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Publication date:
2023-06

Permanent link:
https://doi.org/10.3929/ethz-b-000605288

Originally published in:
Journal of Psychopathology and Behavioral Assessment 45(2), https://doi.org/10.1007/s10862-023-10025-z

Journal of Psychopathology and Behavioral Assessment (2023) 45:277–293
https://doi.org/10.1007/s10862-023-10025-z

Identifying Symptoms of ADHD and Disruptive Behavior Disorders Most Strongly Associated with Functional Impairment in Children: A Symptom-Level Approach

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Accepted: 23 January 2023 / Published online: 3 March 2023

Abstract

To enhance the understanding of how symptoms of attention-deficit/hyperactivity disorder (ADHD) and disruptive behavior disorders such as oppositional defiant disorder (ODD), conduct disorder (CD), including callous-unemotional (CU) traits, differentially relate to functional impairment (FI). Participants were 474 German school-age children (age: $M = 8.90$, $SD = 1.49$, 81% male) registered for participation in the ESCAschool trial (ESCAschool: *Evidence-based, Stepped Care of ADHD in school-aged children*). Clinicians assessed the severity of individual symptoms and five FI domains specifically associated with ADHD symptoms or ODD/CD/CU symptoms using a semi-structured clinical interview. We conducted two multiple linear regression analyses, combined with relative importance analyses, to determine the impact of individual symptoms on global FI associated with ADHD and ODD/CD/CU symptoms. Next, we estimated two networks and identified the strongest associations of ADHD symptoms or ODD/CD/CU symptoms with the five FI domains. Symptoms varied substantially in their associations with global FI. The ADHD symptom *Easily Distracted* (15%) and ODD symptom *Argues with Adults* (10%) contributed most strongly to the total explained variance. FI related to academic performance, home life and family members, and psychological strain were most strongly associated with ADHD inattention symptoms, whereas FI related to relationships with adults and relationships with children and recreational activities were most strongly associated with hyperactivity-impulsivity symptoms. By comparison, the ODD/CD/CU symptoms most closely linked to FI domains originated from the ODD and CD dimensions. Our findings contribute to a growing body of literature on the importance of analyzing individual symptoms and highlight that symptom-based approaches can be clinically useful.

Keywords Functional impairment · Attention-deficit/hyperactivity disorder · Oppositional defiant disorder · Conduct disorder · Callous-unemotional traits · Network analysis

Introduction

Attention-deficit/hyperactivity disorder (ADHD) and disruptive behavior disorders such as oppositional defiant disorder (ODD) and conduct disorder (CD) with its specifier for callous-unemotional (CU) traits are common and highly impairing mental disorders in childhood and adolescence (Herpers et al., 2012; Polanczyk et al., 2015). In the field of disruptive behavior disorders, symptoms of affective dysregulation have gained increasing attention in recent years. Yet, diagnostic classification systems still disagree in the assignment to diagnostic categories. While symptoms of affective dysregulation are conceptualized as core to the diagnosis of disruptive mood dysregulation disorder (DMDD) diagnosis in the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) and in the 10th edition of the International

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Classification of Diseases (ICD-10; World Health Organization, 1992), the ICD-11 (World Health Organization, 2019) confines to adding a specifier for chronic irritability/anger to the ODD diagnosis because of the difficulty in empirically distinguishing DMDD from other mental disorders, particularly ADHD and ODD (Evans et al., 2017; Lochman et al., 2015). According to both classification systems, the diagnosis of any of these mental disorders requires the presence not only of symptoms with a certain frequency and severity, but also of functional impairment (FI). Although symptoms and FI are often interrelated, they are not identical (Palermo et al., 2008). FI manifests across a wide range of domains and can be defined as *"the extent of restriction in a child's ability to perform important daily life activities including physical, social, and personal activities due to their health condition or to specific symptoms"* (Palermo et al., 2008, p. 984). For example, the presence and severity of symptoms may interfere with children's ability to attend school or to maintain friendships. In fact, many children and adolescents or their parents seek help because of FI rather than the presence of symptoms (Epstein & Weiss, 2012). Studies assessing the relationship between symptoms and FI have yielded mostly moderate associations (reviewed by Rapee et al., 2012). In line with this, not all individuals meeting the symptom criteria for an ADHD or ODD/CD diagnosis demonstrate FI as a result of their symptoms, while others with only subthreshold symptoms may show marked levels of impairment (Arildskov et al., 2022; DuPaul et al., 2014; Pickles et al., 2001). The assessment of FI is not only important for making diagnoses and verifying the need for treatment, but also for treatment planning, identifying maintaining factors of psychiatric symptoms and treatment targets, and evaluating treatment success (DuPaul, 2022; Haack & Gerdes, 2011; Winters et al., 2005). Therefore, measures of FI provide important additional information to measures of symptoms.

Relationship between Symptom Dimensions and Functional Impairment Domains

Previous studies have demonstrated considerable variability in how symptom dimensions (e.g. ADHD inattention, hyperactivity-impulsivity) relate to various domains of FI. With regard to ADHD, the findings generally suggest that the inattention dimension is especially associated with academic impairment (Garner et al., 2013; Massetti et al., 2008; Willcutt et al., 2012; Zoromski et al., 2015). By comparison, the ADHD hyperactivity-impulsivity dimension generally shows the strongest associations with impaired social functioning, e.g. in the form of classroom disruption or peer exclusion (Garner et al., 2013; Willcutt et al., 2012). In terms of symptoms of disruptive behavior disorders, previous findings generally suggest that a greater severity of ODD problems is particularly related to impaired relationships with peers and family members (Burke et al., 2014; Dose et al., 2019; Kernder et al., 2019). Similarly, CD problems were found to predict workplace problems in young adults (Burke et al., 2014), and CU traits were found to predict impaired social functioning in children (Haas et al., 2018). Notably, most of these associations remained significant after controlling for demographic factors and comorbid symptoms (Burke et al., 2014; Garner et al., 2013; Haas et al., 2018; Massetti et al., 2008; Power et al., 2017; Willcutt et al., 2012).

Yet, despite the growing body of literature on FI associated with symptoms of ADHD and disruptive behavior disorders, there is still a need for clarification regarding the relationship between *individual* symptoms and different domains of FI. For example, it remains unclear whether certain symptoms are more impairing than others, and if so, what the relative importance of these symptoms is compared to other symptoms. This gap in the research is highly clinically relevant given the large variability in the symptoms experienced by patients (Mota & Schachar, 2000; Zoromski et al., 2015).

Relationship between Individual Symptoms and Global Functional Impairment

To address this need for clarification, some studies have investigated the impact of individual symptoms, rather than symptom dimensions, on global FI. With respect to ADHD, Mota and Schachar (2000) suggested that some individual ADHD symptoms, including, for example, the teacher-rated *leaves seat* and the parent-rated *blurts out*, predict global FI in children better than other symptoms. In a more recent study, Zoromski et al. (2015) examined teacher ratings and found that certain symptoms of inattention (i.e. *does not listen* during early childhood, *does not follow through* during adolescence) and certain symptoms of hyperactivity-impulsivity (i.e. *on the go* during early childhood, *leaves seat* during middle childhood, *interrupts or intrudes* during adolescence) showed the most robust relationships with classroom impairment. Regarding other externalizing behavior problems, research has shown that particularly ODD symptoms reflecting irritability (e.g. *anger* and *temper outbursts*) are associated with FI in children (Kolko & Pardini, 2010; Wesselhoeft et al., 2019) and that these symptoms predict greater FI than do other symptoms, even after controlling for other mental disorders (Dougherty et al., 2015). While this previous work has provided valuable insights into the relationship between symptoms and FI, additional exploration is needed. In particular, in previous studies, ratings for various domains of FI were combined into an overall, global score (Dougherty et al., 2013, 2015; Mota & Schachar, 2000) or the assessment of impairment was limited

to classroom settings (Zoromski et al., 2015). A more nuanced approach, which considers the associations between individual symptoms and different FI domains in more detail while simultaneously accounting for ADHD as well as ODD, CD, and CU symptoms within a common approach, could help to enhance the understanding of these probably complex interrelations.

Network Analysis

Network analysis offers such a more nuanced approach, which could potentially uncover individual symptom relations and associations with different FI domains (Borsboom & Cramer, 2013). From a network perspective, mental disorders are conceptualized as networks of mutually interacting symptoms (Borsboom & Cramer, 2013). Psychological networks may be depicted as structures comprising nodes (e.g. symptoms, FI domains), which are connected via edges (e.g. positive or negative associations). Some nodes can have a more dominant, central position in a network, for example, as expressed by stronger connections with other nodes (Borsboom & Cramer, 2013; Epskamp et al., 2018). Moreover, network analysis helps to uncover the unique strongest connections between nodes by relying on regularized partial correlations. This approach is somewhat similar to conducting multiple linear regressions at once, but with the advantage of reducing the risk of false positives (Epskamp & Fried, 2018). Hence, it is possible to determine which individual symptom shows the strongest association with a particular FI domain.

In recent years, many studies have applied network analysis to investigate how symptoms of different mental disorders are interrelated, particularly in the fields of anxiety and mood-related disorders (reviewed by Contreras et al., 2019). In the field of externalizing disorders, network analysis has been applied to symptoms of ADHD (Burns et al., 2022; Goh et al., 2020, 2021a, b; Martel et al., 2016, 2021; Preszler et al., 2020; Silk et al., 2019), ODD (Smith et al., 2017), or ADHD and ODD together (Martel et al., 2017; Preszler & Burns, 2019), to CU traits (Bansal et al., 2020; Deng et al., 2021), and to CU traits in conjunction with ODD and CD (Bansal et al., 2021), in samples ranging from preschool age to adulthood. Furthermore, a recent study explored the relations between ADHD symptoms, executive functioning, and temperament traits, and found support for the primary role of effortful control as a potential risk marker for the characterization of ADHD across childhood and adolescence (Goh et al., 2021a, b).

To the best of our knowledge, so far, only three studies have focused on the associations between ADHD symptoms and different FI domains using network analysis (Burns et al., 2022; Goh et al., 2020, 2021a, b). Goh et al. (2020) explored individual ADHD and sluggish cognitive tempo symptoms and their relations with multiple domains of FI in a nationally representative sample of 1,742 children and adolescents (age: $M = 11.51$, $SD = 3.36$, range 6 – 17 years). The results revealed that in particular, the following eight symptoms were related to various FI domains and especially to the domains of academic and social impairment: *difficulties following through on instructions, inability to stay seated, acting without thinking, impatience, disinhibition, apathy/withdrawal, slowness*, and *lacking initiative*. Similarly, Goh et al., (2021a, b) explored individual ADHD symptoms (with an expanded impulsivity set) and their relations with multiple FI domains using network analysis and random forest regression in a nationally representative sample of 1,249 adults. The results from both techniques revealed that in particular, three inattention symptoms (*difficulty organizing, does not follow through, makes careless mistakes)* and one hyperactivity symptom (*difficulty engaging in leisure activities*) were strongly associated with global FI and FI, especially in the domains of social and interpersonal relationships, and difficulties maintaining structure in daily life. Finally, Burns et al. (2022) applied network and latent variable models to mother, father, and teacher ratings of ADHD inattention symptoms, sluggish cognitive tempo, and depressive symptoms in a sample of 2,142 Spanish children (age range 8–13 years; $M = 10.30$, $SD = 1.21$). Most interestingly, across all three sources, the same two ADHD inattention symptoms *difficulty keeping attention focused during tasks* and *avoids, dislikes or is reluctant to engage in tasks that require sustained mental efforts* showed unique relations with academic impairment. To summarize, each of these network studies uncovered important aspects of psychopathology, including the mutual associations among symptoms and the centrality of symptoms in a mental disorder network. However, the important role of FI has rarely been considered. To our knowledge, no study to date has identified which individual ADHD, ODD, CD, and CU symptoms show the strongest associations with particular domains of FI in a clinical sample of school-age children, in whom the associations between symptoms and impairments are probably more pronounced and relevant than in a community sample (Borsboom, 2017).

The Present Study

The overall aim of this study was to enhance the understanding of how individual symptoms of ADHD and disruptive behavior disorders (i.e. ODD, CD, CU symptoms) may differentially relate to global FI and to FI in the five domains of psychological strain; home life and family members; relationships with adults; relationships with children and recreational activities; and academic performance. We extended previous research according to four important

aspects: (a) We assessed FI domains specifically related to ADHD symptoms and, likewise, specifically related to ODD/CD/CU symptoms. (b) Consistent with current evidence, we included not only symptoms of ODD, but also affective dysregulation symptoms, as suggested in the ICD-11 for the subtype ODD with chronic irritability/anger (Evans et al., 2017; World Health Organization, 2019). (c) We provided another rater perspective (i.e. clinician ratings), since structured clinical interviews may be considered as the gold standard for diagnosing mental disorders (Rettew et al., 2009). (d) We extended previous findings by using a clinical sample of school-age children.

First, we determined the impact of individual ADHD symptoms or ODD/CD/CU symptoms, respectively, on global FI using linear regression, combined with relative importance analyses. In line with the results of previous studies, we assumed that the ADHD symptoms *leaves seat, blurts out*, *interrupts,* or *organizational skills* (Goh et al., 2021a, b; Mota & Schachar, 2000; Zoromski et al., 2015) and the ODD-related symptoms of irritability, such as *loses temper, touchy*, or *angry* (Dougherty et al., 2013; Wesselhoeft et al., 2019) would have the highest impact on global FI. Second, we estimated two psychological networks to identify the unique strongest associations between individual ADHD symptoms or ODD/CD/CU symptoms, respectively, and multiple FI domains. For the ADHD network, we expected that the symptoms most strongly associated with academic FI would originate from the inattention domain (Burns et al., 2022; Garner et al., 2013; Goh et al., 2020; Massetti et al., 2008; Willcutt et al., 2012; Zoromski et al., 2015), while symptoms most strongly associated with social impairment would originate from the hyperactivity-impulsivity domain (Garner et al., 2013; Goh et al., 2021a, b; Willcutt et al., 2012). For the ODD/CD/CU network, we expected the symptoms most strongly associated with academic FI to originate from the CD domain (Burke et al., 2014), the symptoms most strongly associated with impaired home life and family members and with relationships with adults to originate from the ODD or CD domain (Dose et al., 2019; Kernder et al., 2019), and the symptoms most strongly associated with impaired relationships with children to originate from the ODD or CU domain (Burke et al., 2014; Dose et al., 2019; Haas et al., 2018; Kernder et al., 2019).

Methods

Participants and Procedure

Data for the present analyses were collected within the ESCAschool study (ESCAschool: *Evidence-based, Stepped Care of ADHD in school-aged children*), which is part of the ESCAlife consortium and involves multiple study sites in Germany. The ESCAschool study was designed to investigate an evidence-based, individualized, stepwise- intensifying treatment program for children diagnosed with ADHD, which is based on behavioral and pharmacological interventions.

Children and their families were eligible for participation if the child met diagnostic criteria for ADHD according to the DSM-5, was aged between 6;0 and 11;11 years, and attended school. The following exclusion criteria were applied: child IQ < 80; a child diagnosis of a pervasive developmental disorder, schizophrenia, bipolar disorder, severe depressive episode, epilepsy, or heart disease; insufficient German language or reading skills of the parents; a current or planned behavior therapy for child ADHD or ODD occurring at least weekly; a known non-response of the child to all standard ADHD medication; and psychotropic medication of the child other than for the treatment of ADHD/antipsychotic medication other than for the treatment of disturbances of impulse control. Further details on the background and procedures are outlined in the study protocol (Döpfner et al., 2017).

The present study analyzed baseline data (i.e., data collected before any intervention) of 474 children ($M = 8.90$, $SD = 1.49$; 81% males). The screening to check whether the participants met the diagnostic criteria for ADHD relied on the DSM-5-based *Clinical Parent Interview for Externalizing Disorders in Children and Adolescents [Interview-Leitfaden für Externale Störungen]* (ILF-EXTERNAL; Görtz-Dorten et al., 2022; see Measures section). If children were receiving ADHD medication prior to the study, parents described their child's behavior with and without medication. For the present analyses, we investigated the children's symptomatology without medication.

Clinical diagnoses of ADHD, ODD, CD, and CU symptoms were based on the interview ILF-EXTERNAL according to the DSM-5. In addition, to assess comorbid symptoms, all clinicians applied a clinical diagnostic checklist (DCL-SCREEN) from the *Diagnostic System for Mental Disorders in Children and Adolescents based on the ICD-10 and DSM-5 [Diagnostik-System für psychische Störungen nach ICD-10 und DSM-5 für Kinder und Jugendliche—III]* (DISYPS-III; Döpfner & Görtz-Dorten, 2017). The sample used in the present study also included children who did not fulfill DSM-5 criteria for an ADHD diagnosis. These screening negatives ($n = 32$, 72% males) were characterized by subclinical ADHD symptoms (Thöne et al., 2020). The ESCAschool study was registered at the German Clinical Trials Register (identifier: DRKS00008973).

Measures

Clinical Parent Interview for Externalizing Disorders in Children and Adolescents (ILF-EXTERNAL)

The ILF-EXTERNAL is part of the German semi-structured *Interview for Diagnosing Mental Disorders According to the DSM-5 in Children and Adolescents* [*Interview-Leitfäden zum Diagnostik-System für psychische Störungen nach DSM-5 für Kinder und Jugendliche*] (DISYPS-ILF; Görtz-Dorten et al., 2022) and comprises two interview sections. The first section assesses ADHD criteria and the second assesses criteria for ODD, CD, including CU traits according to the DSM-5.

In terms of ADHD criteria, the ILF-EXTERNAL measures inattention symptoms (nine items), hyperactivity-impulsivity symptoms (nine items), and FI associated with ADHD symptoms (five items) in the domains of home life and family members, relationships with adults, relationships with children and recreational activities, academic performance, and psychological strain.

In terms of ODD, CD, and CU criteria, the ILF-EXTERNAL assesses ODD symptoms (eight items), CD symptoms (15 items), disruptive mood dysregulation symptoms (five items in total; two items assessing affective dysregulation and three items assessing irritability/anger associated with ODD), CU symptoms (11 items) and, resembling the ADHD section, functioning and psychological strain associated with these symptoms (five items).

Following a semi-structured interview format, clinicians rate each item on a 4-point Likert scale ranging from 0 (age-typical / not at all), to 3 (very much), with higher scores reflecting higher symptom severity. Item scores of 2 and higher are interpreted as clinically relevant and considered to fulfill the DSM-5 symptom criteria. It should be noted that the ILF-EXTERNAL captures the full set of diagnostic criteria for a given mental disorder (i.e. each item explores a DSM-5 symptom criterion), thereby avoiding issues associated with skip outs in symptom networks (Hoffman et al., 2019). However, for the present analyses, we excluded the CD items assessing aggressive and antisocial symptoms, which are recommended for use in participants aged 11 years or older, due to obvious floor effects.

Interview Training All interviewers involved in the recruitment of patients for the ESCAschool study were trained psychologists or educators with a master's degree, doctoral students, or in training to become a child and adolescent psychotherapist/psychiatrist. The interviewers received standardized training on how to administer and score the ILF-EXTERNAL, which included viewing a practice video. Finally, all interviewers were given guidance by supervisors if they experienced any difficulties in scoring the ILF EXTERNAL.

Psychometric Properties of the ILF-EXTERNAL Psychometric evaluations revealed a good to excellent interrater reliability [intraclass correlation (ICC) on the scale level: ICC(1,1) = .83–.95; ICC(1,3) = .94–.98] as well as convergent and divergent validity of the ILF-EXTERNAL scale scores with parent ratings of the respective constructs (Thöne et al., 2020). Furthermore, the basic factorial configuration of the ILF-EXTERNAL scale scores was confirmed (Thöne et al., 2021). In the current sample, internal consistencies (Cronbach's alpha: $.60 \leq \alpha \leq .87$) and item-total correlations ($.22 \leq r_{it} \leq .68$) of the corresponding scales were, for the most part, satisfactory to good (see Table S1). The internal consistencies of the ADHD FI scale ($\alpha = .62$) and the CD scale ($\alpha = .60$) were somewhat below the satisfactory range. The following items demonstrated item-total correlations below $r_{it} = .30$: A01 *Careless*, A06 *Concentration* (both ADHD symptoms), F05 *Interferes with Educational Activities* (FI related to ADHD), B03 *Cruel to Animals*, B05 *Steals Without Confrontation* (both CD items), C04c *Manipulates* (CU item). However, excluding any of these items did not noticeably change the Cronbach's alpha of the respective scales.

Multicollinearity and Missing Data Checks Since symptoms of ADHD and, likewise, ODD/CD/CU symptoms are usually correlated with each other, we performed multicollinearity checks using the variance inflation factor. The variance inflation factor did not exceed the cut-off value of 5 for any symptom (Table S2), indicating no considerable multicollinearity problems (Craney & Surles, 2002). The amount of missing data per item is reported in Table S2 and varied from 0% (ADHD symptoms) through 5% (ODD, CD symptoms) to 6% (CU symptoms) and 7% (FI related to ODD/CD/CU symptoms).

Data Analytic Plan

First, we performed two multiple linear regression analyses, combined with relative importance analyses, in order to estimate the impact of individual symptoms on global FI. Second, we estimated two networks, one comprising ADHD symptoms and FI and the other comprising ODD/CD/CU symptoms and FI. Both networks included five FI domains (nodes F01 – F05), which were specifically associated with symptoms of ADHD or ODD/CD/CU, respectively. Descriptive statistics were calculated using SPSS version 27. The network and regression analyses were carried out using the R statistical software version 4.0.3 in RStudio 1.3.1093 for macOS.

Multiple Linear Regressions and Relative Importance Analysis

To examine the impact of individual symptoms on global FI, we computed the average score across the five FI domains (F01 – F05) associated with ADHD or ODD/CD/CU

symptoms, respectively. We used the 18 ADHD symptoms and the 26 ODD/CD/CU symptoms, respectively, as predictors of global FI in a multiple linear regression model, additionally controlling for age and gender as covariates. An a priori power analysis using G-Power 3.1 (Faul et al., 2009) yielded a required sample size of $n = 222$ for the ADHD model and $n = 253$ for die ODD/CD/CU model, respectively, assuming a moderate effect size ($f^2 = 0.15$), a power of .95 and a significance level of 5%. Next, we allocated unique R^2 shares (i.e., proportion of explained variance) to each regressor to determine how much unique variance each individual symptom shared with global FI. We used the *R* package RELAIMPO (Grömping, 2006) which provides several metrics for assessing relative importance in linear models. The recommended metric is lmg (like in Lindeman et al., 1980) which estimates the importance of each regressor by splitting the total R^2 into one non-negative R^2 share per regressor. These non-negative R^2 shares sum up to the total R^2. To estimate the importance of each regressor, the contribution of each predictor at all possible entry points into the model is calculated and the average of these contributions is taken (i.e., an estimate for each variable is obtained by computing as many regressions as there are possible orders of regressors, and then the average of the individual R^2 values across all models is taken). The relative importance estimates were then adjusted to add up to 100% to facilitate their interpretation.

Then, we compared two multiple linear regressions models for the ADHD and ODD/CD/CD symptoms, respectively (for a similar analysis, please see Fried & Nesse, 2014). In the first model (unconstrained model), all regression weights for symptoms were free to vary, whilst in the second model (constrained model), the symptom weights were constrained to be equal. While the unconstrained model allows for differential associations between functional impairment and symptoms, the constrained model hypothesizes that symptoms are equally associated with functional impairment. A chi-square difference test was used to compare the two nested models.

Network Analysis

We constructed undirected Gaussian graphical models (GGMs) using the *R* package *bootnet* version 1.4.3 (Epskamp et al., 2018). In these network models, the edges connecting the nodes represent estimates of partial correlations. In undirected GGMs, the edges can be interpreted as conditional dependence relations among nodes. If the analysis reveals that two nodes are connected, they are dependent after controlling for all other symptoms in the network. If no edge emerges, two nodes are interpreted as conditionally independent (Epskamp & Fried, 2018). As stated above, we estimated two network models: Our first network comprised 18 ADHD symptoms and five FI domains and our second network comprised 26 ODD/CD/CU symptoms and five FI domains. We decided to estimate two networks given that we assessed FI specifically related to ADHD symptoms and FI specifically related to ODD/CD/CU symptoms. To prevent spurious edges and to estimate a more parsimonious network model, we adopted the graphical least absolute shrinkage and selection statistical regularization technique, coupled with the extended Bayesian information criterion (EBICglasso) model selection (tuning hyperparameter = 0.5). This regularization technique pulls small associations (edges) to zero, which results in their removal from the network as potentially false positive edges (Epskamp & Fried, 2018). We used Spearman correlations to account for our ordinal data structure and pairwise complete observations to handle missing data (Epskamp et al., 2018). The resulting networks were visualized using the Fruchterman–Reingold algorithm from the *R* package *qgraph* version 1.6.9, which places related nodes closer to each other.

Furthermore, we assessed the accuracy of the edge weights by randomly resampling participants (nonparametric bootstrapping; 2,500 iterations) and estimating the 95% bootstrapped confidence intervals (Epskamp et al., 2018). Then, we performed bootstrapped difference tests (2,500 iterations) to investigate whether two edge weights significantly differed from each other. It should be noted that a correction for multiple testing when carrying out bootstrapped difference tests in network analysis has not yet been developed (Epskamp et al., 2018).

In addition, we ran a simulation study on the performance of network estimation by varying sample size using the *netSimulator* function from the *bootnet* package (2,500 iterations; Spearman correlations; EBICglasso network). The simulation analysis yields plots which demonstrate the sensitivity and specificity of the network as well as correlations between the "true" and estimated edges given our network structure (Epskamp et al., 2018).

Associations of Externalizing Symptoms with Functional Impairment Domains

For each FI domain (nodes F01 – F05), we identified the ADHD symptom and the ODD/CD/CU symptom which was most strongly associated with the respective domain by determining the largest edge weight (i.e., the strongest partial correlation). These partial correlations reflect the associations between individual symptoms and a particular FI domain after controlling for the influence of all other symptoms and FI domains in the network. In this context, it should be mentioned that previous research relied on bridge analysis to explore which symptoms may act as "middlemen" regarding the associations between symptoms and FI (e.g. Goh et al., 2020, 2021a, b). Our

approach contributes to this research insofar as we were interested in identifying the unique strongest associations between different FI domains and individual symptoms. As the EBICglasso regularization technique pulls smaller, potentially spurious edges to zero, the remaining edges may be considered as sufficiently strong for inclusion in the network model (Epskamp & Fried, 2018). Notably, as weaker edges should be interpreted with some caution, our interpretation concentrates on the stronger, and thus likely more stable, edges in the network structures.

Results

Sample Characteristics

The present sample (Table 1) comprised school-age children mainly diagnosed with ADHD (94%) according to the DSM-5. The majority of these children (98%) as well as their mothers (87%) and fathers (84%) were born in Germany. About 90% of the families spoke predominantly German at home. Most of these children met the diagnostic criteria for the ADHD combined type (44%), followed by the ADHD predominantly hyperactive-impulsive type (39%). Probably due to this high percentage of children diagnosed with ADHD, the mean ADHD-related scale scores were generally higher than the ODD/CD/CU-related scale scores (Table S1). The intercorrelations between the ADHD-related items (i.e. symptoms and FI domains) or the ODD/CD/CU-related items (i.e. symptoms and FI domains), respectively, were predominantly positive and low to moderate (see Fig. S1).

Multiple Linear Regression Analyses and Relative Importance Analyses

In our multiple linear regression models, we used 18 ADHD symptoms and 26 ODD/CD/CU symptoms, respectively, as

Table 1 Sample Characteristics

Variable	Total Sample ($N = 474$)
Age Mean (*SD*)	8.90 (1.49)
Male *n* (%)	382 (81)
Primary Diagnosis *n* (%)	
No ADHD diagnosis	32 (7)
ADHD – combined type	208 (44)
ADHD – predominantly inattentive type	184 (39)
ADHD – predominantly hyperactive-impulsive type	50 (11)
Comorbidities *n* (%)	*n* = 454 - 465
Internalizing disorders:	
- Anxiety	29 (6)
- Depression	15 (3)
Externalizing disorders:	
- Oppositional defiant disorder	166 (37)
- Conduct disorder	28 (6)
- Disruptive mood dysregulation disorder	40 (9)
Other disorders:	
- Obsessive-compulsive disorder	2 (< 1)
- Tic disorder	24 (5)
- Autism spectrum disorder	2 (< 1)
Medication *n* (%)	*n* = 462
ADHD medication	150 (33)
Parents' Primary Language *n* (%)	*n* = 458
German	429 (94)
Parents' Highest Educational Attainment *n* (%)	*n* = 455
Higher-track school	261 (57)
Vocational school	26 (6)
Medium-track school	123 (27)
Lower-track school	43 (10)

Clinical diagnoses of ADHD and externalizing behavior disorders were based on the semi-structured *Clinical Parent Interview for Externalizing Disorders in Children and Adolescents* (ILF-EXTERNAL) conducted with the parents. Additional comorbid symptoms were evaluated using a clinical diagnostic checklist

ADHD attention-deficit/hyperactivity disorder

predictors of global FI, additionally controlling for age and gender as covariates.

In the ADHD model, a significant equation was found [F (20, 451) = 12.69, $p < .001$], with an R^2 of 36%. It also emerged that seven out of the 18 ADHD symptoms as well as gender significantly predicted global FI ($p < .05$; see Table S3). A subsequent relative importance analysis revealed that different ADHD symptoms had markedly different effects on global FI, with estimates of the R^2 contributions ranging from 1% (A07 *Loses Things*) to 15% (A08 *Easily Distracted*; Fig. 1a). The relative importance estimates were similar when the inattention dimension and the hyperactivity-impulsivity dimension were considered separately (inattention: $R^2 = 52\%$; hyperactivity-impulsivity: $R^2 = 48\%$). When comparing the ADHD unconstrained model (all regression weights for symptoms were free to vary) and the ADHD constrained model (the regression weights were constrained to be equal), the unconstrained model fit the data significantly better than the constrained model ($\chi^2_{diff} = 50.07$, $df_{diff} = 19$, $p < .001$). Also, the $R^2 = 36\%$ of the ADHD unconstrained model was higher than the $R^2 = 29\%$ of the constrained model.

In the ODD/CD/CU model, a significant equation was found [F (28, 411) = 16.06, $p < .001$], with an R^2 of 52%. It also emerged that 10 out of the 26 ODD/CD/CU symptoms significantly predicted global FI ($p < .05$; see Table S4). A subsequent relative importance analysis revealed that different symptoms had markedly different effects on global FI, with estimates ranging from < 1% (C03a *Indifferent to Poor Performance*; C04a *Shallow, Deficient Affect*) to 10% (A04 *Argues with Adults*; Fig. 1b). When adding up the relative importance estimates of the symptoms belonging to the ODD, CD, and CU dimensions, the results showed differential contributions of the dimensions to explaining the variance in global FI: ODD (55%) was most strongly associated with global FI, while CD (24%) and CU (20%) were less strongly associated with global FI. When comparing the ODD/CD/CU unconstrained model and the ODD/CD/CU constrained model, the unconstrained model fit the data significantly better than the constrained model ($\chi^2_{diff} = 83.35$, $df_{diff} = 27$, $p < .001$). Also, the $R^2 = 52\%$ of the ODD/CD/CU unconstrained model was higher than the $R^2 = 42\%$ of the constrained model.

For interested readers, we provide a supplementary multiple regression analysis with global FI averaged

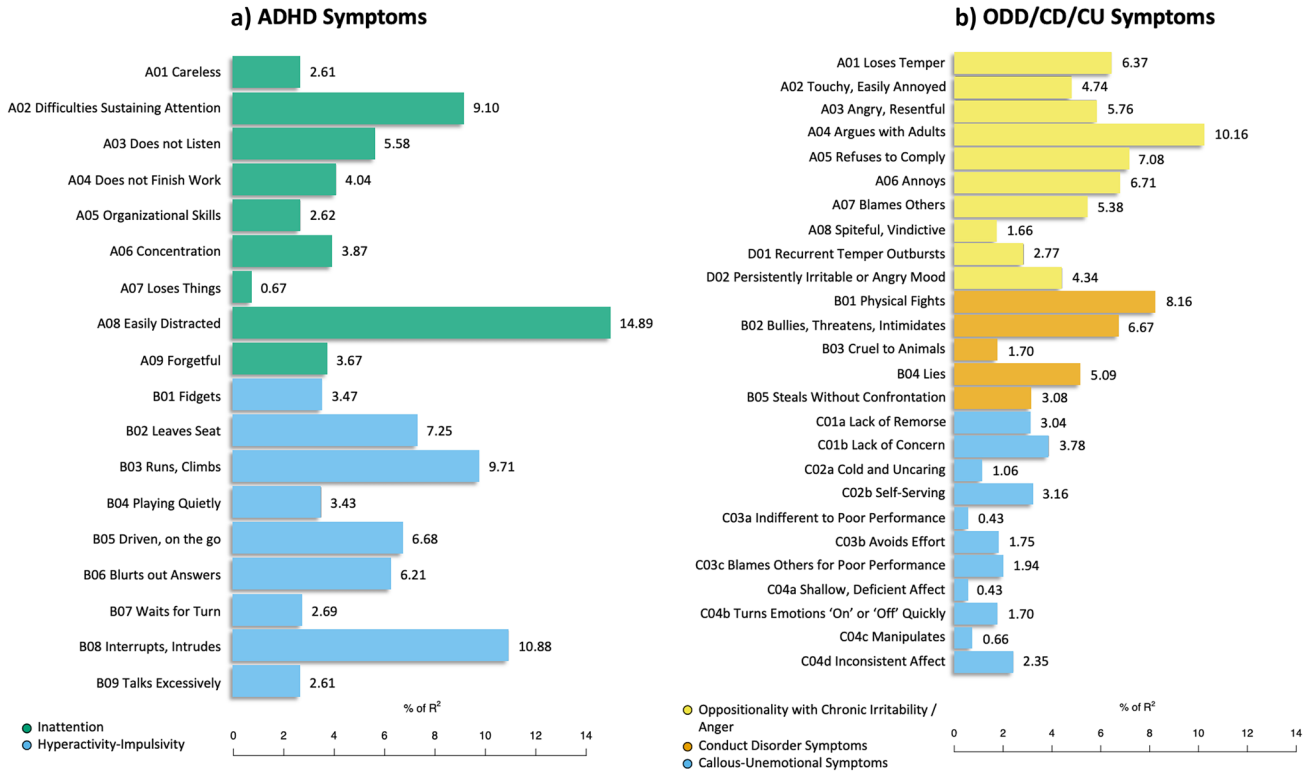

Fig. 1 Relative Importance Estimates of ADHD and ODD/CD/CU Symptoms on Global Functional Impairment. *Note*. Depicted are the relative importance coefficients of ADHD (**a**) and ODD/CD/CU (**b**) symptoms on global functional impairment associated with these symptoms, respectively. Each value represents the unique shared variance (%) between a symptom and functional impairment. Estimates are adjusted to sum up to 100%

across ADHD and ODD/CD/CU as a response variable and all externalizing symptoms as regressors in the online supplement (Table S5). Noteworthy, all significant predictors from this supplementary analysis also emerged as significant predictors in our ADHD and ODD/CD/CU regression analyses, respectively (e.g., ADHD A08 *Easily Distracted* was identified as a highly significant predictor in both analyses).

Network Analysis

Network Structures for the ADHD and ODD/CD/CU Symptoms and Associated Functional Impairment Domains

As visualized in Fig. 2, there were stronger associations with items within the same dimension (e.g. Inattention) than across dimensions. The results of our simulation studies on the performance of the ADHD and ODD/CD/CU network estimations by varying sample size are depicted in Fig. S2.

The Strongest Associations of Functional Impairment Domains with Symptoms

Regarding the ADHD network, the strongest partial correlations were found between FI related to psychological strain (F01) and A08 *Easily Distracted* ($\rho_{xy\bullet z} = .09$), between FI related to home life and family members (F02) and A03 *Does not Listen* ($\rho_{xy\bullet z} = .09$), between FI related to relationships with adults (F03) and B02 *Leaves Seat* ($\rho_{xy\bullet z} = .07$), between FI related to relationships with children and recreational activities (F04) and B08 *Interrupts, Intrudes* ($\rho_{xy\bullet z} = .15$), and between FI related to academic performance (F05) and A06 *Concentration* ($\rho_{xy\bullet z} = .10$).

Regarding the ODD/CD/CU network, the strongest partial correlations were found between FI related to psychological strain (F01) and A01 *Loses Temper* ($\rho_{xy\bullet z} = .07$), between FI related to home life and family members (F02) and A04 *Argues with Adults* ($\rho_{xy\bullet z} = .18$), between FI related to relationships with adults (F03) and B05 *Steals Without Confrontation* ($\rho_{xy\bullet z} = .08$), between FI related to relationships with

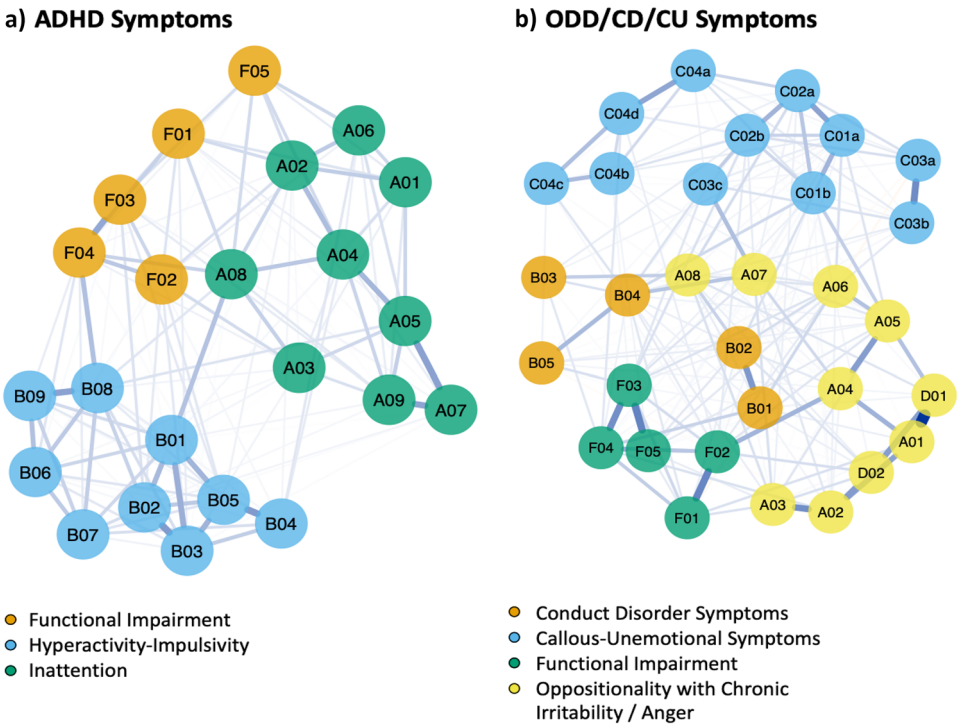

Fig. 2 Networks of ADHD and ODD/CD/CU Symptoms with Associated Functional Impairment Domains. *Note.* The figure depicts the network structures of the ADHD and ODD/CD/CU symptoms and functional impairment related to psychological strain (F01) and in the domains of home life and family members (F02), relationships with adults (F03), relationships with children/adolescents and recreational activities (F04), and academic performance (F05). Item dimensions are differentiated by color. Blue edges represent positive partial correlations and the thickness of an edge represents the strength of the partial correlation. A short description of each item is provided in Fig. 1. ADHD = attention-deficit/hyperactivity disorder; ODD = oppositional defiant disorder; CD = conduct disorder; CU = callous-unemotional

children and recreational activities (F04) and B01 *Physical Fights* ($\rho_{xy\bullet z} = .11$), and between FI related to academic performance (F05) and B02 *Bullies, Threatens, Intimidates* ($\rho_{xy\bullet z} = .06$).

Following our edge-weight accuracy checks, results from non-parametric bootstrapping generally indicate accurate estimations, since the sample values lie within the bootstrapped confidence intervals and the bootstrap mean values are generally well aligned with the sample values (Fig. S3). As the bootstrapped confidence intervals were relatively wide, we recommend some caution when interpreting the presence and strength of weaker edges. The aforementioned associations (i.e. edge weights) between each FI domain and symptoms of the ADHD and ODD/CD/CU networks were significantly stronger than most of the other edge weights in the respective networks (Figs. S4 and S5). Importantly, while the associations may appear to be weak, it should be kept in mind that these are partial correlations after regularization (shrinking). As supplementary analyses, we also report the strongest associations between different domains of functional impairment and all externalizing symptoms in a combined network. The results are mostly consistent with the two separate ADHD and ODD/CD/CU networks (e.g., ADHD F01 *Psychological Strain* is most strongly associated with A08 *Easily Distracted*). However, the results should be interpreted with some caution, as the network may be rather unstable due to the high number of nodes in a relatively small sample (Figs. S6 and S7). Furthermore, we aimed to support the interpretations drawn from our network analyses with additional regression analyses. We therefore calculated separate ordinal logistic regression analyses with the different FI domains as response variables to account for the ordinal data structure (Tables S6 and S7). Most intriguingly, we were able to establish method equivalence insofar as those symptoms from the network analyses that were most strongly associated with a particular FI domain also emerged as significant predictors in the ordinal regression analyses.

Discussion

The present study aimed to enhance the understanding of how individual ADHD and ODD/CD/CU symptoms differentially relate to global FI as well as FI in the five domains of home life and family members, relationships with adults, relationships with children and recreational activities, academic performance, and psychological strain. Our findings contribute to a growing body of literature on the importance of analyzing the associations between individual symptoms and different domains of FI and highlight that symptom-based approaches can be clinically useful.

Distraction (ADHD) and Arguments with Adults (ODD) Explained a Large Proportion of the Variance in Functional Impairment

Overall, individual symptoms had differential impacts on global FI. In particular, A08 *Easily Distracted*, B03 *Runs, Climbs*, and B08 *Interrupts, Intrudes* explained a large proportion of the variance in global FI related to ADHD symptoms. These findings are largely consistent with previous studies, which reported that particularly ADHD hyperactivity-impulsivity symptoms were linked to global FI in children and adolescents (Mota & Schachar, 2000; Zoromski et al., 2015). Furthermore, A04 *Argues with Adults*, A05 *Refuses to Comply*, and B01 *Physical Fights* explained a large proportion of the variance in FI related to ODD/CD/CU, whereas CU symptoms made few unique contributions to global FI. One possible explanation for these findings could be that the nature of "covert" CU-symptoms is assessed to be less functionally impairing relative to typical, "overt" ODD/CD symptoms (e.g., losing temper, arguing) in the clinical interview. Interestingly, however, our additional logistic regression analyses showed that individual CU traits were particularly strongly associated with FI related to relationships with adults. Of note, these conclusions are rather preliminary and require replication before more precise conclusions can be drawn about the relationships between CU traits and FI.

Inattention Strongly Relates to Academic, Family, and Psychological Strain, while Hyperactivity-impulsivity Strongly Relates to Social impairment

The interpretation of the ADHD network structure suggests that symptoms most strongly associated with FI in the domains of academic performance, home life and family members as well as with psychological strain originated from the inattention dimension. These results are consistent with previous studies, which reported that ADHD inattention symptoms show strong associations with academic impairment (Garner et al., 2013; Massetti et al., 2008; Willcutt et al., 2012; Zoromski et al., 2015). Furthermore, our analyses add to previous findings by providing another rater perspective (i.e. clinician ratings), investigating a clinical sample of school-age children, and applying novel analysis techniques. Moreover, we found that the ADHD inattention symptom A08 *Easily Distracted* was the symptom most strongly associated with FI related to psychological strain. This finding is quite interesting from a clinical perspective given that inattention symptoms have previously been regarded as less impairing than hyperactivity-impulsivity symptoms (Willcutt et al., 2012). However, while the combined presentation of inattention and hyperactivity-impulsivity symptoms is

generally associated with a high degree of FI (Willcutt et al., 2012), if inattention symptoms are present, we recommend paying particular attention to exploring psychological strain, both to ensure adequate and appropriate treatment and to inform future research in this area. By contrast, the symptoms most strongly associated with FI in the domains of relationships with children and recreational activities, as well as relationships with adults, originated from the hyperactivity-impulsivity dimension. These results are consistent with previous research indicating that ADHD hyperactivity-impulsivity symptoms are strongly associated with impaired social functioning (Garner et al., 2013; Goh et al., 2021a, b; Willcutt et al., 2012). From a clinical perspective, the present findings highlight the need for a thorough assessment of impairment in the domains of relationships with children and adults in the presence of hyperactivity-impulsivity symptoms (e.g. B02 *Leaves Seat*, B08 *Interrupts, Intrudes*) and the subsequent selection of appropriate interventions, for example interventions focusing on positive parent–child interactions and communication skills.

Symptoms of ODD and CD More Strongly Relate to Impairment than do CU Traits

The interpretation of the ODD/CD/CU network suggests that the symptoms most closely linked to the examined FI domains originated from the ODD and CD dimension, while FI was less strongly associated with CU traits. In particular, the symptoms most strongly associated with FI in the domains of academic performance, relationships with children and recreational activities as well as relationships with adults were CD symptoms, whereas the symptoms most strongly associated with FI related to home life and family members as well as with psychological strain were ODD symptoms. Interestingly, CU traits remained a rather self-contained dimension in the network structure, that is, they were neither strongly associated with any FI domain nor with ODD/CD symptoms. This finding is particularly interesting given that CU traits can be added as a specifier to the CD diagnosis in the DSM-5 (American Psychiatric Association, 2013) and as a specifier to the ODD or CD diagnosis in the ICD-11 (World Health Organization, 2019). Moreover, the finding is in line with previous research on the structure underlying externalizing behavior disorders in children (Castagna et al., 2021; Haas et al., 2018; Thöne et al., 2021).

Clinical Implications

Several clinical implications of these findings with respect to clinical assessment and therapy can be derived. First, given the only low to moderate correlations between externalizing symptoms and related functional impairment, as well as the importance of single, specific symptoms for the prediction of FI in different domains, we agree with the growing consensus that in order to gain a comprehensive understanding of psychopathology, the assessment of FI is as important as the assessment of symptoms (Arildskov et al., 2022; DuPaul, 2022). To further clarify the relationship between symptoms and FI, a recent study by Arildskov et al. (2022) examined whether the relationship between ADHD symptom severity and FI was nonlinear (i.e. whether there was a symptom severity threshold linked to a marked increase in impairment). The authors found a gradual linear increase in impairment with higher symptom severity, suggesting that the current symptom severity threshold for an ADHD diagnosis may be arbitrarily defined with respect to the presence or absence of FI (Arildskov et al., 2022). In line with this, not all individuals meeting the symptom-based criteria for an ADHD or ODD/CD diagnosis suffer from FI as a result of their symptoms, while others with only subthreshold symptoms show marked levels of impairment (DuPaul et al., 2014; Pickles et al., 2001). Arildskov et al. (2022) thus highlight *"the continuing need for the clinical assessment and diagnosis of ADHD to be based on two independent decisions: one about the symptom threshold and one about functional impairment with both decisions having a certain degree of arbitrariness and social subjectivity"* (Arildskov et al., 2022, p. 5). As discussed by DuPaul (2022), in the current diagnostic systems, the functional impairment criterion seems to be considered categorically (i.e., either present or absent), while lacking a precise operationalization and an explicit dimensional threshold. This—along with the influence of co-occurring symptoms on impairment ratings—illustrates the challenges clinicians face when making decisions on functional impairment (DuPaul, 2022).

Second, we emphasize the need for a more nuanced perspective on the association of specific symptoms with FI. For example, in our analyses, the ADHD symptom A08 *Easily Distracted* explained about five times as much variance in global FI as A01 *Careless*, even though both symptoms originate from the inattention dimension. In line with this, we found that constraining regression weights of ADHD and ODD/CD/CU symptoms, respectively, to be equal when predicting global FI led to a significantly reduced model fit and lower R^2 compared freely estimating symptom contributions. These findings suggest that symptoms have differential impacts on functional impairment and that differentially weighing symptoms does indeed lead to notable improvements in predicting impairment. Interestingly, similar findings of variable associations with impairment were also reported for individual depression symptoms (Fried & Nesse, 2014). In light of these differential symptom-impairment relations, we recommend that besides symptom dimensions, *individual* symptoms should be considered in the process of diagnostic assessment. In the long term, research on the

associations between single symptoms and FI in different domains could inform future modifications of the diagnostic criteria. For instance, instead of simple criterion counts in which various DSM-5 criteria are given equal weight (e.g. 6/9 symptoms of ADHD inattention), symptoms that show particularly strong associations with FI could be weighted based on the strength of their relationship with impairment.

Third, the results of the present study may also have important implications for the development of assessment measures, particularly screening instruments. As also suggested by Zoromski et al. (2015), and provided that further research is conducted, results of network analyses on symptom-impairment relations might inform the development of more economical screening instruments, which might initially include only symptoms that have particularly strong associations with FI domains. Such screening instruments might be valuable for both clinical research and practice. In research, they could precede the use of more extensive diagnostic batteries (Zoromski et al., 2015) and, for example, help identify participants eligible for a particular study more efficiently. In practice, several possible applications are conceivable. Such screening instruments might be used by clinical psychologists, but also other health care or educational professionals, to identify children in need for closer observation, more comprehensive diagnostics, or (early) intervention, if possible, before impairment manifests (Zoromski et al., 2015). Moreover, given that impairments rather than the presence of symptoms are often the reason for seeking treatment (Epstein & Weiss, 2012), and provided that the association between particular symptoms and FI domains is replicated, these screening instruments could assist clinicians in identifying target areas for treatment and selecting appropriate interventions accordingly (Zoromski et al., 2015). In addition, the sensitivity and specificity of such screening tools compared with standard screening procedures could be evaluated by comparing both approaches with more extensive current diagnostic practice (Zoromski et al., 2015). Finally, on a more global level, Zoromski et al. (2015) suggest to evaluate gating questions in existing structured interviews in terms of their correspondence to symptoms most strongly associated with FI domains and to further investigate whether having gating questions about symptoms most strongly linked to FI domains can facilitate diagnostics or treatment planning, e.g., by weighing symptoms according to the strength of their relationship with FI.

Limitations and Future Directions

Several limitations need to be considered when interpreting the results of the present study. First, we concede that a cross-sectional data design cannot uncover causal processes, for example in terms of the causal associations between FI and symptoms (e.g. symptoms and FI may potentially influence each other). Moreover, it remains to be investigated how the associations between FI and symptoms develop across age (e.g. whether certain symptoms become more impairing in adolescence). Ideally, future studies should address these gaps using a longitudinal data design. Second, in terms of the diversity of our sample, all children included in this study were registered for participation in a randomized control trial. As these children met stringent inclusion and exclusion criteria, our findings need to be replicated in clinically referred children under routine care conditions. In this context, it might be criticized that our FI items may not be able to differentiate between FI related to ADHD and FI related to ODD/CD/CU symptoms. However, the only moderate scale correlations between ADHD-related FI and ODD/CD/CU-related FI ($r = .53$) indicate that the clinicians (and the parents who were interviewed) were indeed able to differentiate between impairment related to the two symptom domains, and consequently that ADHD- and ODD/CD/CU-related impairment are perhaps overlapping but nevertheless generally distinct constructs. Third, we must acknowledge that we were unable to calculate confidence intervals and associated *p*-values as part of our relative importance analyses due to overly intensive computational efforts. We assume that these computational problems are related to our large number of regressors. Nevertheless, we would like to point out that the statistical significance of individual regressors can also be obtained from the multiple linear regression tables. Fourth, it should be noted that ADHD symptoms explained only 33% and ODD/CD/CU symptoms only 49% of the variance in global FI, underlining the likelihood that there are many sources of influence that contribute to the severity of FI, including variables not assessed in this study (e.g. parenting style, socioeconomic status). Since the DSM-5 diagnoses require the presence of symptom-related impairment, we limited the current analyses to the associated variables. However, the consideration of additional variables influencing FI in future studies could yield valuable contributions to both theoretical reflections and the advancement of treatments.

Conclusion

The current findings demonstrate that symptoms of ADHD or ODD/CD/CU, respectively, vary substantially in their associations with global FI. The total amount of variance in global FI explained by ADHD symptoms ranged from 1% (A07 *Loses Things*) to 15% (A08 *Easily Distracted*) and the amount of variance in global FI explained by ODD/CD/CU symptoms ranged from < 1% (C03a *Indifferent to Poor Performance*; C04a *Shallow, Deficient Affect*) to 10% (A04 *Argues with Adults*). Moreover, ADHD symptoms most

strongly associated with FI in the domains of academic performance, home life and family members as well as with psychological strain originated from the inattention dimension (A03 *Does not Listen*, A06 *Concentration*, A08 *Easily Distracted*), whereas the symptoms most strongly associated with FI in the domains of relationships with children/adolescents and recreational activities as well as with relationships with adults originated from the hyperactivity-impulsivity dimension (B02 *Leaves Seat*, B08 *Interrupts, Intrudes*). By contrast, the symptoms most closely linked to the examined FI domains related to ODD/CD/CU symptoms originated from the ODD and CD dimension (A01 *Loses Temper*, A04 *Argues with Adults*, B01 *Physical Fights*, B02 *Bullies, Threatens, Intimidates*, B05 *Steals Without Confrontation*), while FI was less strongly associated with CU traits. Our study contributes to this growing body of research in that diagnosticians should equally pay attention to both the severity and frequency of symptoms and the degree to which these symptoms are related to academic or social impairment. In particular, the present study provides first evidence on the extent to which individual symptoms are related to specific domains of functional impairment. In clinical practice, this could be of particular interest for both diagnostics and treatment planning purposes, as the presence of certain symptoms might lead clinicians to particularly assess functional impairment in specific domains, which could also be a target for treatment. Of note, the results of this study are preliminary and require replication in larger samples before more precise conclusions can be drawn about the relationships between symptoms and impairment.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10862-023-10025-z.

Acknowledgements We thank all staff members who participated in the ESCAschool study in nine different study recruiting centers and who were involved in recruitment, study organization and management, blind rating, assessment and therapy, and the Clinical Trials Unit Freiburg: Veronika Frommberger, Alexander Hellmer, Lydia Herbstritt, Maria Huber, Carolin Jenkner, Stefanie Lade, Patrick Müller, Barbara Schilling, Carla Schneider, and Ralf Tostmann. Further thanks to Sarah Mannion for English-language proofreading.

Author Contributions **A-KTh** conceptualized the study design, conducted the formal data analysis, interpreted and visualized the results, and developed the first draft of the manuscript. She was involved in the recruitment and data acquisition of the ESCAschool study site in Cologne and is co-author of the DISYPS-ILF on which the results on the present study were based. **MJ** contributed to the interpretation of the results and critically revised the first draft of the manuscript. **CD** contributed to the interpretation of the results, contributed to the management and organization of the study, heads the telephone-assisted self-help trial performed in one treatment arm of the ESCAschool study, and critically revised the first draft of the manuscript. **CH** was involved in the development of the ESCAschool research proposal and organization of the study. **LJ** and **A-KTr** coordinate ESCAschool and contribute to the management and organization of the study. **PV** is a scientific staff member at the Cologne study site and was involved in patient recruitment and data acquisition. **EvW** coordinates the ESCAschool study, contributed to the implementation of the study, and provided supervision for patient treatment. **TB** coordinates the ESCAlife consortium and is co-principal investigator in the ESCAschool study. He made substantial contributions to the conception and design of the ESCAschool research proposal and heads the Mannheim study site of ESCAschool. **KB** heads the Marburg study site of ESCAschool, is PI for the ESCApreschool study, is a member of the ESCAlife consortium, is a co-applicant of the ESCAlife research project, and made substantial contributions to the conception and design of the ESCAlife study. **DB** made substantial contributions to the conception and design of the ESCAschool research proposal and the neuropsychological research battery and heads the sub-project ESCAbrain. **UD** coordinates the Tübingen study site of ESCAschool, contributes to the management and organization of the study, and was involved in patient recruitment and data acquisition. **JG** coordinates the Würzburg study site and contributed to the management and organization of the ESCAlife projects. **JH** heads the Essen study site of ESCAschool and made substantial contributions to the conception and design of the ESCAschool study. **SH** coordinates the ESCAlife consortium and made substantial contributions to the conception of the neuropsychological research battery and the neurofeedback protocol. **MAH** heads the Hamm/Bochum study site of ESCAschool and was involved in the development of the ESCAschool research proposal. **MIH** heads the Mainz study site of ESCAschool and was involved in the implementation of the ESCAlife projects. **TJ** was involved in the planning of the ESCAlife research projects and application for funding, is co-PI for the ESCAadol trial and was involved in the implementation of the ESCAlife projects at the Würzburg study site. **AK** is a scientific staff member at the Mannheim study site, contributed to the implementation of the study, was involved in data acquisition, contributed to the management and organization of the (especially, ESCAbrain) study, and critically revised the first draft of the manuscript. **JK** coordinates ESCAschool at the Marburg study site, contributes to the management and organization of the study, and was involved in patient recruitment and data acquisition. **TL** heads the research department of the Hamm/Bochum study site of ESCAschool, contributed to the implementation of the study in Hamm, and supervised the realization of the trial in Hamm. **SM** heads the Mannheim study site of ESCAschool, coordinates the ESCAlife consortium, and made substantial contributions to the conception of the neuropsychological research battery and the neurofeedback protocol. **LP** heads the Göttingen study site of ESCAschool and was involved in the implementation of the ESCAlife projects. **TR** heads the Tübingen study site of ESCAschool and contributed to the implementation of the ESCAschool study. **MR** was involved in the planning of the ESCAlife research projects and application for funding, is co-PI for the ESCAadol trial, and was involved in the implementation of the ESCAlife projects at the Würzburg study site. **HUS** coordinates ESCAschool at the Göttingen study site, contributed to the management and organization of the study, and was involved in patient recruitment and data acquisition. **PS** coordinates the Tübingen study site of ESCAschool, contributes to the management and organization of the study, and was involved in patient recruitment and data acquisition. **JW** coordinates ESCAschool at the Essen study site and contributed to the management and organization of the study. **MZ** is a scientific staff member at the Mannheim study site, contributed to the implementation of the study, and was involved in patient recruitment and data acquisition. **AGD** developed the DISYPS-III system, developed the DISYPS-ILF, contributed to the interpretation of the results, and critically revised the first draft of the manuscript. **MD** is principal investigator of the ESCAschool trial, developed the basic ESCAschool study design, is part of the ESCAlife consortium, is head of the Cologne recruiting center for the ESCA children trials (ESCApreschool, ESCAschool and ESCAadol), developed the DISYPS-III system, developed the DISYPS-ILF, conceptualized the study design, contributed to the interpretation of the results, and critically revised the first draft of the manuscript. All authors critically revised the

manuscript, gave final approval of the last version of the manuscript, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding Open Access funding enabled and organized by Projekt DEAL. The ESCAschool study was funded by the German Federal Ministry of Education and Research (BMBF) Grant 01EE1408B. This work was supported by the research consortium on ADHD, ESCA-Life, funded by the German Federal Ministry of Education and Research (FKZ 01EE1408A-E).

Bundesministerium für Bildung und Forschung, FZK 01EE1408B, Manfred Döpfner

Data Availability The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Declarations

Ethics Approval and Consent to Participate Ethical approval was obtained for the study center Cologne from the University of Cologne (ID 15–216), for the study center Essen from the University of Duisburg-Essen (ID 17–7404-BO), for the study center Hamm from the Ruhr-University Bochum (ID 15–5564), for the study center Göttingen from the University Medical Center Göttingen (ID 3/3/17), for the study center Mainz from the Federal Medical Association of Rhineland-Palatinate (ID 837.237.17 [11071]), for the study center Mannheim from the Ruprecht-Karls-University Heidelberg (ID 2015–646 N-MA), for the study center Marburg from the Philipps-University Marburg (ID Studie 03/16), for the study center Tübingen from the Eberhard-Karls-University Tübingen (ID 791/2015BO2), and for the study center Würzburg from the Julius-Maximilians-University Würzburg (ID 332/15_z).

Conflicts of Interest **A-KTh**, **AGD** and **MD** were involved in the development of the DISYPS-ILF and will receive royalties from the publisher Hogrefe after publication of this instrument. **AGD** and **MD** are AKiP supervisors and lecturers and received income as heads of the School for Child and Adolescent Behavior Therapy at the University of Cologne and royalties from treatment manuals, books, and psychological tests published by Guilford, Hogrefe, Enke, Beltz, and Huber. **MD** received consulting income and research support from Medice, Shire, and eyelevel. **AGD** received consulting income and research support from Medice and eyelevel. **TB** served in an advisory or consultancy role for ADHS digital, Infectopharm, Lundbeck, Medice, Neurim Pharmaceuticals, Oberberg GmbH, Roche, and Takeda. He received conference support or speaker's fee by Medice and Takeda. He received royalities from Hogrefe, Kohlhammer, CIP Medien, Oxford University Press. **KB** receives or has received research grants from the German Research Foundation (DFG), German Federal Ministry for Education and Research (BMBF), Philipps-University Marburg, Federal Joint Committee (G-BA), German Ministry for Health, University Hospital Giessen and Marburg and Rhön Klinikum AG. Further she receives royalties and honorary from Georg Thieme Publisher. **DB** served as an unpaid scientific advisor for an EU-funded neurofeedback trial unrelated to the present work. **JG** has received a research grant from the Bavarian State Ministry of Family, Labor and Social Affairs. She receives royalties from Hogrefe for the publication of an ADHD treatment manual. **MAH** served in an advisory role for Shire and Medice and received conference attendance support or was paid for public speaking by Medice, Shire. and Neuroconn. He receives research support from the German Research Foundation and the German Ministry of Education and Research. He receives royalties as Editor-in-Chief of the German Journal for Child and Adolescent Psychiatry and for textbooks from Hogrefe. **MIH** has served as a member of the advisory boards of Eli Lilly and Co., Engelhardt Arzneimittel, Janssen-Cilag, Medice, Novartis, Shire, and Steiner Arzneimittel within the past five years; served as a consultant to Engelhardt Arzneimittel, Medice, and Steiner Arzneimittel; received honoraria from Eli Lilly and Co., Engelhardt Arzneimittel, Janssen-Cilag, Medice, Novartis, and Shire; and received unrestricted grants for investigator-initiated trials from Eli Lilly and Co., Medice, Engelhardt Arzneimittel, and Steiner Arzneimittel. **LP** served in an advisory or consultancy role for Shire, Roche, and Infectopharm. She has received speaker's fees from Shire and royalties from Hogrefe, Kohlhammer, and Schattauer. **HUS** served in an advisory or consultancy role for Medice. He has received speaker's fees from Shire and Medice. **CD, MJ, CD, CH, LJ, A-KTr, PV, EvW, UD, JH, SH, TJ, AK, JK, TL, SM, TR, MR, PS, JW, MZ** are not aware of any biases that might be perceived as affecting the objectivity of this manuscript and declare that they have no competing interests.

Experiment Participants Patients and parents or guardians were informed verbally and received information sheets about the scope and the relevance of the study as well as the study procedures. All participants were able to clarify questions about the study with research staff members. For study participation, patients and their parents or guardians were required to give their assent and informed consent.

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