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GENETIC FACTORS IN FAMILIES: PARENTAL PSYCHOPATHOLOGICAL RISK AND OFFSPRING'S DEVELOMPMENTAL OUCOMES

Silvia Cimino (a), Luca Cerniglia (b), Michela Erriu (a)*, Renata Tambelli (a)
*Corresponding author

(a) Department of Dynamic and Clinical Psychology, Faculty of Medicine and Psychology, Sapienza University of Rome, Via dei Marsi n. 78, 00185 Rome, Italy, silvia.cimino@uniroma1.it; michela.erriu@uniroma1.it; renata.tambelli@uniroma1.it
(b) Uninettuno Telematic International University, Faculty of Psychology, Corso Vittorio Emanuele II, 39, 00186, Rome, Italy, l.cerniglia@uninettunouniversity.net

Abstract

Recent international research has highlighted the relevance of genetic elements in children's behavioral and emotional functioning, together with several environmental elements. In particular, parental psychopathology has turned out as crucial environmental factors in children's maladaptive outcomes. While previous research has analyzed preschool-age children and adolescents, no-few studies, to our knowledge, has focused on youths and pre-adolescents. In order to explain the complexity of the relationship between genetic and environmental elements in children's adaptive or maladaptive functioning during developmental age, this study proposes a longitudinal evaluation of genetic and psychological characteristics in families with 6- to 18-year-old sons. The sample consisted in total of 20 families (mothers, fathers, children). Parents' psychopathological symptoms were assessed using the SCL-90-R, while offspring emotional–behavioral functioning was assessed through CBCL-6–18. Dopamine transporter gene (DAT1) was also tracked. Interestly, while no significant correlations emerged between maternal and children's DAT methylation, significant correlations were found between fathers' and children's methylations. The study points out the necessity to better investigate offspring's psychological functioning in relation to parental psychopathological risk, with the addition of epigenetic elements. This may be useful to implement early assessment and treatment programmes for children and their parents.

Keywords: Epigenetic, emotional-behavioral functioning, parental risk.

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1. Introduction

Nowadays an increasing number of children and adolescents show several behavioral and/or emotional difficulties that can lead to negative consequences for their psychological and physical wellbeing (Cabaj et al., 2014; Cerniglia et al., 2018; Maguire et al., 2015; Ogundele, 2018). Both genetic and environmental elements have been posited to be an even more significant variable in the onset and maintaining of youth's problems. In fact, the recent international scientific literature suggested that difficulties in childhood might stem from a gene-environment interaction (GxE) (Bakermans-Kranenburg & Van Ijzendoorn, 2006; Duncan & Keller, 2011; Lemery-Chalfant et al., 2013; Nigg et al., 2010; Sameroff, 2010). More specifically, as highlighted by the Developmental Psychopathological theoretical framework, psychopathological risk can be predicted by a complex interplay between genetic and environmental risk factors (Cicchetti & Blender, 2006; Cicchetti & Rogosch, 1996). It may be noted that this specific interaction appears relatively understudied and only in the last two decades studies have identified a clear need for research to better understand adolescents' and children's psychological problems (Cimino et al., 2018; Lavigne et al., 2014).

The scientific literature in the epigenetic field has specifically investigated the link between genetic and environmental factors, highlighting that relational experiences can interact with genes at multiple levels (Birnbaum & Jung, 2011; Cicchetti & Blender, 2006; Meaney, 2010). This complex interaction has been indicated as a possible mechanism underpinning children's emotional and behavioral functioning (Faraone et al., 2014; Tissen et al., 2015). Research has also identified epigenetic patterns linked with biological and environmental factors (Giana et al., 2015; Schuch et al., 2015). Consistently with these empirical evidences, epigenetic alterations seems to be a biological response to environmental experiences (Lahey et al., 2011; Xu et al., 2015). In particular, emotional and behavioral problems have been reported to be related to epigenetic modification (such as DNA methylation) and genotype vulnerability (allelic polymorphism) (Adam, 2012; Haas et al., 2016). In addition, consistent research data showed that various neurotransmitters (such as dopamine) influence individual emotion regulation and behavior. Dopaminergic system has been reported as the most important center of emotional and behavioral regulation (Johnson & Young, 2015; Okita et al., 2016; Villani et al., 2018). Research has focused its attention on the gene dopamine transporter (DAT), which controls dopamine levels in the brain and also seems to be susceptible to epigenetic modification (Rajala et al., 2014; Shumay et al., 2010). As a consequence, the literature suggests that problems in emotional and behavioral functioning can be related to an alteration in neurotransmitter activity that in turn stems from genetic modification or variability (genetic polymorphism-DNA methylation) (Albert, 2011). Moreover, epigenetic modification such as DNA methylation has been reported to be associated with a gene modification (reduced gene expression) that in turn can lead to children's psychopathological problems (Roth, 2013). This risk can be further increased by negative environmental experiences, such as parental psychopathology and childhood abuse or maltreatment (Suderman et al., 2014).

With specific regard to environmental factors, some authors have recently reported that several environmental factors can have a relevant role in the onset and maintenance of maladaptive outcomes in childhood (Bornstein & Bradley, 2014; Herring et al., 2006). In particular, family elements such as parental psychopathology have turned out as crucial environmental factor in offspring's developmental

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difficulties (Ramchandani & Psychogiou, 2009; Tambelli et al., 2015; van der Pol et al., 2016). Moreover, studies that assessed the parental psychopathological risk suggested that maternal and paternal psychopathological problems can impair in deleterious way children's mental health (Wlodarczyk et al., 2017). In this regard, evidence from recent studies has indicated that children's internalizing and externalizing difficulties are strictly related to parent's psychopathological problems (van der Pol et al., 2016). Additionally, as highlighted by some authors, among which Hannigan and collegues (Hannigan et al., 2017), children could show a stability of psychopathological symptoms over time. This core aspect is likely to be an important element for intergenerational transmission of psychopathological risk from parents to offspring across the life span.

Taking into account these scientific evidences from the genetic and environmental field, epigenetic mechanism deserves to be even more investigated.

2. Problem Statement

Although children's genetic features have been found to be a relevant factor in the relationship between relational and environmental factors (i.e. parent's psychopathology) and offspring's emotional-behavioral functioning, research findings are mixed. There have been still some reasoning about the specific mechanism through which epigenetic elements influence of the genotype and environment interact on children's psychological functioning (Adriani et al., 2018; Schuch et al., 2015). Currently, research have attempted to synthesize this complex process but there's still a lot to clarify on biological, genetic and environmental interplay in children's developmental well-being.

3. Research Questions

Thus, in order to explain the complexity of the relationship between genetic and environmental elements in children' adaptive or maladaptive functioning during developmental age, this study proposes a longitudinal evaluation of genetic and psychological characteristics in families with 6 to 18 years old sons. To date, previous researches have analyzed preschool-age children and adolescents, whereas, to our knowledge, less studies have examined youths and pre-adolescents belonging to non-clinical samples.

4. Purpose of the Study

Hence, the aim of the study was to determine genetic aspects and associated risk factors in normative families in order to improve the understanding of individual and relational variables related to children's and adolescents psychological functioning. In particular, the present research was aimed at analyzing the correlation or causal relation between parents' and children's genetic (DAT methylation) and environmental factors (children's emotional-behavioral functioning and parental psychopathological risk).

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5. Research Methods

5.1. Sample

The sample consisted in a total of 20 families (mothers, fathers and children aged between 6 and 18 years of age). Participants were recruited in primary schools located in central Italy. The majority of them were Caucasian (92%). Prior permission was obtained from the Ethical Committee of the Medicine and Psychology Faculty at Sapienza, University of Rome, in accordance with the Declaration of Helsinki.

All parents were told about the aims and scope of this study. After obtaining a written informed consent, an appointment was given to the participants by a trained psychologist. Psychologists gave oral information about the research project also to the children, using an age-adequate language). None of the parents refused to participate in the study.

Parents' psychopathological symptoms were assessed using the SCL-90-R, while offspring's emotional–behavioral functioning was assessed through CBCL-6–18. Dopamine transporter gene (DAT1) was also tracked. Participants were assessed with biological sampling (buccal cells). Buccal cell sampling is a non-invasive procedure that allows collecting epithelial cells through swabs. Buccal swabs were collected for each child (Isohelix Swab Pack, Cell Product Ltd, Harriestam, UK) and carefully transported to laboratories for the next procedures.

5.2. Measures

The *Symptom Checklist-90-Items-Revised* (SCL-90-R; Derogatis, 1994) is a 90-item self-report questionnaire that assess psychological and/or psychopathological symptoms and psychological distress of adults or adolescents. It is composed of nine symptom dimensions (somatization, obsessive-compulsivity, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism) and a Global Severity Index (GSI). The Italian validated version of this tool was developed by Prunas et al. (2012), who showed that the instrument have good internal coherence (α coefficient=0.70–0.96), both for adolescents and adults.

The *Child Behavior Checklist* (CBCL 6-18; Achenbach & Rescorla, 2001; Italian version by Frigerio & Montirosso, 2002) is a report form scale including 99 items used to assess children's and adolescents' emotional and behavioral functioning in different areas of daily psychological functioning (age range: 6-18 years). The items are scored on a three-point scale (three alternative answer: not true, somewhat or sometimes true, very true or often true). It is composed of three different symptomatic scales: Internalizing, Externalizing, and Neither Internalizing Nor Externalizing. The Internalizing scale includes the syndromes: Emotionally Reactive, Anxious/Depressed, Withdrawn, Somatic Complaints; the Externalizing scale includes: Attention Problems and Aggressive Behavior; the Neither Internalizing Nor Externalizing scale identifies the syndromes of Sleep Problems and Other Problems. The instrument shows a good internal consistency (Cronbach's α, 0.65 to 0.96).

To isolate buccal cell DNA the Buccal-Prep Plus DNA isolation kit (Isohelix, Cell Product Ltd, Harriestam, UK) was adopted.

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5.3. Statistical analysis

To verify possible correlations between parental and offspring genetic characteristics, a Pearson correlation analyses were carried out. To verify the possible effect of parental psychopathological risk on offspring genetic characteristic regression analyses were performed. All data were performed with IBM SPSS software version 25.0 (IBM, Chicago, IL, USA).

6. Findings

To verify in the study variables the possible correlation between parental and children's genetic characteristics (DAT methylation) bivariate Pearson correlations were performed. Results showed a not significant correlation between maternal and offspring DAT methylation. Interestingly, results obtained revealed a significant correlation between father's DAT methylation and children's DAT methylation at different site of DAT methylation (CpG). More specifically, the examination evidenced significant correlation between fathers' methylation at CpG M1 and children's methylation at CpG M3 (r= .45; p<.05), In addiction significant correlation between father's methylation at CpG M 5 and children's methylation at CpG M 3 was found (r= .53; p <.05).

To verify the possible effect of parental psychopathological risk on offspring genetic characteristic linear regression analyses were used. We entered as independent variables parental scores on the SCL-90-R GSI, and as dependent variables children's DAT methylation. Results revealed a significant predictive effect of maternal GSI on children's DAT methylation (i.e. at CpG M2: $R^2$0 .33; β=.57; t=3.07; p <.01). Contrary, a significant predictive effect of paternal GSI on children's DAT methylationat M2 was found (R^2 0 .45; β=.67; t=3.98; p <.01) and at another different methylation sites, such as M6 and M5.

7. Conclusion

Epidemiological studies showed that emotional and behavioral dysfunctional functioning has recently increased among children and adolescents (Barker et al., 2019; Herbert, 2008; Hölling et al., 2014; Steiger & Thaler, 2016). Nowadays several school-age children and young adolescents develop difficulties in emotion and/or in behavior regulation that can impair their psychological and physical wellbeing (Cabaj et al., 2014; Cerniglia et al., 2018; Maguire et al., 2015; Ogundele, 2018).

Children's and adolescents' maladaptive patterns should be investigated through the conceptual framework of *Developmental Psychopathology* (Cicchetti & Rogosch, 1996), a recent theoretical model which emphasizes the role of relationships and the relevance of risky and protective factors in the onset and maintenance of psychological maladjustment. Several risk factors exist which link children and adolescents to the development of many psychopathological problems, such as internalizing and externalizing problems (Costello et al., 2011; Manfro et al., 2019; Miranda et al., 2011; Theunissen et al., 2014). Thus, according to this theory and consistent with a large amount of empirical work, psychopathological problems across development has been mainly investigated referring to the issue of parental psychopathological risk factors within family relationships (Ramchandani & Psychogiou, 2009; Tambelli et al, 2015; van der Pol et al., 2016; Wlodarczyk et al., 2017).

Moreover, an important contribution to the understanding of developmental psychopathology stems from studies in the field of epigenetic, the discipline that focus on the complex interplay between

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environmental factors (family experiences and relationships) and genetic modifications (DNA alteration and allele polymorphism) during childhood (Birnbaum & Jung, 2011; Meaney, 2010). In particular, there have been many empirical contributions about genetic and biological elements in children's behavioral and emotional functioning (Davidson et al., 2002; Van Goozen et al., 2007). Within this line of research studies that assess the genetic patterns in emotional and behavioral problematic functioning suggested that difficulties in emotion regulation may be linked to epigenetic modification (such as DNA methylation) and genotype vulnerability (allelic polymorphism) (Adam, 2012; Haas et al., 2016). Moreover, dopaminergic system has also been described as a crucial center of neurobiological control from which emotional and behavioral functioning depends. In this mechanism, gene dopamine transporter (DAT) that controls dopamine levels in the brain seems to be susceptible to epigenetic modification (Rajala et al., 2014; Shumay et al., 2010). Currently recent research have attempted to synthesize this complex process but nowadays there's still a lot to clarify on biological, genetic and environmental interplay in children's developmental well-being.

In the light of the current state of research, our study was aimed to explore genetic and psychological characteristics in families belonging to non-clinical samples. In order to achieve this aim we intended to examine the relationship (possible correlation or causal link) between individual genetic features (DAT methylation) and environmental variables (parental psychopathology) in children's psychological functioning during developmental age. Since previous studies have mainly focused on preschool-age children and adolescents, we choose to examined youths and pre-adolescents (6 to 18 years old sons).

Our results showed a significant correlation between fathers' DAT methylation and children's DAT methylation at different site (CpG). Moreover, no significant correlation was found between maternal and children's methylation. In addition, to verify the possible causal link between parental psychopathology and offspring genetic characteristic (DAT methylation), we conducted a linear regression analyses. Our results show a predictive effect of paternal symptomatology and DAT methylation in children at all site of methylation examined, compared to the significant predictive effect of maternal GSI on children's DAT methylation at sites M2 M3 M6.

A possible explanation for all these findings may be that fathers' genetic features play an even more relevant role in the transmission of biological information to offspring. Traditionally, in fact, it is expected, as suggested by the epigenetic topic, that mothers will have a privileged way in passing biological characteristic to children (due to mother-infant biological relationship). Actually it may be noted that a great deal of research have paid much attention to the role of paternal psychopathological and genetic variables on children's psychological adjustment (Finegersh et al., 2015; Strober et al., 2014). Thus, it would have been interesting to better explore difference between maternal and paternal transmission of epigenetic and biological features.

This study has important limitations: first, the sample is numerically limited so that there is no possible to generalize our findings to child population. Moreover, only self-reported measures were adopted to collect the information. Despite the limitations this study provided relevant information about the complex interplay between gene and environment lighting the need for clarification on the mechanisms of epigenetic intergenerational transmission in family with children.

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Taking into account all these considerations we strongly think that psychological problems among children and adolescents should be addressed by empirical studies based on both genetic and family (psychopathology) factors. In fact, since offspring's adaptive psychological functioning results strictly related to first environmental experiences (Cerniglia et al., 2018), many problems during development (such as subclinical forms) can be solved especially through an early assessment focused on individual and relational topics.

References

Achenbach, T. M., & Rescorla, L. A. (2001). *Manual for the ASEBA School-Age Forms and Profiles.* University of Vermont, Research Center for Children, Youth, and Families

Adam, E. K. (2012). Emotion—cortisol transactions occur over multiple time scales in development: implications for research on emotion and the development of emotional disorders. *Monographs of the Society for Research in Child Development*, *77*, 17-27.

Adriani, W., Romano, E., Pucci, M., Pascale, E., Cerniglia, L., Cimino, S., & Laviola, G. (2018). Potential for diagnosis versus therapy monitoring of attention deficit hyperactivity disorder: a new epigenetic biomarker interacting with both genotype and auto-immunity. *European child & adolescent psychiatry*, *27*, 241-252.

Albert, P. R. (2011). What is a functional genetic polymorphism? Defining classes of functionality. *Journal of psychiatry & neuroscience: JPN*, *36*, 363.

Bakermans-Kranenburg, M. J., & Van Ijzendoorn, M. H. (2006). Gene-environment interaction of the dopamine D4 receptor (DRD4) and observed maternal insensitivity predicting externalizing behavior in preschoolers. *Developmental Psychobiology: The Journal of the International Society for Developmental Psychobiology*, *48*, 406-409.

Barker, M. M., Beresford, B., Bland, M., & Fraser, L. K. (2019). Prevalence and incidence of anxiety and depression among children, adolescents, and young adults with life-limiting conditions: a systematic review and meta-analysis. *JAMA pediatrics*, *173*(9), 835-844.

Birnbaum L. S., & Jung, P. (2011). From endocrine disruptors to nanomaterials: advancing our understanding of environmental health to protect public health. *Health Affairs, 30*, 814–22.

Bornstein, M. H., & Bradley, R. H. (2014). Socioeconomic Status. *Parenting, and Child Development.* Routledge.

Cabaj, J. L., McDonald, S. W., & Tough, S. C. (2014). Early childhood risk and resilience factors for behavioral and emotional problems in middle childhood. *BMC pediatrics*, *14*, 166.

Cerniglia, L., Cimino, S., Erriu, M., Jezek, S., Almenara, C. A., & Tambelli, R. (2018). Trajectories of aggressive and depressive symptoms in male and female overweight children: Do they share a common path or do they follow different routes? *PLoS one*, *13*, e0190731.

Cicchetti, D., & Blender, J. A. (2006). A multiple-levels-of-analysis perspective on resilience: Implications for the developing brain, neural plasticity, and preventive interventions. *Annals of the New York Academy of Sciences*, *1094,* 248–258.

Cicchetti, D., & Rogosch, F. A. (1996). Equifinality and multifinality in developmental psychopathology. *Development and psychopathology*, *8*, 597–600.

Cimino, S.; Cerniglia, L.; Ballarotto, G.; Marzilli, E.; Pascale, E.; D'Addario, C., & Tambelli, R. (2018). DNA Methylation at the DAT Promoter and Risk for Psychopathology: Intergenerational Transmission between School-Age Youths and Their Parents in a Community Sample. *Frontiers in psychiatry*, *8*, 303.

Costello, E. J., Copeland, W., & Angold, A. (2011). Trends in psychopathology across the adolescent years: what changes when children become adolescents, and when adolescents become adults?. *Journal of Child Psychology and Psychiatry*, *52*, 1015-1025.

Davidson, R. J., Lewis, D. A., Alloy, L. B., Amaral, D. G., Bush, G., Cohen, J. D., & Nolen-Hoeksema, S. (2002). Neural and behavioral substrates of mood and mood regulation. *Biological psychiatry*, *52*, 478-502.

Derogatis, L. R. (1994). *Symptom Checklist-90-Revised: Administration, scoring and procedures manual.* National Computer Systems.

Duncan, L. E., & Keller, M. C. (2011). A critical review of the first 10 years of candidate gene-by-environment interaction research in psychiatry. *American Journal of Psychiatry*, *168*, 1041–1049.

Faraone, S. V., Bonvicini, C., & Scassellati, C. (2014). Biomarkers in the diagnosis of ADHD–promising directions. *Current psychiatry reports, 16*, 497. https://doi.org/10.1007/s11920-014-0497-1

Finegersh, A., Rompala, G. R., Martin, D. I., & Homanics, G. E. (2015). Drinking beyond a lifetime: New and emerging insights into paternal alcohol exposure on subsequent generations. *Alcohol*, *49*, 461-470.

Frigerio, A. & Montirosso, R. (2002). La valutazione su base empirica dei problemi emotivocomportamentali in età evolutiva. *Infanzia e Adolescenza*, *1*, 38–48.

Giana, G., Romano, E., Porfirio, M. C., D'Ambrosio, R., Giovinazzo, S., Troianiello, M., & Tarani, L. (2015). Detection of auto-antibodies to DAT in the serum: Interactions with DAT genotype and psycho-stimulant therapy for ADHD. *Journal of neuroimmunology*, *278*, 212-222.

Haas, B. W., Filkowski, M. M., Cochran, R. N., Denison, L., Ishak, A., Nishitani, S., & Smith, A. K. (2016). Epigenetic modification of OXT and human sociability. *Proceedings of the National Academy of Sciences*, *113*, E3816-E3823.

Hannigan, L. J., Walaker, N., Waszczuk, M. A., McAdams, T. A., & Eley, T. C. (2017). Aetiological influences on stability and change in emotional and behavioural problems across development: a systematic review. *Psychopathology review*, *4*(1), 52-108.

Herbert, M. (2008). *Developmental problems of childhood and adolescence: Prevention, treatment and training*. John Wiley & Sons.

Herring, S., Gray, K., Taffe, J., Tonge, B., Sweeney, D., & Einfeld, S. (2006). Behavior and emotional problems in toddlers with pervasive developmental disorders and developmental delay: associations with parental mental health and family functioning. *Journal of intellectual disability research*, *50*, 874-882.

Hölling, H., Schlack, R., Petermann, F., Ravens-Sieberer, U., Mauz, E., & KiGGS Study Group. (2014). Psychopathological problems and psychosocial impairment in children and adolescents aged 3-17 years in the German population: prevalence and time trends at two measurement points (2003-2006 and 2009-2012): results of the KiGGS study: first follow-up (KiGGS wave 1). *Bundesgesundheitsblatt, Gesundheitsforschung, Gesundheitsschutz*, *57*, 807-819.

Johnson, Z. V., & Young, L. J. (2015). Neurobiological mechanisms of social attachment and pair bonding. *Current opinion in behavioral sciences*, *3*, 38-44.

Lahey, B. B., Rathouz, P. J., Lee, S. S., Chronis-Tuscano, A., Pelham, W. E., Waldman, I. D., & Cook, E. H. (2011). Interactions between early parenting and a polymorphism of the child's dopamine transporter gene in predicting future child conduct disorder symptoms. *Journal of Abnormal Psychology*, *120*, 33.

Lavigne, J. V., Herzing, L. B., Cook, E. H., LeBailly, S. A., Gouze, K. R., Hopkins, J., Bryant, F. B. (2014). Gene x environment effects of serotonin transporter, dopamine receptor D4, and monoamine oxidase A genes with contextual and parenting risk factors on symptoms of oppositional defiant disorder, anxiety, and depression in a community sample of 4-year-old children. *Development and psychopathology*, *25*, 555–575.

Lemery-Chalfant, K., Kao, K., Swann, G., & Goldsmith, H. H. (2013). Childhood temperament: passive gene-environment correlation, gene-environment interaction, and the hidden importance of the family environment. *Development and psychopathology*, *25*, 51.

Maguire, S. A., Williams, B., Naughton, A. M., Cowley, L. E., Tempest, V., & Kemp, A. M. (2015). A systematic review of the emotional, behavioral and cognitive features exhibited by school-aged children experiencing neglect or emotional abuse. *Child: care, health and development*, *41*, 641-653.

Manfro, A. G., Santoro, M., Polanczyk, G. V., Gadelha, A., Pan, P. M., Bressan, R. A., & Salum, G. A. (2019). Heterotypic trajectories of dimensional psychopathology across the lifespan: the case of

youth-onset attention deficit/hyperactivity disorder. *Journal of Child Psychology and Psychiatry*, *60*(5), 533-544.

Meaney, M. J. (2010). Epigenetics and the biological definition of gene × environment interactions. *Child development*, *81*, 41-79.

Miranda, J. K., de la Osa, N., Granero, R., & Ezpeleta, L. (2011). Maternal experiences of childhood abuse and intimate partner violence: Psychopathology and functional impairment in clinical children and adolescents. *Child abuse & neglect*, *35*, 700-711.

Nigg, J., Nikolas, M., & Burt, S. A. (2010). Measured gene-by-environment interaction in relation to attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, *49*, 863-873.

Ogundele, M. O. (2018). Behavioral and emotional disorders in childhood: a brief overview for paediatricians. *World journal of clinical pediatrics*, *7*, 9.

Okita, K., Ghahremani, D. G., Payer, D. E., Robertson, C. L., Dean, A. C., Mandelkern, M. A., & London, E. D. (2016). Emotion dysregulation and amygdala dopamine D2-type receptor availability in methamphetamine users. *Drug and alcohol dependence*, *161*, 163-170.

Prunas, A., Sarno, I., Preti, E., Madeddu, F., & Perugini, M. (2012). Psychometric properties of the Italian version of the SCL-90-R: a study on a large community sample. *European Psychiatry*, 27, 591–597.

Rajala, A. Z., Zaitoun, I., Henriques, J. B., Converse, A. K., Murali, D., Epstein, M. L., & Populin, L. C. (2014). Dopamine transporter gene susceptibility to methylation is associated with impulsivity in nonhuman primates. *Journal of neurophysiology*, *112*, 2138-2146.

Ramchandani, P., & Psychogiou, L. (2009). Paternal psychiatric disorders and children's psychosocial development. *The Lancet*, *374*, 646-653.

Roth, T. L. (2013). Epigenetic mechanisms in the development of behavior: Advances, challenges, and future promises of a new field. *Development and psychopathology*, *25*, 1279.

Sameroff, A. (2010). A unified theory of development: A dialectic integration of nature and nurture. *Child Development*, *81*, 6–22.

Schuch, V., Utsumi, D. A., Costa, T. V. M. M., Kulikowski, L. D., & Muszkat, M. (2015). Attention deficit hyperactivity disorder in the light of the epigenetic paradigm. *Frontiers in psychiatry*, *6*, 126.

Shumay, E., Fowler, J. S., & Volkow, N. D. (2010). Genomic features of the human dopamine transporter gene and its potential epigenetic states: implications for phenotypic diversity. *PLoS One*, *5*, e11067.

Steiger, H., & Thaler, L. (2016). Eating disorders, gene-environment interactions and the epigenome: roles of stress exposures and nutritional status. *Physiology & behavior*, *162*, 181-185.

Strober, M., Peris, T., & Steiger, H. (2014). The plasticity of development: how knowledge of epigenetics may advance understanding of eating disorders. *International Journal of Eating Disorders*, *47*, 696-704.

Suderman, M., Borghol, N., Pappas, J. J., Pereira, S. M. P., Pembrey, M., Hertzman, C., ... & Szyf, M. (2014). Childhood abuse is associated with methylation of multiple loci in adult DNA. *BMC medical genomics*, *7*(1), 13.

Tambelli, R., Cimino, S., Cerniglia, L., & Ballarotto, G. (2015). Early maternal relational traumatic experiences and psychopathological symptoms: a longitudinal study on mother-infant and father-infant interactions. *Scientific reports*, *5*, 1-11.

Theunissen, S. C., Rieffe, C., Netten, A. P., Briaire, J. J., Soede, W., Schoones, J. W., & Frijns, J. H. (2014). Psychopathology and its risk and protective factors in hearing-impaired children and adolescents: a systematic review. *JAMA pediatrics*, *168*, 170-177.

Tissen, A. J., Bralten, J., Rommelse, N. N., Arias-Vasquez A., Greven, C. U., Heslenfeld, D., & Franke, B. (2015) The role of age in association analyses of ADHD and related neurocognitive functioning: a proof of concept for dopaminergic and serotonergic genes. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*, *168*, 471-479.

van der Pol, L. D., Groeneveld, M. G., Endendijk, J. J., van Berkel, S. R., Hallers-Haalboom, E. T., Bakermans-Kranenburg, M. J., & Mesman, J. (2016). Associations between fathers' and mothers'

psychopathology symptoms, parental emotion socialization, and preschoolers' social-emotional development. *Journal of child and family studies*, *25*, 3367-3380.

Van Goozen, S. H., Fairchild, G., Snoek, H., & Harold, G. T. (2007). The evidence for a neurobiological model of childhood antisocial behavior. *Psychological bulletin*, *133*(1), 149.

Villani, V., Ludmer, J., Gonzalez, A., Levitan, R., Kennedy, J., Masellis, M., & Atkinson, L. (2018). Dopamine receptor D2 (DRD2), dopamine transporter solute carrier family C6, member 4 (SLC6A3), and catechol-O-methyltransferase (COMT) genes as moderators of the relation between maternal history of maltreatment and infant emotion regulation. *Development and psychopathology*, *30*, 581-592.

Wlodarczyk, O., Pawils, S., Metzner, F., Kriston, L., Klasen, F., Ravens-Sieberer, U., & BELLA Study Group. (2017). Risk and protective factors for mental health problems in preschool-aged children: cross-sectional results of the BELLA preschool study. *Child and Adolescent Psychiatry and Mental Health*, *11*, 12.

Xu, Y., Chen, X. T., Luo, M., Tang, Y., Zhang, G., Wu, D., & Wang, H. L. (2015). Multiple epigenetic factors predict the attention deficit/hyperactivity disorder among the Chinese Han children. *Journal of psychiatric research*, *64*, 40-50.