77), indicating factorial invariance in particular for component 2. Component 1 appears as a "general factor of antisocial behaviour and comorbid psychopathology" with high loadings on all scales that capture the broader spectrum of antisocial behaviour, for both sexes, with the highest loading on aggression. Component 2 was labelled "narcissistic traits" based on the highest loadings on manipulation, dishonest charm, and grandiosity (YPI). Component 3 shows similar loadings for both sexes, but considering the lowest of all correlations (r3=.77) it also shows an indication of factorial non-invariance by sex. Component 3 was named "callous-unemotional" for girls as it loaded on scales of callousness (λ=.73) and unemotional (λ=.35). For boys, component 3 was named "callous-blunt" as it loaded positively on the scale callousness (λ=.56) and negatively on lying (λ=-.40). This latter dimension also showed high loadings on conduct disorder itself, alcohol and drug use and proactive aggression. All three components account for 61.4% of the variance for girls and 59.4% of the variance for boys.

********** INSERT TABLE 1 ABOUT HERE **********

3.2 Correlations between antisocial behaviour, ANS measures and covariates

Table 2 shows a correlation matrix between the three principal components of antisocial behaviour and comorbid psychopathology identified in our analyses (see Table 1), the four ANS measures as well as covariates which are relevant for cardio-respiratory physiology and/or psychopathology. Correlations are shown for both sexes separately (females below the diagonal) and partial correlations controlled for covariates are superscripted. In females, significant correlations were observed between respiration rate and the general factor of antisocial behaviour (r=.12, p<.01) and callous-unemotional traits (r=.08, p<.05), and between heart rate and callous-unemotional traits (r=.09, p<.05), and pre-ejection period with the general factor of antisocial behaviour (r=.14, p<.001) and callous-unemotional traits (r=-.09, p<.05). In males, the pre-ejection period correlated positively

with the general factor of antisocial behaviour (r=.13, p<.05) and callous-blunt traits (r=.18, p<.01), while respiratory sinus arrhythmia correlated negatively with narcissistic traits (r=-.13, p<.05). All significant correlations were rendered non-significant when we controlled for covariates.

Several significant correlations were observed between covariates, antisocial behaviour, and comorbid psychopathology. The most prominent association was found for smoking with the general factor of antisocial behaviour, with a higher correlation for girls (r=.48, p<.001) than for boys (r=.38, p<.001). In contrast, callous-blunt traits correlated significantly with smoking only in boys (r=.41, p<.001). Among the relation between covariates and ANS measures, age showed the strongest association with all of the ANS measures, especially in boys, whereas in females only respiration rate was not related to age. In boys, among the covariates, smoking was only related to pre-ejection period (r=.23, p<.01) whereas in girls smoking was related to respiratory sinus arrhythmia (r=-.12, p<.01), pre-ejection period (r=.12, p<.01), and respiration rate (r=.20, p<.001). Among ANS measures, significant correlations were observed in the expected direction, e.g., between respiratory sinus arrhythmia and heart rate (girls: r=-.54, p<.001; boys: r=-.48, p<.001), except for an unexpected negative correlation between respiratory sinus arrhythmia and pre-ejection period (r=-.14, p<.01) in girls. The analyses suggest that these significant, though weak correlations between ANS measures and psychopathological components are influenced by covariates, potentially by smoking and age which show the highest correlations with these measures.

********** INSERT TABLE 2 ABOUT HERE **********

3.3 Predictors of antisocial behaviour

Figure 2 demonstrates the result of a multi-group SEM for both sexes (CFI=.988 RMSEA=.021) using the principal components of antisocial behaviour and comorbid psychopathology from Table 1 as outcome variables. None of the ANS measures significantly predicted PCA dimensions (general factor of antisocial behaviour, narcissistic traits, callous-unemotional/blunt traits). The covariates “smoking” and “age” outperformed all ANS measures with respect to predicting PCA dimensions. Smoking showed the strongest association with the general factor of antisocial behaviour and comorbid psychopathology (girls: β=.44***, p<.001; boys: β=.33***, p<.001) and with callous-unemotional/blunt traits (girls: β=.12**, p<.01; boys: β=.41***, p<.001). Several paths are significant only for one sex, e.g., age predicts callous-unemotional traits only in girls (β=-.18***, p<.001), whereas in boys the association of age and callous-blunt traits is non-significant (β=.06). Age is only negatively correlated with respiration rate in boys (β=-.24***, p<.001) and smoking only positively correlated with respiration rate in females (β=.19***, p<.001). Residual errors (ε1, ε2, ε3) which are

expected to be uncorrelated (since PCA produces uncorrelated components), are correlated in males (ε1 with ε3, r=.20***, p<.001). Figure 2 shows that ANS measures do not function as predictors of principal components underlying antisocial behaviour and psychopathology when controlling for age and smoking behaviour.

********** INSERT FIGURE 2 ABOUT HERE **********

3.4 Physiological phenotypes

Figure 3 illustrates the results of a k-means Cluster Analysis performed on ANS measures based on a two-cluster solution for both sexes according to the Bayesian Information Criterion. For girls, the "high arousal" cluster (40.7% of the sample) is characterized by low respiratory sinus arrhythmia, high heart rate and high respiration rate. This cluster is also characterized by significantly higher levels of caffeine consumption and lower age. The second cluster (59.3% of the sample) displays an inverse pattern and therefore appears as a "low arousal" type. For boys, both clusters show similar ANS patterns compared to girls. One difference between the two sexes, however, relates to the pre-ejection period. For boys, the pre-ejection period is significantly higher in the "low arousal" cluster (67.9% of the sample). Contrarily, the clusters in girls do not differ with regard to pre-ejection period. The "high arousal" cluster (32.1% of the sample) is characterized by significantly lower age and lower smoking levels. In females and males, there were no significant associations between cluster membership and psychopathological outcome variables (conduct disorder and principal components). Only in males, the "general factor of antisocial behaviour and comorbid psychopathology" showed evidence for a substantial difference between the two clusters. However, this association was no longer significant when controlling for multiple testing (Bonferroni correction), nor when controlling for covariates. ANOVAs were also performed on the subscales of each questionnaire, showing no significant associations between cluster membership and specific correlates of antisocial, aggressive, comorbid symptoms, callous-unemotional traits, and traumatic experiences (MAYSI, YPI, RPQ; data not shown). The cross-validation with findings from Latent Class Analysis using Mplus resulted in Phi coefficients of 0.75 for females and 0.83 for males.

********** INSERT FIGURE 3 ABOUT HERE **********

4. Discussion

The aim of our study was to examine relationships between different dimensional measures of antisocial behaviour and several ANS measures determined under resting conditions.

Furthermore, we investigated how different clusters of ANS activity relate to antisocial behaviour and comorbid psychopathology. We studied four ANS measures (heart and respiration rate, respiratory sinus arrhythmia and pre-ejection period) together capturing SNS and/or PNS activity. We carefully controlled for several covariates, including cigarette smoking. We studied those aspects with respect to sex using a large international sample including data acquired across seven European countries and containing not only healthy adolescents, but additionally those with clinically significant levels of antisocial behavior. This meant that we captured the full spectrum of antisocial behaviour – from very low to very high.

In our study, the weak correlations between baseline ANS measures and antisocial behaviour and psychopathology were rendered non-significant after controlling for age and smoking. Additionally, a cluster analysis suggested for both, girls and boys, a low and a high arousal cluster. Again, potentially significant (bivariate) associations between these ANS clusters and the general factor of antisocial behaviour and comorbid psychopathology were rendered non-significant when controlling for covariates.

No evidence for a relationship of low heart rate and antisocial behaviour

Some of our findings are in contrast to existing evidence regarding ANS functioning and antisocial behaviour. We did not find evidence for a relationship with low heart rate which had been shown in many previous studies (Latvala, Kuja-Halkola, Almqvist, Larsson, & Lichtenstein, 2015; Murray et al., 2016; Portnoy & Farrington, 2015). This is surprising, considering the statistical power based on a large sample size which tends to result in even small effects to become significant. However, in line with the present findings, a recent meta-analysis reported a trend showing the relationship between low resting heart rate and antisocial behaviour to become weaker with increasing publication year (Portnoy & Farrington, 2015). They explain this trend by referring to the "proteus phenomenon" describing an effect occurring in the early phase of a scientific investigation in which most likely significant findings are published in both directions. Later, findings refuting the original results become more interesting. Thus, the findings from Ortiz and Raine (2004) might have encouraged researchers to publish null findings refuting their results. One possible explanation of the weak relationship between antisocial behaviour and ANS parameters could be related to the severity of conduct problems in our study: Latvala et al. (2015) found a stronger relationship between violent crimes and low heart rate, as opposed to the comparison with non-violent crimes. Correspondingly, Portnoy and Farrington (2015) showed the strongest effect size (d=−.35) for violence compared to the other categories of antisocial behaviour (aggression, behaviour problems, conduct disorder/oppositional defiant disorder, offending, psychopathy). The conduct disorder/oppositional defiant disorder category, which is also present in our sample, only exhibited an effect size of d=−.19

in their analysis for low heart rate. One might also argue that the use of an inclusive sample with patients and typically developing individuals could have masked possible relationships. To investigate this, a categorical approach was performed on the same sample by Oldenhof et al. (this volume). The authors compared the conduct disorder group with controls and found no relation between antisocial behaviour and heart rate - only a higher respiration rate in female cases compared to female controls was detected.

Weak relations between the remaining ANS measures and antisocial behaviour

All remaining ANS measures showed significant, but weak associations to antisocial behaviour and psychopathology. We found positive associations between pre-ejection period and antisocial psychopathology for both sexes. A lengthened resting pre-ejection period, indicating less sympathetic activity was previously found in relation to conduct problems in children (Beauchaine et al., 2013). Further, the positive relation between respiration rate and psychopathology in females had been shown before (Blom et al., 2014). A negative association between respiratory sinus arrhythmia and our narcissistic component in males is not in line with other findings indicating a positive link (Hansen, Johnsen, Thornton, Waage, & Thayer, 2007). After controlling for covariates, none of the associations remained significant. In general, our findings of weak ANS associations with antisocial psychopathology align with previous research. For example, heart rate variability exhibited quantitatively small to moderate associations to different types of psychopathology, with the exception of schizophrenia, exhibiting a large effect size (Alvares et al., 2016), which is hypothesised to be at the peak of severity of the general psychopathology factor (Caspi et al., 2014).

Considerations on the covariate smoking

Findings regarding the covariate smoking should be considered further. The positive association between smoking and antisocial and comorbid psychopathology is in line with prior research (Jennings et al., 2013; Pagani et al., 2017; Talati, Keyes, & Hasin, 2016). Interestingly, the association of smoking and antisocial psychopathology strengthened in more recent study cohorts, whereas at the same time the prevalence of smoking decreased (Talati et al., 2016). It is argued that as social desirability of smoking decreases, the prevalence of biologically vulnerable persons among the population of smokers increases. It is further discussed by Talati et al. (2016) that the risk for deviant behaviour and for psychiatric conditions, including substance use, share common genetic variance. Accordingly, two genome-wide association studies have found genes in adults with alcohol dependence to be possibly related to conduct disorder in the past (Dick et al., 2011; Jian, Wang, Wu, Hillhouse, & Mullersman, 2011) and a strong overlap between substance abuse and antisocial behaviour has previously been shown (Krueger, Markon, Patrick, Benning, & Kramer, 2007).

ANS clusters

A further aim was to examine if reversing the common approach of relating psychopathology to physiology would benefit the investigation of the ANS and antisocial behaviour. For boys and girls a high and a low arousal cluster arose from our analysis. The results showed two opposite and physiologically plausible clusters, i.e., the ANS measures showed the expected relationships with each other (e.g., for heart rate and respiratory sinus arrhythmia an inversed activity pattern in both clusters). Previous research would suggest differential associations to psychopathology for these patterns, e.g., internalizing symptoms being related to higher ANS activity, and callous-unemotional traits being linked to lower ANS activity (Fanti, 2016). Our data does not provide evidence for such associations. The male clusters show a significant bivariate difference on the general factor of antisocial behaviour and comorbid psychopathology. However, the difference did not remain significant, neither after correcting for multiple testing, nor when controlling for covariates. Further, from a methodological point of view, an artificial division of study populations based on continuous variables, in our study the clustering based on ANS measures, may impact on results: It has been argued that a dichotomization of continuous measures leads to a loss of information and potentially leads to spuriously increased or decreased effects (MacCallum, Zhang, Preacher, & Rucker, 2002). In conclusion, also the reversed approach of creating groups of individuals based on resting ANS activity does not account for substantial variance in antisocial behaviour and comorbid psychopathology. The finding that patients were equally distributed over both clusters highlights the limited value for classifying individuals based on baseline ANS measures.

Limitations

Limitations of this study are considered, notably that we only assessed basal ANS measures. Growing evidence highlights the importance of ANS reactivity for adaptive functioning (Graziano & Derefinko, 2013). It is possible that we would have found associations between ANS activity and antisocial behaviour if we had included ANS reactivity measures in our analyses (e.g., heart rate increases to stress or in response to aversive stimuli). Despite acceptable reliability of SES (Cronbach's Alpha =.74), further limitations concern the inter-rater reliability of SES.

Suggestion for future research

Our study leads to some suggestions for future research. Considering the close relationship between smoking and respiration rate, at least in females, it would be worthwhile to include other respiratory variables in future studies (e.g., tidal volume, variability, pCO2), as they have been related to internalizing problems which are of direct relevance to the study of antisocial behaviour. Considering the strong relationship between antisocial behaviour and smoking and its relevance to

ANS functioning, we recommend to assess smoking routinely in studies of ANS and antisocial behaviour. Ideally, it should be assessed as a continuous variable, given its non-linear relationship to pre-ejection period (Hu et al., 2017), allowing a more informative analysis.

Conclusion

In conclusion, we found that baseline ANS measures showed only weak associations with antisocial behaviour and comorbid psychopathology, all of which become insignificant when controlling for covariates. Smoking was strongly related to the general factor of antisocial behaviour and comorbid psychopathology, as well as callous-blunt traits, which implies the importance to consider this variable when studying antisocial behaviour. The finding of opposing ANS clusters for both sexes did not help to elucidate the relationship between resting ANS activity and antisocial behaviour. The positive association between respiration rate and antisocial behaviour in females warrants the inclusion of this measure in future studies on ANS activity and antisocial behaviour. Finally, our results suggest the importance of a dimensional assessment of antisocial behavior in order to target this multi-faceted construct.

Practical implications

Given the small associations between the ANS and antisocial behaviour and comorbid psychopathology, our results do not support a potential of the ANS markers, as measured in a resting state, for profiling or predicting antisocial behaviour. However, future research should examine, if ANS markers examined under conditions of reactivity, for example, using an induction of emotions with film clips, provide such potential applications for the criminal justice practice. The strong relationship between smoking and antisocial behaviour suggests the relevance to target it in intervention and prevention programs, given its detrimental health effects to adolescents and their environment. Even passive smoking in households has been shown to increase the risk of antisocial behaviour (Pagani et al., 2017). Furthermore, females should be considered more carefully in intervention and prevention programs, as prenatal smoking constitutes a risk factor for the development of antisocial behaviour (Paradis, Shenassa, Papandonatos, Rogers, & Buka, 2017). Thus, the continuity of antisocial behaviour could potentially be decreased by placing a stronger focus on smoking prevention.

Competing interest

CMF has served as consultant for Desitin and Roche on Autism Spectrum Disorder. She receives royalties for books on ASD, ADHD, and depressive disorder. SDB has received speaker fees from the

Child Mental Health Centre and the Centre for Integrated Molecular Brain Imaging. All other authors declare that there is no potential conflict of interests.

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Table 1. Principal Component Analysis (PCA) using measures of antisocial behavior and psychopathology

		FEMALES (N=659)			MALES (N=351)		
		Component 1	Component 2	Component 3	Component 1	Component 2	Component 3
		„General Factor“	**„Narcissistic Traits“**	**„Callous-Unemotional“**	**„General Factor“**	**„Narcissistic Traits“**	**„Callous-Blunt“**
Conduct Disorder	K-SADS	**.70**	-.15	.27	**.50**	-.25	**.44**
Dishonest Charm	YPI	**.63**	**.52**	-.26	**.61**	**.55**	-.15
Grandiosity	YPI	**.36**	**.54**	-.22	**.45**	**.50**	-.26
Lying	YPI	**.59**	**.34**	-.20	**.53**	**.37**	**-.40**
Manipulation	YPI	**.67**	**.50**	-.24	**.62**	**.57**	-.11
Remorselessness	YPI	**.67**	**.35**	.16	**.67**	**.38**	.04
Unemotional	YPI	**.50**	**.46**	**.35**	**.48**	**.49**	.19
Callousness	YPI	**.41**	.18	**.73**	**.39**	.24	**.56**
Thrill seeking	YPI	**.70**	.23	-.12	**.62**	**.34**	-.09
Impulsivity	YPI	**.73**	.05	-.09	**.67**	.20	-.16
Irresponsibility	YPI	**.75**	.01	.10	**.68**	.05	.26
Alcohol / Drug Use	MAYSI	**.68**	-.19	.00	**.60**	-.15	**.37**
Angry-Irritable	MAYSI	**.80**	**-.32**	-.01	**.76**	-.41	-.03
Depressed-Anxious	MAYSI	**.74**	**-.46**	-.02	**.66**	**-.50**	-.27
Somatic Complaints	MAYSI	**.50**	**-.48**	**-.32**	**.51**	**-.52**	-.27
Suicidal Ideation	MAYSI	**.68**	**-.34**	.07	**.53**	**-.40**	-.08
Thought Disturbance	MAYSI	**.58**	-.25	-.08	**.57**	**-.37**	-.23
Traumatic Experience	MAYSI	**.78**	**-.33**	.00	**.71**	**-.41**	-.17
Proactive Aggression	RPQ	**.75**	.01	.03	**.67**	-.12	**.30**
Reactive Aggression	RPQ	**.82**	-.13	-.01	**.75**	-.20	.16
Eigenvalue		8,33	2,24	1,09	7,14	2,86	1,29
% Variance		43,9%	11,8%	5,75%	37,6%	15,0%	6,8%

Note. Component extraction based on Kaiser-Gutmann-Criterion (Eigenvalue > 1); Bold loadings > .30 or <-.30;
K-SADS-PL = Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version; YPI = Youth Psychopathic traits Inventory; MAYSI-2 = Massachusetts Youth Screening Instrument 2; RPQ = Reactive-Proactive aggression Questionnaire; ”General factor” (GF) of antisocial behaviour and comorbid psychopathology

Table 2. Correlation matrix of psychopathological principal components, autonomic nervous system (ANS) measures and covariates for females (below diagonal) and males (above diagonal)

		PCA of Antisocial and comorbid Psychopathology[1]			ANS measures				Covariates							
		GF	Narc.	CU	lgRSA	PEP	HR	RR	BMI	Caffeine	Smoking	Sports	Age	SES	Medication	CP
PCA of	GF		0 (.11)	0 (-.28***)	-.03 (.08)	.13* (-.00)	.00 (.10)	-.02 (-.02)	.14*	.27***	.38***	.02	.25***	-.16**	.10	-.03
Antisocial and comorbid Psycho-pathology[1]	Narc.	0 (.15**)		0 (.16*)	-.13* (-.12)	-.10 (-.03)	.03 (.12)	.03 (.00)	.05	-.02	-.03	.12	.09	.10	-.05	.01
	CB	0 (-.04)	0 (-.03)		-.10 (.03)	.18** (-.04)	-.07 (-.03)	.03 (.01)	.04	.11	.41***	-.07	.22***	-.20***	.12*	.02
ANS measures	lgRSA	-.04 (.04)	.07 (.03)	.00 (-.03)		-.10	-.48***	-.29***	-.14*	-.04	-.08	.02	-.21***	.10	-.09	.11*
	PEP	.14*** (.05)	0 (.01)	-.09* (-.05)	-.14**		-.22***	-.09	.20**	.09	.23**	-.03	.38***	-.06	-.01	-.01
	HR	-.02 (-.02)	-.03 (-.06)	.09* (.06)	-.54***	-.14**		.21***	-.07	.00	-.08	-.09	-.35***	-.03	.21***	-.02
	RR	.12** (.07)	-.03 (.00)	.08* (.04)	-.32***	.02 (.02)	.08*		-.05	.03	-.01	.04	-.27***	-.07	.16**	.02
Covariates	BMI	.21***	-.06	.04	-.00	.12**	-.07	.02		.07	.14*	.19**	.39***	-.14*	-.11	.04
	Caffeine	.18***	-.07	.09*	-.01	.05	-.03	.09*	.15***		.24***	.04	.19**	-.10	-.03	-02
	Smoking	.48***	-.08	.07	-.12**	.12**	.06	.20***	.19***	.31***		.13*	.38***	-.21**	.06	.11
	Sports	-.16***	.05	.09*	.07	-.08	-.05	-.05	-.09*	.01	-.12**		.12	-.04	-.03	.08
	Age	.25***	-.08*	-.14***	-.14***	.31***	-.21***	-.03	.37***	.23***	.31***	-.10*		-.05	-.14*	.01
	SES	-.27***	.09*	-.09**	.03	-.06	.02	-.07	-.16***	-.13**	-.24***	.12**	-.07		-.15**	-.04
	Medication	.21***	-.08*	.00	-.01	.01	.06	.03	.10*	.07	.17***	.00	-.02	-.09*		.09
	CP	.10**	-.07	-.03	-.11**	.03	.03	.02	.01	.10*	.16***	-.02	.06	-.01	.02	

Note. Pearson correlations. The results of partial correlations controlling for covariates are reported in parentheses and superscripted. GF=General factor of antisocial behaviour and comorbid psychopathology , Narc. = narcissistic traits, CU=callous-unemotional traits, CB=callous-blunt traits, RSA=respiratory sinus arrhythmia, PEP=pre-ejection period, HR=heart rate, RR=respiration rate, BMI=body-mass-index, CP=cardiac problems.

[1] Antisocial and comorbid Psychopathology relates to the dimensions identified by the Principal Component Analysis (PCA), which are reported in Table 1. *p<.05, **p<.01, ***p<.001

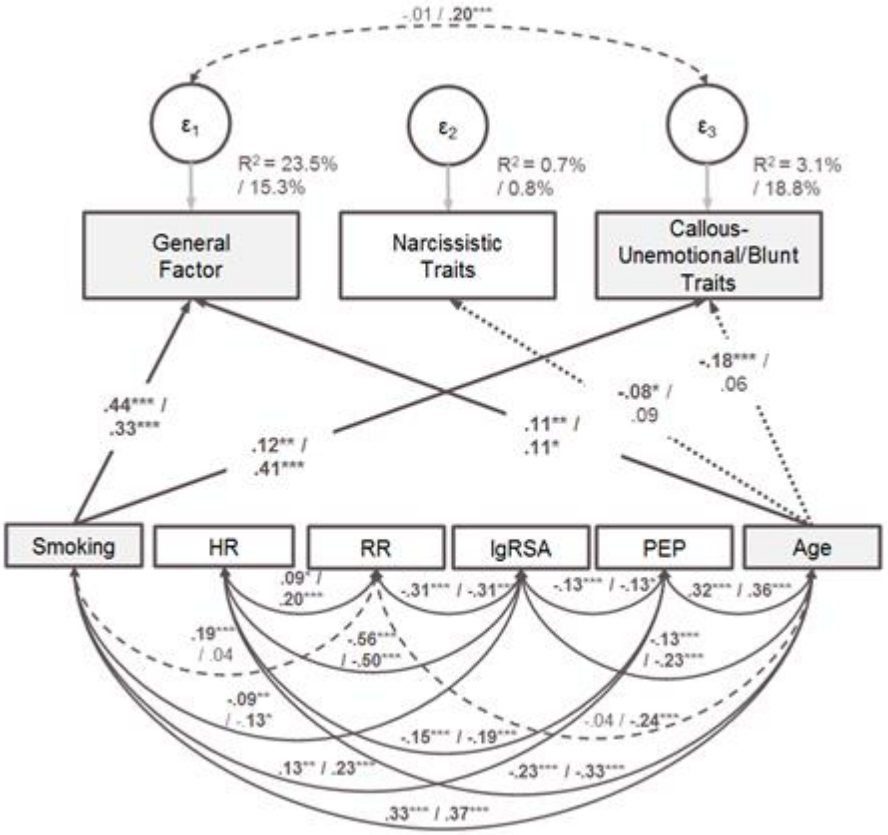

Figure 2. Structural Equation Model (SEM) using autonomic nervous system (ANS) measures as predictors of principal components analysis (PCA) dimensions of antisocial behavior and psychopathology controlling for age and smoking (CFI=.988 RMSEA=.021 df=34, N=1010) separately for females (parameters before slash) and males (parameters after slash) solid / dashed arrows represent significant paths for both sexes / significant paths only for one sex (*p<.05, **p<.01, ***p<.001). HR = heart rate, RR = respiration rate, RSA = respiratory sinus arrhythmia, PEP = pre-ejection period.

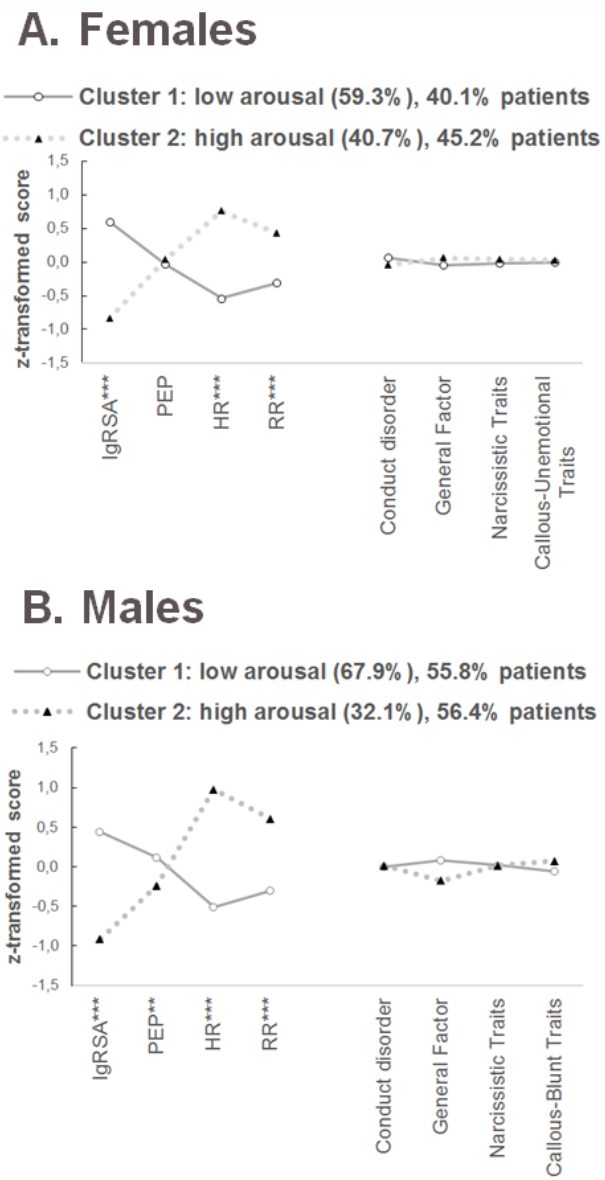

Figure 3. K-means cluster analysis performed using autonomic nervous system (ANS) measures as clustering variables and its relation to profiles across psychopathological principal components and conduct disorder for females (figure A) and males (figure B). Significant p-values of ANOVAs are shown (*** p<.001; **p<.01; * p<.05). RSA = respiratory sinus arrhythmia, HR = heart rate, PEP = pre-ejection period, RR = respiration rate.

Appendix 2 – Additional Co-Author Paper

Störung des Sozialverhaltens mit fehlenden prosozialen Emotionen – sind vorliegende Behandlungsprogramme weniger wirksam?

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Einleitung

Störungen des Sozialverhaltens (SSV) gelten als ein schwer zu behandelndes Störungsbild mit hohem Risiko für eine persistierende Verhaltenssymptomatik. Eine Vielzahl von Längsschnittstudien weist übereinstimmend auf ein höheres Risiko für die Entwicklung von Persönlichkeitsstörungen, späterer strafrechtlicher Verfolgung und Verurteilung, Inhaftierung oder Drogenmissbrauch hin (Übersicht bei [1]). Insbesondere so genannte kühl unemotionale Persönlichkeitseigenschaften (callous-unemotional traits, im Folgenden abgekürzt als CU Eigenschaften), die im DSM-5 durch die Klassifikation eines eigenen Subtyps berücksichtigt werden, sind mit einem schwerwiegenden und ungünstigen Verlauf assoziiert. Dieser Beitrag beginnt mit einer allgemeinen Einführung zur Klassifikation nach ICD-10 und den Neuerungen im DSM-5, gefolgt von einer näheren Beschreibung der Befundlage zu dieser Risikogruppe. Im Anschluss wird insbesondere der Frage nachgegangen, inwieweit sich differentielle Aussagen zur Therapiewirksamkeit und entsprechende Behandlungsempfehlungen aufgrund der vorliegenden Evidenz ableiten lassen.

Phänotyp und Klassifikation von Störungen des Sozialverhaltens

Die Diagnose einer SSV, deren Prävalenz bei 2-5.4 % liegt [2], setzt nach den aktuellen Leitlinien ein durchgängiges Muster oppositionell-aggressiver Verhaltenssymptome voraus, wie beispielsweise häufige oder schwere Wutausbrüche, welche vor dem Hintergrund des Entwicklungsstandes des Kindes und in Bezug zur Altersgruppe deutlich normverletzend und mindestens sechs Monate beobachtbar sind. Störungen des Sozialverhaltens umfassen nach der ICD-10 aber gleichermaßen dissoziale Symptome wie Schule schwänzen, Tiere quälen, oder delinquentes Verhalten wie Stehlen und gewaltsame Übergriffe. Die derzeitigen psychiatrischen Diagnosekriterien umfassen demzufolge eine breite und sehr heterogene Verhaltenssymptomatik (siehe Tabelle 1).

Während die Symptome, die einer SSV zugeordnet werden, im DSM-5 und ICD-10 weitgehend übereinstimmen, unterscheidet sich die Art der Klassifikation zwischen den beiden Systemen ICD-10 und DSM-5.

In der ICD-10 werden SSV nach folgenden Kriterien eingeteilt:

Tabelle 1: Grundlegende Symptome von oppositionellem Trotzverhalten und Störungen des Sozialverhaltens.

Oppositionelles Trotzverhalten	Aggressives Verhalten gegenüber Menschen und Tieren
• Wird schnell ärgerlich	• Bedroht andere, schüchtert ein
• Streitet sich häufig mit Erwachsenen	• Beginnt häufig Schlägereien
• Widersetzt sich häufig Anweisungen und Regeln von Erwachsenen	• Fügt anderen mit Waffen schwere körperliche Schäden zu
• Verärgert andere häufig absichtlich	• Körperlich grausam gegenüber Menschen
• Gibt anderen Schuld für eigene Fehler	• Quält Tiere
• Häufig empfindlich, leicht verärgert	• Erpressung, bewaffneter Raubüberfall
• Häufig wütend und beleidigt	• Zwingt andere zu sexuellen Handlungen
• Häufig boshaft und nachtragend	<u>Zerstörung von Eigentum</u>
	• Begeht vorsätzliche Brandstiftung
	• Zerstört fremdes Eigentum
	<u>Betrug oder Diebstahl</u>
	• Bricht in Autos oder Gebäude ein
	• Lügt zur Erlangung von Vorteilen
	• Stiehlt wertvolle Gegenstände
	<u>Schwere Regelverstöße</u>
	• Bleibt nachts ohne elterliche Erlaubnis von zu Hause weg (vor dem 13. L.j.)
	• Lief schon zweimal über Nacht von zu Hause weg
	• Schwänzt häufig Schule (vor 13. L.j.)

Störungen des Sozialverhaltens: DSM-5: mindestens drei Symptome der rechten Spalte müssen über einen Zeitraum von 12 Monaten (ICD-10: sechs Monate) und mindestens eins dieser Symptome während der letzten sechs Monate vorgelegen haben.
Störung mit oppositionellem Trotzverhalten: mindestens 4 Symptome der linken Spalte

In der ICD-10 werden SSV nach dem vorwiegenden Ort des Auftretens (familiär vs. generalisiert), der Beziehungsfähigkeit des Kindes oder Jugendlichen (mit vs. ohne soziale Bindungen) und dem Schweregrad (oppositionelle Störung ohne Verletzung der Gesetze oder Grundrechte anderer vs.

Vollbild der Störung) eingeteilt. Zudem können nach ICD-10 SSV gemäss Störungsbeginn (vor 10. Lebensjahr/ nach 10. Lebensjahr) differenziert werden. Übereinstimmung besteht darin, dass es sich bei SSV um eine heterogene Störungsgruppe handelt. Wenn sowohl die allgemeinen Kriterien für eine hyperkinetische Störung (F90.0) als auch für eine Störung des Sozialverhaltens (F91.-) erfüllt sind, wird nach ICD-10 die Diagnose einer hyperkinetischen Störung des Sozialverhaltens vergeben; bei gleichzeitigem Vorliegen einer depressiven Symptomatik die Diagnose Störung des Sozialverhaltens mit depressiver Störung (F92.0) oder bei Vorliegen einer anderen emotionalen Störung die Diagnose einer sonstigen kombinierten Störung des Sozialverhaltens und der Emotionen (F92.8).

Dahingegen orientiert sich die Klassifikation des DSM-5 am Beginn der vorhandenen Symptomatik und teilt ein in früh- und spät (childhood vs. adolescent-onset) beginnende SSV. Die Subtypisierung nach dem Störungsbeginn wurde im DSM-IV, aber auch im DSM-5 als mögliches prognostisches Kriterium berücksichtigt. Bedeutsam für den Entwicklungsverlauf ist insbesondere jedoch auch die Anzahl und Schwere früher psychosozialer Risikofaktoren. Eine explizite Klassifikation psychosozialer Risikofaktoren ist im DSM-5 nicht vorgesehen, jedoch im Rahmen der multi-axialen Klassifikation im ICD-10 auf der Achse 5 vorgesehen. Sowohl die kindlichen, als auch die elterlichen sowie umweltbezogenen Risiken haben einen erheblichen Einfluss auf den Verlauf und auf die Behandlung von SSV [3-5]. Darüber hinaus liegen mittlerweile mehrere Studien vor, die darauf hinweisen, dass sowohl bei früh-beginnenden, aber auch den spät-beginnenden SSV neurobiologische Auffälligkeiten gegeben sind, die auf Defizite in der Verarbeitung emotionaler Prozesse hinweisen. Es wird diskutiert, dass insbesondere die Qualität frühkindlicher Erfahrungen die Beziehung zwischen individueller Vulnerabilität und Beginn der Störung moderiert (siehe zusammenfassend [6]).

Zentrale individuelle, familiäre und psychosoziale Risikofaktoren

- Kind/Jugendlicher: Früher Beginn von Verhaltensproblemen (< 8. Lebensjahr), komorbide Störungen insbesondere Vorliegen einer ADHS, geringe kognitive Leistungsfähigkeit, Vorliegen einer hohen Ausprägung von kühl-unemotionalen Persönlichkeitseigenschaften
- Eltern: Psychische Erkrankungen eines oder beider Elternteile, häufige Konflikte zwischen Eltern, Misshandlungs- und Vernachlässigungs-erfahrungen, dysfunktionale Erziehungsmethoden, elterliche Kriminalität oder Alkoholkerkrankungen.
- Sozio-ökonomische Faktoren wie ein geringes familiäres Einkommen verbunden mit ungünstigen gesellschaftlichen und schulischen Faktoren.

(**##Merksatz-Anfang##**) Die Klassifikation psychosozialer Risikofaktoren, welche einen bedeutenden Einfluss auf den Verlauf von SSV haben, sollte im Rahmen der multiaxialen Klassifikation der ICD-10 vorgenommen werden, da diese nicht nur den Verlauf der Störung des Sozialverhaltens entscheidend beeinflussen können, sondern ebenso die Wirksamkeit empfohlener Behandlungsmassnahmen. (**##Merksatz-Ende##**)

Subtyp SSV mit mangelnden prosozialen Emotionen

Charakterisierung

Die entscheidende Modifikation im DSM-5 ist die Hinzunahme von kühl-emotionslosen Persönlichkeitszügen (callous-unemotional traits, im Folgenden kurz CU Eigenschaften) zur Klassifikation des Suptyps SSV mit mangelnden prosozialen Emotionen.
Für diesen Subtyp müssen zusätzlich zu den Kriterien für das Vorliegen einer SSV in den letzten 12 Monaten und in verschiedenen Lebensbereichen (und gegenüber mehreren Personen) mindestens zwei von vier Kriterien erfüllt sein, die eine defizitäre interpersonelle und emotionale Funktionstüchtigkeit beschreiben (siehe Infobox 1).

Infobox 1: Klassifikation nach DSM-5: SSV mit mangelnden prosozialen Emotionen.

1. Die Kriterien für das Vorliegen einer Störung des Sozialverhaltens sind erfüllt.

2. Zeigt in einem Zeitraum von mindestens 12 Monaten durchgängig zwei oder mehr der folgenden Merkmale. Bei der diagnostischen Beurteilung sind mehrere Informationsquellen zu berücksichtigen. So zum Beispiel, ob die Person selbst berichtet, dass diese Merkmale charakteristisch für sie sind oder ob diese von anderen (Eltern, andere Familienmitglieder, Lehrer, Gleichaltrige) beobachtet wurden.

- Mangel an Reue oder Schuldgefühlen (*Lack of Remorse or Guilt)*: Fühlt sich nicht schlecht oder schuldig, wenn er oder sie etwas Falsches tut (mit Ausnahme von Situationen, wenn er oder sie entdeckt wurde und Strafe zu erwarten ist).
- Mangel an Empathie (*Callous-Lack of Empathy)*: Missachtet die Gefühle anderer oder zeigt sich den Gefühlen anderer gegenüber gleichgültig.
- Gleichgültigkeit gegenüber der eigenen Leistung (*Unconcerned about Performance):* Zeigt keine Besorgnis bei schlechten Leistungen in der Schule, der Arbeit oder anderen wichtigen Bereichen.
- Oberflächliche oder defizitäre Emotionalität (*Shallow or Deficient Affect):* Drückt keine Gefühle aus oder zeigt anderen gegenüber keine Gefühle, mit Ausnahme von vordergründigen oder oberflächlichen Situationen (z. B. keine Konsistenz zwischen Verhalten und Emotionen, Emotionen können «an- » und «abgeschaltet» werden) oder Emotionen werden eingesetzt, um etwas Bestimmtes zu erreichen (z. B. um zu manipulieren oder andere einzuschüchtern).

Befundlage

Kinder und Jugendliche mit SSV und mangelnden prosozialen Emotionen zeigen einen schweren und chronischen Verlauf, sie sind charakterisierbar durch ein hohes Ausmaß an instrumenteller (proaktiver) Aggression, mangelnder Empathie und erhöhter Sensationssuche [7]. Zwillingsstudien belegen eine moderate bis hohe Vererbbarkeit von SSV bei Vorliegen hoher CU Eigenschaften [8]. Längsschnittliche Studien lassen jedoch vermuten, dass ein reziproker Einfluss zwischen genetisch determinierten kindlichen Verhaltensproblemen und elterlichem Erziehungsverhalten im Sinne einer evokativen Gen-Umwelt Korrelation anzunehmen ist [9]. Die beschriebenen neurobiologischen und neuropsychologischen Auffälligkeiten weisen insbesondere auf eine beeinträchtigte Verarbeitung aversiver emotionaler Reize, insbesondere Furchtreize, hin [10, 11]. Zudem konnten wiederholt Defizite im Bereich des passiven Vermeidungslernens nachgewiesen werden, das heisst ein beeinträchtigtes Lernen aus negativen Konsequenzen, was auch mit einer unzureichenden moralischen Entwicklung in Zusammenhang gebracht wird (siehe zusammenfassend [12]).
Diskutiert wird in diesem Zusammenhang auch, dass die geringe Reaktivität auf emotional saliente Hinweisreize mit einer geringeren Aufmerksamkeit auf die Augen von Bezugspersonen einhergeht [13]. Dadds und Mitarbeiter nehmen an, dass gerade in der frühen Kindheit der fehlende Augenkontakt mit den primären Bezugspersonen, den Erwerb sozial-emotionalen Wissens und den Erwerb von Kompetenzen zur Emotionsregulation und Empathie beeinträchtigen kann [13].

(**##Merksatz-Anfang##**) Eine mangelnde neurobiologische Responsivität auf emotionale Reize - insbesondere Furchtreize – kann das Erkennen von Empathie und prosozialem Verhalten erschweren. (**##Merksatz-Ende##**)

Die vorliegende Datenlage weist zusammenfassend relativ einheitlich darauf hin, dass CU Eigenschaften mit einem ungünstigen Entwicklungsverlauf assoziiert sind, die sowohl unabhängig von der Schwere der SSV Symptomatik, als auch unabhängig von Geschlechtseffekten zu sein scheinen (siehe zusammenfassend [14, 15]).
Diese Studien, die sowohl an nicht-klinischen als auch klinischen Stichproben durchgeführt wurden, unterstreichen somit weitgehend übereinstimmend die Bedeutung von CU Eigenschaften zur Vorhersage von antisozialem, aggressivem und delinquenten Verhalten. Inwieweit hohe CU Eigenschaften auch bei anderen Diagnosen oder unabhängig von einer psychiatrischen Diagnose mit klinischen Beeinträchtigungen assoziiert sind, ist auf der Basis der vorliegenden Datenlage jedoch nicht zu beantworten. Assoziiert mit einer Störung des Sozialverhaltens stellen sie jedoch ein bedeutendes und weitgehend spezifisches Entwicklungsrisiko dar (siehe hierzu auch [16]), was die Definition des Subtyps rechtfertigt.

(**##Merksatz-Anfang##**) Eine hohe Ausprägung an CU Eigenschaften bei Vorliegen einer Störung des Sozialverhaltens steht mit einem schweren und oft persistierenden Entwicklungsverlauf in Zusammenhang. (**##Merksatz-Ende##**)

Therapie

Allgemeine Behandlungsempfehlungen

Elterntraining im Kindesalter. Aufgrund der aktuell vorliegenden empirischen Evidenz sind für den Altersbereich zwischen 3 und 11- Jahren in erster Linie Elterntrainingsprogramme und Eltern-Kind Behandlungsprogramme für Kinder mit SSV empfehlenswert [17]. Diese Empfehlung gilt nach der vorliegenden Datenlage auch für Kinder mit hohen CU Merkmalen. Hauptfokus der meist im Gruppensetting durchgeführten Programme liegt dabei auf der Verbesserung der Erziehungskompetenz der Eltern, der Einführung von Familienregeln sowie der Verringerung negativer Interaktionskreisläufe und dem Aufbau positiver Strategien im Umgang mit dem Kind, um das Familienklima und die Familienkommunikation zu verbessern. Die Programme sollten sich an einem in wissenschaftlichen Studien überprüften Behandlungsmanual orientieren, wenn möglich beide Eltern einschliessen und die individuellen Schwierigkeiten der Eltern mit ihrem Kind berücksichtigen. Die Umsetzung von Übungen, Rollenspielen, Hausaufgaben und Feedback haben sich als evidenzbasierte Behandlungsstrategien erwiesen.

Die Vielzahl der Studien konnte zeigen, dass bei Kindern mit hohen CU Merkmalen nach einem durchgeführten Elterntraining weiterhin eine grössere Beeinträchtigung besteht als bei Kindern mit niedrigen CU Merkmalen. Allerdings gibt es empirische Hinweise, dass diese Kinder trotzdem hinsichtlich einer Reduktion der Verhaltensprobleme und der CU Merkmale profitieren können. Jedoch ist zu berücksichtigen, dass in dieser Gruppe möglicherweise nicht alle Module eines Elterntrainings in gleicher Weise wirksam sind. So scheinen insbesondere diejenigen Module, die an einer Förderung einer positiven, warmherzigen Eltern-Kind Beziehung ansetzen, positive Effekte zu erzielen, insbesondere im Hinblick auf die Reduktion von CU Merkmalen. Es sind jedoch weitere randomisiert-kontrollierte Studien notwendig, um den Einfluss von CU Eigenschaften als Moderator auch in verschiedenen Altersbereichen, aufzuklären.

(**##Merksatz-Anfang##**) Im Kindesalter sind Elterntrainings sinnvoll, welche die Erziehungskompetenz, das Familienklima und die Kommunikation in der Familie verbessern und auf die Förderung einer warmherzigen Eltern-Kind Beziehung abzielen. (**##Merksatz-Ende##**)

Im Alter zwischen 9 und 14 Jahren sind Gruppentrainingsprogramme zu empfehlen, die an einer Förderung emotionaler Kompetenzen und Problemlösestrategien ansetzten. Ebenso wie Elterntrainings sollten sie auf einem kognitiv-behavioralen Erklärungsmodell basieren und sich an einem evidenzbasierten und wissenschaftlich überprüften Manual orientieren [17].

Multimodale Behandlungsprogramme. Bei chronifizierter oder umfassender Symptomatik sind Interventionen zu empfehlen, die die gesamte Familie und das weitere soziale Umfeld des Jugendlichen in der Behandlung berücksichtigen. Zu den Interventionen mit nachgewiesener Evidenz zählen Programme, die an einer Verbesserung der Erziehungskompetenz der Eltern ansetzen, gegebenenfalls mit enger Unterstützung eines multiprofessionellen Teams, das die Familie in Krisensituationen unterstützt. Darüber hinaus steht die Verbesserung des Familienklimas und der Kommunikation im Zentrum der Behandlung sowie bei Bedarf die Integration individueller therapeutischer Elemente. Zu den mehrfach in randomisiert-kontrollierten Studien nachgewiesenen hoch wirksamen Behandlungsprogrammen zählt die Multisystemische Therapie (MST, [18]), oder auch andere familienbezogene Interventionen (siehe [19]) wie beispielsweise die multidimensionale Behandlung in Pflegefamilien (Multidimensional Treatment Foster Care), bei der Jugendliche während der Behandlung sechs bis neun Monate bei einer speziell geschulten Pflegefamilie bleiben oder die Funktionale Familientherapie. Auch für den deutschen Sprachraum liegen bereits erste Hinweise für die Wirksamkeit von MST vor [20].

(**##Merksatz-Anfang##**) Bei einer chronifizierten schwerwiegenden Verhaltenssymptomatik ist es für eine effektive Behandlung besonders wichtig, das Umfeld miteinzubeziehen. Dies wird beispielsweise mit guten Wirksamkeitsnachweisen in der Multisystemischen Therapie umgesetzt (**##Merksatz-Ende##**)

Schulbezogene Interventionen. Zu den präventiven Behandlungsprogrammen, die im Lebensumfeld ansetzen, gehören schulbezogene Interventionen und Interventionen im Kindergarten. Wesentlicher Ansatzpunkt ist die Verbesserung von Problemlösefertigkeiten und Ärgerkontrolle sowie Förderung sozialer Kompetenzen. In einer aktuellen Metaanalyse mit 60 eingeschlossenen Studien konnte gezeigt werden, dass schulbezogene Interventionen einen mittleren Effekt haben, um aggressives Verhalten und fehlende Selbstkontrolle zu reduzieren 21]. Die Programme sollten insbesondere in den Schulen und Kindergärten angeboten werden, in deren Klassenpopulationen ein hoher Anteil an Kindern besteht, bei denen nicht nur individuelle, sondern auch familienbezogene Risiken vorliegen, die zur Entstehung einer Störung des Sozialverhaltens prädisponieren [17]. Hierzu zählen beispielsweise kindliche Missbrauchserlebnisse, Scheidung der Eltern, elterliche psychische Probleme, Substanzmissbrauch oder chronische Konflikte.

(**##Merksatz-Anfang##**) Schulbezogene Interventionen zeigen bei der Therapie von fehlender Selbstkontrolle einen mittleren Effekt (**##Merksatz-Ende##**)

Haben Patienten mit CU-Eigenschaften einen schlechteren Behandlungsverlauf?

Prädiktoren für den Behandlungserfolg

Familiäre und psychosoziale Faktoren. Neben dem Einfluss möglicher individueller, den Therapieerfolg beeinflussender Faktoren wie beispielsweise hohe CU Eigenschaften sind elterliche und psychosoziale Faktoren zu berücksichtigen [22 - 24]. So kann die Durchführung eines Elterntrainings durch eine psychische Erkrankungen eines Elternteils, aber auch eine hohe familiäre Belastung, sozio-ökonomische und sozio-kulturelle Faktoren nicht nur mit einem ungünstigen Verlauf, sondern auch mit einem reduzierten Behandlungserfolg oder mit einem erhöhten Risiko für einen vorzeitigen Abbruch einer Behandlung assoziiert sein. Im Jugendalter können Umfeldfaktoren wie etwa der Einfluss der Gleichaltrigengruppe eine entscheidende Rolle spielen. So weisen die Ergebnisse von Van Ryzin und Leve darauf hin, dass der Erfolg einer evidenzbasierten Behandlung davon beeinflusst wurde, inwieweit durch die Intervention der Kontakt zur devianten Gleichaltrigen verändert werden konnte [25].

Individuelle Faktoren. Der im Hinblick auf die differentielle Wirksamkeit von Interventionen am häufigsten untersuchte Prädiktor ist das Vorliegen von hohen CU Eigenschaften. Aktuelle Übersichtsarbeiten weisen darauf hin, dass insbesondere Jugendliche mit ausgeprägten CU Eigenschaften weniger von einer Intervention profitieren [15]. Dies gilt besonders für Jugendliche in institutionellen oder forensischen Einrichtungen: Sie nehmen mit geringerer Wahrscheinlichkeit an einem Interventionsprogramm teil, die Anpassung an die institutionellen Bedingungen sind geringer und die Rate der Rückfälle höher. Die Studie von Waschbusch und Kollegen lässt vermuten, dass bei Vorliegen einer externalen Verhaltensproblematik und ausgeprägten CU Eigenschaften eine begleitende Stimulantienbehandlung wirksam sein kann [26]. Auch weisen einige Studien darauf hin, dass intensive modular ausgerichtete Therapieangebote Verhaltensprobleme auch bei Kindern mit schwerwiegenden CU Eigenschaften reduzieren können [27]. Therapieansätze, die stärker zugeschnitten sind auf die emotionalen, motivationalen und behavioralen Charakteristika von Kindern und Jugendlichen mit hohen CU Eigenschaften und die individuelle Interessen der Patienten berücksichtigen und Empathie fördern, sollten ebenfalls grössere Effekte zu erzielen.

So zeigen die Ergebnisse von Hawes und Dadds, dass die Module eines Elterntrainings, die auf die Vermittlung positiver Verstärkerprinzipien abzielen, bei Vorschulkindern mit hohen CU Eigenschaften gleichermassen wirksam sind während die Module des Trainings, in denen Eltern die Durchsetzung

konsequenter Erziehungsstrategien vermittelt wurde, weniger geeignet schienen [28]. Bei Kindern im Vorschulalter mit hohen CU Merkmalen scheint eine Intensivierung der Behandlung durch die Realisierung von mehr Sitzungen und der stärkeren Einbeziehung der Eltern notwendig und erfolgversprechend, um Verhaltensprobleme, aber auch CU Eigenschaften zu reduzieren [29]. Es wird diskutiert, dass die positiven Effekte insbesondere durch die Zunahme adaptiver Erziehungskomponenten wie elterliche Wärme und die Reduktion ungünstiger Erziehungsstrategien vermittelt wird. Auch ein intensives Elterntraining, Coaching und emotionale Unterstützung im häuslichen Umfeld hat sich für diese Gruppe im Vorschulalter als wirksam erwiesen [30]. Darüber hinaus wurde untersucht, ob der zusätzliche Einsatz eines Trainings zur Verbesserung der Emotionserkennung für Kinder mit hohen CU Eigenschaften wirksam ist. Die von Dadds und Mitarbeitern berichteten mittleren Effekte auf die erfassten Verhaltensprobleme scheinen jedoch nicht auf eine Verbesserung der Emotionswahrnehmung zurückzuführen zu sein, sondern auf den während der Intervention zusätzlich intensivierten Eltern-Kind Kontakt [31].

(**##Merksatz-Anfang##**) CU Eigenschaften können die Wirksamkeit evidenzbasierter Interventionen beeinträchtigen. Bei Vorliegen dieser Eigenschaften ist häufig eine Intensivierung der Behandlung indiziert, die eine umfassende Psychoedukation und Anleitung der Eltern einschliessen sollte. (**##Merksatz-Ende##**)

Behandlungsprognose im Jugendalter

Zur Frage, inwieweit CU Eigenschaften durch spezifische Interventionen auch im Jugendalter modifizierbar sind, liegen bisher wenige und zum Teil widersprüchliche Befunde vor. Manders und Kollegen untersuchten in einer randomisiert kontrollierten Studie die differentielle Wirksamkeit einer multisystemischen Intervention und konnten zeigen, dass diese bei Jugendlichen mit hohen CU Eigenschaften eine geringere Wirksamkeit aufweist [32]. Butler und Kollegen fanden entsprechende Ergebnisse nur im Selbsturteil von Jugendlichen nach einer MST Behandlung, während im Elternurteil positive Effekte der Intervention nachgewiesen werden konnten [33]. Die vorliegenden Ergebnisse können zusammenfassend nicht dahingehend interpretiert werden, dass evidenzbasierte Verfahren bei Jugendlichen mit CU Eigenschaften generell nicht wirksam sind. Jedoch zeigen Jugendliche mit hohen CU Eigenschaften nach der Therapie nach wie vor mehr Verhaltensprobleme im Vergleich zu Jugendlichen mit niedrigen CU Merkmalen [34].

Hawes und Kollegen schlussfolgern in ihrer Übersichtsarbeit, dass die geringere Effektivität der Interventionen bei Kindern und Jugendlichen mit hohen CU Eigenschaften nicht als Folge einer stärkeren Verhaltensbeeinträchtigung zu verstehen ist und auch unabhängig von familienbezogenen

Faktoren wie elterlichem Stress oder sozio-ökonomischem Stress zu sein scheint [35].

(**##Merksatz-Anfang##**) Zusammenfassend deuten die Ergebnisse darauf hin, dass CU Eigenschaften nicht als unbehandelbar einzuschätzen sind. Dies scheint insbesondere für Interventionsprogramme zu gelten, die im frühen Kindesalter ansetzen und besonders die Eltern-Kind Interaktion in den Fokus der Behandlung setzen. (**##Merksatz-Ende##**)

Forensisches Setting und Jugendhilfeeinrichtungen

Besonders hohe Prävalenzraten sind in der stationären Jugendhilfe festzustellen, wo bis zu 50%, häufig in Kombination mit anderen psychischen Störungen, unter einer Störung einer Störung des Sozialverhaltens leiden [36, 37]. Bei Stichproben von Jugendlichen, die aufgrund ihrer Delikte bereits Kontakt zur Polizei und Strafverfolgungsbehörden haben, steigen die Prävalenzraten bis zu 75% [38].

Abschreckungsprogramme. Auf der Basis durchgeführter Evaluationsstudien konnte gezeigt werden, dass im forensischen Setting eingesetzte Abschreckungsprogramme wie das Programm „Scared Straight“, bei dem delinquente Jugendliche mit Strafgefangenen Kontakt aufnehmen, nicht wirksam sind und sogar negative Effekte aufweisen, im Sinne einer Zunahme kriminellen Verhaltens nach Durchführung des Programms (siehe zusammenfassend [39]).

Evidenzbasierte Programme. Im forensischen als auch im stationären Jugendhilfebereich ist die Implementierung evidenzbasierter Programme aufgrund der hohen Prävalenzraten psychischer Störungen dringend indiziert. Die Metaanalyse von De Swart et al. weist darauf hin, dass bei Jugendlichen, die in Jugendhilfeeinrichtungen platziert waren, dann positive Verhaltensänderungen zu beobachten waren, wenn während der Plazierung psychosoziale Interventionen durchgeführt wurden [40]. Die Effekte fielen dabei nicht geringer aus im Vergleich zu einer multimodalen evidenzbasierten Behandlung wie beispielsweise MST. Insbesondere kognitiv-verhaltenstherapeutische Programme, auch unter Einbezug dialektisch-behavioraler Strategien können effektiv sind, um Probleme der Emotionsregulation bei aggressiven Verhaltensproblemen signifikant zu reduzieren und gleichzeitig Problemlösestrategien zu verbessern [41].

(**##Merksatz-Anfang##**) Zu den evidenzbasierten Behandlungsprogrammen zählen im Alter von 3-11 Jahren insbesondere Elterntrainingsprogramme, im Kindesalter kognitiv-behavioral ausgerichtete Gruppenprogramme, die an einer Verbesserung der Problemlösefertigkeiten und sozialen Kompetenz ansetzten. Bei chronischer und schwerwiegender Symptomatik sind multimodale Programme indiziert, die sowohl beim Jugendlichen, den Eltern und der Schule ansetzten und auch

darauf abzielen, ein förderliches Umfeld aufzubauen - auch mit einer nicht-devianten Gleichaltrigengruppe. (**##Merksatz-Ende##**)

Diagnostik und Risikofaktoren. Jeder wirksamen Behandlung muss eine umfassende Diagnostik vorausgehen - sowohl hinsichtlich der Erfassung persönlichkeits- und umweltbezogener Risikofaktoren, als auch hinsichtlich komorbider, insbesondere internaler Symptome, die ebenfalls das Risiko für einen ungünstigen Entwicklungsverlauf entscheidend erhöhen können [42]. Da sich verschiedene Risikofaktoren unterschiedlich auf die Wirksamkeit einer Intervention auswirken, sollten zukünftige Studien verstärkt der Frage nach der differentiellen Wirksamkeit verschiedener Behandlungskomponenten berücksichtigen, um optimale, den spezifischen Schwierigkeiten der heterogenen Patientengruppe angepasste Behandlungsmöglichkeiten entwickeln und anbieten zu können.

Vernetzung zwischen Versorgungssystemen. Für eine erfolgversprechende Behandlung ist insbesondere auch die verstärkte Vernetzung verschiedener Behandlungsmassnahmen und Fachstellen empfehlenswert. Eine Koordination der verschiedenen Systeme ist zentral, um die Übergänge in den Versorgungssystemen optimal zu gestalten. Insbesondere bei Vorliegen familiärer oder ausserfamiliärer Risikofaktoren, können ergänzende Maßnahmen indiziert sein, die nicht nur das medizinische, sondern auch erweiterte Unterstützungssysteme einschliessen.

(**##Merksatz-Anfang##**) Wichtig ist das Ineinandergreifen verschiedener Systeme der medizinischen und sozialen Unterstützung betroffener Familien. (**##Merksatz-Ende##**)

Bezugspersonensystem und Motivation. Eine wirksame Behandlung zeichnet sich neben der Schaffung optimaler Versorgungsketten über unterschiedliche Altersbereiche auch durch die angemessene Einbeziehung der wichtigen Bezugspersonen sowie der betroffenen Kinder aus. Oft sind gerade bei geringer Behandlungs- oder Veränderungsmotivation entsprechende therapeutische Techniken wie beispielsweise der Einsatz motivierender Gesprächstechniken vielversprechend, um für eine Behandlung zu motivieren oder einen frühzeitigen Abbruch zu verhindern [43].

Fazit

Die bisherige Datenlage zeigt, dass vorliegende Interventionen auch bei einer Störung des Sozialverhaltens mit mangelnden prosozialen Emotionen zu empfehlen sind, auch wenn die Effekte im Allgemeinen geringer ausfallen. Weitere Forschung ist notwendig, um die Entwicklung wirksamer Behandlungsangebote voranzutreiben, die vermehrt an den spezifischen neuropsychologischen und persönlichkeitsspezifischen Defiziten dieser Kinder ansetzten. Die Vernetzung zwischen

Versorgungssystemen, die Bereitstellung von umfassenden Angeboten, die die ganze Familie einschliessen sowie die Förderung der Behandlungsmotivation sind auch in dieser Subgruppe wichtige zu berücksichtigende Aspekte einer erfolgreichen Behandlung.

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