

The influence of the serotonin transporter gene (5-HTT) on the relationship between prenatal maternal stress and delayed gratification



Douglas
INSTITUT
MENTAL HEALTH
UNIVERSITY
INSTITUTE



Sandra Lafontaine^{1,2}, Marwa Kaffel¹, David P Laplante¹, Guillaume Elgbeili¹, Lei Cao^{1,3},
Sue Kildea⁴, Gabrielle Simcock⁵, Suzanne King^{1,3}

¹Douglas Hospital Research Centre, Montreal, Quebec, Canada.

²University of Montreal, Montreal, Quebec, Canada. ³McGill University, Montreal, Quebec, Canada.

⁴Mater Research Institute, South Brisbane, Queensland, Australia. ⁵University of Queensland, Brisbane, Queensland, Australia.



ABSTRACT

Background – Delayed gratification (DG) is the ability to resist temptation of an immediate reward in order to obtain a larger or better one afterwards and has been shown to be predictive of physical and psychological health, academic success, and social competence. Animal studies suggest that the serotonin transporter gene (5-HTT) plays a role in emotional and behavioral conduct, through its effect on the executive attention network involved in self-regulation. The SS 5-HTTLPR polymorphism is linked to the risk of aggression in childhood. Specifically, prenatal maternal stress (PNMS) has been shown to be associated with externalizing problems during childhood.

Objective – The objective of this study was to determine whether the serotonin transporter gene moderated the relationship between PNMS and DG.

Methods – DG (time to failure) was assessed in 95, 4 year-old children. The serotonin transporter gene was available for 81 children. PNMS (i.e., objective hardship, subjective distress and cognitive appraisal) were assessed by questionnaires following the 2011 Queensland Flood in mothers who faced the disaster.

Results – Our results indicate that negative maternal cognitive appraisal of the flood was associated with increased risk of failing the DG task in children with the SS 5-HTTLPR polymorphism ($p=.003$).

Conclusion – These results suggest that PNMS may increase the risk of hindering the development of DG in children already genetically susceptible for problems in self-regulation. Further research is required to determine if problems in delayed gratification predict outcomes in the present cohort.

INTRODUCTION

DG has been shown to be predictive of positive life outcomes such as better SAT scores, educational attainment and body mass index (BMI). In one measure of DG (the marshmallow task), children who resisted temptation later scored an average of 210 points higher on the SAT than individuals who ate the marshmallow before the time elapsed. Inability to demonstrate DG in childhood has also been associated with adolescent behaviour problems, drug addiction, and obesity (1).

Animal studies suggest that early disruption of the serotonin transporter gene (5-HTT) has various consequences regarding emotional and behavioral conduct, through its effect on the executive attention network involved in self-regulation(2). The SS 5-HTTLPR polymorphism is associated with the risk of aggression in childhood. In addition, this gene is linked to neutral areas of the brain which are part of the executive attention network involved in self-regulation (3). It has also been shown that the inability to demonstrate DG in childhood is related to later problems in aggression, particularly in boys (4).

Furthermore, studies have shown that PNMS is also associated with externalizing problems during childhood (5).

OBJECTIVE and HYPOTHESIS

The objective was to determine whether the 5-HTTLPR polymorphism moderated the relationship between disaster-related PNMS and DG.

Based on previous findings, it was hypothesized that a disaster-related PNMS would be associated with poorer DG abilities, and that the SS genotype of the serotonin transporter gene (5-HTT) would moderate this relationship.

5-HTTLPR



PNMS

DG

METHODS

Sample

Queensland Flood Study Project (QF2011) is a prospective longitudinal study that evaluates the effects of disaster-related PNMS on mothers and their children. DG data were available for 95 4 year-old children (43 girls, 52 boys). Genetic data were available for a subset of 80 children (38 girls, 42 boys).



Outcome variables

Delayed gratification was assessed using a modified version of The Stanford marshmallow experiment in which the child is offered a choice between one small reward (a single treat) provided immediately or two treats if they waited for a short period (10 minutes) without eating the treat. The child was told that (s)he could end the task at any time by ringing a bell. The task was also terminated if the child ate the treat before the 10 minute period elapsed. Time to failure was used in the analyses.

Predictor variables

PNMS was evaluated using a survey that included three flood-related scales:

Objective hardship was calculated using a large number of questions related to the women's flood experiences that provided information on four disaster-related categories: threat, loss, scope and change. Each category had a maximum possible score of 50 points. Categories were summed to obtain a total score. The total score (log-transformed) was used in the analyses.

Subjective distress was assessed using a composite score from three validated scales: the Peritraumatic Distress Inventory, the Peritraumatic Dissociative Experiences Questionnaire, and the Impact of Event Scale – Revised. The scores were centered around a mean of 0 and SD = 1.

The women's **cognitive appraisal** of the flood was assessed using the following item: 'Overall, what were the consequences of the flood on you and your family?'; response options were on a five-point scale of 'Very negative' (1), 'Negative' (2), 'Neutral' (3), 'Positive' (4) and 'Very positive' (5). A dichotomous score (negative vs neutral/positive) was used in the analyses.

Moderator variables

Genotyping of the 5-HTTLPR polymorphism from DNA extracted from saliva using PrepIT-L2P kits (DNA Genotek Inc.) according to the manufacturer's instructions. Polymerase chain reaction (PCR) was performed to span the central portion of the repeats in the 5-HTTLPR polymorphism and genotyping was conducted using agarose gel analysis of PCR product. The three genotypes SS, SL, and LL were analyzed.

Statistical analysis

Means and standard deviations were obtained for all continuous variables. Survival analysis was used since our data consist of censored times, i.e. the times for participants who failed are known, but those for participants who succeeded are truncated at the end of the task. As such, Cox regression models were used, with time to task completion (eat the treat, ring the bell for failure, or successful end of task) as the time variable and task success or failure as the status variable. PNMS and 5-HTTLPR variables, as well as their interactions, were entered as covariates.

RESULTS

Table 1: Descriptive analysis

Continuous Variables	Min	Max	Mean	SD	Categorical Variables	Categories	%
Objective Hardship	1.10	4.41	2.82	0.80	Cognitive Appraisal	Negative	32.5
						Neutral/Positive	67.5
Composite Subjective Stress	-1.08	3.44	0.06	0.10	Child Sex	Male	52.5
						Female	47.5
Failure Time	00:00	10:19	06:28	04:15	5-HTTLRP	LL	23.8
						LS	63.7
Eat Time	00:00	10:19	06:55	04:01		SS	12.5
Ring Bell Time	00:04	10:19	06:38	04:03			

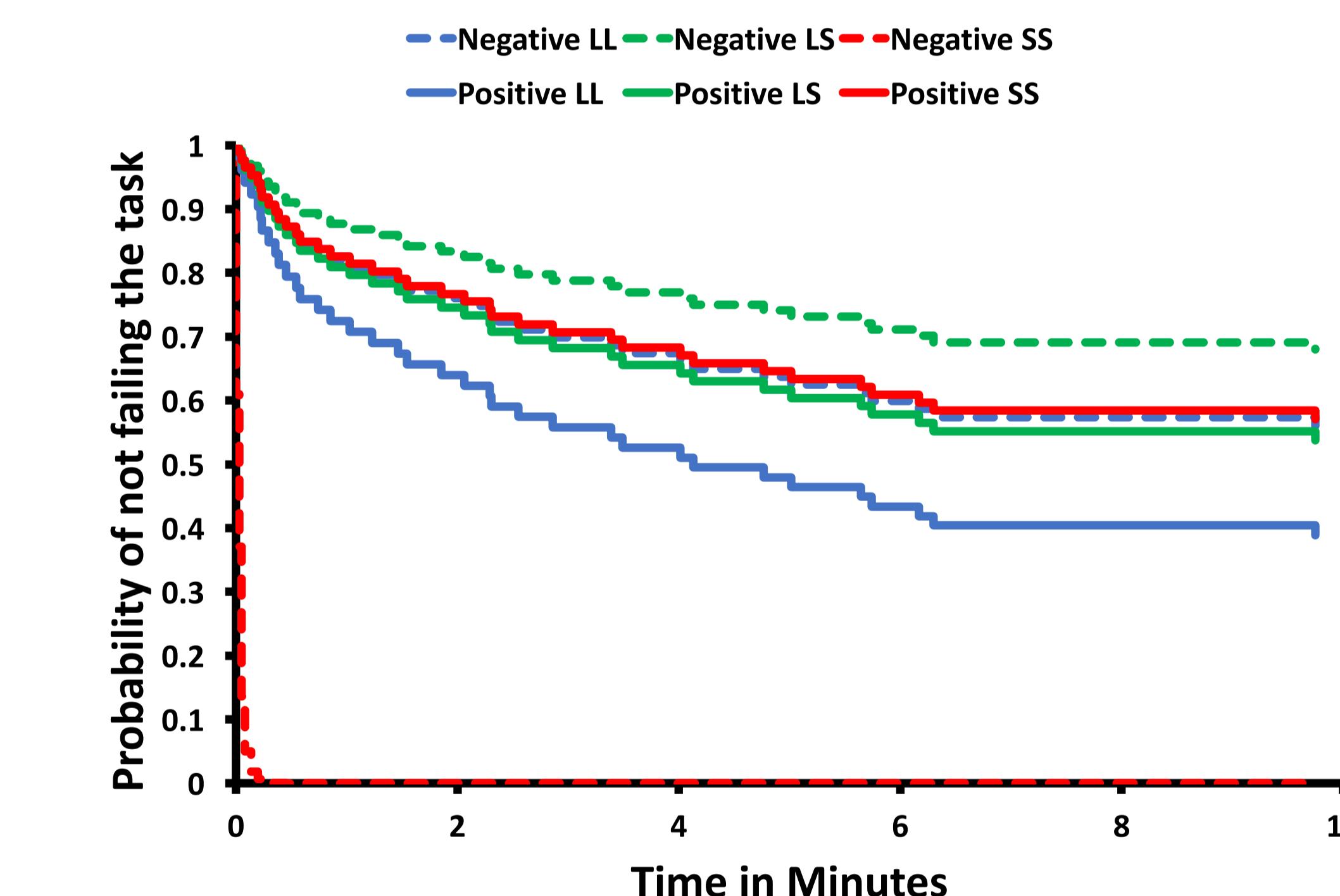


Figure 1: Survival graph representing the effect of the interaction between the child's 5-HTTLPR genotype and the mother's cognitive appraisal on delayed gratification

The analyses demonstrated that the combination of negative maternal cognitive appraisal and the SS genotype of 5-HTTLPR polymorphism decreased the probability of the child completing the task ($p=.003$).

The graph also demonstrates that the rate of not failing the task decreases with increased time.

DISCUSSION and CONCLUSION

These results suggest that PNMS may hinder the development of DG abilities in children already genetically susceptible for problems in self-regulation.

Further research is required to determine if problems in DG predict later outcomes in the present cohort.

REFERENCES

- Casey, B. J., L. H. Somerville, I. H. Gotlib, O. Ayduk, N. T. Franklin, M. K. Askren, J. Jonides, M. G. Berman, N. L. Wilson, T. Teslovich, G. Glover, V. Zayas, W. Mischel and Y. Shoda (2011). "Behavioral and neural correlates of delay of gratification 40 years later." *Proc Natl Acad Sci U S A* 108(36): 14998-15003.
- Posner, Rothbart, & Sheese, 2007
- Kochanska, G., R. A. Philibert and R. A. Barry (2009). "Interplay of genes and early mother-child relationship in the development of self-regulation from toddler to preschool age." *J Child Psychol Psychiatry* 50(1): 1331-1338.
- Funder, D. C., Block, J. H., & Block, J. (1983). Delay of gratification: Some longitudinal personality correlates. *Journal of personality and social psychology*, 44(6), 1198.
- King, S., Laplante, D., & Joober, R. (2005). Understanding putative risk factors for schizophrenia: retrospective and prospective studies. *Journal of psychiatry& neuroscience: JPN*, 30(5), 342.