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Genetic and Psychosocial Predictors of Child Dental Cooperation: The Interplay of Maternal Attachment and OXTR/5-HTTLPR Polymorphisms

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Abstract

Background: Uncooperative behavior in pediatric dentistry remains a significant barrier to effective care. While the correlation between maternal and child anxiety is established, the biological mechanisms moderating this relationship specifically the interaction between attachment styles and genetic susceptibility remain unexplored. This study investigated the combined predictive power of mother-child attachment and polymorphisms in the Oxytocin Receptor (OXTR) and Serotonin Transporter (SLC6A4) genes on children's behavior during dental treatment.

Methods: A prospective cohort study was conducted with 200 mother-child dyads (children aged 4–8 years). Maternal attachment was assessed using the Experiences in Close Relationships-Revised (ECR-R) questionnaire. Child cooperation was rated during restorative procedures using the Frankl Behavior Rating Scale. Genomic DNA was extracted from peripheral blood samples. Genotyping for the OXTR rs53576 polymorphism was performed using the Amplification Refractory Mutation System (ARMS-PCR), and the 5-HTTLPR region was amplified via standard PCR.

Results: Secure maternal attachment was significantly associated with positive child cooperation ($p<0.001$). Genetically, children carrying the Short (S) allele of 5-HTTLPR exhibited lower cooperation scores ($p=0.04$). A hierarchical regression model revealed a significant Gene-Environment interaction ($\beta=-0.38$, $p<0.01$), indicating that children with the 'risk' genotype (S-carriers) were significantly more vulnerable to the effects of insecure maternal attachment than children with the protective genotype (L/L).

Conclusion: The child's behavioral phenotype in the dental operatory is shaped by a complex interplay of maternal emotional availability and the child's genetic stress sensitivity. These findings support a move toward personalized behavioral management strategies based on psychosocial and biological risk profiling.

Key Words: Attachment Theory, Behavioral Genetics, Dental Anxiety, Pediatric Dentistry.

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1- INTRODUCTION

Managing behavior is a fundamental aspect of pediatric dentistry. Despite advancements in techniques, dental anxiety impacts around 10-20% of children and adolescents, leading to avoidance behaviors and negative oral health outcomes (1, 2). Traditionally, research has focused on environmental factors, particularly the "emotional contagion" between mother and child. It is well-documented that maternal dental anxiety is a significant predictor of child distress (3).

However, environmental theories alone do not fully explain why some children of anxious parents cope well, while others do not. Attachment theory provides a framework for understanding this variability. Bowlby suggested that a secure attachment figure serves as a "secure base" from which a child can manage stress (4). In the context dentistry, a securely attached child should theoretically regulate fear more effectively.

Recent advancements in molecular genetics indicate that social bonding and stress response are also biologically influenced. Two genes are particularly relevant:

1. ***The Oxytocin Receptor Gene (OXTR):*** Oxytocin plays a central role in social bonding and maternal behavior. Variations in maternal sensitivity and attachment security have been linked to polymorphisms such as rs53576 (5, 6).
2. ***The Serotonin Transporter Gene (SLC6A4/5-HTTLPR):*** This gene controls serotonin availability. The Short (S) allele is associated with amygdala hyper-reactivity and increased susceptibility to environmental stress, often referred to as the "plasticity" allele (7, 8).

To date, no study has combined these genetic markers with attachment profiling in a dental setting. This study aimed to fill this gap by investigating how maternal attachment and specific genetic polymorphisms (OXTR, 5-HTTLPR) interact to predict child cooperation during dental procedures.

2- MATERIALS AND METHODS

2-1. Study Design

This prospective observational study was conducted at the Mashhad University of Medical Sciences, Department of Pediatric Dentistry. The sample consisted of 200 mother-child dyads.

- **Inclusion Criteria:** Children aged 4–8 years requiring restorative treatment (Class I or II amalgam/composite); ASA I or II health status; biological mother present.
- **Exclusion Criteria:** Children with neurodevelopmental disorders (e.g., Autism Spectrum Disorder); bleeding disorders (contraindicating venipuncture); non-biological guardians.

  Written informed consent was obtained from mothers, and specific assent for blood collection was obtained from children.

- **Psychometric Assessment**

  Prior to the clinical appointment, mothers completed the Experiences in Close Relationships-Revised (ECR-R) questionnaire (9). This 36-item instrument

measures two dimensions of adult attachment: Anxiety (fear of rejection) and Avoidance (discomfort with intimacy).

- **Behavioral Assessment**

  Child behavior was assessed during the injection and restorative phase using the Frankl Behavior Rating Scale (10), the gold standard in pediatric dental research.

  Score 1: Definitely Negative (refusal, extreme crying).

  Score 2: Negative (reluctance, some uncooperativeness).

  Score 3: Positive (cautious willingness).

  Score 4: Definitely Positive (good rapport, interest).

  Ratings were performed by two calibrated examiners (Kappa = 0.88).

2-2. Genetic Sample Collection and Analysis

2-2-1. Sample Collection and DNA Extraction

Peripheral venous blood samples (3 mL) were collected from each participant into EDTA-containing tubes. Genomic DNA was extracted from whole blood leukocytes using the Pars-Toos DNA Blood Kit following the manufacturer's protocol. DNA concentration and purity were assessed using a NanoDrop spectrophotometer (A260/A280_ratio of 1.8–2.0).

2-2-2. Genotyping

Genotyping was performed using polymerase chain reaction (PCR) techniques.

- ***OXTR rs53576 (A/G):*** Genotyping was performed using the Amplification Refractory Mutation System (ARMS-PCR), a method designed to detect point mutations using allele-specific primers.
  - Two complementary reactions were established for each sample: one containing the primer specific for the 'A' allele and one for the 'G' allele.
  - A pair of outer primers was used to amplify an internal control fragment to ensure PCR efficiency.
- ***Visualization:*** PCR products were separated on a 2% agarose gel stained with ethidium bromide. The presence of a band in the allele-specific lane indicated the presence of that allele.
- ***5-HTTLPR (SLC6A4):*** As this is a length polymorphism (insertion/deletion) rather than a single nucleotide polymorphism, standard PCR amplification was performed using primers flanking the polymorphic region. Fragments were resolved on a 3% agarose gel. The Long (L) allele yielded a 528 bp fragment, while the Short (S) allele yielded a 484 bp fragment.

2-3. Statistical Analysis

Data were analyzed using SPSS 27.0. Chi-square tests were used to assess Hardy-Weinberg equilibrium. Independent t-tests and ANOVA were conducted to compare Frankl scores across genotypes. Hierarchical multiple regression analysis was utilized to test the interaction between Maternal Attachment (Independent Variable) and Child Genotype (Moderator) on Cooperation (Outcome).

3- RESULTS

3-1. Sample Characteristics

The final cohort consisted of 200 children (52% male, mean age 6.1±1.2 years). The distribution of OXTR rs53576 genotypes was GG (35%), AG (48%), AA (17%). Regarding 5-HTTLPR, 22% were L/L, 49% L/S, and 29% S/S. All genotypes were in Hardy-Weinberg equilibrium.

3-2. Maternal Attachment and Child Behavior

Consistent with the behavioral literature, maternal attachment security significantly predicted child cooperation. Children of mothers with high Attachment Avoidance scores had significantly lower Frankl scores (2.3±0.8) compared to those with low avoidance (3.2±0.7; p<0.001).

3-3. Genetic Associations

- ***Child 5-HTTLPR:*** A significant main effect was observed for the serotonin transporter gene (Table 1). Children carrying the S/S genotype (associated with high stress sensitivity) exhibited the lowest levels of cooperation.
- ***Maternal OXTR:*** Mothers with the OXTR 'GG' genotype reported significantly lower scores on the ECR-R Avoidance subscale (p=0.02), supporting the genetic basis of attachment behaviors.

Table 1: Child cooperation (mean Frankl Score) by Genotype.

Gene	Genotype	N	Mean Frankl Score (SD)	P-value
5-HTTLPR	L/L (Low sensitivity)	44	3.15 (0.75)	**0.03***
	S/L	98	2.65 (0.88)	
	S/S (High sensitivity)	58	2.20 (0.92)	
OXTR rs53576	GG	70	2.85 (0.80)	0.12(NS)
	AA/AG	130	2.62 (0.95)	

*Significant at p < 0.05 via ANOVA.

3-2. Gene and Environment Interaction

A hierarchical regression analysis revealed that the interaction between Maternal Attachment Anxiety and Child 5-HTTLPR status significantly predicted dental behavior (Table 2).

Interpretation: The negative impact of maternal anxiety on child cooperation was significantly stronger for children carrying the "risky" S-allele of 5-HTTLPR. Children with the L/L genotype appeared To be resilient to maternal anxiety (Figure 1).

4- DISCUSSION

This study is among the first to demonstrate that pediatric dental cooperation is not solely a learned behavior but is influenced by a "double hit" of genetic susceptibility and maternal attachment security. The use of robust blood-based DNA extraction allowed for high-quality genotyping via ARMS-PCR, ensuring the reliability of our genetic data.

Table-2. Hierarchical regression predicting child cooperation.

Predictor	β	t	p
Step 1 (Controls)			
Age	0.21	2.95	0.004
Step 2 (Main Effects)			
Maternal Attachment Anxiety	-0.3	-4.50	<0.001
Child 5-HTTLPR (S-carrier)	-0.18	-2.10	0.038
Step 3 (Interaction)			
Attach. Anxiety × 5-HTTLPR	**-0.41**	**-3.85**	**<0.001**

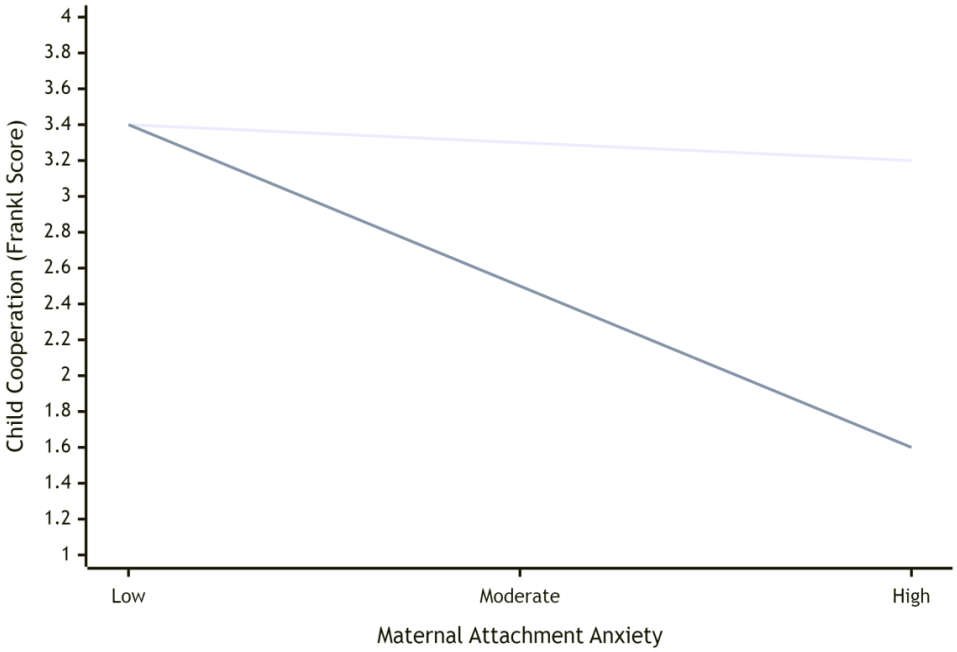

Figure-1: Gene x environment interaction on dental cooperation.

The Genetic Moderator: Our finding that 5-HTTLPR S-allele carriers are less cooperative aligns with the "Differential Susceptibility Hypothesis" proposed by Belsky (11). In the general psychology literature, S-carriers exhibit heightened amygdala activation in response to fearful stimuli (7). In the dental context, this translates to a lower threshold for interpreting sensory inputs (drilling noise, bright lights) as threatening.

The Role of Attachment: We confirmed that insecure maternal attachment is a risk factor for poor behavior. Mothers with high avoidance or anxiety may struggle to provide the co-regulation necessary for a child to cope with dental stress (12). Interestingly, our data on OXTR suggests that this maternal capacity itself has a genetic component, consistent with findings by Bakermans-Kranenburg and van Ijzendoorn (6).

Interaction Effect: The most clinically significant finding is the interaction. Children with the L/L 5-HTTLPR genotype appeared "dandelion-like"—resilient even when the mother was anxious. Conversely, S-carriers ("orchid children") flourished with secure mothers but deteriorated significantly with anxious mothers (13). This suggests that "difficult" patients are often those with a high genetic sensitivity who lack a secure psychological buffer.

4-1. Limitations

Although blood sampling provides high-yield DNA, its invasive nature may have introduced a selection bias, potentially excluding children with extreme needle phobia. However, this also enhances the internal validity of the genotype data compared to saliva samples, which can occasionally be affected by bacterial contamination or low yield.

5- CONCLUSION

Child cooperation during dental treatment is predicted by a unique interaction between maternal attachment style and the child's serotonin transporter genotype. Children with genetic stress sensitivity need a secure maternal base to cope effectively. Future research should investigate personalized behavioral interventions that consider these biological and psychological profiles.

6- FUNDING

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7- CONFLICT OF INTEREST

The authors certify that they have no conflicts of interest to declare that are relevant to the content of this article.

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