ORIGINAL ARTICLE

Increased Frontotemporal Activation During Pain Observation in Sexual Sadism

Preliminary Findings

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Context: Sexual sadism is a psychiatric disorder in which sexual pleasure is derived from inflicting pain, suffering, or humiliation on others. While the psychological and forensic aspects of sexual sadism have been well characterized, little is known about the neurocognitive circuitry associated with the disorder. Sexual sadists show increased peripheral sexual arousal when observing other individuals in pain. The neural mechanisms underlying this unusual response are not well understood. We predicted that sadists relative to nonsadists would show increased responses in brain regions associated with sexual arousal (amygdala, hypothalamus, and ventral striatum) and affective pain processing (anterior cingulate and anterior insula) during pain observation.

Objective: To study the neural correlates of pain observation in sadists and nonsadists.

Design: Case-control cross-sectional study. Sadists and nonsadists viewed 50 social scenes, 25 that depicted a person in pain (eg, one person stabbing another person's hand with scissors) and 25 thematically matched no-pain pictures (eg, one person stabbing a table with scissors, with another person's hand nearby). Pain severity ratings (range, 0 [none] to 4 [severe]) were acquired following each picture presentation.

Setting: Sand Ridge Secure Treatment Center, Mauston, Wisconsin.

Participants: Fifteen violent sexual offenders, including 8 sadists and 7 nonsadists (defined using the Severe Sexual Sadism Scale) who were matched for age, IQ, and education.

Main Outcome Measures: Hemodynamic response revealed by functional magnetic resonance imaging and pain severity ratings.

Results: Sadists relative to nonsadists showed greater amygdala activation when viewing pain pictures. They also rated pain pictures higher on pain severity than nonsadists. Sadists but not nonsadists showed a positive correlation between pain severity ratings and activity in the anterior insula.

Conclusion: These results provide neurobehavioral evidence of unusually heightened sensitivity to the pain of others in sadists.

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SEXUAL SADISM IS A PSYCHIATRIC disorder in which sexual pleasure is derived from inflicting pain, suffering, or humiliation on others. The prevalence of sexual sadism is unknown, and estimates have varied widely from 5% to 11% to 45% to 50% of sexual offenders.[1-4] Sexual sadism is relevant to the assessment of sexual offenders and may be underdiagnosed in forensic settings.[5]

While the psychological and forensic aspects of sexual sadism have been well characterized,[6,7] little is known about the neurocognitive circuitry associated with the disorder. Sadists convicted of sexual assault have shown impairment on some neuropsychological tests (eg, Speech Perception and Trailmaking subtests of the Halstead-Reitan test),[8] and computed tomographic images have shown a significant dilation of the right temporal horn in sadists relative to nonsadists.[9-11] Garnett et al[12] recorded positron emission tomographic findings in 1 sadist and 2 nonsadists during the presentation of erotic and neutral auditory stimuli and reported right lateralized activity during both stimuli in nonsadists, whereas the sadist showed more bilateral activity. However, this finding has not been replicated in a larger study.

The defining characteristic of sexual sadism is the derivation of sexual pleasure by inflicting pain and suffering on others. Sadists are also aroused by passively

watching others in painful situations. Seto et al[13] used penile plethysmography (PPG) to record penile tumescence in sexual sadists and control subjects as they viewed stimuli depicting physical injury caused to others. Relative to controls, sadists had increased PPG responses. The increased responses occurred to sexual and nonsexual stimuli and in consenting and nonconsenting scenarios. The neural mechanisms underlying this unusual response are not well understood. Studies[14,15] comparing individuals with sadomasochistic interests vs those without have reported greater neural and hemodynamic activity in regions of the frontotemporal cortex in response to pictures with sadomasochistic content. However, the participants in these studies did not meet *DSM-IV* criteria for sexual sadism because they preferred consensual sadomasochistic activities and did not derive sexual pleasure from victimizing others. Furthermore, the studies included individuals with sadistic and masochistic interests in the same group. Therefore, the brain mechanisms related to sexual sadism remain unknown.

The lack of neuroimaging studies of sexual sadism may reflect the reluctance of sadists to volunteer for community research because of the risk of drawing attention to their sexual preferences and the potential risk for criminal behavior. It has previously been challenging to conduct neuroimaging research in forensic settings, where the prevalence of sadism is 50 times higher than in nonforensic settings,[16] because they do not contain imaging facilities. Herein, we used a mobile magnetic resonance (MR) imaging system, which was transported to a sexual offender treatment facility, to conduct the first (to our knowledge) functional MR (fMR) imaging study of sexual sadists convicted of a violent sexual offense and committed for treatment. The comparison group of nonsadists were also convicted violent sexual offenders. This ensured that the groups did not differ in deviant sexual behavior, violence, incarceration-related stress, or psychological characteristics that may be more prevalent among violent criminals, such as psychopathic personality.

To investigate the neural mechanisms underlying pain observation in sadists and nonsadists, participants were evaluated using fMR imaging as they viewed picture clips depicting the intentional infliction of pain on others (eg, one person slamming a door on another person's hand) and matched clips depicting nonpainful situations (eg, one person slamming a door shut, with another person's hand nearby) and rated the "pain severity" of each clip. The task was a modified version of a similar task that has been used in healthy controls[17] and engages frontotemporal brain regions, including the anterior midcingulate cortex and the anterior insula. These regions are involved in "affective pain" processing or emotions evoked when observing someone in pain.[18] Our prediction was that sadists would show increased hemodynamic activity in these regions when viewing pain clips, reflecting heightened sensitivity to others' pain. We further predicted that sadists would show increased activity in brain regions implicated in sexual arousal, including amygdala, hypothalamus, and ventral striatum.[19-21] We also conducted a parametric modulation analysis of pain severity ratings. This identifies brain regions whose activity when viewing pain clips is correlated with the subsequent pain severity rating. Because the anterior insula is involved in subjective emotion (awareness of one's own emotional states),[22] we predicted that sadists would show a positive correlation with pain severity ratings in this region. Functional connectivity was also compared across groups using a psychophysiological interaction analysis that investigates the covariation between activity in a selected brain region and other regions by experimental condition. We predicted that sadists would show greater connectivity between brain regions involved in the perception of others' pain (anterior cingulate and anterior insula) and those involved in sexual arousal (amygdala, hypothalamus, and ventral striatum) during pain observation.

METHODS

PARTICIPANTS

Seventeen adult male volunteers were recruited from the Sand Ridge Secure Treatment Center, Mauston, Wisconsin, which provides treatment for persons committed under Wisconsin's sexually violent persons law. Exclusion criteria were age younger than 18 years or older than 65 years, nonfluency in English, reading level lower than fourth grade, IQ less than 75, seizure history, current *DSM-IV* Axis I diagnosis,[23] lifetime psychotic disorder in self or a first-degree relative, and current alcohol or drug use. Information was obtained via self-report and institutional file review. All participants were right-handed, except for 1 sadist who was ambidextrous. All had committed at least 2 violent sexual offenses. Most had committed between 2 and 10, although 1 sadist and 1 nonsadist claimed too many to recall. Each offender's victims were primarily adult females, except for 1 nonsadist whose victims were adolescents and children (his file indicated no diagnosis of pedophilia or hebephilia) and 1 sadist whose victims were male. Except for 1 nonsadist (the participant with child victims), none were incest offenders.

Assignment to sadist and nonsadist groups was based on scores from the Severe Sexual Sadism Scale,[24] an 11-item scale rated according to history of sexual behavior. Items are rated yes (1 point) or no (0 points) and include the following: (1) engages in gratuitous violence toward or wounding of victim; (2) exercises power, control, or domination over victim; (3) humiliates or degrades victim; (4) is sexually aroused by the act; (5) tortures victim or engages in acts of cruelty to victim; (6) shows evidence of ritualism in offense; (7) abducts or confines victim; (8) inserts object or objects into victim's bodily orifice or orifices; (9) mutilates sexual parts of victim's body; (10) mutilates nonsexual parts of victim's body; and (11) keeps trophies (eg, underwear or identification) of victim or keeps records of the offense. To meet sexual sadist criteria, an offender's behavior must include at least 4 items (3 of which must be items 2-5 or item 9).[25] These criteria distinguished between 100 sadists and nonsadistic sexual offenders (diagnosed using the *International Statistical Classification of Diseases, 10th Revision,* or the *DSM-IV*) with 100% accuracy,[24] and the Severe Sexual Sadism Scale has shown high reliability (interrater reliability across all items, $\kappa = 0.86$; range, 0.65-1) and structural validity (coefficient of scalability, $H = 0.83$). In contrast, *DSM-IV* and PPG-based diagnoses have shown lower reliability.[6,7,26] Information was obtained via institutional file review (family, education, social, and criminal history) and was supplemented by interviews (described herein). Each participant was assigned to the sadist or nonsadist group, except for 1 participant who met criteria for 5 Severe Sexual Sadism Scale items but for whom less than 3 were items 2 through 5 or item 9. There were also

Table 1. Participant Characteristics

Characteristic	Sadists (n = 8)	Nonsadists (n = 7)	*t* Statistic	*P* Value
Demographic				
Age, mean (SD), y	51.6 (7.4)	49.9 (9.3)	0.41	.69
Race/ethnicity, No.				
White	5	6	1.03[a]	.57
Nonwhite	3	1		
Education, mean (SD), y	12.5 (0.9)	11.5 (1.7)	1.44	.17
Cognitive				
IQ, mean (SD)	96.9 (14.0)	92.1 (10.1)	0.74	.47
Severe Sexual Sadism Scale				
Total score, mean (SD)	5.9 (0.8)	2.3 (0.8)	7.30	<.001
Psychopathy				
Hare Psychopathy Checklist–Revised				
Total score, mean (SD)	23.9 (5.6)	22.7 (3.8)	0.46	.66
Score range	16-30	16-27		
Factor, mean (SD)				
1, Interpersonal/affective	8.0 (4.7)	7.4 (3.2)	0.27	.79
2, Lifestyle/antisocial	13.1 (2.2)	12.1 (2.8)	0.77	.46
Past Substance Use				
Total time used, mean (SD), y				
Alcohol	5.7 (6.8)	4.6 (4.4)	0.38	.71
Cannabis	10.7 (10.4)	4.3 (7.3)	1.37	.19
Cocaine	1.0 (2.5)	0.01 (0.03)	1.06	.31
Methamphetamine	0.3 (0.7)	0	0.93	.37
Heroin	0	0	. . .	. . .

[a] χ^2 Statistic.

conflicting sadism evaluations in his file. To ensure a clear separation of sadists and nonsadists, this participant was excluded. The sadists' Severe Sexual Sadism Scale scores (n=8) ranged from 5 to 7, slightly lower than the score range of 6 to 8 among a large sample of sadists residing in forensic institutions.[24] The nonsadists' scores (n=7) ranged from 1 to 3. Except for 1, all sadists had a *DSM-IV* sadism diagnosis listed in their institutional files.

One sadist had comorbid paraphilias (eg, voyeurism and fetishism). One nonsadist had exhibitionism; however, this participant was excluded because of motion in the MR image. Four sadists and 2 nonsadists were diagnosed as having paraphilia not otherwise specified (nonconsent). No other comorbid paraphilias were present. The sadists did not significantly differ from the nonsadists in age, race/ethnicity, IQ,[27] education, or past substance use[28] (**Table 1**). Except for 2 nonsadists, all participants were undergoing a 4-phase treatment program and were in phase 1 or phase 2. Phase level did not differ between the groups ($P=.94$), nor did duration (years) of treatment ($P=.83$) or facility commitment ($P=.88$).

Several of the core characteristics of sexual sadism, including callousness and low empathy, are also characteristics of psychopathy.[29] To evaluate psychopathic traits, all participants completed the Hare Psychopathy Checklist–Revised,[30] which uses a detailed interview and file review to rate 20 psychopathic traits (eg, grandiosity, remorselessness, and impulsivity) on a scale of 0 to 2. A score of 30 or more indicates high psychopathic traits. Scores on the Hare Psychopathy Checklist–Revised were used to ensure that sadists and nonsadists did not significantly differ on psychopathic traits (Table 1).

Participants were paid $7.00 per hour, a rate commensurate to pay for work assignments at the facility. Participants provided written informed consent, and the study was conducted in accord with institutional ethical standards.

STIMULI AND TASK

The fMR imaging task is shown in **Figure 1**. Participants viewed 50 dynamic stimuli that depicted action in a 3-picture format timed to mimic natural motion. Each picture series, which lasted for 2.2 seconds, belonged to 1 of the following 2 categories: (1) two people were shown, and one caused pain to the other (eg, one person stabbing another person's hand with scissors), and (2) two people were shown, and one caused no pain to the other (eg, one person stabbing a table with scissors, with another person's hand nearby). A third condition was included in which one person caused damage to an object; however, this was not of interest in the present study. Overall, 25 nonrepeating stimuli were presented in each category. The 3-picture trials from each condition were randomly presented and were followed by a rating scale in which participants rated the preceding trial on the severity of pain caused to a person. The scale displayed a red bar that began at 0 (none) and progressed to 4 (severe) for 4 seconds (Figure 1). The participant pressed a button to stop the bar when it reached his chosen rating. This format was used for simplicity (pressing one button rather than several). A 4-second delay then preceded the next picture. Picture trials were randomly interspersed with fixation trials of the same duration, which were analyzed as a no-picture baseline. This created variable rest periods (10.2, 20.4, or 30.6 seconds when a picture trial was followed by 1, 2, or 3 fixation trials), which induced jitter. The 100 total trials (25 pain, 25 no pain, 25 damage, and 25 fixation) were presented across 2 separate runs lasting approximately 9 minutes each (50 trials per run). Images were projected into the imaging system using an LCD projector, controlled by a PC. Tasks were presented and responses recorded using available software (Presentation; http://www.neurobs.com/).

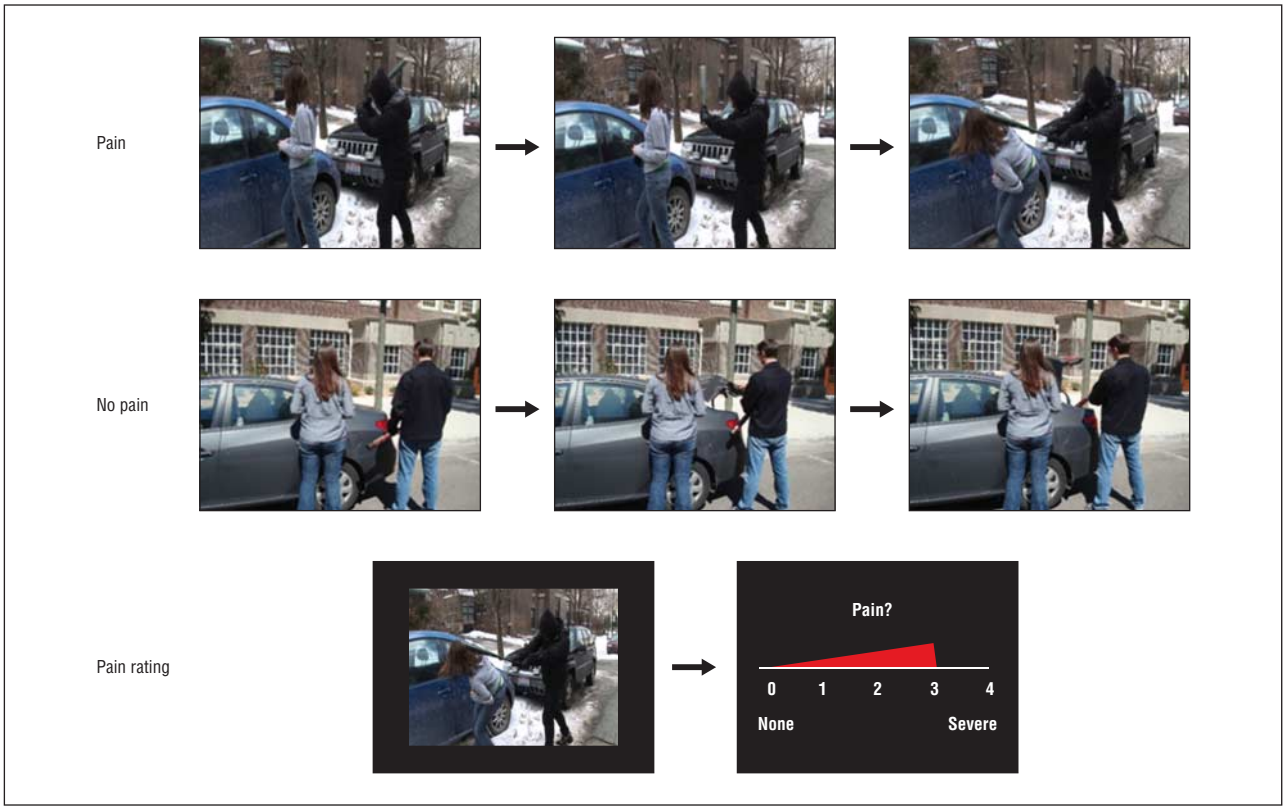

Figure 1. Example of pain and no-pain picture sets, along with the pain severity rating scale.

MR IMAGING DATA ACQUISITION AND ANALYSIS

Magnetic resonance images were collected using a mobile 1.5-T system (Avanto; Siemens) with advanced SQ gradients (maximum slew rate of 200 T/m/s, vector summation of 346 T/m/s, and rise time of 200 ms) equipped with a 12-element head coil. The echoplanar imaging gradient-echo pulse sequence (repetition time, 2000 milliseconds; echo time, 39 milliseconds; flip angle, 90°; field of view, 24 × 24 cm; pixel matrix, 64 × 64; in-plane resolution, 3.4 × 3.4 mm; section thickness, 3.4 × 3.4 mm; and 30 sections) covers the entire brain (150 mm) in 2.0 seconds. Head motion was limited using padding and restraint. Any participant with motion greater than 6 mm was not analyzed, resulting in the exclusion of 1 nonsadist.

Functional images were analyzed using available software (Statistical Parametric Mapping [SPM5]; http://www.fil.ion.ucl.ac.uk/). Images were realigned using a motion correction algorithm unbiased by local signal changes.[31,32] Motion parameters (3 translation and 3 rotations) were entered as covariates of no interest in the model to regress motion-related variance. Functional images were spatially normalized to the Montreal Neurological Institute (MNI) template[33] and smoothed (8-mm full width at half maximum). High-frequency noise was removed using a low-pass filter (cutoff, 128 seconds). All trial types (pain, no pain, damage, and fixation) were modeled as separate events with the canonical hemodynamic response function (2.2-second duration). The rating period was modeled as one regressor for all ratings (4-second duration).

Functional images were computed for each participant that represented hemodynamic responses associated with viewing pain pictures, no-pain pictures, or no pictures (fixation). Group differences were analyzed using a 2 (sadist or nonsadist) by 3 (pain, no pain, or fixation) analysis of variance in SPM5, which included between-participant and within-participant effects.

Hemodynamic responses associated with pain severity ratings were also analyzed using a parametric modulation analysis in SPM5, in which the participant's ratings of each picture were entered as covariates in the first-level analysis. A functional image was computed for each participant that represented the correlation between brain activity and pain severity ratings across all pain pictures. No-pain pictures were excluded because almost all were rated between 0 and 1 on severity by participants. This analysis determined whether increased activity in any brain regions during picture viewing was associated with higher (positive modulation) or lower (negative modulation) pain severity ratings. Including each participant's ratings in the first-level analysis also controlled for potential associations between different ratings across participants and brain activity in main-effect analyses (eg, pain or no pain). One-sample *t* tests were conducted in each group to assess whether positive or negative modulatory effects were present in any brain regions. To determine whether modulatory effects differed across sadists and nonsadists, a 2-sample *t* test was conducted on the parametrically modulated images.

A psychophysiological interaction analysis was also conducted in SPM5. This identifies changes in the coupling between activity in brain regions across different conditions. The maximally activated cluster in the left amygdala was entered as the seed region. The analysis produced statistical maps displaying brain regions whose activity changed significantly with the time course in the amygdala during the pain, no-pain, and fixation conditions. These maps were compared across groups using 2-sample *t* tests.

For all analyses, we defined regions of interest related to affective pain processing, including bilateral anterior midcingulate cortex and anterior insula using central coordinates of these regions previously identified by a meta-analysis[18] of fMR imaging studies examining pain observation. We also defined regions of interest related to sexual arousal, including the bilateral amyg-

dala, hypothalamus, and ventral striatum, by averaging coordinates from fMR imaging studies[19-21] of sexual arousal. Spheres with 8-mm radius were defined around the center coordinate of each region and corrected with a familywise error threshold of $P<.05$ using small volume correction in SPM5. Whole-brain analyses were also conducted to examine activation in other regions during pain observation (thresholded at $P<.05$, corrected; 10 contiguous voxels) and differential effects in sadists and nonsadists (thresholded at $P<.001$, uncorrected; 10 contiguous voxels). Activations were overlaid on a high-resolution structural T1-weighted image from the SPM5 canonical image set, coregistered to MNI space. All coordinates are reported in MNI space.

RESULTS

PAIN SEVERITY RATINGS

A group (sadist or nonsadist) by condition (pain or no pain) analysis of variance was used to assess group differences in pain severity ratings. A group × condition interaction was found ($F_{1,6}=8.24$, $P<.03$), indicating higher pain severity ratings of pain pictures given by sadists relative to nonsadists ($F_{1,14}=7.79$, $P<.02$) (**Figure 2**). No group differences were found for no-pain pictures ($F_{1,14}=0.04$, $P=.86$). Both groups rated pain pictures higher than no-pain pictures ($F_{1,7}=916.62$ for sadists and $F_{1,6}=47.95$ for nonsadists) ($P<.001$ for both).

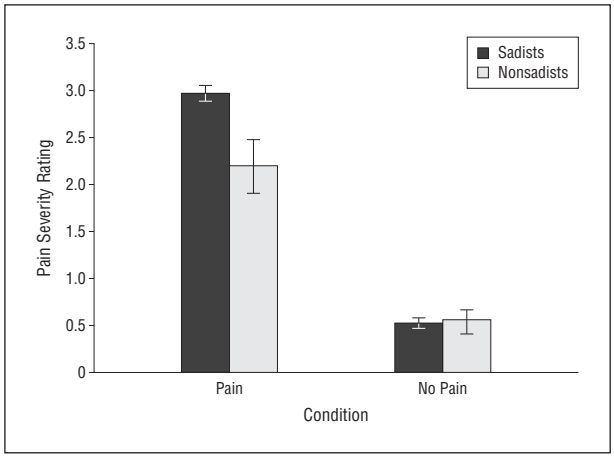

Figure 2. Pain severity ratings by condition in sadists vs nonsadists. Bars indicate standard errors.

BRAIN ACTIVITY DURING PAIN PICTURE VIEWING

The group (sadist or nonsadist) by condition (pain, no pain, or fixation) analysis revealed a main effect of group in the ventral striatum (**Table 2**). Sadists relative to nonsadists showed greater hemodynamic responses to pain pictures ($t_{14}=3.53$, $P=.02$; x=−9, y=15, z=6) and no-pain pictures ($t_{14}=3.50$, $P=.03$; MNI coordinates, x=−6, y=9, z=9) but not during fixation. An interaction was present in the left amygdala (Table 2), indicating greater responses to pain pictures vs no-pain pictures in sadists ($t_7=3.49$, $P=.04$; MNI coordinates, x=−18, y=6, z=−18) but not in nonsadists (**Figure 3**). When the pain condition was examined without reference to the no-pain condition, sadists again showed increased amygdala response relative to nonsadists ($t_6=3.28$, $P=.04$; MNI coordinates, x=−18, y=6, z=−18). An interaction was also present in the right temporoparietal junction (Table 2 and **Figure 4**). Sadists relative to nonsadists showed increased temporoparietal activity when viewing both pain and no-pain pictures. Nonsadists did not show greater responses relative to sadists in any condition.

BRAIN REGIONS MODULATING PAIN SEVERITY RATINGS

One-sample *t* tests conducted on the parametric modulation results for each group separately revealed a significant positive modulation in the left anterior insula in sadists, indicating that increased activity in this region during pain picture viewing was associated with higher pain severity ratings. A similar effect was found in the right anterior insula at a reduced statistical threshold ($P<.001$, uncorrected). This effect was not present in the nonsadists, and the between-group difference was significant (**Table 3** and **Figure 5**). Compared with sadists, nonsadists showed a greater modulation in the more dorsal region of the left insula, as well as the left parahippocampal gyrus, but these effects were not explained by a significant positive modulation in the nonsadists or by a significant negative modulation in the sadists (Table 3).

PSYCHOPHYSIOLOGICAL INTERACTION

The psychophysiological interaction analysis showed greater functional connectivity between the left amygdala and the right anterior insula in sadists relative to nonsadists during pain vs fixation ($t_{13}=3.96$; $P=.06$; MNI coordinates, x=39, y=21, z=3). Functional connectivity did not differ between groups during the pain vs no-pain and no-pain vs fixation conditions.

COMMENT

This study explored whether sexual sadists differ from nonsadists in neural systems underlying pain observation. Consistent with hypotheses, sadists showed increased activity in the left amygdala in response to pain pictures relative to no-pain pictures, whereas nonsadists did not. Sadists rated pain pictures higher on pain severity than nonsadists and showed a positive association between pain severity ratings and activity in the left anterior insula that was not present in nonsadists. Relative to nonsadists, sadists also showed increased activity in the right temporoparietal junction when viewing both pain and no-pain pictures. Sadists but not nonsadists showed greater connectivity between the left amygdala and right anterior insula when viewing pain pictures. These results are indicative of heightened sensitivity to others' pain in sadists, are consistent with prior evidence demonstrating increased sexual arousal during pain observation in sadists, and point to underlying neural mechanisms.

Sadists showed a greater pain vs no-pain picture distinction in the left amygdala relative to nonsadists. The

Table 2. Brain Regions Showing Differential Response to Pain Pictures in Sadists vs Nonsadists

Region (Brodmann Area)	Montreal Neurological Institute Coordinate			*t* Statistic	Small Volume Correction Value[a]	Cluster Size
	x	y	z			
Group × Condition Interaction						
Left amygdala[b]	−18	6	−18	9.50[c]	.045	31
Right cuneus (19)	27	−90	33	16.40[c]	. . .	11
Right temporoparietal junction (39)	42	−63	27	14.07[c]	. . .	15
Main Effect of Condition						
Pain > fixation						
Left insula (13)[b]	−48	12	6	5.51	<.001	59
Right insula (13)[b]	30	21	3	7.88	.002	30
Right anterior cingulate (32)[b]	9	21	36	5.85	.001	71
Hypothalamus[b]	0	−3	−12	3.17	.073	38
Right occipitotemporal junction (39)	30	−75	27	13.81	. . .	4723
Right inferior frontal gyrus (9)	48	9	27	11.51	. . .	122
Left inferior frontal gyrus (6)	−45	0	36	9.46	. . .	136
Right middle frontal gyrus (6)	30	6	60	7.70	. . .	27
Left precentral gyrus (44)	−48	6	12	7.54	. . .	15
Right thalamus	9	−24	−3	7.32	. . .	12
Fixation > pain						
Right precentral gyrus (6)	48	−9	9	8.06	. . .	26
Pain > no pain						
No differences	. . .	. . .	. . .	. . .	. . .	. . .
No pain > pain						
No differences	. . .	. . .	. . .	. . .	. . .	. . .
No pain > fixation						
Right insula (13)[b]	30	21	3	5.17	.001	28
Left insula (13)[b]	−48	12	6	4.17	.011	52
Right anterior cingulate (32)[b]	9	21	36	4.90	.002	50
Left parahippocampal gyrus (19)	−30	−54	−12	13.52	. . .	2024
Right occipitotemporal junction (39)	30	−75	27	13.35	. . .	2288
Right inferior frontal gyrus (9)	48	9	27	12.52	. . .	192
Right thalamus	9	−21	6	9.07	. . .	24
Left inferior frontal gyrus (6)	−45	0	36	9.06	. . .	44
Left midbrain	−6	−21	−9	9.03	. . .	26
Right inferior parietal cortex (40)	33	−48	48	8.11	. . .	80
Left insula (13)	−33	24	3	7.60	. . .	11
Left superior parietal cortex (7)	−18	−66	60	7.54	. . .	19
Left postcentral gyrus (2)	−51	−30	36	7.23	. . .	18
Left middle frontal gyrus (6)	−27	−3	48	7.09	. . .	17
Fixation > no pain						
No differences	. . .	. . .	. . .	. . .	. . .	. . .
Main Effect of Group						
Sadists > nonsadists						
Right ventral striatum	−6	9	9	3.83	.012	26
Nonsadists > sadists						
No differences	. . .	. . .	. . .	. . .	. . .	. . .

[a] Familywise small volume correction values are listed for regions of interest.
[b] Region of interest.
[c] *F* score.

amygdala has been implicated in sexual arousal in healthy controls,[20,21] is more active in men than in women when viewing erotic stimuli (particularly in the left hemisphere),[21] and may be related to sexual orientation and regulation of sexual behavior.[34,35] Increased amygdala activity is not typically reported in studies of pain observation in healthy controls (although not all pain observation studies depict pain caused by another person)[18] and was not found in our nonsadists. This is consistent with our prediction that only sadists would find pain pictures sexually arousing. However, the amygdala is also implicated in general positive and negative arousal,[36] particularly the left amygdala.[37] It is possible the increased amygdala activity in sadists represents a more general positive emotion than sexual arousal, such as excitement. It is unlikely that pain pictures evoked negative emotions in sadists, given their clinical pathologic condition. The study by Seto et al,[13] which used stimuli similar to ours, found that sadists showed increased sexual arousal (measured by PPG) during pain observation. Finally, all sadists had voluntarily consented to treatment, meaning they had previously admitted sexual arousal in causing pain to others.

Compared with nonsadists, sadists also rated pain pictures higher on pain severity. This result is consistent with

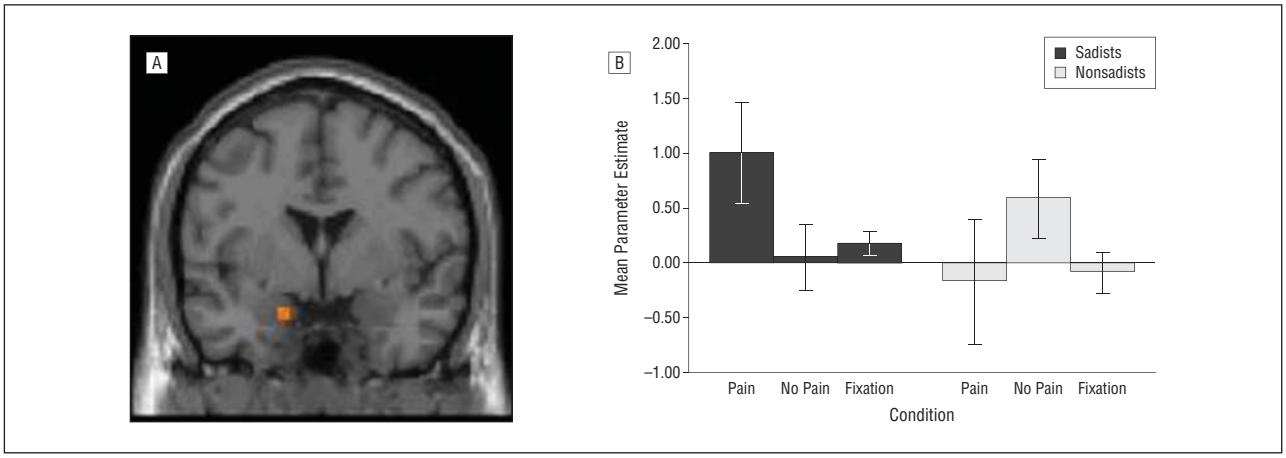

Figure 3. A, Interaction in the left amygdala, representing increased response during pain vs no-pain picture viewing in sadists but not in nonsadists. B, The mean parameter estimates are for the cluster at Montreal Neurological Institute coordinates x=–21, y=–6, z=–21. Bars indicate standard errors.

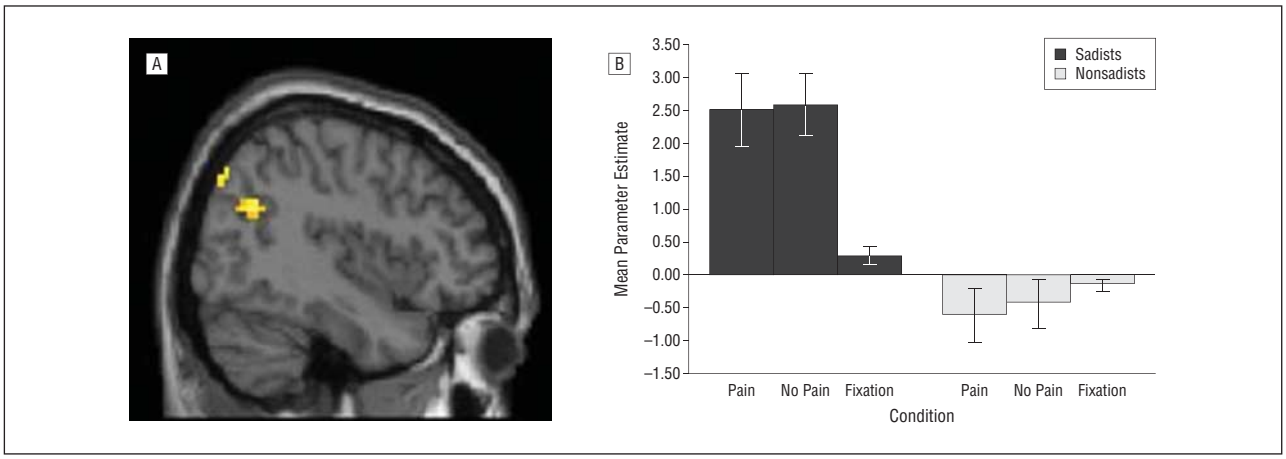

Figure 4. A, Interaction in the right temporoparietal junction, representing increased response during pain vs no-pain picture viewing in sadists but not in nonsadists. B, The mean parameter estimates are for the cluster at Montreal Neurological Institute coordinates x=42, y=–63, z=27. Bars indicate standard errors.

Table 3. Brain Regions Associated With Pain Severity Ratings

Region (Brodmann Area)	Montreal Neurological Institute Coordinate x	y	z	*t* Statistic	Small Volume Correction Value[a]	Cluster Size
Sadists > Nonsadists						
Left insula (13)[b]	–45	12	–6	6.21	.001	18
Right hypothalamus[b]	6	6	–12	3.59	.099	23
Nonsadists > Sadists						
Left insula (13)	–42	12	15	9.83	. . .	13
Left parahippocampal gyrus (36)	–36	–30	–12	6.72	. . .	14
Positive Modulation in Sadists[c]						
Left insula[b]	–45	12	–6	7.87	.009	17

[a] Familywise small volume correction values are listed for regions of interest.
[b] Region of interest.
[c] There were no modulatory effects for positive modulation in nonsadists, negative modulation in sadists, or negative modulation in nonsadists.

sadists' heightened sensitivity to others' pain. To explore the association between brain activity and pain severity ratings, we conducted a parametric modulation analysis of pain severity ratings and brain activity in response to pain pictures. Consistent with predictions, sadists showed a positive correlation between pain severity ratings and activity in the left anterior insula, meaning that increased activity was associated with higher subsequent pain severity ratings. The anterior insula is implicated in the subjective experience of emotion (being

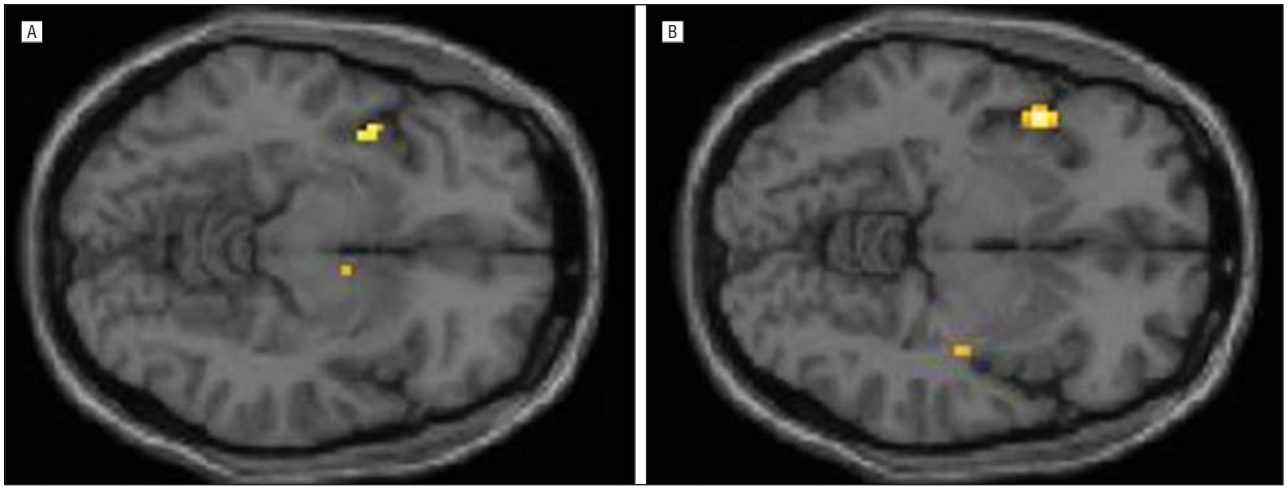

Figure 5. Positive association between left insula activity and pain severity ratings in sadists (A), which is greater than that in nonsadists (B).

aware of one's own emotional states).[22] While both sadists and nonsadists showed increased insula activity when viewing pain pictures, the association between insula activity and pain severity ratings was present only in sadists. Therefore, sadists may draw from subjective emotional experience when evaluating others' pain severity. Nonsadists showed a significant modulation in a more dorsal region of the left anterior insula, which is implicated in executive attention and cognitive control.[38] The parametric modulation analysis cannot determine whether associations between brain activity and pain severity ratings are causal. The association may occur because subjective emotional experience influenced the subsequent rating, or it may occur because the pain severity rating influenced the emotional experience.

Our prediction that sadists would show greater activity relative to nonsadists in the anterior cingulate was not confirmed. Both groups showed increased anterior cingulate activity during the pain and no-pain conditions. This may reflect nonspecific effects in the anterior cingulate related to picture viewing.[39,40] Another possibility concerns the demonstrated involvement of the anterior cingulate in pain anticipation.[41,42] The close thematic matching of the pain and no-pain pictures likely engenders pain anticipation in both conditions because each series consisted of 3 pictures leading up to the pain or no-pain event in the third picture. In addition, sadists may have experienced anticipatory arousal, as suggested by their greater response in the ventral striatum during the pain and no-pain conditions. This region has shown selective recruitment during reward anticipation.[43] In contrast, sadists' heightened amygdala activity to pain pictures but not no-pain pictures suggests specificity to pain outcome, a critical point given that sadists may be aroused by other sadistic activities, such as control or domination. A person using a knife to strike a table, with someone's hand nearby (no pain) rather than directly striking the person's hand (pain), would still be considered the "dominant" actor in the scenario. The association between left insula activity and pain severity ratings in the sadists also seems specific to pain outcome because no such association was present in the no-pain condition.

Sadists also showed increased right temporoparietal activity relative to nonsadists in response to both pain and no-pain pictures. The role of the temporoparietal junction in mentalizing (attribution of mental states, such as beliefs and intentions, to others) is well established.[44] However, investigations have highlighted other functions of this region. It has been implicated in empathy, agency, self-other discrimination, and redirection of attention.[45,46] Decety and Lamm[45] proposed that the right temporoparietal junction is associated with multiple lower-level processes that contribute to higher-level functions, including mentalizing. An explanation that encompasses all of these proposals may lie in the fact that sadists showed increased activity to both pain and no-pain pictures. As already discussed, the close thematic matching of the pain and no-pain pictures likely engenders pain anticipation during no-pain pictures. In any scenario where pain is imminent, sadists may pay closer attention than nonsadists to the thoughts and feelings of the victim because this enhances their sexual arousal when pain is inflicted. In other words, whereas sadists lack sympathy for their victims, they may exhibit empathy (simulating their victims' feelings) when consistent with their goals.

Relative to nonsadists, sadists showed greater functional connectivity between the left amygdala and right anterior insula during pain observation. This result is consistent with our predictions and suggests covariation between the perception of others' pain and sexual arousal in sadists but not in nonsadists. The difference in connectivity was significant between pain pictures and baseline (fixation) but not between pain and no-pain pictures. Therefore, the group difference in connectivity might include pain perception and pain anticipation. These results do not indicate causation. It is possible that increased insula activity represents the detection of others' pain and feeds information to the amygdala, resulting in increased sexual arousal, but the opposite (or both) may also occur.

It is interesting to consider whether the neural abnormalities that characterize incarcerated sexual sadists generalize to individuals in the community with sadistic sexual preferences. Sadists who offend may differ from those who do not in early environment (eg, abuse or inadequate social and family environment).[7] Individuals involved in con-

senting sadomasochistic relationships are also different from criminal sadists because criminal sadists do not generally engage in sadomasochism, nor do those in sadomasochistic relationships generally victimize others.[47] Nonetheless, all experience sexual arousal to pain infliction. Therefore, whether the present results generalize to all sadists is a question for future research.

Limitations of this study should be noted. First, all participants were from an antisocial incarcerated population. Although the study results were consistent with those that have been demonstrated in healthy populations (eg, increased anterior cingulate and anterior insula activity in response to pain pictures), it will be important to directly compare these populations in future studies. Second, our exclusion criteria and controls for potentially confounding variables across sadists and nonsadists (eg, IQ and comorbid psychiatric conditions) resulted in a specialized sample of sadists. However, we note that only 2 sadists were excluded from the study (one because of reading level and another because of MR imaging incompatibility), and the remaining sadists and nonsadists were matched on all relevant variables, with no specific matching efforts (eg, further exclusions) necessary. Nevertheless, the sample size was small, and the results should be replicated in additional samples to help generalize the results to the larger population of sexual sadists. Third, we did not collect self-report ratings regarding sexual arousal to the pictures because we wanted to get a spontaneous reaction rather than one that was complicated by participants' conscious considerations of the degree of sexual arousal they were experiencing (especially if they made responses that did not truly reflect what they were feeling). Although all sadists previously admitted sexual arousal in causing pain to others in general, it will be helpful in future studies to assess this during imaging. Fourth, the participants were older and had resided in a treatment facility for several years. Although to date there are no published studies similar to ours among younger or noninstitutionalized populations with which to compare our results, it is possible we would have observed even stronger group differences in offenders who were temporally closer in proximity to their most recent sexual offense.

The results of the present study may not indicate inherent abnormalities (eg, structural) within these brain regions in sexual sadists but may reflect context-dependent engagement of brain regions that differs across groups. Furthermore, the results could reflect atypical brain mechanisms for pain processing that result in sadism, or sadism could result in atypical recruitment of regions involved in pain processing. These questions can be addressed in future studies using anatomical MR imaging and longitudinal studies of the development of sadism over time.

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