Disruptive Behaviour Disorders:
The challenge of delineating mechanisms in the face of heterogeneity

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Abstract: Causal pathways to Disruptive Behavior Disorders, even within the same diagnostic category, are varied. Both equifinality and multifinality pose considerable challenges to uncovering underlying mechanisms and understanding varied developmental trajectories associated with Disruptive Behavior Disorders. Uncovering genetic causes requires improved granularity in how we operationalise presentation and developmental trajectories associated with Disruptive Behavior Disorders. If we want to integrate the study of genetic, environmental and neurocognitive factors within a longitudinal framework, we need to improve measurement. Furthermore, brain changes associated with Disruptive Behavior Disorders should not simply be understood as outcomes of genetic and environmental influences, but also as factors that reciprocally influence future social environments over time in ways that are important in contributing to risk and resilience. Advancing the field with regard to these challenges will result in more truly integrated investigation of Disruptive Behavior Disorders, which holds the promise to improve our ability to develop more effective preventative and intervention approaches.

Disruptive behaviour disorders (DBDs) in childhood are classified at the level of behaviour. Although current diagnostic categories identify clinically disturbed functioning, they arguably do not identify etiologically delineated groups with distinct risk factor profiles (1,2) – something would come as no surprise to mental health practitioners and teachers who work

with children and young people with DBDs. Children can be diagnosed with the same disorder with limited symptom overlap (3). Even those with relatively comparable behavioral presentation, can differ in underlying mechanisms and developmental trajectories associated with their DBD (1,4). Furthermore, not all children who are diagnosed with DBD in childhood will develop into adults with antisocial behavior. Some remain on a stable DBD trajectory, but others remit in their disruptive behaviors (5,6) and many migrate to different diagnostic categories over development (7,8).

In the light of the heterogeneity in presentation of DBDs, their underlying mechanisms and outcomes, how can we best advance our understanding? DBDs have spawned research into genetic, environmental, and neurocognitive risk factors, but we are far from truly integrating our understanding across these different levels of analyses. Here we outline several key inter-related areas that need to be considered if we are to advance a genuinely holistic explanatory model that has the potential to account for multiple developmental trajectories (and indeed variation in treatment approaches/outcomes) in children with DBDs.

Equifinality and multifinality

The term 'equifinality' refers to the notion that a particular outcome/end state can be reached by many potential means (9). In other words, two individuals may display comparable DBD symptoms, but may do so for different underlying reasons. If these individuals are treated with a single intervention, possibly targeting the underlying causal factors important for person A, it is by no means inevitable that person B will be helped.

We can use conduct disorder (CD), as an example of the challenge of advancing our understanding of DBDs in the face of equifinal outcomes. Typically, when we try to study mechanisms that are related to CD, we select individuals based on their behavioural symptoms and try to find an underlying cause or causes for their presentation. There is a clear circularity of argument here. We already know that children and young people who qualify for a CD diagnosis are not all alike. In fact, they may have very different symptom profiles or they may display the same symptoms for different reasons. Despite this heterogeneity, we use behaviourally defined diagnostic criteria to select individuals for our studies, then try and look for causes and mechanisms. If we accept that in all likelihood there are *conduct disorders*, rather than *a* conduct disorder, then such an approach is inherently limited.

One way researchers, ourselves included, have attempted to get around this problem, has been to use differences in behaviour/trait indicators to subgroup individuals with CD and then investigate these subgroups at different levels of analyses. Although this approach explicitly recognizes heterogeneity within the disorder, it does not resolve the circularity problem. This is because the heterogeneity is still defined at the behavioural level, and we cannot assume that the behavioural indicators we have chosen, or our ability to observe them, are sufficiently accurate or discriminating with respect to underlying causes or mechanisms. We should therefore view work in this tradition as one approach for triangulating the

'heterogeneity problem' and reducing the problem space – whilst continuing to recognize its inherent limitations.

Research into children with CD with high vs. low levels of callous-unemotional (CU) traits (CD/HCU vs. CD/LCU) can be used to more fully illustrate this approach and its limitations (1, 10, 11). The 5th Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; 12) included measurement of CU traits (termed 'Limited Prosocial Emotions') as a specifier for children with Conduct Disorder, based on findings from different methodological traditions indicating divergence between children with CD/HCU and their peers with CD/LCU (1, 10, 11). For example, twin data from our group have indicated that conduct problems may be more heritable in the presence of HCU, while reflecting predominantly environmental risk in the presence of LCU (13, 14). Neuroimaging and experimental data across different research groups have suggested that children with CD/HCU show diminished neural, psychophysiological and behavioral responses to other people's pain, fear and laughter (1,15,16), while those with CD/LCU may have exaggerated neural and behavioral responses to threat (1,17,18). These findings are consistent with the view that there are distinct subgroups of children presenting with CD that can be differentiated at multiple levels of analyses and may have different underlying vulnerabilities for their disruptive behavior. This gives some cause for optimism for the use of subgrouping as one approach for triangulating the heterogeneity problem.

However, as we have noted above, even with this approach it is not possible to avoid circularity that stems from basing grouping on behavioral criteria or traits that are ultimately inferred based on behavior. In recent years, data has accumulated indicating that not all children presenting with CD/HCU are the same. For some children with CD, HCU traits are

accompanied by high levels of anxiety and trauma histories and different cognitive/affective presentation compared to other children where HCU traits are associated with an absence of anxiety symptomatology and prior trauma histories (19-21). In other words, children may present with CD and HCU traits as a result of different etiological pathways.

The recognition of the problems of relying on behavioural diagnoses has contributed to a range of initiatives including the US National Institute of Mental Health's Research Domain Criteria (RDoC; 22), which encourages researchers to focus on basic dimensions of functioning (e.g. threat reactivity variously specified) rather than diagnostic criteria. The aim of such initiatives is to elucidate how individual differences in a particular domain/construct, such as negative valence representation probed by paradigms targeting the functioning of threat circuitry, may increase the risk (for example), of developing aggressive symptomatology that we know characterises some children with DBDs.

The research focus advocated by the RDoC initiative is important, but has its own set of challenges. Most practitioners recognize that particular shared risk indicators can characterize two individuals who in fact qualify for different diagnoses or may even be present in some individuals who appear largely free from mental health problems. Genetically informative studies indicate that substantial amount of genetic risk is common across different DBDs, as well as DBDs and psychopathological outcomes more broadly (23,24). This is in line with the notion of there being general vulnerability to psychopathology that is likely to explain why most risk indicators for DBDs are transdiagnostic (25). How particular DBDs that share risk indicators with other disorders canalise over development, or why some individuals with initial DBD symptoms remit over time, is likely to depend on the degree of general psychopathology risk, as well as unique genetic and environmental risk and protective factors, over and above those related to general psychopathology. Cicchetti and Rogosch (9)

described the phenomenon of common risk indicators being associated with different outcomes as 'multifinality'. They proposed the following: *'The principle of multifinality (Wilden, 1980) suggests that any one component may function differently depending on the organization of the system in which it operates.' (*9, pp. 597–598). Individuals who share particular characteristics, for example, higher reactivity of the amygdala to threat, often differ in their genetic and environmental endowments in multiple ways. This accounts for individual differences in the ability to regulate the amygdala response and the range of likely choices and behaviours available to a particular person. In other words, developmental outcomes for people with similar amygdala responsivity in childhood may vary considerably, with only a subset of those with exaggerated amygdala response to threat developing a persistent DBD.

Both equi- and multifinality need to be considered as we seek to understand development of DBDs. Cicchetti and Rogosch (9, pp. 599) wrote the following:

"This attention to diversity in origins, processes, and outcomes in understanding developmental pathways does not suggest that prediction is futile as a result of the many potential individual patterns of adaptation (Sroufe, 1989). There are constraints on how much diversity is possible, and not all outcomes are equally likely (Cicchetti & Tucker, 1994a; Sroufe et al., 1990). Nonetheless, the appreciation of equifinality and multifinality in development encourages theorists and researchers to entertain more complex and varied approaches to how they conceptualize and investigate development and psychopathology."

In nearly 25 years since Cicchetti and Rogosch's article was published, we have not made as much progress in entertaining more complex and varied approaches to conceptualizing and

investigating DBDs as we might have hoped for. Below we outline a set of issues that need meaningful attention if we are to realise this ambition. Given the constraints of space, we have chosen to focus on those issues that appear to us most salient at the current time. Of course there are other factors that are important and require further consideration as the field progresses.

Challenges around finding risk genes

Despite robust and well replicated findings from twin and adoption studies indicating substantial heritability of DBDs (23,26,27), success in molecular genetic research has been modest (28-30). In other words, we have not yet found a substantive proportion of genes that increase risk of developing DBDs or identified how these might vary for different patterns of DBD development. This limits both our ability to understand how genetic risk for DBDs operates and constrains our capacity for effective multi-level study of DBDs. There is no doubt that much larger samples will be needed to find common genetic variants with small effect size that probabilistically increase risk of DBDs (30). Studies of other phenotypes indicate that the ability to find common variants rises exponentially as sample sizes increase from tens of thousands to hundreds of thousands or million participants (31); to date the largest studies of DBDs have involved samples in the thousands (e.g. 28). Studies should also be conducted to search for rare variants associated with DBD risk. However, the success of molecular genetic research will not just depend on large samples or latest analytic technologies, although both are important.

If molecular genetic studies focus on generic measures of disruptive behaviour and do not pay attention to the particular presentation or age of the participants, we are biasing our

studies for finding those variants that are responsible for what is common across subgroups and ages. One might argue that if we want to find those genes, we should focus on screening for variants that increase risk for general psychopathology, as twin data indicate that these will also increase risk of DBDs (24). We should additionally consider that partly divergent risk genetic factors may be important when we seek to understand different DBD developmental profiles (HCU, LCU, persistent, remitting, increasing, heterotypically continuous, co-morbid with anxiety etc.) (27,13,5).

Recent findings in relation to 'genetic innovation' serve as a sobering illustration of this issue. Genetic innovation refers to novel heritable effects that become apparent over the course of development with genes that were previously inactive coming 'online'. It has been shown that those genetic factors which increase early *risk* of developing conduct problems are largely independent of those genetic factors that explain subsequent *change* in these behaviours (32). A comparable pattern is seen in relation to CU traits (33). We have speculated that genetic risk factors influencing the baseline level of conduct problems/CU traits may be related to the temperamental make-up of the child, including those genetic variants that influence emotional reactivity or drive social affiliation and resonating with other people (34,15). A second set of genetic factors influencing the developmental course of DBDs may relate more specifically to traits and capacities that mature in childhood and adolescence and are likely to impact upon expression of behaviour and trait profile over time. As an example, the capacity to engage in complex, goal-oriented thinking substantially increases across childhood and adolescence (35), as does sensitivity to what other people think (36). Both are thought to be linked to changes in the adolescent brain structure and function (35,36). These processes may be important for assessing best strategies for executing one's own goals, which may result in less or more adaptive ways of interacting with others. Developmental changes such as these could lead to genuine changes in the

appreciation and understanding of others' emotions, for example, or might reflect masking or unmasking of baseline dispositional traits – as superior or inferior (compared to the age group) planning and regulatory capacities emerge.

In conclusion, advances in our understanding DBDs will be impeded if the granularity of molecular genetic studies does not mirror the granularity of how we operationalise etiology, presentation and trajectories. This will, in turn, constrain our capacity for effective multi-level study of different DBD trajectories where molecular genetic risk is successfully integrated into any analytic approach.

Challenges around harmonising and improving neuroimaging and experimental studies

To date there is a burgeoning body of functional neuroimaging and experimental research, aimed at elucidating the information processing patterns associated with DBDs (1,37). The extant studies have documented e.g. atypical affect perception, empathy, affect regulation and decision making in DBD populations and suggest that the specific patterns may differ by subgroup (1). While some of these findings have been replicated, in many instances it is difficult to interpret the not infrequent inconsistencies reported in the literature. There is no doubt that some of these inconsistencies are driven by variation in who these studies sample and the field needs more consistency in participant selection practices. We also want to highlight three further challenges if we want to build a stronger evidence base of neurocognitive risk to DBDs.

First, task parameters and task demands often vary considerably between studies claiming to assess the same cognitive/affective constructs. Just because two investigators both state that they assess, for example, emotion regulation, does not mean that they are actually quantifying

the same information processing parameters. We need more precision in definitions of constructs and an agreed set of measures for quantifying those constructs. A related issue concerns the degree of inference afforded by the choice of paradigm. For example, if a task conflates a number of cognitive processes without parsing them, it is not possible to use it as equivocal evidence of atypical processing in a single domain. It would substantially advance the field to agree on a core set of paradigms that more precisely and reliably measure a set of clearly defined candidate cognitive/affective functions.

Second, we need considerably more work on psychometric validation of functional neuroimaging and experimental measures if we want to advance the longitudinal study of DBD development. Unfortunately, the functional neuroimaging and experimental paradigms that are currently available, have largely been adopted from cognitive neuroscience and experimental psychology studies that were originally developed to study 'species universals'. That is, these paradigms are designed to minimise between individual variation and to reliably capture effects across all humans or within a specific group. In other words, they are optimized to capture group effects. These paradigms have not, as a rule, been psychometrically validated to sensitively and reliably capture individual differences (38). This currently limits their utility for inclusion in large scale, longitudinal studies of individual differences in developmental trajectories – particularly our ability to relate functional neuroimaging and experimental data to behavioural (including clinical) outcomes.

A third challenge relates to dearth of work validating paradigms that could be used to assess the same neurocognitive domains across the lifespan. For example, how we might experimentally index a process such as emotion regulation is unlikely to be the same for pre-school children as it would be for adolescents. There is an intrinsic challenge here in how we

can have confidence that our various measures employed at different ages are indexing the same underlying cognitive process. Furthermore, as developmental researchers, we must grapple with the reality that such processes themselves will, in almost all instances, evolve and change over time.

Until these challenges are addressed, the most reliable indices of individual differences in neurocognitive development are likely to be indices of brain structure. These do sensitively chart individual differences, as evidenced by the utility of brain structural measures in charting heritable individual differences on brain development (39,40). Recent studies have shown that longitudinal structural brain phenotypes can be reliably associated with development of behaviors related to DBDs, such as impulsivity (e.g. 41). However, measures of brain structure are naturally limited in the insight they can offer regarding information processing patterns that may underlie development of particular DBD profiles (or remission thereof).

Challenges around embedding the study of the brain into the social context

One critical shortcoming in our understanding of DBDs has been the failure to systematically consider the complex and reciprocal relationships between the brain/cognition and the social world. Research has either focused on genetic or neurocognitive vulnerability, often conceptualised as 'located within the child', or in social/environmental risk factors, often conceptualised as external to the child. However, the complex psychological and behavioral features that characterise DBDs are clearly emergent phenomena that are the product of dynamic interplay between these domains. Brain changes do not mean that vulnerability is simply located in the child. Rather, vulnerability unfolds in a relational context. That is, through the interaction of a child's social behaviour and capacities, and the responses of

peers, adults and systems around them. We need to advance study of the 'embedded brain', that neither denies biology, nor adopts a biologically reductionist approach in the study of DBDs. We need to better understand how neurocognitive endowments or adaptations impact specific aspects of social functioning in order to inform approaches to prevention and intervention.

DBDs should not be seen as just an outcome, but rather viewed through a developmental lens, whereby atypical behaviours (by children themselves and those around them) shape and maintain social interactions. Five decades ago Patterson introduced the notion of 'coercive cycles' as a model of how disruptive behaviours escalate and are reinforced within the family ecology (42). His theory described a process of mutual reinforcement, where caregiver behaviors reinforce the child disruptive behavior, which in turn evoke anger and hostility in the caregiver, which then escalate the child behavior (43). Genetically sensitive studies have since demonstrated that many social risk factors associated with DBDs include genetic confounding – providing some insight into sources of individual differences in family social interactions (44). For example, harsh and inconsistent discipline is associated with higher levels of DBDs, but this in part reflects shared genetic vulnerabilities between parents and children (passive gene-environment correlation) and reactions that a child with difficult DBD evokes in parents (evocative gene-environment correlation) (44). Although gene-environment correlation in the context of DBDs has not been studied using neuroimaging or experimental probes, it is not unreasonable to propose that genetic endowments calibrate children's (and caregivers') cognitive and affective functioning in ways that constrain subsequent building and maintaining of social relationships (34,15). For example, difficulty in empathising with other people's distress (1) or sharing in their joy (45), as seen in children with CP/HCU, may evoke fear, discomfort and even hostility in child-caregiver interactions.

The genetic endowments of the parent may also constrain their ability to respond to a challenging child.

Environmental risk, for example extreme childhood adversity, can also lead to neurodevelopmental adaptations that may confer latent vulnerability to subsequent development of DBDs (46). In brief, the brain may adapt to an adverse environment; however, these calibrations may mean that a child may be less well equipped to function in more normative environments. For example, children who have experience maltreatment in the past show heightened reactivity to threat (47,48). Being alert to potential threat will clearly serve a purpose in an environment that is not safe. However, it may result in threat reactive aggression in response to perceived threat, even if threat was not intended, causing problems in school, for example. We have argued that this 'mismatch' - where brain systems calibrated for an adverse environment function less well in a more normative environment - may lead to mental health vulnerability that is socially mediated. That is, neurocognitive adaptations associated with early adverse environments may impact how a child shapes and experiences the social world in ways that become problematic. For example, altered brain functioning may contribute to the generation of *new* stressful events ('stress generation') that in turn contribute to an increased risk of future internalising symptoms, and plausibly externalising symptoms (49). For example, if conflict escalates for a child at school, and this ultimately leads to exclusion, this would likely result in significant stress for the child and their family in addition to that which may have been experienced by the child earlier in life. Equally, brain adaptations associated with exposure to childhood adversity may lead to what has been termed 'social thinning' (50). Here, the range and quality of social interactions of a child are reduced over time (50,51), attenuating the protective effects associated with social support.

It is regrettable that there is such a dearth of research into how different cognitive/affective biases may feed into generating and maintaining atypical social interactions, and how the social interactions in turn calibrate future brain/cognitive development in children with DBDs. In order to achieve longitudinal, multi-level study of the 'embedded brain', we will need advances in our understanding of the etiology of different DBD trajectories and refinement of neuroimaging and experimental study protocols, as outlined in the previous sections. We will also need improvements in sensitive measurement of social functioning over development (via e.g. observational, experience sampling, and social network measures), so that we can examine how particular cognitive and affective biases shape social experiences at different developmental stages, and how those social experiences in turn shape brain development in ways that either increase risk of or protect against developing a DBD.

Improving our ability to study the 'embedded brain' is a challenging, but important task. Social learning principles used in many therapeutic programmes of DBDs emphasise the ways in which adult behaviour can impact on the child outcome. However, children also play a key role in shaping the responses of adults around them, often evoking particularly negative or conflictual reactions. Furthermore, caregivers may share some of the vulnerabilities of their child, augmenting the challenge of delivering a systemic intervention. Helping caregivers and teachers understand cognitive and affective biases of the child may help them reframe the child's behaviour and change how they consequently experience and respond to that behavior. Therapeutic programmes also target child cognitions, aiming to shift the way in which a child with DBD processes information (e.g. emotion regulation or empathy training). A more precise understanding the neurocognitive processes that contribute to a particular child's disruptive behaviour could help clinical formulation. If the child displays aggressive responses in the face of perceived threat, then shifting how affective cues are perceived (52) or emotion regulation training (53) may be appropriate and feed into reduction of aggression

and subsequent improvement in social functioning. If the child displays diminished responses to other people's positive affect (45), it may be possible to pair positive affect stimuli with something that the child finds rewarding. This could, over time, make the child more receptive to adult positive affect/feedback and improve the quality of social interactions. In both cases the breakdown in social relationships or the outcome after intervention may be very similar, but the reasons for the breakdown or who benefits from which approach is not.

Conclusions

There are structural barriers inherent in the scientific world where we all specialise in particular methods, schools of thoughts, or disorders. Increasingly, data are accumulating that challenge our traditional notions of diagnoses and shine a light onto complexities of developmental risk and resilience. Causal pathways to DBDs, even within the same diagnostic category, are varied. If we are to advance the study of DBDs, we do not just need bigger samples or larger quantities of data. We need a more systematic approach to uncover underlying mechanisms and need to creatively address the current reliance on behaviour as the primary organising framework. The field needs to work together to generate an integrated conceptual framework that articulates the relationships between levels of explanation, but also across development and across domains of functioning. Genetic advances in our understanding of DBDs will be impeded if they do not occur alongside improved granularity in how we operationalise presentation and developmental trajectories. Improvement in measurement is essential, particularly in relation to neurocognitive and social risk factor indices. Unless we achieve this goal, we will not be able to place what we are learning about brain function in a systemic, multilevel context, where brain changes are understood not simply as outcomes of genetic and environmental influences, but also as factors that reciprocally influence future social environments in ways that are important in understanding

risk and resilience. The ultimate goal of advancing the field in this way is to improve our ability to develop effective preventative approaches and more targeted, and therefore more effective, approaches to intervention.

References

1. Blair R, Leibenluft E, Pine D: Conduct Disorder and Callous–Unemotional Traits in Youth. N Engl J Med 2014;371(23):2207-2216

2. Frick P, Viding E: Antisocial behavior from a developmental psychopathology perspective. Dev Psychopathol 2009;21(4):1111-1131

3. NICE: Antisocial behaviour and conduct disorders in children and young people: recognition and management 2017

4. Viding E, Fontaine N, McCrory E: Antisocial behaviour in children with and without callous-unemotional traits. J R Soc Med 2012;105(5):195-200

5. Odgers C, Moffitt T, Broadbent J, et al: Female and male antisocial trajectories: From childhood origins to adult outcomes. Dev Psychopathol 2008;20(2):673-716

6. Gutman L, Joshi H, Schoon I: Developmental Trajectories of Conduct Problems and Cumulative Risk from Early Childhood to Adolescence. J Youth Adolesc 2019;48(2):181-198

7. Lahey B, Zald D, Hakes J, et al: Patterns of Heterotypic Continuity Associated With the Cross-Sectional Correlational Structure of Prevalent Mental Disorders in Adults. JAMA Psychiatry 2014;71(9):989-996

8. Caspi A, Houts R, Ambler A, et al: Longitudinal Assessment of Mental Health Disorders and Comorbidities Across 4 Decades Among Participants in the Dunedin Birth Cohort Study. JAMA Netw Open 2020;3(4):e203221

9. Cicchetti D, Rogosch F: Equifinality and multifinality in developmental psychopathology. Dev Psychopathol 1996;8(4):597-600

10. Frick P, Ray J, Thornton L, et al: Can callous-unemotional traits enhance the understanding, diagnosis, and treatment of serious conduct problems in children and adolescents? A comprehensive review. Psychol Bull 2014;140(1):1-57

11. Viding E, McCrory E: Understanding the development of psychopathy: progress and challenges. Psychol Med 2018;48(4):566-577

12. American Psychiatric Association: Diagnostic and statistical manual of mental disorders (DSM-5). Arlington, VA: American Psychiatric Association; 2013

13. Viding E, Blair R, Moffitt T, et al: Evidence for substantial genetic risk for psychopathy in 7-year-olds. J Child Psychol Psychiatry 2005;46(6):592-597

14. Viding E, Jones A, Paul J, et al: Heritability of antisocial behaviour at 9: do callous-unemotional traits matter?. Dev Sci 2008;11(1):17-22

15. Viding E, McCrory E: Towards understanding atypical social affiliation in psychopathy. Lancet Psychiatry 2019;6(5):437-444

16. de Wied M, van Boxtel A, Matthys W, et al: Verbal, Facial and Autonomic Responses to Empathy-Eliciting Film Clips by Disruptive Male Adolescents with High Versus Low Callous-Unemotional Traits. J Abnorm Child Psychol 2012;40(2):211-223

17. Viding E, Sebastian C, Dadds M, et al: Amygdala Response to Preattentive Masked Fear in Children With Conduct Problems: The Role of Callous-Unemotional Traits. Am J Psychiatry 2012;169(10):1109-1116

18. Sebastian C, McCrory E, Dadds M, et al: Neural responses to fearful eyes in children with conduct problems and varying levels of callous–unemotional traits. Psychol Med 2014;44(1):99-109

19. Cecil C, McCrory E, Barker E, et al: Characterising youth with callous–unemotional traits and concurrent anxiety: evidence for a high-risk clinical group. Eur Child Adolesc Psychiatry 2018;27(7):885-898

20. Kimonis E, Frick P, Cauffman E, et al: Primary and secondary variants of juvenile psychopathy differ in emotional processing. Dev Psychopathol 2012;24(3):1091-1103

21. Viding E, Kimonis ER: Callous–unemotional traits. In Patrick CJ, editor. Handbook of psychopathy. The Guilford Press; 2018. p. 144-164

22. National Institute of Mental Health: Research Domain Criteria Initiative 2009

23. Bornovalova M, Hicks B, Iacono W, et al: Familial Transmission and Heritability of Childhood Disruptive Disorders. Am J Psychiatry 2010;167(9):1066-1074

24. Allegrini A, Cheesman R, Rimfeld K, et al: The p factor: genetic analyses support a general dimension of psychopathology in childhood and adolescence. J Child Psychol Psychiatry 2020;61(1):30-39

25. Caspi A, Moffitt T: All for One and One for All: Mental Disorders in One Dimension. Am J Psychiatry 2018;175(9):831-844

26. Viding E, McCrory E: Genetic and neurocognitive contributions to the development of psychopathy. Dev Psychopathol 2012;24(3):969-983

27. Lahey B, Waldman I: Annual Research Review: Phenotypic and causal structure of conduct disorder in the broader context of prevalent forms of psychopathology. J Child Psychol Psychiatry 2012;53(5):536-557

28. Tielbeek J, Johansson A, Polderman T, et al: Genome-Wide Association Studies of a Broad Spectrum of Antisocial Behavior. JAMA Psychiatry 2017;74(12):1242-1250

29. Viding E, Hanscombe K, Curtis C, et al: In search of genes associated with risk for psychopathic tendencies in children: a two-stage genome-wide association study of pooled DNA. J Child Psychol Psychiatry 2010;51(7):780-788

30. Salvatore J, Dick D: Genetic influences on conduct disorder. Neurosci Biobehav Rev 2018;91:91-101

31. Plomin R, von Stumm S: The new genetics of intelligence. Nat Rev Genet 2018;19(3):148-159

32. Pingault J, Rijsdijk F, Zheng Y, et al: Developmentally dynamic genome: Evidence of genetic influences on increases and decreases in conduct problems from early childhood to adolescence. Sci Rep 2015;5(1):10053

33. Takahashi Y, Pease C, Pingault J, et al. Genetic and environmental influences on the developmental trajectory of callous-unemotional traits from childhood to adolescence. J Child Psychol Psychiatry 2020

34. Bird G, Viding E: The self to other model of empathy: Providing a new framework for understanding empathy impairments in psychopathy, autism, and alexithymia. Neurosci Biobehav Rev 2014;47:520-532

35. Crone E, Steinbeis N: Neural Perspectives on Cognitive Control Development during Childhood and Adolescence. Trends Cogn Sci 2017;21(3):205-215

36. Foulkes L, Blakemore S: Studying individual differences in human adolescent brain development. Nat Neurosci 2018;21(3):315-323

37. Alegria A, Radua J, Rubia K: Meta-Analysis of fMRI Studies of Disruptive Behavior Disorders. Am J Psychiatry 2016;173(11):1119-1130

38. Elliott M, Knodt A, Ireland D, et al: What is the Test-Retest Reliability of Common Task-fMRI Measures? New Empirical Evidence and a Meta-Analysis. Biol Psychiatry 2020;87(9):S132-S133

39. Schmitt J, Neale M, Fassassi B, et al: The dynamic role of genetics on cortical patterning during childhood and adolescence. Proc Natl Acad Sci 2014;111(18):6774-6779

40. Jansen A, Mous S, White T, et al: What Twin Studies Tell Us About the Heritability of Brain Development, Morphology, and Function: A Review. Neuropsychol Rev 2015;25(1):27-46

41. Ziegler G, Hauser T, Moutoussis M, et al: Compulsivity and impulsivity traits linked to attenuated developmental frontostriatal myelination trajectories. Nat Neurosci 2019;22(6):992-999

42. Patterson GR, Reid JR: Reciprocity and coercion: Two facets of social systems. In Neuringer C, Michael JL, editors. Behavior modification in clinical psychology. New York: Appleton-Century-Crofts; 1970. p. 133-177

43. Patterson G: Coercive family process (vol 3). Eugene, Oregon: Castalia Publishing Company; 1982

44. Moffitt T: The New Look of Behavioral Genetics in Developmental Psychopathology: Gene-Environment Interplay in Antisocial Behaviors. Psychol Bull 2005;131(4):533-554

45. O'Nions E, Lima C, Scott S, et al: Reduced Laughter Contagion in Boys at Risk for Psychopathy. Curr Biol 2017;27(19):3049-3055

46. McCrory E, Viding E: The theory of latent vulnerability: Reconceptualizing the link between childhood maltreatment and psychiatric disorder. Dev Psychopathol 2015;27(2):493-505

47. McCrory E, De Brito S, Sebastian C, et al: Heightened neural reactivity to threat in child victims of family violence. Curr Biol 2011;21(23):R947-R948

48. Hein T, Monk C: Research Review: Neural response to threat in children, adolescents, and adults after child maltreatment - a quantitative meta-analysis. J Child Psychol Psychiatry 2017;58(3):222-230

49. Gerin M, Viding E, Pingault J, et al: Heightened amygdala reactivity and increased stress generation predict internalizing symptoms in adults following childhood maltreatment. J Child Psychol Psychiatry 2019;60(7):752-761

50. McCrory E: The case for a preventative approach to mental health: Childhood maltreatment, neuroimaging, and the theory of latent vulnerability. In Davies W, Savulescu J, Roache R, Loebel, editors. Psychiatry Reborn: Biopsychosocial psychiatry in modern medicine. Oxford: Oxford University Press; 2020

51. Sperry D, Widom C: Child abuse and neglect, social support, and psychopathology in adulthood: A prospective investigation. Child Abuse Negl 2013;37(6):415-425

52. Penton-Voak I, Thomas J, Gage S, et al: Increasing Recognition of Happiness in Ambiguous Facial Expressions Reduces Anger and Aggressive Behavior. Psychol Sci 2013;24(5):688-697

53. Sukhodolsky D, Smith S, McCauley S, et al: Behavioral Interventions for Anger, Irritability, and Aggression in Children and Adolescents. J Child Adolesc Psychopharmacol 2016;26(1):58-64