SUPPLEMENTARY INFORMATION

METHODS

Subjects

In our adolescents, trait aggression (mean±sd: 42.2±6.8) was assessed with the Aggression Questionnaire (1) and exposure to community violence (14.9±5.3) and media violence (14.3±2.0) were assessed with the Children's Report of Exposure to Violence (2).

Stimuli

In a pre-study, another group of 22 age- and education-matched males (age: 15.3±1.3, range 14–17, yrs. of education: 9.0±1.6, range 7-12) rated the videos for aggression and excitement. In the rating experiment, videos were presented in a randomized order to subjects on a computer screen using the SuperLab Pro software (Cedrus Corporation, San Pedro, CA). On a second screen, two horizontal bars (approximately 10.5 inches of length) with an internal scale ranging from 0 to 100 were presented to allow for a continuous rating (in steps of 1) of excitement ("How exciting do you find the video?") and aggression ("How aggressive do you find the video?"). The bars were labeled at the left extreme point (0), center (50), and right extreme point (100) using "not exciting", "moderately exciting", and "extremely exciting" and "not aggressive", "mildly aggressive", and "moderately aggressive", respectively, accounting for the fact that the videos that were presented to adolescents contained no more than moderate aggression. Prior to the rating, adolescents were informed that they would not be shown any scenes of severe aggressive behavior involving guns, blood, killing, or scenes that focus on the suffering of a person. Moreover, three videos were shown as anchors that represented example videos at the extreme points and center point of the aggression scale.

Procedure

Immediately after scanning, adolescents completed the state anger subscale of the State Trait Anger Expression Inventory (STAXI) (5), the state anxiety subscale of the State Trait Anxiety Inventory (STAI-C for 14-year-old subjects or STAI-Y for 15- to 17-year-old subjects) (6, 7), and the SAM rating to assess their mood state after viewing the videos. We also performed follow-up emotional evaluations to assess adolescents' mood one day and two weeks after exposure to the videos used in our fMRI experiment. (Note that after the experiment and at follow-ups, all subjects had anger and anxiety levels that were clinically within normal limits. The ratings of emotional valence, arousal, and dominance using the Self-Assessment Manikin did not differ significantly between pre- and post experiment measures).

Data analyses

Behavioral data

Behavioral data were analyzed using SPSS 15.0 (SPSS Inc., Chicago, IL, USA) with applying a significance level of $P < 0.05$ (two-tailed). All data were normally distributed as determined by the Kolmogorov-Smirnov test and homogeneity of variance was verified with Bartlett's test. Note that we were primarily focusing on the video viewing phase and not the decision phase of the fMRI experiment, and therefore analyzed the skin conductance responses (SCR) and brain activation changes during that phase in detail but we also report the reaction times and missing response rate for the decision phase.

FMRI data

Structural and functional imaging data were preprocessed as follows: slice scan time correction was performed using sinc interpolation; small serial head movements were corrected by spatially aligning all volumes to the first volume using rigid body transformation; a linear trend removal was applied; low frequency non-linear drifts of three or fewer cycles for the time series were removed by temporal high-pass filtering; and spatial smoothing of the functional images was performed with a Gaussian filter of 12 mm FWHM. Preprocessing of the anatomical data included reassembling into 1 mm resolution and normalizing into Talairach space using a piecewise linear transformation.

Brodmann areas (BAs) were determined by using the Talairach Daemon Client software (Research Imaging Center, San Antonio, http://ric.uthscsa.edu/) and the co-planar stereotaxic atlas of the human brain (8).

Design

For the fMRI study, a 3 (Aggression) x 3 (Time) factorial design was applied with Aggression (low, mild, moderate) and Time (time1, time2, time3) as within-subject factors. The factor Aggression (low, mild, moderate) reflected the severity of aggressive behavior shown in the videos. The factor Time (time1, time2, time3) reflected the number of exposures to aggressive videos which was implemented by three different fMRI runs.

Multivariate Granger Causality Analysis

The Granger causality concept draws on the principle of temporal predictability (9) assuming that if the current temporal progression of brain activity in one brain region allows the prediction of future temporal progression of activity in another brain region, then the first brain region is assumed to have a causal influence on the second brain region.

To determine whether ROIs were either predominantly driving other ROIs or being driven by other ROIs (or, alternatively, a given ROI may be driven as much as it is driving the other ROIs), we computed input-output ratios for each ROI. Accordingly, for a network represented by a matrix G with ROIs $v_1 \ldots v_k$, where k is the number of ROIs and the causal influence from v_j to v_i is represented by the ij^{th} element of G, the total strength of the causal influence incident on, or emanating from, a particular ROI i is calculated as $I(i)$ and $O(i)$, respectively, as given below (10)

(1) $$I(i) = \sum_{j=1}^{k} G(v_i, v_j) \qquad \text{for } i = 1 \Lambda\ k$$

(2) $$O(j) = \sum_{i=1}^{k} G(v_i, v_j) \qquad \text{for } j = 1 \Lambda\ k$$

The ratio of input to output, I/O, for any given ROI is an indicator of whether it is predominantly driving, being driven, or is neutral.

Note that GC networks were obtained separately for low and moderate aggressive videos for both time1 and time3. The input-output ratio was calculated for each ROI using networks from the resulting four conditions, i.e. time1-moderate aggression $I/O^{(1M)}$, time1-low aggression $I/O^{(1L)}$, time3-moderate aggression $I/O^{(3M)}$ and time3-low aggression $I/O^{(3L)}$. For each ROI, the change undergone by *I/O* with respect to time and aggression were calculated as follows:

(3) Change with Time = $(I/O^{(3M)} + I/O^{(3L)}) — (I/O^{(1M)} + I/O^{(1L)})$

(4) Change with Aggression = $(I/O^{(1M)} + I/O^{(3M)}) — (I/O^{(1L)} + I/O^{(3L)})$

In addition, the Time × Aggression interaction was ascertained as follows:

(5) Interaction = $(I/O^{(3M)} — I/O^{(3L)}) — (I/O^{(1M)} — I/O^{(1L)})$

The statistical significance of each of the above effects were determined using surrogate data where in a null distribution of the corresponding effect parameter was calculated for each ROI using surrogate data, and compared with the corresponding value obtained from real data (10, 11).

RESULTS

Behavioral results

The 3 Aggression (low, mild, moderate) x 3 Time (T1, T2, T3) ANOVA for response times during the decision phases in the fMRI experiment revealed a significant main effect of Aggression ($F_{2,42}$=23.63.65, P<0.001), indicating that response times decreased with level of aggression (Fig. S1). There was a significant main effect of Time ($F_{2,42}$=15.65, P<0.001), indicating that response times decreased over time. In addition, there was a significant interaction effect of Aggression x Time ($F_{4,84}$=6.05, P<0.001), indicating that response times equalized over time for level of aggression. The average missing response rate was less then 2.2% for the entire experiment.

REFERENCES

1. Buss, AH & Warren, WL (2000) *The Aggression Questionnaire* (Western Psychological Services, Los Angeles, CA).
2. Cooley, MR, Turner, SM & Beidel, DC (1995) Assessing community violence: the children's report of exposure to violence. *J Am Acad Child Adolesc Psychiatry* 34:201-208.
3. Spielberger, CD (1999) *State Trait Anger Expression Inventory* (Psychological Assessment Resources, Inc., Lutz, FL).
4. Spielberger, CD (1973) *State-Trait Anxiety Inventory for Children: Professional Manual* (Mind Garden, Redwood City, CA).
5. Spielberger, CD (1983) *State-Trait Anxiety Inventory for Adults: Manual* (Mind Garden, Redwood City, CA).
6. Talairach, J & Tournoux, P (1988) *Co-planar stereotactic atlas of the human brain* (Thieme Medical Publishers, Inc., New York).
7. Granger, C (1969) Investigating causal relations by econometric models and cross-spectral methods. *Econometrica* 37:424-438.
8. Deshpande, G, *et al.* (2008) Multivariate Granger causality analysis of fMRI data. *Hum Brain Mapp*.
9. Deshpande, G, Hu, X, Stilla, R & Sathian, K (2008) Effective connectivity during haptic perception: a study using Granger causality analysis of functional magnetic resonance imaging data. *Neuroimage* 40:1807-1814.

FIGURE LEGENDS

Figure S1. Response times (mean±s.e.m.) during the decision phase. The response times decreased with level of aggression and equalized over time.

Figure S2. Main effect of aggression. The main activation effect of Aggression revealed activation in the bilateral lOFC (left, BA 47; right, BA 45) in addition to a fronto-parieto-temporo-occipital network including the left inferior frontal gyrus (BA 9), rostral anterior cingulate cortex (BA 32), right posterior cingulate cortex (BA 23), bilateral middle temporal gyri (left, BA 39; right, BA 37), and bilateral middle occipital gyri (BAs 19).

Figure S3. Main effect of time. The main activation effect of Time revealed activation in a fronto-temporo-parietal network including the bilateral middle frontal gyri (BAs 10), right precuneus (Prec, BA 31), right lingual gyrus (BA 18), and left middle temporal gyrus (BA 37).

Figure S4. Interaction effect of aggression x time. The main interaction effect of Aggression x Time revealed activation in the left lOFC (BA 10) in addition to the right Prec (BA 31), and bilateral intraparietal lobules (left IPL, BA 39; right ILP, BA 7).

Figure S5. Adaptation for brain regions emerged from the interaction effect of aggression x time. Adaptation factors are shown for low, mildly, and moderately aggressive videos. **A) Right precuneus (Prec) adaptation.** A linear downward trend in

Prec adaptation was observed with increasing aggression in the videos. Right Prec adaptation was positive (sensitization) for the low, mildly, and moderately aggressive videos. **B) Left Intraparietal Lobe (IPL) adaptation.** A linear downward trend in left IPL adaptation was observed with increasing aggression in the videos. Left IPL adaptation was positive (sensitization) for the low, mildly, and moderately aggressive videos. **C) Right Intraparietal Lobe (IPL) adaptation.** A linear downward trend in right IPL adaptation was observed with increasing aggression in the videos. Right IPL adaptation was positive (sensitization) for the low aggressive videos and negative (desensitization) for the mildly and moderately aggressive videos.