

## Prospects of studies on violence, adolescence and cortisol: a systematic literature review

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**Abstract** *Violence has a negative impact on adolescents and affects their quality of life. It causes stress and requires the victim's adaptive capacity, which can cause psychological and biological changes. Hormone cortisol levels have been used as stress biomarker in several studies. This paper aims to perform a systematic literature review of publications on cortisol and violence involving teenagers from 2000 to 2013. Descriptors "cortisol", "violence" and "adolescent" were used in both English and Portuguese in this review, which included bibliographic databases PubMed/Medline, Lilacs, BVS and SciELO. Twelve papers were analyzed. Most studies involve participants from the United States, of both genders and without a control group. Different types of violence are studied, especially family violence, victimization or testimony. All studies used saliva to measure cortisol and no standard methodology was used for the analysis. Most studies (83.3%) found a statistically significant association between cortisol levels and exposure to violence. Results regarding gender, type of violence, socioeconomic status or cortisol analysis methods are not yet uniform.*

**Key words** *Cortisol, Violence, Adolescent, Stress*

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## Introduction

The World Health Organization<sup>1</sup> defines violence as “the intentional use of physical force or power, threatened or actual, against oneself, another person, or against a group or community that either results in or has a high likelihood of resulting in injury, death, psychological harm, maldevelopment, or deprivation.” Violence derives from a network of diverse socioeconomic, political, and cultural factors that have great interdependence and influence the lives of individuals and/or social groups. It can affect all human beings, regardless of gender, geographical location, socioeconomic and cultural status, with significant disparities in their prevalence in different populations.

Violence is a particularly harmful and stressful event, requiring the victim’s adaptive capacity, which can lead to psychological and biological changes that, in turn, affect health<sup>2</sup>. Violence and stress have an intrinsic relationship, where they both provide feedback to one another, since chronic stress can lead to more violent acts and new victimizations, leading to additional stress and health problems. Miller *et al.*<sup>3</sup> warn that exposure to chronic stress increases by three to fourfold the odds of an adverse medical situation.

From the late 1980s, eminently experimental studies began to be developed on the physiological and biochemical analysis of the hypothalamic-pituitary-adrenocortical (HPA) axis, the hormone cortisol and its biological function in the body, as well as cortisol’s response on awakening and its circadian rhythm. The HPA axis is a hormonal response system activated by a series of physical or psychological stressor events. From a biological perspective, one of the objectives of this line of research is to understand how the activation of specific physiological systems modulated by physical and psychological conditions<sup>2</sup> occurs.

One of HPA axis’ main biochemical products is hormone cortisol, which is produced by the adrenal glands and is a great modulator of the immune response, as well as a mediator of the glycogenic chain for the quick retrieval of energy when facing a stressful situation<sup>4,5</sup>. The production and secretion of cortisol grow in increasing amounts during and after exposure to some stressors. Usually, cortisol has an excellent association between its production and HPA axis activity; it is easily detected in saliva, blood and urine<sup>6</sup>. It is an excellent biomarker of HPA function and, consequently, of the study on the impact of stress in humans<sup>7</sup>.

From this context, in the late 1990s, studies were developed in several countries where the relationship between stress and cortisol began to be investigated through reliable methods of detecting free cortisol in the body, and exposure to violence was an important issue in this research scenario. War veterans with severe emotional disorders were the particularly investigated population groups, in addition to clinical groups with mental health problems, including posttraumatic stress disorder, depression and anxiety<sup>8</sup>.

In the interface between violence and health, psychosocial problems are commonly studied, but there are few studies examining their association with physiological issues. Reflecting from the biopsychosocial approach of human development, it is important to look at how much the environment is impacting on organic (physiological, genetic, epigenetic, among others) manifestations, understanding it in a relation of interdependence. Thus, it is important for public health to understand how states of alertness and stress caused, for example, by the violence that affects children and adolescents, impact human development, therefore resulting in a social issue that must be investigated, prevented and confronted. It is also important to understand the relationship between levels of cortisol and violence in adolescence, since this moment is already characterized as a naturally more critical and stressful stage, with physical, psychological and social transformations, where polarities of courage and restrained fear, the transition to secondary education, conflicts with parents and grief and learning are evident<sup>9,10</sup>. Taking as a starting point the relevance of investigating the setting of this matter, this paper intends to present a systematic bibliographical review of national and international publications on the subject.

## Methodology

This is a systematic review of the literature, which according to Greenhalgh<sup>11</sup> involves the elaboration of an overview of primary studies that explicitly contain their objectives, methods and materials so that they may be replicated by other authors. This review followed the guidelines proposed by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses - PRISMA<sup>12</sup> and Amstar<sup>13</sup>, which includes the following steps: identification of the material (search in the bibliographic bases), selection and eligibility (exclusion of duplicate records and application of

exclusion criteria), and definition of publications to be analyzed (Figure 1).

This review accessed the following bibliographic bases: BVS (Virtual Health Library), SciELO (Scientific Electronic Library Online), Lilacs (Latin American and Caribbean Health Sciences Literature) and Medline/Pubmed (Medical Literature Analysis and Retrieval System Online). Papers search was performed with same descriptors in both English and Portuguese, namely, “adolescent”, “violence” and “cortisol”. These descriptors were selected due to their recurrence in the indexing of papers on the subject. Boolean descriptor “AND” was inserted between descriptors for a better qualification of search results.

The selected timeline period of the publications analyzed in this study was 2000-2013, since studies on violence and cortisol became more frequent from the 2000s onwards. All data were collected between March and April 2014.

Table 1 shows the number of publications identified, according to the bibliographical database consulted, reaching a final number of 121 scientific papers.

In the selection stage, 32 papers were excluded due to duplication among bibliographic bases. Then, we performed partial (abstract only) or total reading of all identified papers. Partial reading was done initially and, when only the abstract was not conclusive, we proceeded with the full reading of the paper. Two independent researchers selected the papers. Discrepancies among the selected papers to be analyzed were decided by joint discussion among the researchers. At this stage, 69 articles were eliminated due to lack of adequacy to the object of research.

Then, at the eligibility stage, the following exclusion criteria were applied: (A) those that mostly included samples of children or adults, with a limit of 10 years for children and above 19 for adults; (B) those who did not include analyzes of cortisol results; and (C) those who had no methodological description for cortisol analysis. As a result, eight papers were discarded ((A) = 2; (B) = 3; and (C) = 3).

Figure 1 shows the flowchart for the identification and selection of articles for systematic review on the topic of violence in adolescence and

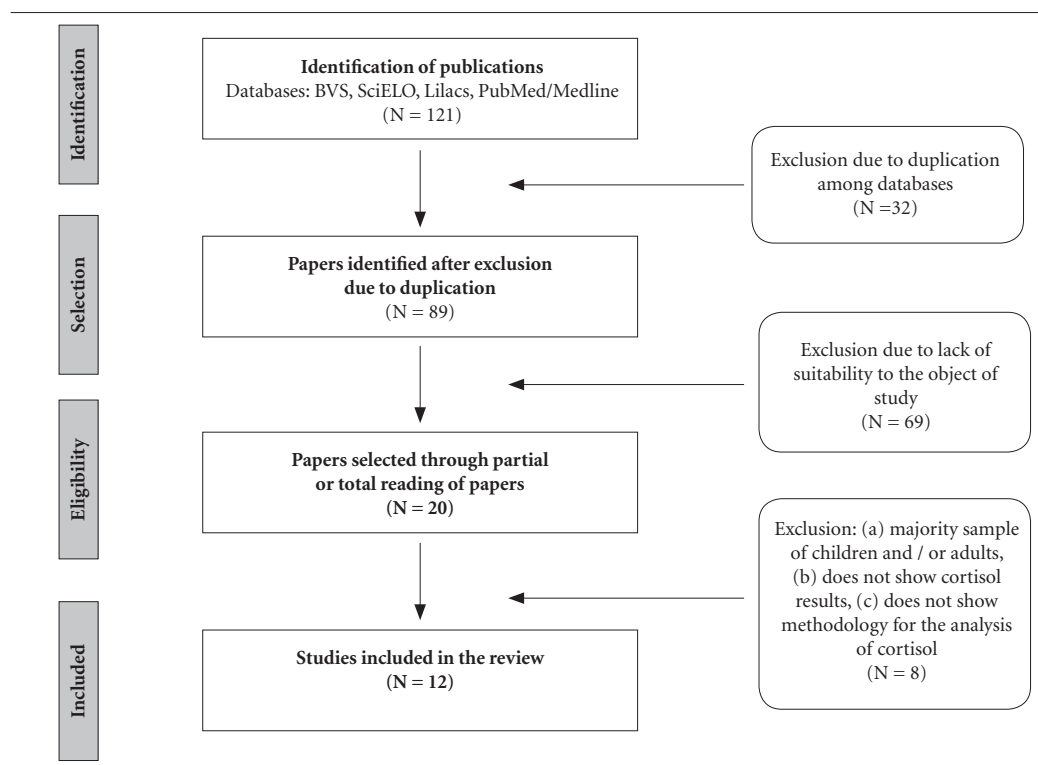


Figure 1. Flowchart of the main steps of the systematic bibliographic review.

**Table 1.** Number of scientific papers located, by bibliographic base.

Descriptors	BVS	SciELO	Lilacs	Medline	Pubmed
adolescente AND violência AND cortisol	0	0	0	18	0
adolescent AND violence AND cortisol	22	0	0	3	78
General Total: 121 scientific papers					

cortisol, achieving a final result of 12 papers to be analyzed in this study.

## Results

Chart 1 shows the main characteristics of the selected studies. Of the 12 publications included in this review, six papers (50.0%) were published in the last three years (2011, 2012 and 2013) and only three (25.0%) before 2006, the other three articles were published between 2006 and 2011.

As for the populations studied, most participants were from the United States (eight papers, 66.7%), Canada (two papers, 16.7%), Sweden and the Palestinian Region (one paper each). There are no papers originating from research conducted in South America or in Portuguese. The main ways of selecting participants were from a larger study<sup>14-18</sup>, advertising<sup>19-21</sup> and in health and education services<sup>22-25</sup>. Due to the very nature of the research object, it is difficult to use samples with strict designs. Only three studies used control groups. Most worked with a single sample, which was then subdivided into statistical analyzes in groups exposed to violence or not. Most studies included individuals of both genders (58.3%). However, three papers covered only girls<sup>14,15,18</sup> (25.0%) and two included only males<sup>23,25</sup> (16.7%). Regarding the age of participants, most of them worked exclusively with adolescents (five papers, 41.7%), two included children and adolescents<sup>16,22</sup> (16.7%), two adolescents and adults<sup>14,19</sup> (16.7%) and the rest reported only the average age of the participants<sup>21,23,24</sup>. In those involving children and adults, the proportion of adolescents overlapped, as foreseen in the exclusion criteria described. In this group of five adolescent-only papers, only one<sup>25</sup> selected only individuals at a fixed age (14 years of age).

Regarding the socioeconomic status of the research participants, five articles<sup>14,17,18,24,25</sup> (41.6%) stated that all participants were from poor regions or low-income population, quoting the average income of families in the region and/or low

human development index as poverty indicators. The remaining papers analyzed comprised populations of different socioeconomic conditions, or this information was not revealed in the text of the paper.

Different types of violence are addressed in the articles analyzed. Most<sup>14,15,17-19,21,22</sup> (58.3%) refer to family violence, where victimization or witnessing are addressed. Two studies<sup>16,24</sup> focus on community violence, one<sup>25</sup> on violence motivated by political and religious issues, another<sup>23</sup> on media violence, and one<sup>20</sup> that addresses witnessing of situations of violence in various contexts. The evidence of mental disorders (anxiety, depression, suicide attempt and post-traumatic stress disorder) is the most frequently addressed issue in the publications and is studied concomitantly with violence and cortisol.

Different methods are developed in the 12 articles analyzed. Most of the analyzed publications<sup>14,15,17,22,23,26</sup> use structured and validated tools, such as the Conflict Tactic Scale<sup>14</sup>, to verify an exposure to violent acts or actions suffered or perpetrated by adolescents, and the Trier Social Score Test<sup>15,17,19,22</sup>. Two other applied methodological lines were the realistic laboratory simulation of violent acts, such as the screening of a movie with violent scenes or staging of actors showing a violent act, and the application of a mixed work plan, containing the realistic simulation and application of questionnaires.

Regarding the collection of cortisol, all the articles used the saliva to carry out analyzes. Collection done in the morning; in the afternoon; performed before, during and after the emergence of the stressful event; with short and long time intervals; and before and after the application of the questionnaire are some of the situations observed. Regarding the number of samples collected, it was verified that the analyzed studies used from one<sup>20</sup> to 7<sup>17</sup> collections, of which four were the most usual number<sup>14,16,23,25</sup>.

Regarding cortisol analysis, most studies (75.0%) used enzyme immunoassay (ELISA) methods. Only three articles<sup>14,16,25</sup> (25.0%) used

**Chart 1.** Characteristics of studies on cortisol, violence and adolescence, by chronological order of publication (from the most recent to the oldest).

Reference (year of publication)	Study location	Sample	Objectives
Linares et al. <sup>18</sup> (2013)	New York, U.S.A.	N = 40 Females (14-17 years). Low-income population	To identify the relationship between history of sexual abuse and the perpetration of dating violence with changes in cortisol patterns before and after a stressor.
Cook et al. <sup>17</sup> (2012)	Northeast of the United States	N = 175 Males and females (14-16years) Age average = 15.4 years Low-income population	To examine the relationship between the physiological response of adolescents to an acute laboratory stressor, anger management and interpersonal competence.
Saxbe et al. <sup>21</sup> (2012)	United States	N = 54 Males and females Age average = 15.2 years	To identify whether the history of family violence is associated with changes in cortisol levels.
Peckins et al. <sup>22</sup> (2012)	United States	N = 124 Males and females (8-13 years)	To examine the impact of exposure to violence with cortisol reactivity in adolescents with no mental health or history of ill-treatment problems.
Victoroff et al. <sup>25</sup> (2011)	Gaza Territory, Palestine	N = 52 Males (14 years) Poverty areas	To examine the association between daytime cortisol levels and political-religious assault.
Harkness et al. <sup>19</sup> (2011)	Ontario, Canada	N = 71 Males and females (12-21 years) Average age = 15.39 years	To examine the relationship between child maltreatment, severity of depression and its relation to cortisol reactivity.

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radioimmunoassay (RIA), with the affirmation that the results found are compatible with enzyme immunoassays<sup>14</sup>. Regarding the indicators

of quality and analytical precision of cortisol results, different methods were used: intra-assay and inter-assay coefficients of variability-

Chart 1. continuation

Reference (year of publication)	Methodology (Tools/Collection of cortisol)	Cortisol analysis	Results
Linares et al. <sup>18</sup> (2013)	Subjects divided into 2 groups regarding exposure to sexual abuse. Measurement of the level of cortisol (saliva) at rest and after watching a video involving a situation of violence among teenage couples. Six saliva samples were collected in two phases: three before and three after the presentation of the vignette, with identical intervals between the samples. Collection in the afternoon.	Fluorescent immunoassay. Duplicate tests and mean values were used.	Higher reactivity of cortisol in victims of childhood sexual abuse and violence in comparison between groups who suffered violence or not.
Cook et al. <sup>17</sup> (2012)	Structured questionnaire on childhood violence, interpersonal relations, among others and interview. Application of the Trier Social Stress Test (TSST). Seven collections of saliva samples: 40 minutes before the TSST, one just before the start of the test, another just after and three more every 15 minutes. Collection in the afternoon.	Enzyme immunoassay. Duplicate tests.	History of family violence in childhood was associated with higher levels of cortisol.
Saxbe et al. <sup>21</sup> (2012)	Structured questionnaire on family violence, antisocial behavior, among other topics and simulation of family discussion. Collection of five saliva samples, one before the simulation and four after the simulation. Collection in the afternoon.	Enzymatic immunoassay, with the lower limit of 0.0031µg / dl. Duplicate and repeated tests if any pair of results differed more than 7%.	Decreased levels of cortisol in young people with a history of family violence and during family conflict simulations. Increased cortisol in young people from families with no history of assault during family conflict simulations.
Peckins et al. <sup>22</sup> (2012)	Structured questionnaire on violence and mental health. Application of TSST. Five 4ml-saliva samples were collected: two before TSST, another during the application of the test and two more after. Collection in the afternoon.	Enzyme immunoassay. Duplicate tests and mean values were used.	Decreased levels of cortisol in boys with a history of exposure to violence, without variation in relation to girls.
Victoroff et al. <sup>25</sup> (2011)	Structured questionnaires on violence, depression, political views and anxiety. Collection of 5ml morning saliva. Four samples, one per week. Collection in the morning.	Modified enzyme radioimmunoassay. Sensitivity 2pg / ml	No evidence of association between cortisol levels and religious-political assault was found.
Harkness et al. <sup>19</sup> (2011)	Application of TSST. Five saliva samples: two before TSST application, one soon after and two more after an interval of one hour. Collection in the afternoon	Enzyme immunoassay. Duplicate tests. Samples with coefficients of variation greater than or equal to 15% were repeated.	A history of childhood maltreatment associated with higher levels of cortisol. Greater reactivity to cortisol in coping with stressful situations. Increased levels of cortisol in adolescents with mild / moderate depression. Decreased cortisol levels in moderate / severe depression.

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Chart 1. continuation

Reference (year of publication)	Study location	Sample	Objectives
MacMillan et al. <sup>15</sup> (2009)	Ontario, Canada	N = 67 Females (12-16 years). Control Group = 25 adolescents, matched by age and place of residence.	To examine differences between participants who are victims of violence and those not exposed to this event through cortisol level assessment.
Suglia et al. <sup>16</sup> (2009)	Boston, U.S.A.	N = 43 Males and females (7-13 years)	To examine the influence of community violence victimization and cortisol response
Ivarsson et al. <sup>23</sup> (2009)	Stockholm, Sweden	N = 21 Males Average age = 13.3 years	To investigate whether (violent and non-violent) videogames affect cortisol levels.
Kliewer <sup>24</sup> (2006)	Richmond, U.S.A.	N = 101 Males and females Average age = 11,14 years Low-income population	To investigate the physiological cost of exposure to violence in African American adolescents living in violent areas.
Murali & Chen <sup>20</sup> (2005)	St .Louis, U.S.A,	N = 115 Males and females (16-19 years, average of 16.85 years)	To investigate the influence of exposure of violence to cardiovascular and neuroendocrine responses.
Young et al. <sup>14</sup> (2004)	Michigan, U.S.A.	N = 632 Females (18-54 years) Single mothers. Low-income population	To assess cortisol and associated response with childhood abuse and posttraumatic stress disorder.

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ty<sup>16,18,19,21,22,25</sup>, biochemical test sensitivity<sup>20,22,24,25</sup> and duplicate analyzes<sup>15,17,18,19,21,22</sup>. Tests repetition if the intra- or inter-assay coefficient was higher than a fixed value<sup>14,19</sup> was also mentioned, however, different cut-off points were used, without indication as to whether value used was arbitrary or based on the literature.

Regarding studies' results, most papers (10 papers, or 83.3%) found a statistically significant association between cortisol level and exposure to violence. Of the articles describing a change in cortisol reactivity, more than half of them<sup>14,16-20</sup> (60,0%, 6 articles) found increased cortisol levels in adolescents exposed to violence and four

Chart 1. continuation

Reference (year of publication)	Methodology (Tools/Collection of cortisol)	Cortisol analysis	Results
MacMillan et al. <sup>15</sup> (2009)	Application of TSST. Six samples were collected: three before TSST and three after. Collection in the afternoon.	Enzyme immunoassay. Duplicate tests.	The control group evidenced increased cortisol levels after the test. An attenuated response to cortisol levels was noted among those who suffered violence.
Suglia et al. <sup>16</sup> (2009)	Three days of saliva collection. Four saliva samples, one on awakening, one at lunch, one before dinner, and one before bedtime. Collection throughout the day.	Enzymatic radioimmunoassay. The sensitivity limit was $8 \times 10^{-4}$ pmol / l for all samples.	Victims of community violence with greater posttraumatic stress symptoms evidence higher cortisol levels, especially in the afternoon and evening samples, even when adjusted for gender, age, race, and socioeconomic status.
Ivarsson et al. <sup>23</sup> (2009)	Four samples were collected, two during the game session, and two on awakening. Collection throughout the day.	Enzyme immunoassay.	There are no significant changes in cortisol in violent or non-violent game players
Kliwer <sup>24</sup> (2006)	Three samples taken: one before a film screening, one after and the last just after 20 minutes. Collection in the morning.	Enzyme immunoassay. Sensitivity of 0.007 µg / dL.	Cortisol levels found were low. In boys, witnessing more violent acts was associated with a reduced cortisol response on awakening, while in girls showed an increase. The average profile of cortisol found in boys is greater than that of girls.
Murali & Chen <sup>20</sup> (2005)	Interviews on exposure to violence. One saliva collection after the interview. Collection in the afternoon.	Enzyme immunoassay. Sensitivity of 0.43 nM and a coefficient of variation of less than 10%	History of maltreatment in childhood was associated with higher levels of cortisol in both genders.
Young et al. <sup>14</sup> (2004)	3 5 ml-saliva samples collected on awakening, 30 minutes after awakening and at bedtime. One sample was taken at another time. Collection throughout the day.	Enzymatic radioimmunoassay. Samples with results greater than 2 µg / dL were discarded.	Recent trauma has led to increased cortisol.

articles<sup>15,21,22,24</sup> (40,0%) showed a decrease in the level of cortisol. Two publications<sup>23,25</sup> reported no changes in hormone levels. Saxbe<sup>21</sup> highlights the cumulative effect of prior history of family violence in association with cortisol levels. It is worth mentioning that the expression of cortisol varied between males and females in two studies<sup>22,24</sup>. However, it should be noted that not all studies included both genders in the sample.

## Discussion

This literature review on cortisol and violence involving adolescents is unprecedented nationally and internationally, and shows the methodological trend and the main findings of studies on the subject. Their analysis shows the growing interest and knowledge of the international scientific community, starting in the 2000s, on the



relation of the subject, with a clear highlight on the largest volume of publications in recent years, especially in the United States, which points to a certain unprecedented topic worldwide. It is worth highlighting the growing trend of more sophisticated protocols developed and the use of more robust methods. This setting increases the knowledge on the subject and leads to more reliable results<sup>6,17</sup>.

In general, this literature review clearly shows the following methodological trend in the articles analyzed: the use of saliva as the main source for cortisol analysis, the duplication of saliva collection, the collection of several samples from the same person during one day, the use of enzyme immunoassay in cortisol analysis and the subject's exposure to a realistic and laboratory-produced situation.

The methodological options used are directly related to the scope of the research, the financial budget and the availability of participants. For example, a very critical aspect is in relation to the number of collections from the same individual. The higher the number of samples, the greater the reliability of the study. Another point that evidences great variation between studies refers to the period of collection during the day, whether in the morning or in the afternoon, which induces the lack of consensus regarding the most appropriate moment for collection. The option to perform the afternoon collection seems to be the most indicated and is justified by the lower cortisol variation in this period of the day<sup>17,18,26</sup>.

Although most articles demonstrate that there is a change in cortisol levels in adolescents who are victims of violence, they differ enormously when compared by chronicity, intensity and types of violence situations, as well as methodological aspects. There is no consensus on the direction of the association between exposure to violence and cortisol levels, and different explanations are given for increased and reduced levels of the hormone. One of the most accepted arguments for the diversity of results in the relationship between violence and cortisol lies in the fact that studies do not take into account the particular expression of each individual about their life experience and the stressful episodes<sup>19</sup>. Other authors state that individuals only express significant physiological changes after some exposure to a major stressing situation<sup>8</sup>. The explanation of the positive association is due to the abrupt activation of the biological response to the stressful situation, which, in the long run, is no longer protective and can become toxic to the metab-

olism<sup>7</sup>. On the other hand, scholars explain that the reduction of cortisol levels in victims of violence can generate a phenomenon called hypocortisolism, which may represent an individual's poor adaptation to deal with a situation of threat and cause future health problems<sup>27,28</sup>. Heim et al.<sup>29</sup> further add that early life stress can alter the response to stress, with a cumulative effect with acute and current stressful situations. Thus, Yehuda & Seckl<sup>30</sup> hypothesize about a negative feedback system of the HPA axis, which could cause a change in glucocorticoid catabolism as adaptation to higher levels of cortisol at some earlier stage of life.

It is interesting to note that, in this review, the two papers that differ most from the others in relation to the type of violence (religious and virtual) were not associated with changes in cortisol levels. The non-association between adolescent exposure to realistic simulations of violent videogames and cortisol alteration may be related to the lack of stress in the situation, which can often be a pleasurable and unrealistic activity to adolescents. Another argument is that, in violent videogames, the teenage player is the perpetrator of the violent act and is rarely victimized, which produces an inverse relationship between violence and cortisol levels. In relation to religious violence, Victoroff et al.<sup>25</sup> point out the need for further studies in order to understand how aspects of human development, innate psychological factors and exposure to prolonged stress from conflicts between religious groups interact with biological issues.

It is worth mentioning that being male or female is an important issue to be considered in research on violence and cortisol. Kliewer<sup>24</sup> explains that boys who engage in violent situations tend to worry more than girls do with negative ratings directed at them and have more concerns about the possible loss of relationships. Compared to girls, they tend to have fewer protective resources and internal resources to deal with situations of violence. Regarding the witnessing of violence, the meaning is also different for boys and girls and, consequently, their processing. Witnessing violence seems to affect adolescents in the way social information is processed, whereas direct victimization seems to affect the adjustment of young people by means of emotional deregulation<sup>24</sup>. Harkness et al.<sup>19</sup> further add that mental health problems, such as depression, can mediate the relationship between violence and cortisol for underlying biological, personal, and social issues.

Another factor that draws attention in studies

on cortisol and violence in adolescents is the use of samples from population groups with low socioeconomic status<sup>14,17,18,24,25</sup>, which may result in selection bias, since these populations are more likely to face stressful situations, to have worse health and more difficulty accessing health services<sup>2</sup>. However, no methodological procedure was reported by authors analyzed to control possible biases.

A crosscutting issue that discusses the findings of this review is the serious biological, emotional and cognitive damage that violence can cause in the course of human development, and this is a public health issue, especially in childhood and adolescence. The National Scientific Council on the Developing Child<sup>31</sup> highlights that chronic alterations of the HPA (Hypothalamic-Pituitary-Adrenal) axis may affect the cerebral re-constitution of children who are devel-

oping. The toxic stress has already been shown to be associated with a deficit in the development of cerebral structures, that is, a decrease in their size; as well as changes in the biological responses to the adverse event, causing damage to the auto-immune system and greater vulnerability to the development of physical and mental diseases<sup>31-33</sup>.

Finally, the greater fragility of this work stems from the lack of standardized methods and techniques of cortisol analysis concomitant to violence, either by not explicitly explaining in the works the methodological path used or the still incipient theoretical knowledge. In addition, much of what is known about this subject derives from small samples and studies with sectional designs. More studies that use more robust techniques that combine the qualitative approach and that are developed in Latin America and in other regions of the world are required.

### **Collaborators**

LP Lugarinho, JQ Avanci and LW Pinto participated in the design and final writing of this paper.

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