



## I9 Serotonin and Aggression in Children and Adolescents: A Systematic Review

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**Learning Overview:** After attending this presentation, attendees will gain knowledge concerning the relationship between low serotonin (5H-T) and aggression in children and adolescents. Attendees will understand that the burden of predicting violence and homicide risk assessment increasingly falls on the clinical psychiatrist.<sup>1</sup> This presentation will also discuss the potential of using serotonergic genetic markers to aid in the possible identification of aggression.

**Impact on the Forensic Science Community:** This presentation will impact the forensic science community by demonstrating the genetic and biological relationship between low 5H-T and aggression in children and adolescents. Aggression is one of the most frequent concerns that trigger a child and adolescent psychiatric referral.<sup>2</sup> Youth homicides and assault-related injuries result in an estimated \$18.2 billion in combined medical and work-loss costs.<sup>3</sup> Studies have shown that low 5H-T has been associated with aggression in animal and adult studies. However, there has been a paucity of studies in relation to children and adolescents and the results have been inconsistent.

Aggressive behavior is complex and associated with multiple biological, psychological, and environmental factors. Aggression is often divided into two types: impulsive and premeditated. Neuromodulators associated with aggression include dopamine, norepinephrine, MAOA, and nitrous oxide synthetase. Serotonin remains one of the better-understood neuromodulators involved in impulsive aggression. A systematic literature search was conducted of the following databases: Embase®, PubMed®, PsycINFO®, and Google® Scholar. Studies published through January 25, 2018, were considered. The key words aggression, violence, adolescent, adolescents, juveniles, serotonin, 5-HT, 5-HIAA, 5-hydroxyindoleacetic acid, tryptophan, serotonin transporter gene polymorphism, 5-HTTLPR, and serotonin plasma membrane transport proteins were used, which included a PubMed® “Mesh” search. Inclusion criteria for the review included children and adolescents <18 years old, English language peer reviewed journals, physical aggression as the dependent variable, and serotonin as the independent variable. Exclusion criteria were the following: case reports, review articles, posters, abstracts, published in languages other than English, studies that defined aggression solely as suicide, greater than >18 years old, animals studies, and participants with co-morbid substance use disorders. One hundred fourteen studies were initially identified, and 12 studies were included for the review. The 12 studies can be grouped by how serotonin is measured into the following categories: cerebrospinal fluid (3), acute tryptophan depletion (1), prolactin response to fenfluramine (1) and genetic studies (7). The genetics articles reviewed included studies of the 5HT1B receptor polymorphism and the serotonin transporter gene (5-HTT or SLC6A4). Two common serotonin transporter gene polymorphisms include the 5-HTTLPR (promoter polymorphism), and the 5-HTT Variable Number Tandem Repeat (VNTR). Both are believed to regulate the transcription of the serotonin transporter gene.

The review found that the adolescent CSF studies had strong correlation with aggression. Studies of the 5-HTT (VNTR) and the 5HT1B polymorphism found no association with aggression. The rs16859448 TT Single Nucleotide Polymorphism (SNP) of the serotonergic FEV transcription factor had strong association with aggression. The studies looking at the 5-HTTLPR (promoter polymorphism), had mixed results but the strongest correlation in two gene X environmental studies that included other neuromodulators and environmental risk factors. Low childhood 5-HT function appears important but not sufficient for childhood aggression in the prolactin response to fenfluramine. Finally, in a study of Acute Tryptophan Depletion (ATD), the overall sample indicated increased aggression under the ATD. This presentation will also discuss behavioral and pharmacological treatments for youth aggression.

Limitations of the studies included relatively small sample sizes, adult controls in some studies, and primarily male and Caucasian samples. The use of broadband rating scales was often used rather than the more narrowband youth aggression rating scales. In conclusion, there appears to be a relationship to low 5-HT and aggression in children and adolescents. Further research is needed, particularly in the study of genetics and identifying potential future markers for identifying youth aggression.

### Reference(s):

1. Glick, A.R. The Role of Serotonin in Impulsive Aggression, Suicide, and Homicide in Adolescents and Adults: A Literature Review. *International Journal of Adolescent Medicine and Health* 27, no. 2 (May, 2015): 143-150.
2. Dulcan, Mina K., ed. *Dulcan's Textbook of Child and Adolescent Psychiatry*. Second ed. Arlington, VA: American Psychiatric Association, 2016.
3. Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. *Web-Based Injury Statistics Query and Reporting System (WISQARS)*. Accessed 05/17, 2018. [www.cdc.gov/injury](http://www.cdc.gov/injury).

### Aggression, Serotonin, Adolescents