

icCSBs 2020**The Annual International Conference on Cognitive - Social and Behavioural
Sciences****THE POSSIBLE ROLE OF GENETIC FEATURES IN CHILDREN'S
INTERNALIZING-EXTERNALIZING PROBLEMS**

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Abstract

Gene-environmental interaction has been implied to be an even more significant relevance in shaping children's development. The scientific relevance of the issue of epigenetic modifications in children is underlined by the fact that recent researchers have tried to better identify the relationships between genes and parental elements in children's emotional behavioral profiles. In particular, in the relationship between parental psychopathological factor and offspring's adaptive or maladaptive functioning, the dopaminergic system appear to be crucial for the affective and behavioral regulation in school-age children. Investigating this interaction may provide knowledge about the complex mechanism of mutual influence between members of families with developing age children. On the basis of bio-psycho-social model, this study aims to empirically investigate the possible moderator role of children's genes on the relationships between parental psychopathological risk and offspring's emotional behavioral profiles in families with school-age children. Participants were 79 families (children and their parents). Parental and children's psychological profiles were assessed using Symptom Checklist-90-R and CBCL 6-18. Children's biological samples was measured using the buccal swabs. Dopamine active transporter DAT1 gene was found to moderate the relationship between parent' psychological functioning, particularly externalizing problems, and children's emotional-behavioral profiles. Also a relevant effects of paternal psychological profiles on offsprings' psychological functioning emerged. Overall, the results are consistent with previous research, suggesting the association between environmental risk factors and children's psychological conducts. This study provided information about epigenetic issue that may be useful to implement early assessment and treatment programs for children and their parents.

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



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1. Introduction

Nowadays psychopathological problems represent a very relevant public health issue among children and youth (Cerniglia et al., 2018; Maguire et al., 2015). Since many school age children show psychological problems and discomfort (Barker, Beresford, Bland, & Fraser, 2019; Ogundele, 2018) the developmental period of childhood is very crucial both to understand children's psychological adjustment and to promote programs of intervention (van der Pol et al., 2016). In particular, internalizing and externalizing difficulties represent a distinguishing characteristic of a complex phenomenon that can impair children's development even in a severe way (Cabaj, McDonald, & Tough, 2014). It has been suggested that these types of conditions might be related to children's genetic features (Caspi et al., 2002) but also to environmental negative elements, such as maltreatment, poor parenting, and parental psychopathology (Breux, Harvey, & Lugo-Candelas, 2014; Cimino et al., 2016). In this sense, relational and family context on one hand, and children's genetic vulnerabilities on the other hand, are often indicated as having an important relevance in the onset and maintenance of offspring psychopathological problems (Hyde, Bogdan, & Hariri, 2011; Silberg, Maes, & Eaves, 2012).

The international scientific literature has increasingly focused on the complex interplay between genetic and environmental factors in offspring's psychopathological outcomes (Anreiter, Sokolowski, & Sokolowski, 2018; Duncan & Keller, 2011), highlighting in particular the role of vulnerability in response to various environmental experiences (Roth, 2013; van IJzendoorn, 2017). Within the field of research addressing the relationship between genes and environment, the perspective of *Developmental Psychopathology* (Sroufe & Rutter, 1984) represents a new conceptual framework that looks at developmental trajectories both in terms of risk and resilience. According to this theoretical and empirical model, the human behavior and psychological characteristics stem from a complex interplay between risk factors (that is the set of individual or contextual characteristics that increase the onset and maintenance of difficulties, problems or diseases) and protective aspects (the set of individual or contextual characteristics that reduce the impact of risk factors and increase the likelihood of positive outcomes in developmental age). These reciprocal influences occur between multiple levels, ranging from genetic and hereditary vulnerabilities to environmental experiences, particularly those within the family context (Cicchetti & Curtis, 2007). Within such a model of understanding child development, different risk factors, such as genetic and environmental conditions, can act in a cumulative and dynamic way, predisposing subjects to negative psychological outcomes (Cicchetti & Curtis, 2007; Lask & Bryant-Waugh, 2007; Tronick & Hunter, 2016).

Starting from the theoretical model of *Developmental Psychopathology* researchers have focused on the individual as an integrated system of biological, psychological and social elements (Zipfel, Lowe, & Herzog, 2006), trying to understand children's difficulties. In particular, several empirical studies have shown that dysfunctional psychological functioning in children is linked to both genetic characteristics and exposure during childhood to potentially negative environmental experiences (e.g. parental conflict, parental psychopathology, inadequate parent-child relationships, poverty in parental care) (Cimino et al., 2016; Oladeji, Makanjuola, & Gureje, 2010). Recently, many studies from the field of epigenetic research have focused on the gene-environment interaction to better identify the processes involved in the individual risk for psychopathology (Tronick & Hunter, 2016).

2. Problem Statement

In recent years, the integration between different disciplinary fields and new technological tools improved the investigation of genetic vulnerability, offering additional elements in order to understand the interaction between genetic and environmental variables in influencing psychopathological risk (Hyde, Bogdan, & Hariri, 2011). Studies on genetic factors and vulnerability in children's psychopathology (Hayden et al., 2013) have further redefined previous theories, suggesting a possible environmental impact on genetic vulnerability (Patrono et al., 2015). Thus, current research is increasingly focusing on the relationship between gene and environment and on their mutual interplay in shaping children's maladjustment outcomes (Davies, Cicchetti, & Hentges, 2015). Precisely, the gene-environment interaction (GxE) refers to the moderation that some genetic factors (e.g. polymorphism) can operate on individual vulnerability to particular environmental experiences. In particular, the gene-environment interaction occurs in situations where: the effect of genetic variation (e.g. genotype; genetic polymorphism) on the psychopathological risk (e.g., the risk of the environment). Internalizing-externalizing problems (developmental outcome) depend on the presence of specific socio-environmental experiences (Uher, 2014); or when the effect of environmental factors (stress, parental psychopathology, negative experiences) on the development of dysfunctional behavioral, emotional, and physiological responses is conditioned by individual differences related to the genetic disposition (e.g. genotype) (Shanahan & Hofer, 2005).

With regard to the genetic aspects in children's maladaptive functioning, international literature has highlighted the relevance both of genetic and biological factors in children's behavioral and emotional difficulties (Davidson et al., 2002; Van Goozen, Fairchild, Snoek, & Harold, 2007). In particular, among the human biological systems involved in mental and behavioral diseases, the dopaminergic neuro-transmittorial system is indicated as a crucial center of emotional and behavioral functioning (Bachner-Melman et al., 2007; DeYoung, 2013). The regulation of dopamine in the limbic brain system has received much scientific attention, due to the serious consequences that alterations in the functioning of this neurotransmitter can have on the individuals (emotional regulation, risk behaviors, motivation) (Karrer, Josef, Mata, Morris, & Samanez-Larkin, 2017). Studies on dopaminergic neurotransmission have shown that a gene controlling the synaptic levels of dopamine in the brain, DAT1 gene (dopamine active transporter), influences the children's emotional and behavioral functioning. This gene has received even more scientific attention and appears to be susceptible to epigenetic changes (Frieling et al., 2010; Rajala et al., 2014). In fact, since dopamine is implicated in mood and behavior regulation, many studies have considered the DAT1 gene the crucial genetic factor in the pathogenesis of several childhood disorders, including ADHD, behavior disorder and mood disorder (Fernandez-Jaen et al., 2015; Thissen et al., 2015). Moreover, some studies have specifically focused on role of the DAT1 genotype in developmental psychopathological risk, investigating the relationship between DAT1 and childhood negative environmental conditions (Hayden et al., 2013). The DAT1 genotype, according to this evidence, would act as a moderator in the relationship between negative parental care and dysfunctional developmental outcomes in children (Del Giudice, Ellis, & Shirtcliff, 2013), so that both environmental risks, such as parental psychopathology, and genetic factors can predispose the child to psychopathological symptoms (Cents, 2016).

Research has also indicated epigenetic modifications as a possible process through which relational experiences interact with genes and cause or support behavioral change (e.g. emotional and behavioral functioning in children). In this sense it has been suggested that epigenetic alterations are biological responses to environmental stimuli and that such changes have a relevant role in the development and maintenance of psychopathology (Birnbaum & Jung, 2011). More precisely, studies have basically indicated that epigenetic changes may occur in response to exposure to environmental situations not only in early childhood but also during development (Moore, Le, & Fan, 2013). Among the epigenetic mechanisms related to environmental risk factors, methylation has been particularly studied, considered a central process to explain the long-term effects on gene transcription and/or translation and the consequent changes in physiology (e.g. plasticity and neuronal functioning), cognition and emotional-behavioral functioning (Blaze, Scheuing, & Roth, 2013). While several studies have investigated the DNA methylation process in relation to the effects of environmental risk factors on the onset of developmental psychopathology, including early negative experiences and parental psychopathology (Rusiecki, Uddin, Alexander, & Moore, 2016), relatively few studies, to date, have focused on methylation of the DAT1 gene in humans, a mechanism that could have interesting implications in the relationship between environmental risk factors and the development of psychopathology (Schuch, Utsumi, Costa, Kulikowski, & Muszkat, 2015).

With regard to environmental factors, international literature has shown growing interest on parental psychological risk and children's problems (Crandall, Deater-Deckard, & Riley, 2015). In particular, many studies focused on parental psychopathology risk have widely stressed parental mental illness as the most important risk factors for offspring's mental diseases (Breux et al., 2014). Indeed, studies and research have showed that parental psychopathology can lead to a wide range of maladaptive outcomes in children, including both internalizing and externalizing problems (van der Pol et al., 2016). Among the risk factors for children's emotional and behavioral problems, research points to a set of family and parental elements, including also having parents with psychiatric disorders (Fairburn, Cooper, Doll, & Welch, 1999), as well as positive familiarity for emotional disorders, depressive episodes in mothers or specific personality traits (Westerberg-Jacobson, Edlund, & Ghaderi, 2010). Thus, it would be very important to investigate the mechanisms involved in the transmission of psychopathological risk over generations, with particular attention to factors that can mediate the relationship between the psychopathological risk of parents and the development of children's difficulties (Breslend et al., 2016; Cimino et al., 2016).

3. Research Questions

Despite being focus of growing scientific interest, the specific relationship between genes and environmental (such as parental) elements in shaping children's development has not yet been fully clarified. Considering, as discussed, that the phenotypic expression of the genotype (internalizing or externalizing problems) depends on a various genetic and behavioral elements (age, physical, pathological, developmental conditions, activity) which in turn interact with environmental factors (particularly relational and family factors, such as parental psychopathological risk), children's psychological functioning can be better understood and evaluated through an empirical study focused on

the relationship between genes and environmental factors (GxE). In this attempt, investigating the interaction between parental psychopathological factor and children's genotype may provide knowledge about the relationships between family members and the intergenerational transmission of psychopathological risk from parent to offspring. Moreover, investigating the potential protective and/or risk factors for the adaptive functioning of children in families may also help to promote prevention programs. Along with the need to understand the mutual interaction between children's genetic vulnerabilities and quality of environmental experiences such as parental psychopathology, it would be very relevant including paternal psychopathological profiles and their possible role in children's internalizing and externalizing problems. In addition, to our knowledge, there is a scarce empirical literature on parental psychopathological risk in general population, even more studies were focused on paternal psychological profiles taking into account gene-environment interaction.

4. Purpose of the Study

In the light of the above considerations, and according to a bio-psycho-social model, we propose an empirical study aimed at detecting children's genetic factors and parental psychopathological profiles in families with school age children. More in particular, this study intends to analyze the relationship between mothers' and fathers' psychopathological risk and offspring's emotional and behavioural functioning, taking into account the possible moderator role of children's genotype (DAT1 polymorphism). Precisely, we intend to verify the role of gene dopamine transporter DAT, the DAT1 methylation state, and their possible relationship with environmental factors such as parents' psychopathological risk. In this attempt we hypothesized that children's DAT1 genotype would have moderated the relationship between parents' psychological profiles and children's emotional and behavioral functioning. In addition, this study aims to gather more information about the possible process of gene-environment interaction implied in intergenerational transmission of psychopathological risk in families with children belonging to general population.

5. Research Methods

5.1. Sample

Participants were a total of 79 families (mothers, fathers and their school age children, age range between 6 to 11 years), recruited in primary schools located in central Italy. 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. The majority of the subject were Caucasian (92%). All parents were told about the goals of this study. After obtaining a written informed consent, trained psychologists made an appointment in which information about the research project to the participants was given.

Parental psychopathological profiles were assessed using the SCL-90-R, and children's emotional-behavioral functioning was assessed using CBCL-6-18. Dopamine transporter gene (DAT1) was traced. Children were assessed with non-invasive procedure of biological sampling (buccal cells-Isohelix Swab Pack, Cell Product Ltd, Harriestam, UK).

5.2. Measures

The *Symptom Checklist-90-Items-Revised* (SCL-90-R; Derogatis, 1994) is a 90-item self-report tool that measures psychopathological symptoms of adults or adolescents. It is composed of nine different scales (somatization, obsessive-compulsivity, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism) and a Global Severity Index (GSI). Prunas and colleagues (Prunas, Sarno, Preti, Madeddu, & Perugini, 2012) developed the Italian validated version of SCL-90-R, showing that the instrument have good internal coherence (α coefficient=0.70–0.96).

The *Child Behavior Checklist* (CBCL 6-18; Achenbach & Rescorla, 2001; Italian version by Frigerio & Montiroso, 2002) is a report form questionnaire that assesses children's emotional and behavioral functioning through 99 items. It is composed of three different symptomatic scales (Internalizing, Externalizing, and Neither Internalizing Nor Externalizing). The Internalizing scale includes: Emotionally Reactive, Anxious/Depressed, Withdrawn, Somatic Complaints, whereas the Externalizing scale includes: Attention Problems and Aggressive Behavior. The tool has 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.

5.3. Statistical analysis

To verify possible correlations between offspring's genotype and parents' psychopathological risk a Pearson correlation analyses were performed. To verify whether children's DAT1 genotype moderate the relationship between parental psychopathological risk and offspring psychological functioning a hierarchical regression analyses were carried out. Moderation analyses were carried out through the Process macro for SPSS (Hayes, 2017). All data were performed with IBM SPSS software version 25.0 (IBM, Chicago, IL, USA).

6. Findings

The preliminarily Pearson's correlation test, assessing the possible association between children's genotype and parents' psychopathological symptoms, shows no significant associations between parental psychological scores at SCL-90-R and children's DAT1 genotype ($p > .05$). Next, hierarchical regression analyses were carried out to verify the possible children's DAT1 genotype moderator role on the relationship between parental psychopathological profiles and offspring's emotional-behavioral functioning. In step 1 children's DAT1 genotype and parents' scores on SCL-90R GSI were used as independent variables; children's scores on Internalizing, Externalizing and Total Problems scales were entered as dependent variables. In step 2 the gene-environment interaction (interaction between children's genotype and each parental psychopathological variable) were included.

Results obtained evidenced no significant main or interactive effect for children's internalizing scale ($p > .05$). Moreover, results showed a significant interaction effect of children's DAT1 genotype x fathers' externalizing problems on children's externalizing symptoms in step 2 ($\beta = -0.60$; $t = 2.07$; $p < .05$). In addition, to explore moderation effect in the study variables the PROCESS macro for SPSS was

performed and a significant positive relation between fathers' externalizing problems and children's externalizing problems was found ($\beta = -0.18$; $SE = .07$; $t = 2.44$; $p = .01$).

7. Conclusion

Depending on a variety of individual, social and contextual aspects, children are often indicated as having various forms of psychological suffering, including emotional and behavioural problems (Rijlaarsdam et al., 2013; Tao et al., 2016). In fact, developmental psychopathological trajectories in childhood represent a complex issue in which is possible to track down many individual, relational and environmental factors, giving shape to psychological well-being or maladaptive functioning (Cabaj, McDonald, & Tough, 2014). Nowadays the outcomes may include a variety of problems, from severe psychopathological forms and disease to difficulties in regulating emotion or behavior, such as internalizing and externalizing symptoms (Cerniglia et al., 2018).

The scientific relevance of children's psychological problems is proved by the fact that researchers have shown increasing interest in investigating the variable linked to the onset or maintenance of children's psychopathologies (Cimino et al., 2018; Faraone, Bonvicini, & Scassellati, 2014). In particular, in the last years, the attention of researchers has focused on both individual (biological and genetic) factors (Birnbaum & Jung, 2011) and environmental factors (relational and family) (Tambelli, Cimino, Cerniglia, & Ballarotto, 2015; van der Pol et al., 2016). Recently, many studies from the field of epigenetic research and *Developmental Psychopathology* theoretical framework have focused on the gene-environment interaction to better understand children's risk for psychopathology (Tronick & Hunter, 2016). Although some genetic and environmental characteristics, such as children's genotype (Nigg, Nikolas, & Burt, 2010) and parent's psychological profiles (Lemery-Chalfant, Kao, Swann, & Goldsmith, 2013; Cimino et al., 2016), have been found to be very important to identify potential risk factors, the mechanism from which children's difficulties stem is not fully delineated. Hence, investigating the relationship between family context and children's genetic vulnerabilities may provide knowledge about maladaptive outcomes in childhood.

On the basis of these premises and in according to a bio-psycho-social model, this study aimed to explore gene-environment interaction in family of general population with school age children. In particular, the present study was focused on the children's genotype (DAT1 polymorphism) and its possible mediator role on the relationship between parental psychopathological symptoms and offspring's emotional and behavioral functioning. Our results showed that both genetic and environmental influences may contribute to child's development outcomes. In particular, the present study confirms that offspring's adaptive or maladaptive psychological functioning is related to a complex interplay between individual and environmental factors, particularly parental psychopathological symptoms, as suggested by theory and research from *Developmental Psychopathology* framework (Cicchetti & Blender, 2006). Moreover, according with many authors (Okita et al., 2016; Villani et al., 2018) our study shows that biological and genetic factor, particularly those linked to dopaminergic system, can influence children's emotional and behavioral functioning. Thus, this research also reinforces the relevance of vulnerability aspects in the onset of developmental problems. Yet, the interesting associations between fathers' psychological symptoms and children's emotional and behavioral problems shed light on the importance of the

involvement of paternal profiles in the assessment procedures and also in the treatment programs for children's problems.

This study has some limitations. First, parents' and children's variables were assessed using only report-form and self-report instruments. Moreover, we specifically assessed parental psychopathological risk factors without taking into account other possible family risk factor that can influence offspring's psychological functioning, such as couple distress. Despite these limitations, we hope that the current study may improve the knowledge about the relationship between children's psychological problems and environmental risk provided by parents, especially in families belonging to general population. Indeed, since according to *Developmental Psychopathology* framework and consistent with a large amount of empirical work psychopathology from childhood to adolescence and adulthood tends to maintain stability (Nivard et al., 2015), an early evaluation and intervention is crucial to safeguard children's psychological well-being.

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