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Violence and Latin-American preadolescents: A study of social brain function and cortisol levels

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Abstract

The present study investigated exposure to violence and its association with brain function and hair cortisol concentrations in Latin-American preadolescents. Self-reported victimization scores (JVQ-R2), brain imaging (fMRI) indices for a social cognition task (the 'eyes test'), and hair cortisol concentrations were investigated, for the first time, in this population. The eyes test is based on two conditions: attributing mental state or sex to pictures of pairs of eyes (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001). The results showed an association among higher victimization scores and (a) less activation of posterior temporoparietal right-hemisphere areas, in the mental state condition only (including right temporal sulcus and fusiform gyrus); (b) higher functional connectivity indices for the Amygdala and Right Fusiform Gyrus (RFFG) pair of brain regions, also in the mental state condition only; (c) higher hair cortisol concentrations. The results suggest more exposure to violence is associated with significant differences in brain function and connectivity. A putative mechanism of less activation in posterior right-hemisphere regions and of synchronized Amygdala: RFFG time series was identified in the mental state condition only. The results also suggest measurable effects of exposure to violence in hair cortisol concentrations, which contribute to the reliability of self-reported scores by young adolescents. The findings are discussed in light of the effects of exposure to violence on brain function and on social-cognitive development in the adolescent brain. A video abstract of this article can be viewed at https://www.youtube.com/watch?v=qHcXq7Y9PBk.

KEYWORDS

amygdala, cortisol, fusiform gyrus, preadolescents, superior temporal sulcus, violence

1 | INTRODUCTION

Stress impacts human behavior and cognition in all stages of life. Its effects in early childhood (early-life stress) as a result of trauma, violence, and institutionalization have been largely investigated (Birn, Roeber, & Pollak, 2017; Bremne & Vermetten, 2001; Pechtel & Pizzagalli, 2011; Rahdar & Galván, 2014; Silvers, Goff, Gabard-Durnam, Gee, Fareri, Caldera, & Tottenham, 2016; Taylor, 2010; Walker, Wachs, Grantham-McGregor, Black, Nelson, Huffman, & Richter, 2011). Physical and mental health effects of stress emerge as a factor of chronicity (of exposure to violence, for example) and the period in which exposure occurs (Lupien, McEwen, Gunnar, & Heim, 2009): stress also

affects adolescent and adult mental health (Bick & Nelson, 2016; Birn *et al*., 2017; Hanson, Nacewicz, Sutterer, Cayo, Schaefer, Rudolph, & Davidson, 2015; Moffitt & Tank, 2013; Mueller, Maheu, Dozier, Peloso, Mandell, Leibenluft, & Ernst, 2010; Shonkoff, Garner, Siegel, Dobbins, Earls, Garner, & Wood, 2012).

Adolescence is a period of heightened susceptibility to the environment (Schriber & Guyer, 2016). It is also a second window of opportunity for extending and safeguarding early childhood policies (The Lancet, 2017; UNICEF, 2017): The investments in adolescent health and wellbeing may bring triple dividends (Patton, Sawyer, Santelli, Ross, Afifi, Allen, & Viner, 2016). Most mental health issues begin in early adolescence and youth (Patel, Flisher, Hetrick, & McGorry, 2007). The combination of exposure to violence and susceptibility may help trigger maladaptive processes and mental health disorders that impact the quality of adolescent and adult life (Eiland & Romeo, 2013; Lamblin, Murawski, Whittle, & Fornito, 2017; Lupien *et al*., 2009; Schriber & Guyer, 2016). The effects of stress in the adolescent brain may also be dormant: In animal models, the effects did not emerge until adulthood (Isgor, Kabbaj, Akil, & Watson, 2004; Lupien *et al*., 2009).

Violence promotes chronic stress, it affects learning and cognition, and it is a major public health concern (WHO, 2014). It affects school attendance and dropout rates (Abramovay, 2002; Werthein, 2003), among other health, education, and social aspects (Shonkoff *et al*., 2012; Werthein, 2003; WHO, 2014). In Latin America, violence (e.g. homicide) affects youths disproportionately (Consejo Ciudadano para la Seguridad Pública y Justicia Penal A.C., 2014), and permeates the school ground: 84% of Brazilian students perceive their schools as violent environments and 70% report being direct victims of violence at school, including physical violence, social discrimination, and social exclusion (Waiselfisz, 2016). The school setting is not perceived as a safe harbor for learning and growth, but it offers an unique opportunity to reach youths and investigate environmental effects on cognition (Lupien, 2017).

The present study investigated preadolescent brain function in a social cognition and perception task adapted for functional magnetic resonance imaging (fMRI). We aimed to investigate brain and biological correlational effects of exposure to violence based on a multilevel combination of self-reports of victimization, fMRI indices, and biological markers of stress (hair cortisol concentration). We investigated preadolescents in one of Latin America's 50 most dangerous cities in the world (Cerqueira et al., 2017; Consejo Ciudadano para la Seguridad Pública y Justicia Penal A.C., 2014; Waiselfisz, 2016).

1.1 | The social brain: frontolimbic and right posterior brain networks

Humans are highly social beings. Brain networks associated with social cognition skills vary as the skills themselves (Fonzo, Ramsawh, Flagan, Simmons, Sullivan, Allard, & Stein, 2016; Moll, De Oliveira-Souza, & Zahn, 2008; Moll & Schulkin, 2009; Tsavoussis, Stawicki, Stoicea, & Papadimos, 2014). Social perception, for example, is the ability to glean mental states from facial expressions. It feeds social cognition, which in turn informs behavior (Adolphs, 2001).

Research Highlights

Preadolescent exposure to violence was associated with:

- Less activation of right-hemisphere areas involved in social perception and cognition, including the right superior temporal sulcus and right fusiform gyrus.
- Higher *Z*-score for the correlation between amygdala and right fusiform gyrus (RFFG) time series in the mental state condition.
- Higher levels of cortisol concentrations in hair samples.

Social perception processes capture information from facial expression (Engell & Haxby, 2007; Haxby, Hoffman, & Gobbini, 2000; Hoffman & Haxby, 2000; Schilbach, 2015) eye gaze direction (Allison, Puce, & McCarthy, 2000; George & Conty, 2008; Zilbovicius, Meresse, Chabane, Brunelle, Samson, & Boddaert, 2006), and speech (Ethofer, Bretscher, Wiethoff, Bisch, Schlipf, Wildgruber, & Kreifelts, 2013). For example, facial cues allow a speaker to identify rapport during a conversation (e.g. a smile combined with mutual gaze). The social perception brain circuitry includes the right superior temporal sulcus and inferior temporal lobe (Adolphs, 2003; Haxby *et al*., 2000; Moll & Schulkin, 2009; Saxe, 2006) and the fusiform gyrus (fusiform face area) (Grill-Spector, Knouf, & Kanwisher, 2004; Kanwisher, McDermott, & Chun, 1997; McCarthy, Puce, Gore, & Allison, 1997). Face processing is associated with activation of the right fusiform gyrus (RFFG) (Kanwisher *et al*., 1997; McCarthy *et al*., 1997; Rossion, Caldara, Seghier, Schuller, Lazeyras, & Mayer, 2003; Vuilleumier, Armony, Driver, & Dolan, 2001) and of the right superior temporal sulcus (RSTS) (Allison, Ginter, McCarthy, Nobre, Puce, Luby, & Spencer, 1994; Deen, Koldewyn, Kanwisher, & Saxe, 2015; Engell & Haxby, 2007). The fusiform face area (FFA) is a portion of the right fusiform gyrus (RFFG), its function is associated with detection and identification of faces (Grill-Spector *et al*., 2004). The RFFG and right superior temporal sulcus (RSTS) operate in association with a distributed brain circuitry that includes the amygdala, the orbitofrontal cortex, somatosensory areas, and the insular cortex in the processing of facial cues and emotions (Adolphs, 2001); they form a frontal, limbic, and temporal network of regions involved in social perception and cognition.

The frontolimbic system includes the amygdala, hypothalamus, the basal forebrain, and the orbitofrontal and anterior temporal regions (Fonzo *et al*., 2016; Moll & Schulkin, 2009; Moll *et al*., 2008; Tsavoussis *et al*., 2014). The right occipitotemporal social perception hubs interact with frontolimbic regions, such as the amygdala, in the processing of affective visual stimuli (Pessoa & Adolphs, 2010). The amygdala is involved in the processing of emotional faces, especially ones that carry fearful expressions (Pessoa, 2008; Pessoa, McKenna, Gutierrez, & Ungerleider, 2002). Evidence suggests that activation of the amygdala is partial to processing emotional facial cues. Recently, a combination of machine-learning

algorithms and fMRI data was used to decode face-selective regions. The study showed that only the amygdala and the posterior superior temporal sulcus (STS) accurately discriminated between neutral faces and emotional faces (Zhang, Japee, Nolan, Chu, Liu, & Ungerleider, 2016).

Brain imaging has shown atypical amygdala function and connectivity associated with adolescent anxiety disorders (Toazza, Franco, Buchweitz, Molle, Rodrigues, Reis, & Manfro, 2016), early-life stress and institutionalization (Herringa, Burghy, Stodola, Fox, Davidson, & Essex, 2016; Malter Cohen, Jing, *et al*., 2013; Silvers *et al*., 2016), and PTSD (Cisler, Bush, James, Smitherman, & Kilts, 2015). Atypical fusiform gyrus connectivity, in turn, has been shown in association with social anxiety (Frick, Howner, Fischer, Kristiansson, & Furmark, 2013). Based on brain imaging studies of the effects of stress on brain function, we hypothesized that higher levels of exposure to violence in preadolescents would be associated with atypical function and connectivity of right posterior and frontolimbic network regions. We investigated the brain regions that make up the social perception and frontolimbic circuitry for differences in activation and functional connectivity associated with exposure to violence. The hypotheses of the study stem from brain imaging evidence of the effects of stress on social cognition (Malter Cohen, Tottenham, & Casey, 2013; Moulson, Fox, Zeanah, & Nelson, 2009; Pollak, Cicchetti, Hornung, & Reed, 2000; Pollak & Sinha, 2002; Rahdar & Galván, 2014). We construed stress in terms of self-reported victimization scores and hair cortisol concentration.

1.2 | Cortisol: a psychobiological marker of stress in a multilevel approach

Stressful experiences promote biological system changes that increase vulnerability to mental illnesses (McEwen, 2008; Wisse, Reitsma, Vries, Gersons, & Olff, 2007). The neuroendocrine hypothalamic-pituitary-adrenal (HPA) axis is a key mediator of changes that result from stress. It produces the glucocorticoid cortisol in response to external and internal stimuli. Cortisol measurement has thus been used to investigate HPA axis reactivity to acute and chronic stress (Levine, Zagoory-Sharon, Feldman, Lewis, & Weller, 2007). Traditional cortisol reactivity measures are suited for the investigation of acute cortisol exposure, but less so for assessment of cumulative endocrine output (Kirschbaum, Steyer, Erd, & Patalla, 1991; Stalder & Kirschbaum, 2012; Stalder, Kirschbaum, Heinze, Steudte, Foley, Tietze, & Dettenborn, 2010). Cortisol output from plasma, serum, saliva or urine can be used to investigate the dynamics and the concentration of acutely (serum, saliva) or short-term (urine) circulating cortisol concentration. But cortisol secretion has substantial state/situational variability by circadian rhythmicity (Lightman, 2008; Spiga, Walker, Terry, & Lightman, 2014), it presents significant variation during the day and reactivity to acute transient stress (Hellhammer, Fries, Schweisthal, Schlotz, Stone, & Hagemann, 2007). Hair cortisol concentration is a promising matrix for retrospective measures of systemic cortisol exposure (Russell, Koren, Rieder, & Van Uum, 2012; Stalder & Kirschbaum, 2012). We investigated hair cortisol concentrations as a systemic index of exposure to violence in preadolescents as part of an overarching goal of investigation of indices to suggest a mechanistic account of brain function changes associated with exposure to violence in preadolescents.

2 | METHODS

Participants were from elementary schools in one of the 50 most dangerous cities in the world, in southern Brazil (Consejo Ciudadano para la Seguridad Pública y Justicia Penal A.C., 2014; Waiselfisz, 2016). Schools were the choice of setting for reaching preadolescents and their families (Lupien, 2017). Participation followed a citywide invitation by the state Department of Education. Principals of state-run schools were invited to a meeting with the researchers. We presented the project and school principals freely set up school meetings with parents and guardians of students regularly enrolled in the 4th and 5th grades, the last 2 years of the first phase of elementary school in Brazil. The invites reached an estimated 500 families. Approximately 300 families attended the meetings; parents or guardians who consented participation of their children later returned the informed consent forms in a sealed, anonymous envelope provided with the form. In total, 140 parents or guardians consented that their children participate in the study (roughly 28.0% of invites). No financial incentive was given for participation. The study was approved by the Ethics Committee of the Pontifical Catholic University of Rio Grande do Sul (Certificate of Evaluation of Ethics number CAAE 57741516.6.0000.5336).

2.1 | Participants

We invited all 140 preadolescents whose parents or guardians consented participation. Participants were excluded after the first stage of testing due to: IQ score below 75 (seven participants); illiteracy or inability to fill out the self-report questionnaires (10 participants); and frequent truancy–at least two additional attempts at data collection at the school were made if the participant missed school (five participants). Forty-three participants voluntarily withdrew from the study. The remaining 25 participants voluntarily withdrew from the study after completion of the first stage.

We scanned a total 50 participants; the present study reports on 40 right-handed preadolescents (boys: n = 24; girls: n = 16). Nine participants were excluded due to excessive head motion (see below); one participant was excluded due to focal demyelination on the left hemisphere temporal lobe (A neuroradiological reading of the structural scans was carried out to ensure there were no lesions, malformations or other abnormalities in the brain; all readings were reported to the guardians). The average age of the participants was 11.45 years (SD = 1.01; range 10–14 years).

2.2 | Materials and data collection procedures

The first stage of evaluations included IQ tests and self-reports of exposure to violence. IQ was investigated using the Wechsler Abbreviated Scale of Intelligence™ (*M* = 95.27; *SD* = 10.69; range 75–112). Exposure to violence was investigated using the Juvenile Victimization Questionnaire in its reduced format (JVQ-R2) (Finkelhor, Ormrod, Turner, & Hamby, 2005). The second stage included the fMRI session, collection of hair samples, investigation of socioeconomic status, and additional investigation of exposure to violence (JVQ-R2 full format). Socioeconomic status (SES) was established using a standardized questionnaire for SES classification in Brazil (ABEP, 2016), which provides a score based on schooling and possession of consumer goods (range from A, highest, to D, lowest). Parents or guardians filled out the SES questionnaire. The participants were on average from low SES backgrounds: average score of 19.58 (*SD* = 4.63), which corresponds to level C1 (*n* = 39; data missing from one family who did not fill out the form; the SES and their respective number of participants in the study were D = 1; C2 = 16; C1 = 11; B2 = 9; B1 = 2).

2.2.1 | Exposure to violence: Juvenile Victimization Questionnaire 2nd revision (JVQ-R2)

Victimization was assessed using the Juvenile Victimization Questionnaire - 2nd revision (JVQ-R2). The JVQ-R2 was developed to evaluate self-reported interpersonal victimization in youths (Finkelhor *et al*., 2005). The JVQ-R2 gathers information on 34 items that assess five types of victimization as such: nine items for Conventional Crime, four items for Maltreatment, six items for Peer and Sibling Victimization, seven items for Sexual Victimization, and eight items for Witnessing and Indirect Victimization. The JVQ-R2 assesses recency and chronicity of events (last year and lifetime scores). Reported victimization was scored as one based on the item-level scores proposed by the manual,[1] the absence of victimization was scored as zero. The total victimization scores were the sum of all 34 items. The JVQ-R2 was also used to assess the item-level scores of the five modules (Module A = any Conventional Crime; Module B = any Maltreatment; Module C = any Peer and Sibling Victimization; Module D = any Sexual Victimization; and Module E = any Witnessing or Indirect Victimization). The module scores were also used as dichotomous scores. Thus, a 'yes' for a module indicated that at least one form of victimization on that module was reported, whereas a 'no' indicated that no forms of victimization on that module were reported.

The JVQ-R2 full interview was translated and adapted to Portuguese with the permission of its authors. The JVQ-R2 was field-tested and piloted among youths in the target range before administration in the main survey. In the present study, the JVQ-R2 was filled out in two separate occasions. First, at the schools, participants filled out the abbreviated version of the questionnaire in groups of 10–20 individuals. The abbreviated version assesses dichotomous presence or absence of types and instances of victimization. The questionnaires were later scored and evaluated. Second, a trained member of the clinical research team administered the full version of the questionnaire in an individual interview. This interview was carried out on the day of the fMRI scan. The full version of JVQ-R2 gathers additional information about each of the types and instances of victimization reported in the reduced format; for example, recency and frequency of the events. The internal consistency reliability among the reduced version and the full version scores for the JVQ-R2 was excellent (Cronbach's alpha 0.915). The JVQ-R2 has good construct validity and acceptable test-retest reliability. The agreement between two administrations ranged from 77% to 100% (Finkelhor *et al*., 2005). The mean test-retest correlation was estimated at 0.63, and internal consistency was very good (Cronbach's alpha 0.80) (Finkelhor *et al*., 2005).

The JVQ-R2 score may also be divided into last year (recent) and lifetime violence. The correlation among scores for lifetime and last year victimization was excellent (Pearson's $r = 0.870$). Moreover, the internal consistency reliability (Cronbach's alpha) among last year and lifetime scores for the full version was also excellent (alpha 0.923). These analyses suggest that for the average 11-year old in our study, lifetime JVQ-R2 scores reflect mostly victimization in the previous year. Therefore, we investigated the brain-victimization effects using last year JVQ-R2 scores (lifetime scores are reported, nonetheless).

2.2.2 | Hair cortisol: hair sample collection, cortisol extraction and analyses

Hair strands of approximately 3–5 mm in diameter (*M* ± *SEM* = 114.60 mg ± 11.36 of hair strands) and of 2 cm in length were cut from the posterior vertex position of subjects' heads with surgical scissors. After collection, the scalp end of the sample was identified, and hair samples were stored at room temperature for up to 12 months. Subsequently, 1-cm hair sections (representing 1-month periods) were cut and minced with clean and fine-tipped surgical scissors into 1 mm pieces. Based on an average hair growth rate of 1 cm per month (Wennig, 2000), each of the two hair segments should reflect cumulative cortisol secretion for the previous 30 and 60 days, respectively.

Hair cortisol extraction followed a protocol described in the literature (Kirschbaum, Tietze, Skoluda, & Dettenborn, 2009) but with an adaptation (Boeckel, Viola, Daruy-Filho, Martinez, & Grassi-Oliveira, 2017). At least 10 mg of hair per 1-cm section was weighed and manually milled into different clean centrifuge tubes (*M* ± *SEM*: 1-cm hair segment = 43.85 mg ± 4.40, and 2-cm hair segment = 43.28 mg ± 6.08). Powdered hair was prepared in 1.5 ml methanol and incubated in water bath for 24 hr at 50°C. After incubation, ~1.0 ml of supernatant methanol (containing cortisol extract) was removed to a clean microtube and evaporated under a constant stream of nitrogen at 50°C using TurboVap® Classic LV (Biotage, Sweden).

The residues were reconstituted with 0.2 ml of phosphate-buffered saline (pH 8.0) and vortexed for 1 min. For a double-blinded measurement of cortisol in the extracts, we used a commercially available high-sensitivity salivary cortisol enzyme-linked

immunosorbent assay (ELISA) (Salimetrics LLC, State College, PA, USA) according to the manufacturer's instructions. All samples were run in duplicates. We obtained a total of 71 hair samples from the 40 subjects (boys: *n* = 24; girls: *n* = 16): 1-cm hair segment (*n* = 35, boys: *n* = 20, girls: *n* = 15, missing data: *n* = 4 boys and *n* = 1 girl), and 2-cm hair segment (*n* = 31, boys: *n* = 16, girls: *n* = 15, missing data: *n* = 8 boys and *n* = 1 girl) Of the 40 youths, 12.5% (*n* = 5) was excluded from the current analyses due to a failure in hair cortisol extraction and analysis (missing data). In addition, a total of two participants (*n* = 1 boy and *n* = 1 girl) was considered statistical outliers and excluded from the 1-cm analyses due to low levels of hair cortisol concentration in the 1-cm hair sample (mean in pg/mg ± *SD*) (1-cm hair segment: 1.64 ± 0.73). The final analyses for 1-cm hair cortisol included 33 participants (boys: *n* = 19; girls: *n* = 14).

2.2.3 | fMRI parameters

Data were collected on a GE Healthcare HDxT 3.0T MRI scanner with an eight-channel head coil. Three MRI sequences were acquired: a T1 structural scan (TR/TE = 6.16/2.18 ms, isotropic 1 mm^3 voxels), and two task-related functional FMRI EPI sequences using the eyes test (run 1 = 8 min; run 2 = 8 min 04 s). For the task EPI sequence, we used the following parameters: TR = 2,000 ms, TE = 30 ms, 29 interleaved slices, slice thickness = 3.6 mm; slice gap = 0.3 mm; matrix size = 64 × 64, FOV = 240 × 240 mm, voxel size = 3.75 × 3.75 × 3.90 mm.

2.2.4 | Reading the Mind in the Eyes Test (RMET)

The participants performed the 'Reading the Mind in the Eyes Test' (RMET) in the MRI scanner (Baron-Cohen *et al*., 2001). The test was previously adapted to Brazilian Portuguese (Sanvicente-Vieira *et al*., 2014), and it has been previously applied in fMRI investigations of mental state attribution in schizophrenia (Russell *et al*., 2000) and alcohol dependence (Gizewski *et al*., 2013). It includes two conditions, namely 'Mental State' and 'Sex.' The conditions are made up of pictures of pairs of eyes. In the Mental State condition, participants are asked to infer a state of mind from the pictures of pairs of eyes (experimental condition); in the Sex condition, they are asked to identify the sex of the person in the picture (control condition).

The task includes 36 pictures of pairs of eyes. Each picture is presented twice, one in the Mental State condition and once in the Sex condition. The exact same stimuli are used in both conditions (Hence, the task includes a total 72 trials). Participants are instructed to infer the mental state the person is in, or to identify if the eyes belong to a man or woman. The response choices were displayed at the bottom of the screen at the same time the picture is displayed. After the picture of pairs of eyes has been on the screen for 3 s, a question mark cued participants to choose between two options given (two mental states, or man - woman); participants had 3 s to respond. Please see Supplementary Methods for additional task presentation and timing information.

2.3 | fMRI data analyses

Functional data were processed using AFNI's (http://afni.nimh.nih.gov/) afni_proc.py program (Cox, 1996). Preprocessing included slice-time and motion correction, smoothing with a 6 mm FWHM Gaussian kernel and a non-linear spatial normalization to 3.5 × 3.5 × 3.5 mm^3 voxel template (HaskinsPedsNL template) (Molfese, Glen, Mesite, Pugh, & Cox, 2015). Time points between volumes with framewise displacement (motion) >0.9 mm were censored from the data. These timepoints were regressed out within the 1st level multiple regression calculation (see below). Nine participants who finished the scanning session were excluded due to excessive motion. The criterion for exclusion was excessive head motion in 20% of the total TRs. The average head motion for the participants in the study was 0.1262 mm (*SD* = 0.065). To ensure motion artifacts did not have an effect on the correlation among victimization scores and brain imaging, we calculated the correlation between participants average head motion during the scan and their respective JVQ-R2 score: There was no correlation between exposure to violence and the average motion in the scanner ($r = 0.0388$; $p = 0.8121$). During the scan, a real-time motion detection software was used to monitor participant cooperation. In case participants presented more than framewise displacement of 0.9 mm motion in more than 20 TRs before completing the run, we interrupted the experiment, talked with the participant, and ran the task again. We made one attempt to re-run the task if it was stopped due to excessive head motion. Six participants had to redo one of the RMET runs, one had to redo both (see Supplementary Methods for full report and additional analyses; redoing the task had no significant effects on the group results).

First-level analyses included modeling regressors for each condition (Mental State, Sex), which were convolved with the canonical hemodynamic response function as implemented in AFNI (Cox, 1996). The hemodynamic response was modeled for the full duration of each visual stimuli (6 s). To avoid matrix singularity, a random jitter was included between each trial. The jitter intervals were 1.5, 1.75, and 2.5 s. Regressors of no interest were also included in the multiple regression model including six estimated motion parameters (3-translation and 3-rotation) and a 4th-degree polynomial fit. To correct for multiple comparisons, the 3dClustSim program (estimating the blurring of the data by the autocorrelation function) was used to calculate the cluster threshold for a corrected *p*-score of $\alpha < 0.05$. The calculation showed that the threshold of $p < 0.005$ combined with a minimum cluster size of 74 voxels (3172, 8 μl) corresponded to a score corrected for multiple comparisons of $\alpha < 0.05$.

2.3.1 | Correlations: fMRI and exposure to violence

We carried out correlations among the JVQ-R2 scores and individual participants images for the contrast between the two conditions (Mental State > Sex). The rationale for using the Mental State > Sex images was to investigate effects of victimization in association with activation specific to the inference of emotional cues in facial expressions, thus removing lower-level processes

common to the conditions. The Mental State and Sex conditions used the exact same stimuli; thus, the images for the contrast between the two conditions reflect brain activation specific to the inferring of emotions from the pairs of eyes (Newman, Twieg, & Carpenter, 2001). The correlation was calculated using the JVQ-R2 scores and using the 3dRegAna function from the AFNI package (Cox, 1996). We also investigated correlations among age of participants and the brain imaging conditions (Mental State; Sex) and their contrast (Mental State > Sex). There were no significant correlations between age and activation either in the main conditions or in the contrast.

2.3.2 | Impulse Response (IRESP) and functional connectivity analysis

Impulse responses for Mental State and Sex conditions were calculated using the 3dDeconvolve function from the AFNI package. IRESP was modeled for each condition for 36 s for each of the six blocks for the condition. Subsequently, an average IRESP time course for each condition (including all six blocks of 36 s) was calculated for each brain region, each condition and each participant.

Functional connectivity was computed separately for each participant, each condition and pairs of brain regions as a correlation between the 36-s average time course for the pairs of regions of interest. The correlation was calculated between the average time courses for pairs of brain regions, within the condition. For example, for the functional connectivity correlation between the Amygdala and the RFFG (Amygdala:RFFG) in the Mental State condition, we correlated each participant's average time course for the Mental State condition for the amygdala with the participant's average time course for the Mental State condition for the RFFG; likewise, for the Sex condition, we used the average time courses for the pair of regions, for this condition. The average impulse response was measured for the following regions of interest, based on the literature for social cognition and social perception in the brain discussed above (Adolphs, 2001, 2003; Kanwisher *et al*., 1997; Saxe & Kanwisher, 2003): Right Superior Temporal Sulcus (RSTS); Amygdala (left + right Amygdala); Right Inferior Parietal Lobe (RIPL); Right Inferior Frontal Gyrus (RIFG) (triangularis + opercularis); and Left Orbitofrontal Cortex (LOFC).

The correlations reflect the relation between the activation of two brain regions for the duration of the task. Subsequently, Fisher's *r*-to-*z* transformation was calculated using the correlation coefficients calculated for each pair of areas for each participant, and each condition. The participant's individual *Z*-scores for each pair of areas in each condition were subsequently used for statistical analysis. This method for investigation of functional connectivity has been widely used for mechanistic investigations of individual differences of connectivity in the brain, in clinical and healthy populations (Buchweitz, ; Buchweitz, Keller, Meyler, & Just, 2012; Just, Cherkassky, Keller, Kana, & Minshew, 2007; Just, Cherkassky, Keller, & Minshew, 2004; Keller & Just, 2009, 2016; Mason, Williams, Kana, Minshew, & Just, 2008). The method provides task-related indices that indicate differences in brain networks communication between pairs of regions.

2.3.3 | Correlations: functional connectivity indices and JVQ-R2 scores

To investigate a relation among changes in connectivity and self-reported victimization, we calculated the correlations among the Fisher's *Z*-score for each pair of brain regions of interest (described above), for each participant and the participant's JVQ-R2 scores.

2.4 | Victimization and hair cortisol statistical analyses

We tested JVQ-R2 scores and hair cortisol concentration for normality of distribution using the Kolmogorov-Smirnov or Shapiro-Wilk tests. The tests for hair cortisol concentration showed the data were not normally distributed. We log transformed the hair cortisol concentration values, and the transformation effectively reduced the skewness statistic and allowed for the use of parametric models in the analyses. We calculated descriptive statistics for all items and modules of the full version of JVQ-R2. We calculated Cronbach's alpha for the item scores of JVQ-R2 to evaluate scale reliability among lifetime and last year scores.

We used Pearson's correlation to test the relationship among hair cortisol concentration for two hair segments (1-cm and 2-cm) and JVQ-R2 total score. We also used multiple testing correction of *p*-values for the correlations among hair cortisol concentration and JVQ-R2 total score and module scores (Benjamini & Hochberg, 1995). Generalized Estimating Equation (GEE) was carried out after checking for data normality (Kolmogorov-Smirnov or Shapiro-Wilk tests) to analyze within-individual correlations of repeated-measures of hair cortisol concentrations (1-cm and 2-cm hair segments), and to analyze victimization scores. GEE model with linear distribution was carried out using the log-transformed values of the hair cortisol concentration. Repeated measurements in the same subjects were taken into account in an exchangeable matrix. We modeled the log-transformed hair cortisol concentration (dependent variable) using hair segment (factor), last year victimization scores of JVQ-R2 (covariate), and hair segment × last year victimization (interaction effect). All statistical analyses of cortisol and instrument scores were performed using SPSS software 20th version (SPSS, Chicago, IL, USA). A p-value < 0.05 was considered statistically significant. The Scatterplots of the correlations were generated using GraphPad Prism 6 (GraphPad Software Inc., La Jolla, CA, USA).

3 | RESULTS

3.1 | Preadolescents and self-reported victimization

The majority of the sample (82.5%, n = 33) experienced at least one form of victimization in their lifetime. The prevalence of last year victimization was 72.5% (n = 29), which in turn corresponds to 87.8% of the youths who reported lifetime victimization events. The mean lifetime victimization score was 4.20 (SD = 4.40); the mean last year score was = 2.25 ± 3.38 (Supplementary Table S1 shows descriptive

data by module and total scores for the JVQ, last year and lifetime; it also presents analyses of differences between hair cortisol among boys and girls—no sex differences were found). In types of last year victimization, 30% (n = 12) reported two forms of victimization (which corresponds to 48% of the youths who were victimized in their lifetime), 22.5% (n = 9) reported three forms of victimization (60% of the youths who were victimized in their lifetime), 7.5% (n = 3) reported four forms of victimization (42.8% of the youths who were victimized in their lifetime), and 2.5% (n = 1) reported experiencing all five forms of victimization (the same participant who reported five forms of lifetime victimization). A total 62.5% (n = 25) reported two forms of lifetime victimization; 37.5% (n = 15) reported three forms of victimization; 17.5% (n = 7) reported four forms of victimization, and 2.5% (n = 1) experienced all five forms of victimization.

3.2 | fMRI results

3.2.1 | Exposure to violence and less activation of social perception brain circuitry

Results showed that exposure to violence was associated with less activation of a right-hemisphere temporoparietal network of areas for Mental State > Sex activation. The network of areas that negatively correlated with exposure to violence included the right inferior parietal lobe (RIPL), the right superior temporal gyrus and sulcus (RSTG and RSTS), and the posterior cingulate gyrus. Results also showed a negative correlation among victimization scores and activation of the right fusiform gyrus (RFFG). Figure 1 shows the RFFG and right posterior and superior temporal lobe clusters of activation that negatively correlated with the level of victimization. Table 1 reports all clusters negatively correlated with JVQ-R2; there were no clusters that showed significant positive correlation with victimization scores. (Supplementary Tables S2 and S3 report activation for each condition and for the contrast between conditions; Supplementary Figure S1 shows a scatterplot of the correlation among JVQ last year scores and the beta values for each participant in the RSTS and the RFFG regions shown in Figure 1).

3.2.2 | Violence and amygdala-RFFG connectivity in the Mental State condition

Correlations among amygdala:RFFG Z-scores for each condition (Sex and Mental State) with victimization were significant for the Mental State attribution task only. This suggests significant connectivity between the RFFG and the limbic system only when participants were asked to attribute mental states (Figure 2; correlation Z-score Amyg:RFFG for the Mental State condition with last year JVQ-R2 r = 0.313, p = 0.049; correlation Z-score Amyg:RFFG for the Sex condition with last year JVQ-R2 r = 0.083; p = 0.608). The images presented in either condition were the same. Thus, the result suggests an effect of task on connectivity between the fear center of the brain and one of the brain regions that negatively correlated with victimization (RFFG was among the regions that negatively correlated with JVQ-R2). Supplementary Table S4 reports the correlations for the other pair of regions with JVQ-R2 last year scores; there were no other significant correlations among the Z-scores and the victimization score. A Wilcoxon Signed-Ranks Test indicated no statistically significant difference between the Z-scores for the Mental State condition and for the Sex condition for the Amygdala:RFFG pair (Z = −0.121; p = 0.757).

Differences in amygdala-fusiform connectivity have been found in association with adolescent anxiety disorders (Toazza *et al*., 2016),

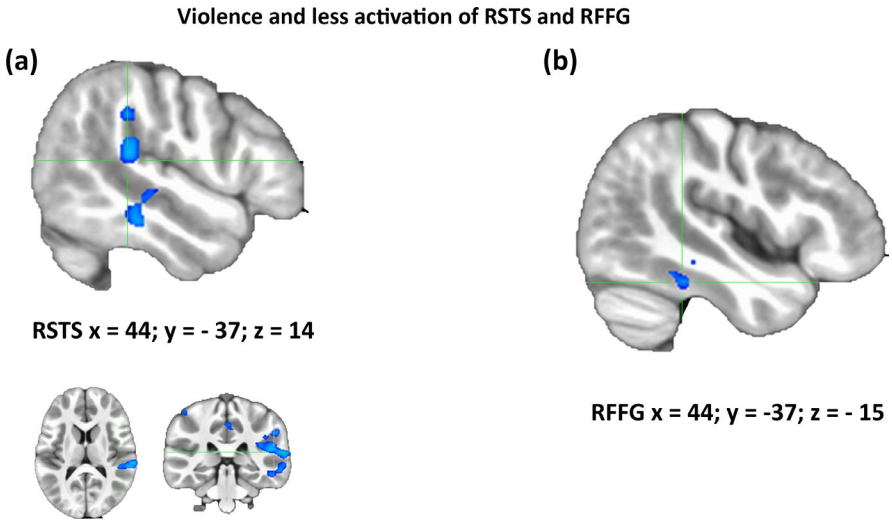

FIGURE 1 Less brain activation associated with increased exposure to violence. Negative correlation for JVQ-R2 last year scores with the images for the Mental State > Sex contrast. Clusters significant at $p < 0.05$ corrected for multiple comparisons (3dClustSim: threshold of $p < 0.005$ for a minimum cluster size of 74 voxels; 3172, 8 μl). (a) Renderings of decreased activation associated with violence and the Right Superior Temporal Sulcus cluster (green crosshairs at x = 44; y = −37; z = 14): Top: lateral view; Bottom: axial and coronal views. (b) Rendering of less activation associated with violence and the Right Fusiform Gyrus (green crosshairs at x = 44; y = −37; z = −15). The number of negatively correlated voxels and their respective regions are described in Table 1

early-life stress and institutionalization (Herringa *et al*., 2016; Malter Cohen, Jing, *et al*., 2013; Silvers *et al*., 2016), and PTSD (Cisler *et al*., 2015). The choice of brain region pairs was not exploratory, but we carried out a correction for multiple comparisons for the correlations among the *Z*-scores for activation time series and the JVQ scores. The significant correlation between Amygdala:RFFG and JVQ scores did not survive correction for multiple comparisons (Benjamini & Hochberg, 1995). Evidently, the result needs to be replicated to establish evidence of an actual mechanism of increased communication among social cognition and limbic system brain regions that emerges in association with violence.

TABLE 1 Right-hemisphere regions, number of voxels and peak coordinates for the brain regions negatively correlated with JVQ-R2 scores. Atlas number and name for the pediatric template region used to extract the voxels significantly negatively correlated with JVQ-R2 scores (parentheses), and coordinates for the peak T value in each cluster. There were no clusters of voxels that positively correlated with victimization. Number of voxels reported based on voxels negatively correlated with the JVQ-R2 score above the corrected threshold of $\alpha < 0.05$

Region (atlas number)		Peak		
Right-Hemisphere	**Voxels**	**x**	**y**	**z**
Sup. Temporal Sulcus (74)	4	59	33	9
Sup. Temporal Gyrus (102)	1	42	30	16
Inf. Temporal (81)	30	56	47	15
Fusiform (79)	7	38	37	15
Inf. Parietal Lobe (80)	27	35	56	54
Sup. Parietal Lobe (101)	33	21	61	51
Mid. Temporal (87)	36	52	33	5
Posterior Cingulate (95)	9	7	37	37
Supramarginal (103)	16	31	30	20
Paracentral (89)	9	14	37	41
Precuneus (97)	80	14	47	34

3.3 | Preadolescents and self-reported victimization

The majority of the sample (82.5%, *n* = 33) experienced at least one form of victimization in their lifetime. The prevalence of last year victimization was 72.5% (*n* = 29), which in turn corresponds to a total of 87.8% of the youths who reported lifetime victimization events. The mean lifetime victimization score was 4.20 (*SD* = 4.40); the mean last year was = 2.25 ± 3.38 (Supplementary Table S1 shows descriptive data by module and total scores for the JVQ, last year and lifetime; it also presents analyses of differences between hair cortisol among boys and girls—no sex differences were found). For reports of last year victimization, 30% (*n* = 12) reported two forms of victimization (which corresponds to 48% of the youths who were victimized in their lifetime), 22.5% (*n* = 9) reported three forms of victimization (60% of the youths who were victimized in their lifetime), 7.5% (*n* = 3) reported our forms of victimization (42.8% of the youths who were victimized in their lifetime), and 2.5% (*n* = 1) experienced all five forms of victimization (the same participant who reported five forms of lifetime victimization). A total 62.5% (*n* = 25) reported two forms of lifetime victimization; 37.5% (*n* = 15) reported three forms of victimization; 17.5% (*n* = 7) reported four forms of victimization, and 2.5% (*n* = 1) experienced all five forms of victimization.

3.4 | Victimization and HPA: hair cortisol concentration reflects youth's self-reported levels of exposure to violence

Participants self-reported victimization scores correlated with individual differences in concentration in hair cortisol. Results showed that last year victimization scores positively correlated with

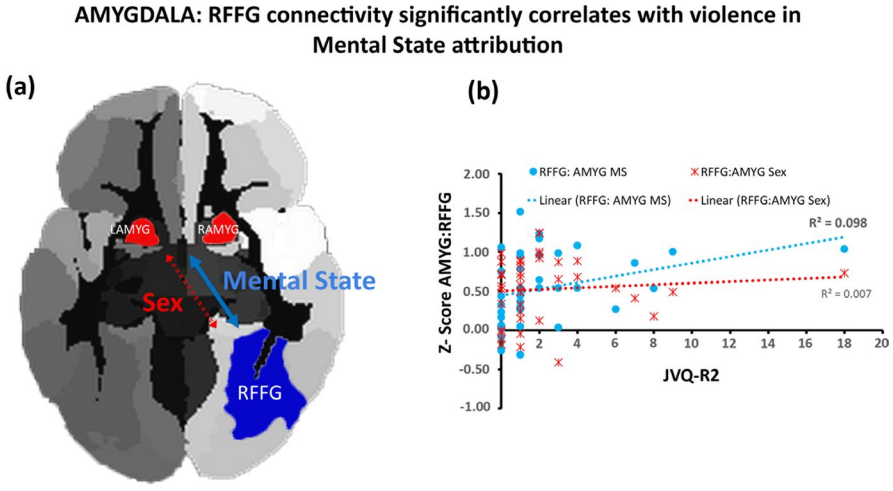

FIGURE 2 Significant correlation among JVQ-R2 and Amygdala:RFFG connectivity (*Z*-scores). Significant correlation found among amygdala and RFFG *Z*-scores for their time courses of activation and the participants victimization scores. (a) shows a rendering of the Haskins pediatric template left and right amygdala and RFFG regions used; (b) shows the scatter plot for the correlations among *Z*-scores for the pair of regions in the Sex and the Mental State condition and JVQ-R2 (*r*-squared for Mental State Amygdala:RFFG = 0.098; for Sex Amygdala:RFFG = 0.007)

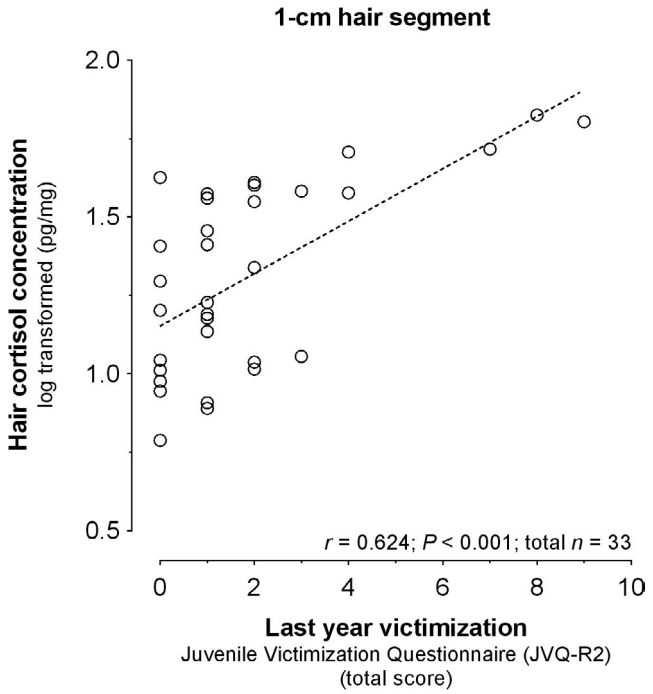

FIGURE 3 Association between hair cortisol concentration and juvenile victimization in the last year. The figure shows the scatterplot of the Pearson correlation among JVQ-R2 total scores (X-axis) and cortisol concentration (pg/mg) after log transformation (Y-axis) in 1-cm hair segment. Data from three participants are missing due to assay failure of cortisol measurement. These participants were excluded from the analyses. Two participants were considered statistical outliers due to low levels of hair cortisol concentration (mean in pg/mg ± SD) (1-cm hair segment: 1.64 ± 0.73). Thirty-three participants were included in the final analyses

hair cortisol concentration for the 1-cm hair segment (r = 0.624, p = 1.06E-04, total n = 33) (Figure 3). The results show a significant last year victimization effect (GEE model with linear distribution, main effect: Wald-χ^2 (1) = 19,606; p = 1E-05) on hair cortisol concentration of preadolescents. Moreover, there was a significant hair segment × last year victimization interaction effect (GEE model with linear distribution, interaction effect: Wald-χ^2 (1) = 8,623; p = 0.003) on hair cortisol levels in 1-cm hair segment. No significant hair segment effect was detected (GEE model with linear distribution, main: Wald-χ^2 (1) = 2,216; p = 0.137). By contrast, last year victimization scores did not correlate with hair cortisol concentration in 2-cm (r = 0.200, p = 0.281, total n = 31) (Supplementary Table S3 presents descriptive results and Figure 4 the correlations with JVQ-R2module scores). The results for cortisol concentration (mg/pg) in hair segments were (M ± SEM): 1 cm (32.23 ± 3.98 in boys and 16.47 ± 3.30 in girls, total n = 33, p = 0.007), and 2 cm (26.04 ± 3.68 in boys and 25.87 ± 3.43 in girls, total n = 31, p = 0.973). The correlations for comparisons among hair cortisol levels and lifetime and last year module scores are reported in Figure 4. The p values were adjusted for multiple comparisons using Benjamini and Hochberg method (Benjamini & Hochberg, 1995).

3.5 | Behavioral results

We analyzed the accuracy and response times (time to making a choice after the question mark was presented) for mental state and sex. Results showed an average accuracy of 0.64 (range 0.33–0.89; SD = 0.13) for the mental state condition and 0.92 (range 0.75–1.00; SD = 0.05) for the sex condition; the average response time after presentation of the question mark for mental state was 998 ms (range 615–1,460; SD = 223), and for sex, 872 ms (range 572–872; SD = 181). The response times were significantly different between conditions [paired t(39) = −5.212; p < 0.001]. There were no significant correlations among response times for Mental State (r = −0.037; p = 0.411) or Sex (r = 0.016; p = 0.460) with the victimization score.

4 | DISCUSSION

Our study shows, for the first time, an association of exposure to violence reported by Latin-American preadolescents with differences in the neural underpinnings of social cognition. Exposure to violence was associated with significantly less activation of right superior temporal sulcus, a brain hub for social perception (Saxe & Kanwisher, 2003; Schurz, Radua, Aichhorn, Richlan, & Perner, 2014), and of the RFFG, which is associated with processing faces. The negative correlation between RFFG and victimization co-occurred with evidence of a correlation among the RFFG and amygdala connectivity with higher victimization scores. The study also showed higher concentrations of cortisol, a psychobiological marker of chronic stress, were associated with youth's self-reported exposure to violence. These results are discussed in light of the corroborating literature.

4.1 | Victimization and decreased activation of right superior temporal sulcus: is violence taking its toll on the social brain?

The results suggest synchronized communication between the limbic system and RFFG associated with higher victimization scores, in the mental state attribution condition only. Synchronized brain function in a pair of areas of the brain suggests more communication, or exchange of information (Just *et al*., 2007); the significantly correlated brain function in the mental state condition could be evidence that RFFG activation is being modulated by the amygdala when more victimized participants infer mental states. The results may be early evidence of a coping mechanism, or a maladaptive process in social brain circuitry as a function of exposure to violence.

Differences in the function of brain networks that regulate emotion, such as the amygdala, may be a prelude to violent behavior (Davidson, Putnam, & Larson, 2000). Animal models of early life stress show alterations in amygdala circuitry and function associated with stress; these alterations, in turn, increase the risk for psychopathologies (Malter Cohen, Jing, *et al*., 2013). Altered fusiform activation and connectivity have been associated with processing negative, emotional faces and with mental disorders: Social anxiety disorder patients

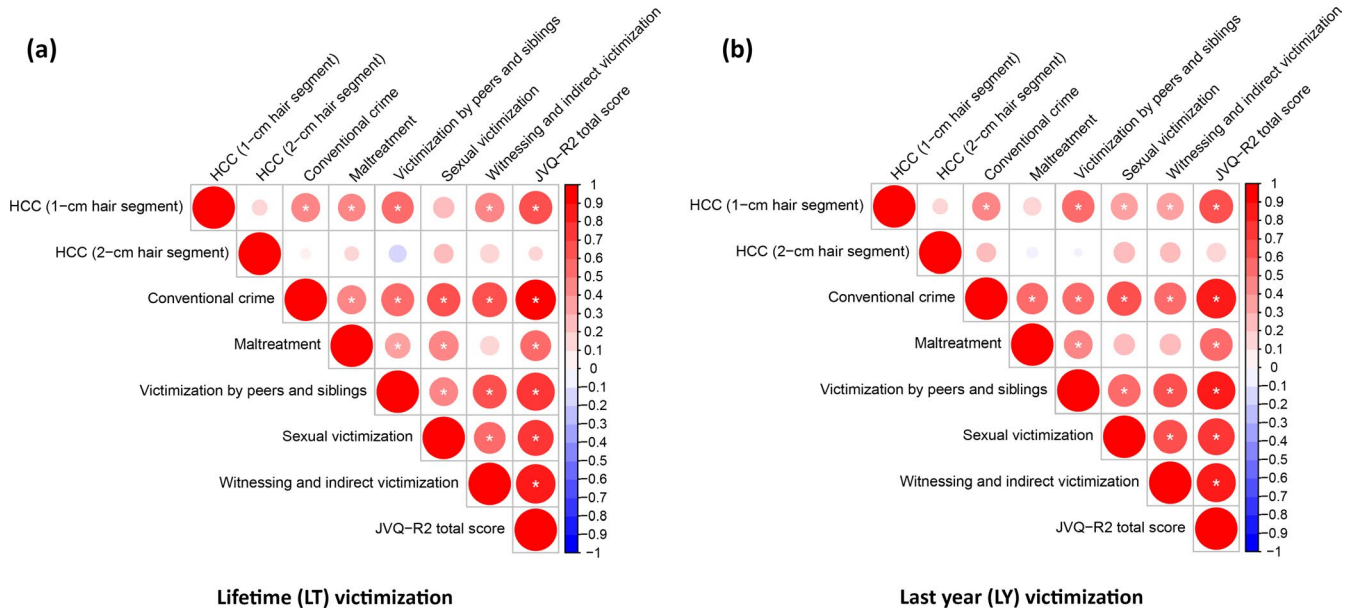

FIGURE 4 Correlation matrix for Hair Cortisol Concentrations (HCC) and JVQ-R2 module scores for lifetime and last year victimization Pearson's correlation test was carried out among HCC and LT (a) and LY (b) victimization subscores: conventional crime, maltreatment, victimization by peers and siblings, sexual victimization, and witnessing and indirect victimization. The circles represent the Pearson's correlation coefficients: the *r* values are color coded and reported in the legend (red color: positive *r*; blue color: negative *r*). Significant correlations are indicated by (*) inside the circle (adjusted *p*-value < 0.05). Correlation coefficient and significant *p*-value for the association among LT victimization scores and HCC 1-cm hair segment: conventional crime ($r = 0.451$, Adjusted *p*-value = 0.020); maltreatment ($r = 0.408$, Adjusted *p*-value = 0.030), victimization by peers and siblings ($r = 0.561$, Adjusted *p*-value = 0.005), and witnessing and indirect victimization ($r = 0.467$, Adjusted *p*-value = 0.020). Correlation coefficient and significant *p*-value for the association among LY victimization scores and HCC 1-cm hair segment: conventional crime ($r = 0.432$, Adjusted *p*-value = 0.024); victimization by peers and siblings ($r = 0.576$, Adjusted *p*-value = 0.004), sexual victimization ($r = 0.392$, Adjusted *p*-value = 0.030), and witnessing and indirect victimization ($r = 0.395$, Adjusted *p*-value = 0.030). Thirty-three participants had 1-cm hair samples (boys: $n = 19$; girls: $n = 14$); 31 participants had 2-cm hair samples (boys: $n = 16$; girls: $n = 15$). Adjusted *p*-value refers to multiple testing correction of *p*-value (Benjamini & Hochberg, 1995). JVQ-R2 = Juvenile Victimization Questionnaire - 2nd Revision (full interview). HCC = hair cortisol concentration (1-cm hair segment or 2-cm hair segment)

present altered amygdala-fusiform connectivity while viewing fearful faces (Frick *et al.*, 2013); phobic patients show decreased activation of the fusiform gyrus for processing angry or negative faces (Gentili, Gobbini, Ricciardi, Vanello, Pietrini, Haxby, & Guazzelli, 2008).

Of course, exposure to violence and adversity in adolescence does not necessarily lead to mental health disorders. Some people thrive despite or in the face of adversity. But the exposure may increase the risk for psychopathologies in a period of heightened susceptibility to the environment (Schriber & Guyer, 2016). Evidence of differences in brain function and connectivity can be more meaningfully interpreted longitudinally as predictors of brain-behavior relationship and of risk for mood disorders, for suicidal ideation, for violent behavior, among other mental health issues. The current study does not link exposure to violence with present or long-term changes in behavior.

Children and adolescents who experience maltreatment, one of the modules in the JVQ-R2, are more likely to become depressed and suicidal (Brown, Cohen, Johnson, & Smailes, 1999). The results show evidence of less activation in a brain network for which (putatively atypical) function has been associated with mental health disorders, stress and early institutionalization (Dien & O'Hare, 2008; Pollak & Sinha, 2002; Silvers *et al.*, 2016; Tottenham, Hare, Quinn, McCarry, Nurse, Gilhooly, & Casey, 2010). RFFG activation also correlated negatively with differences in victimization. Studies have shown differences in FFG activation associated with negative emotional stimuli in PTSD, social anxiety, and phobic patients (Etkin & Wager, 2007). Anatomically, altered gray matter volume in the visual cortex has been associated with experiences of childhood sexual abuse (Tomoda, Navalta, Polcari, Sadato, & Teicher, 2009). In sum, our results corroborate the evidence that different forms of exposure to violence, trauma and maltreatment are associated with differences in neurobiological function that underpins social perception. It remains to be seen whether these differences in social brain function represent early signs of risk for future mental health troubles as a consequence of present chronic exposure to violence.

4.2 | Exposure to violence and cortisol levels: a neuroendocrine telltale sign

Our results showed an association among preadolescents' hair cortisol concentrations and self-reported victimization scores. The correlation supports the notion that increased scores in these reports may

result in increased stress. The differences in concentrations identified in the present study suggest biomarkers of enduring changes due to exposure to chronic stress (Negriff, Saxbe, & Trickett, 2015). Children and adolescent hair cortisol concentration is sensitive to exposure to stressful situations (Rippe, Noppe, Windhorst, Tiemeier, van Rossum, Jaddoe, & van den Akker, 2016; Serwinski, Salavecz, Kirschbaum, & Steptoe, 2016; Ursache, Merz, Melvin, Meyer, & Noble, 2017).

In comparison to other studies, our results suggest an average victimization score at an earlier age. For the last year scores, 72.5% of our population reported at least one victimization experience; this percentage is slightly higher than that found in a study with 4,549 U.S. children and adolescents (69.3%) (Finkelhor, Ormrod, & Turner, 2009), and in a study with 1,107 Spanish adolescents (68.6%) (Pereda, Guilera, & Abad, 2014). In both cases, the population was older than ours. The percentage of participants who reported at least one form of lifetime victimization in our study was slightly higher than that of participants who reported one for of lifetime victimization for a study of 4,053 people in the United States (80% reported victimization) (Turner, Finkelhor, & Ormrod, 2010); also, our lifetime percentage of victimization was comparable to an older, but large sample of 5,960 students (mean age 17.3 years) from Sweden (84.1% reported lifetime victimization) (Aho, Gren-Landell, & Svedin, 2016). The percentage of preadolescents who had experienced at least one form of victimization in our study was comparable to the percentages of older populations, thus suggesting a higher prevalence of at least one experience at an earlier age.

Witnessing and indirect victimization was the most frequently reported type of last year victimization: 42.5% of preadolescents. This prevalence was higher than that for Spanish youths (32.1%) (Pereda *et al*. 2014) and Swedish adolescents (34%) (Aho et al., 2016), who were also generally older than our population. Conventional Crimes were the second most frequent type of victimization in our sample: 37.5%. A similar prevalence was observed in Hong Kong (35.8%) (Chan, Fong, Yan, Chow, & Ip, 2011). Maltreatment in last year was reported by 17.5% of preadolescents, similarly to the Spain (18.1%) (Pereda *et al*. 2014) and Hong Kong (21.1%) (Chan *et al*., 2011) studies. Peer and sibling victimization (30% of preadolescents) was also similar to Spanish (30.6%) (Pereda *et al*. 2014) and Swedish (30%) estimates with adolescents (but again, those studies included older participants) (Aho et al., 2016). The results show 7.5% of youths reported sexual victimization in the last year; this result is higher than the prevalence of sexual abuse in other studies (Chan *et al*., 2011; Pereda *et al*., 2014). Finally, most studies report SES as an intervenient factor for hair cortisol concentrations. Our results showed no association of hair cortisol concentration with SES. There was no correlation among SES scores and the victimization scores for JVQ lifetime ($r = 0.092$; $p = 0.576$) or last year ($r = 0.095$; $p = 0.566$). No correlation between socioeconomic data and hair cortisol concentrations may result from the homogeneity of the sample; all but one participant had low or very low SES (see Methods).

The present findings do not show that social cognition processes are actually compromised, at this point. The cross-sectional evidence suggests associations of exposure to violence with less activation of the social brain, and with synchronized function between limbic and posterior face-processing brain networks. The results corroborate the existing evidence of associations between brain function and violence and contribute to an increasing array of studies that are seeking to better understand the risk and early signs for negative spirals in behavior and mental health with brain-informed evidence.

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ENDNOTE

[1]http://www.unh.edu/ccrc/jvq/scoring.html

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