Research Paper

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Contextual modulation of pain in masochists: involvement of the parietal operculum and insula

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Abstract

Pain can be modulated by contextual stimuli, such as emotions, social factors, or specific bodily perceptions. We presented painful laser stimuli together with body-related masochistic visual stimuli to persons with and without preferred masochistic sexual behavior and used neutral, positive, and negative pictures with and without painful stimuli as control. Masochists reported substantially reduced pain intensity and unpleasantness in the masochistic context compared with controls but had unaltered pain perception in the other conditions. Functional magnetic resonance imaging revealed that masochists activated brain areas involved in sensory-discriminative processing rather than affective pain processing when they received painful stimuli on a masochistic background. The masochists compared with the controls displayed attenuated functional connectivity of the parietal operculum with the left and right insulae, the central operculum, and the supramarginal gyrus. Masochists additionally showed negative correlations between the duration of interest in masochistic activities and activation of areas involved in motor activity and affective processing. We propose that the parietal operculum serves as an important relay station that attenuates the affective-motivational aspects of pain in masochists. This novel mechanism of pain modulation might be related to multisensory integration and has important implications for the assessment and treatment of pain.

Keywords: Contextual modulation, Pain, Masochism, Emotion

1. Introduction

The experience of pain is modulated by contextual factors, such as expectations,[9,41] emotions,[40,43,46] or social factors.[19] The motivational priming hypothesis[29] suggests that the motivational state of a person influences responses to internal and external stimuli, and it has been shown that the experimental induction of a positive or negative mood affects pain perception[18,45] as do stimuli related to personal convictions such as religious beliefs.[56] In patients with chronic pain, a deficient modulation of pain by positive emotional stimuli has been shown.[23,44] The perception of the body itself is associated with emotional responses and can modulate pain perception.[1,6,12,33] Longo et al.,[33] for example, applied painful laser stimuli to the dorsum of the hand while subjects were viewing their hand or a wooden object. They showed that viewing one's own body led to a significant decrease in pain perception. This coincided with an increased functional coupling between a network involved in the visual perception of the body (ie, bilateral superior parietal lobules, posterior lateral occipital cortex, and occipito-temporal cortex) and primary and secondary somatosensory cortices, insula, and anterior cingulate cortex (ACC). However, the mechanisms by which this modulation occurs are so far unknown, although multisensory integration processes might be important.[33]

In an effort to elucidate mechanisms of emotional and body-related pain modulation, we examined persons with masochistic sexual behaviors and compared them with nonmasochistic control subjects. Masochists are persons who prefer painful stimulation during the experience of sexual pleasure and are able to modulate pain in masochistic situations. We chose this population as masochists seek out stimuli that people avoid, and they might thus be an interesting population for the investigation of the emotional modulation of pain perception. We hypothesized that masochists might be able to selectively mask the affective-motivational component of pain evidenced by the suppression of activation of the insula and ACC, regions known to mediate the affective-motivational component of pain. This should be driven by multisensory integration areas such as the operculum. We also assumed that processing in areas such as the somatosensory cortex or the sensorimotor areas show normal responses. Because masochists experience pain as rewarding, we assumed that areas involved in the processing of reward such as the ventral striatum and the orbitofrontal cortex might also participate in this pain modulation.[17,31] Additionally, we expected these alterations to be learnt and thus to be related to the duration and/or intensity of masochistic practices.

2. Materials and methods

2.1. Subject characteristics

Thirty-two participants were included in this study: 16 persons with masochistic behaviors recruited through the Internet and

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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from local meetings and 16 control subjects matched for age, sex, and education (**Table 1** presents sociodemographic data).

Masochists and controls did not significantly differ in age, sex, or years of education (**Table 1**). The mean age of first interest in masochism was 17.07 years (SD = 10.01, range = 7-36 years) and first acting out of masochistic practices was at 29.40 years (SD = 13.36, range = 7-47 years; **Table 1**). Masochistic and control pictures were rated for valence and arousal (general, not sexual) using the Self-Assessment Manikin.[5] The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Medical Faculty Mannheim, Heidelberg University, Germany. All subjects gave their written informed consent to participate in the study and were free to terminate the experiment at any time.

Masochists were screened with a specifically developed questionnaire, which included questions about sexuality, experiences with masochistic activities, preferred activities, and the history of their interest in masochistic activities. To be included in the study, they had to consider themselves to be a masochist with a clear preference for the submissive role and more than 50% of their overall sexuality had to be acted out with pain-related masochistic activities (eg, flogging or whipping) in real life, not exclusively online. Subjects were excluded if they met the criteria for any current mental disorder on axis 1 or 2 in the Diagnostic and Statistical Manual for Mental Disorders IV[57] or had a neurological or a chronic pain disorder. All subjects fulfilled the DSM-IV A criterion for sexual masochism disorder (over a period of at least 6 months, recurrent, intense sexually arousing fantasies, sexual urges, or behaviors involving the act [real, not simulated] of being humiliated, beaten, bound or otherwise made to suffer), but none fulfilled the B criterion (the fantasies, sexual urges, or behaviors cause clinically significant distress or impairment in social, occupational, or other important areas of functioning).

2.2. Painful stimulation

An infrared neodymium yttrium aluminium perovskite laser with a wavelength of 1340 nm (El.En. S.p.A., Calenzano, Italy) was used to apply a total of 250 laser stimuli to the dorsum of the subjects' left hand. Laser stimuli were transmitted through an optic glass fiber. The diameter was set at 6 mm (resulting in an irradiated area of about 28 mm^2) by focusing lenses with a pulse duration of 3 milliseconds. Diameter and duration were kept constant across subjects and sessions. Neodymium yttrium aluminium perovskite laser pulses elicit clearly painful "pinprick-like" stimuli of high intensity and short duration. These pulses directly stimulate nociceptive terminals and selectively activate Aδ and C-fibers.[39] The laser stimuli were applied through a laser-application device that allows for a precise, reliable, and reproducible stimulation.[42] Individual pain thresholds were determined twice: subjects received 10 painful laser stimuli and rated their painfulness on a rating scale (0 = no pain, 1 = slight but distinct pain, and 10 = worst pain imaginable). The laser output intensity that resulted in a subjective pain rating of 3 to 4 in the second determination was used in the experiment so that a distinctly painful but tolerable sensation was elicited.

2.3. Study design

Ten masochistic pictures that were selected from the Internet and had been rated for valence, arousal, and relevance by 18 masochistic subjects before the experiment were used. The 10 pictures we chose had been categorized as being clearly related to masochistic interests, related to the participants' own masochistic experiences (ie, the pictures depicted scenes the participants themselves were interested in), and relevant in a masochistic context (Table S1 Supplementary Digital Content [SDC], available online at http://links.lww.com/PAIN/A172). We also presented painful laser stimuli without a picture background (pain-only trials). Additionally, 10 neutral (International Affective Picture System [IAPS] picture numbers for the neutral set A: 2516, 6150, 7010, 7035, 7090; and neutral set B: 7002, 7031, 7050, 7100, 7950), positive (IAPS picture numbers for the positive set A: 1811, 2050, 4653, 8080, 8200; and positive set B: 2070, 2160, 4660, 8420, 8490), and negative (IAPS picture numbers for the negative set A: 3030, 9050, 9290, 9410, 9421; and negative set B: 2141, 2800, 6300, 9250, 9561) slides were chosen from the IAPS.[30]

The pictures were then divided into 2 sets (A and B) and matched for arousal and valence. Within each set, arousal and valence ratings for the nonneutral pictures were also matched. All pictures were displayed in a random order, with pictures from either set A or B (counterbalanced) being paired with painful laser stimulation. Pictures were presented to the subjects in the scanner through MR-compatible goggles (VisuaStimDigital; Resonance Technology, Inc., Northridge, CA). Each picture was presented to the subjects for 18.3 seconds followed by an off-block of the same duration. For the picture-pain trials, pictures were presented for 18.3 seconds while brief laser stimuli were applied. The first laser stimulus started between 0.0 and 0.3 seconds after picture onset, the intertrial interval between laser stimuli was set at 2 seconds and a total of 10 laser stimuli were delivered. This was followed by an off-block of the same duration and by a rating trial during which subjects were asked to rate the average pain intensity and pain unpleasantness of the previous laser stimuli on a visual analogue scale projected onto the goggles. The subjects conducted the ratings by pressing buttons on a response pad (LUMItouch; Photon Control Inc., Burnaby, British Columbia, Canada) with their right hand. Then, a final fixation cross was presented for 18.3 seconds (off-block-2). The order of the different trials was pseudo-randomized.

2.4. Statistical analysis of the ratings and psychological data

The rating results (intensity and unpleasantness of painful stimulation), demographic data, and thresholds were compared with one-factorial analysis of variance with the factor group (controls, masochists) and pain intensity and pain unpleasantness ratings as dependent variables. Pain intensity and pain unpleasantness ratings during presentation of emotional (negative, neutral, and positive) pictures were analyzed using a repeated-measures analysis of variance with the between-factor GROUP (masochists, controls) and the within-factor RATINGS (ie, pain intensity and pain unpleasantness ratings during negative, neutral, positive, and masochistic picture presentation). The normal distribution of the data was checked beforehand using the Kolmogorov–Smirnov test. For years of education, the assumption of normality was not met and differences between masochists and controls were tested using a nonparametric Mann-Whitney *U* test for independent samples. Effect sizes were calculated using Cohen d, which is defined as the difference between 2 mean values divided by SD for the data.

2.5. Functional magnetic resonance imaging data acquisition

Functional magnetic resonance images (fMRIs) were obtained on a 3T TRIO scanner (Siemens, Erlangen, Germany) (repetition

time = 3.05 seconds, echo time = 45 milliseconds, flip angle 90°, matrix 64 × 64, FOV 190, 3 × 3 × 3 mm voxel-size) using an echo planar imaging T2* sensitive sequence. Additionally, a high-resolution 3D MPRAGE (Magnetization Prepared Rapid Gradient ECHO sequence, repetition time = 2.3 seconds, echo time = 2.98 seconds, flip angle 9°, 1 × 1 × 1 mm voxel-size) was obtained for each subject in the same session.

2.6. Preprocessing of functional magnetic resonance imaging data

Functional magnetic resonance imaging data were analyzed using the FMRIB Software Library.[52] The first 5 volumes of each functional run were discarded from further analyses. Nonbrain tissue was removed in both functional and structural images using the brain extraction tool. Then, the following preprocessing was applied to each subject's time series of fMRI volumes: motion correction using MCFLIRT,[22] spatial smoothing using a 5-mm Gaussian kernel of full width at half maximum; grand-mean intensity normalization of the entire 4D dataset by a single multiplicative factor; and high-pass temporal filtering (cut-off 100 milliseconds). Registration was performed in the following 2-step manner: functional images were first registered to the individual anatomy of each subject using boundary-based registration and in the second step registered to the standard MNI152 space using a 12-parameter nonlinear transformation with a warp resolution of 5 mm. Functional MRI statistical analysis was carried out using fMRI Expert Analysis Tool (FEAT) version 6.0. Lower-level FEAT analysis was carried out for each subject. Functional magnetic resonance imaging signal was modeled using a general linear model. Regressors of interest, such as picture trials (masochistic, negative, neutral, and positive), pain-only trials, masochistic picture–pain trials (masochistic, negative, neutral, and positive), and rating blocks, were constructed using the gamma hemodynamic response function (SD = 3 seconds, mean lag = 6 seconds). To remove variations in signal related to movement artifacts, motion correction parameters were included as regressors of no interest. Group analyses were performed using a mixed-effect approach, which included automatic outlier detection. Z-statistic images were limited using clusters determined by $z > 2.3$ and a corrected family-wise error (FWE) cluster significance threshold of $P = 0.05$.[58] Clusters of activation were labeled with the Harvard-Oxford Cortical Structural Atlas and the Harvard-Oxford Subcortical Structural Atlas as implemented in the FMRIB Software Library.

2.7. Functional connectivity analyses

Task-based functional connectivity analyses were carried out using FEAT. The seed region of interest (ROI) was defined by a 10 mm-diameter sphere centered at the peak voxel resulting from the group contrast (masochists > controls) for masochistic picture–pain trials. Then, this ROI was transformed into each participant's native space using the reversed MNI152 template-to-native transformation matrix, and a new 5-mm-radius ROI was defined centered at the peak of the individual fMRI activation cluster.

2.8. Correlational analyses

Correlations of brain activity with picture valence and years of interest in masochistic activities were carried out using FEAT. Differential contrasts from the masochistic picture–pain trials for each subject were used, and the differences in the slope of the correlations examined. Two subjects (1 masochist and 1 control) were excluded for these analyses as their data (respectively years of interest in masochistic activities and picture valence or arousal) were not available.

Assuming that both masochistic context and pain needed to be present to show a pain reduction, we calculated the result of picture valence divided by pain intensity (Val_{int} = valence/pain intensity) and picture valence divided by pain unpleasantness ratings (Val_{unpl} = valence/pain unpleasantness) for each subject. This formula ensured that subjects with high valence and low pain intensity or pain unpleasantness ratings (ie, subjects who rated the pictures as appetitive and reported low pain intensity and low pain unpleasantness during picture presentation; masochists) would score higher on this ratio than subjects with low valence and high pain intensity or pain unpleasantness ratings (ie, subjects who rated the pictures as highly aversive and reported

Table 1
Subject characteristics.

	Masochistic subjects, M (SD); range	Control subjects, M (SD); range	Significance value
Age, y	41.69 (10.56); 22.00-64.00	40.20 (10.60); 23.00-51.00	$t(30) = -0.391$, $P = 0.698$
Sex (N)	8 male; 8 female	4 male; 12 female	$X^2(1, n = 32) = 2.000$, $P = 0.157$
Education, y	11.88 (1.50); 10.00-13.00	11.88 (1.50); 10.00-13.00	$U = 128.00$, $P = 1.000$
Interest in masochistic activities (beginning with years of age)	17.07 (10.01); 7.00-36.00	—	
First acting out of masochistic activities (age in years)	29.40 (13.36); 7.00-47.00	—	
Valence ratings of masochistic pictures*	6.18 (0.89); 4.50-7.60	3.38 (1.23); 1.40-6.20	$t(29) = -7.317$, $P < 0.001$
Arousal ratings of masochistic pictures*	4.31 (1.40); 2.50-7.50	4.21 (1.81); 1.00-6.50	$t(29) = -0.183$, $P = 0.856$
Stimulation intensity (laser output in J) (threshold determination)	2.19 (0.34); 1.75-2.75	1.95 (0.48); 1.25-3.25	$t(29) = -1.618$, $P = 0.116$
Pain rating at stimulation intensity (threshold determination)†	3.47 (1.18); 1.00-5.00	3.53 (1.73); 1.00-7.00	$t(29) = 0.122$, $P = 0.903$
Pain ratings of pain-only trials‡	2.42 (1.71); 0.00-6.00	2.95 ± 2.00; 0.60-8.00	$t(30) = 0.817$, $P = 0.420$
Unpleasantness ratings of pain-only trials‡	2.23 (1.59); 0.00-6.20	2.69 (2.07); 0.80-7.80	$t(30) = 0.704$, $P = 0.487$

Mean values, SDs, and range are displayed. Demographic data and thresholds were compared with independent sample *t* tests with the 2 groups (controls, masochists) as independent samples.
* Valence and arousal ratings were collected using the Self-Assessment Manikin rating scale (1 = negative valence or no arousal, 9 = positive valence or high arousal).
† Pain ratings were conducted on a 11-point numerical rating scale with 0 = no pain at all and 10 = worst pain imaginable.
‡ Pain ratings were conducted on a 11-point visual analogue rating scale with 0 = no pain at all and 10 = worst pain imaginable.

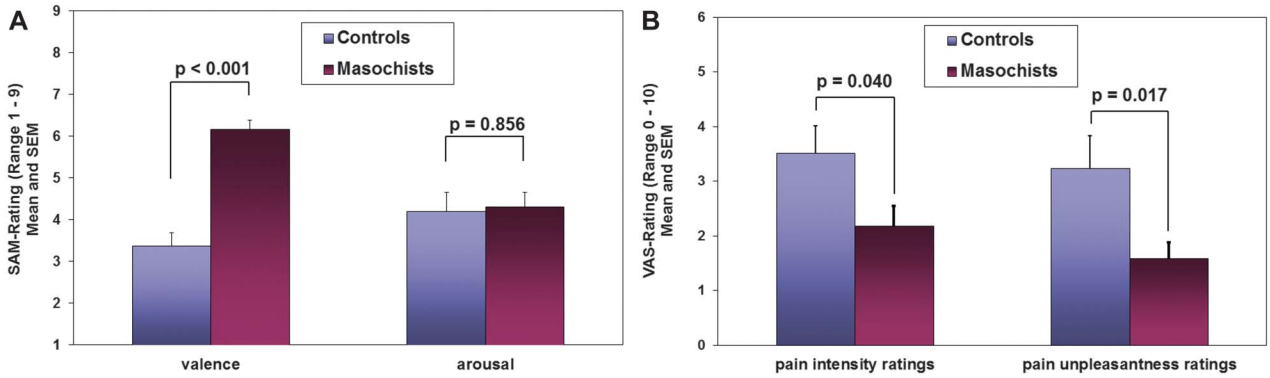

Figure 1. Rating results: (A) Valence and arousal ratings of the masochistic pictures for controls (blue) and masochists (red). (B) Pain intensity and unpleasantness ratings for the masochistic picture–pain trials for controls (blue) and masochists (red), effect sizes for pain intensity rating were Cohen d = 0.72 and for the unpleasantness ratings were Cohen d = 0.82. Data are represented as mean and SEM. SAM, Self-Assessment Manikin scale; VAS, visual analogue rating scale.

high pain intensity and high pain unpleasantness ratings during picture presentation; controls). Rather than assigning the group allocation as masochists or controls, this ratio ensures that possible outliers (ie, subjects who rated the pictures as appetitive while also reporting high pain intensity and high pain unpleasantness ratings and subjects who rated the pictures as aversive while also reporting low pain intensity and low pain unpleasantness ratings) are taken into account. The values obtained were then entered into 2 different FEAT models. One control subject was excluded from this analysis because the data on picture valence were not available.

For the visualization of the correlational results, we first defined a 10-mm-diameter spherical ROI based on the respective group contrast and centered it at the group peak activation cluster. This group ROI was then transformed back into each participant's native space and a new 5-mm-radius ROI was defined centered at the peak of the individual fMRI activation cluster. In the last step, we extracted the time series from this individual ROI and plotted it against the variable of interest (picture valence, years of masochistic activities, picture valence divided by pain intensity ratings, and picture valence divided by pain unpleasantness ratings).

3. Results

3.1. Behavioral and neural processing of pain

As expected, masochists and controls showed no significant differences in pain threshold and tolerance. They did not significantly differ in pain intensity and pain unpleasantness ratings when painful stimuli were presented without an additional emotional context (pain-only trials, **Table 1**). For the imaging data, both groups showed comparable and not significantly different activation in regions involved in the processing of pain, such as the insula, operculum, primary somatosensory cortex, ACC, and thalamus (SDC Figure S1 and Table S2, available online at http://links.lww.com/PAIN/A172).

3.2. Behavioral and neural responses to the pictures

Masochists rated the masochistic pictures as pleasant (mean [M] = 6.18, SD = 0.89, on a scale from 1 "negative" to 9 "positive"), whereas the controls rated them as aversive (M = 3.38, SD = 1.23) ($t(29) = -7.32$, $P < 0.001$, **Fig. 1A** and **Table 1**). Both groups rated the pictures as equally arousing (masochists: M = 4.31, SD = 1.40; controls: M = 4.21, SD = 1.81; $t(29) = -0.18$, $P = 0.86$). There were no significant differences in the evaluation of the other pictures (SDC, available online at http://links.lww.com/PAIN/A172). We found no significant correlation of the valence and arousal ratings of the masochistic pictures for the control subjects ($r = 0.172$, $P = 0.539$) but a significant correlation for masochists ($r = 0.537$, $P = 0.036$).

Both groups showed extended activation in a number of brain regions during the viewing of masochistic pictures (SDC Figure S2, available online at http://links.lww.com/PAIN/A172, and Table S3). The masochists compared with the controls showed significantly higher activation in 2 ventral and dorsal clusters of the right ACC (BA 32) as well as the right anterior insula (**Fig. 2** and **Table 2**). The contrast in the other direction (controls > masochists) did not

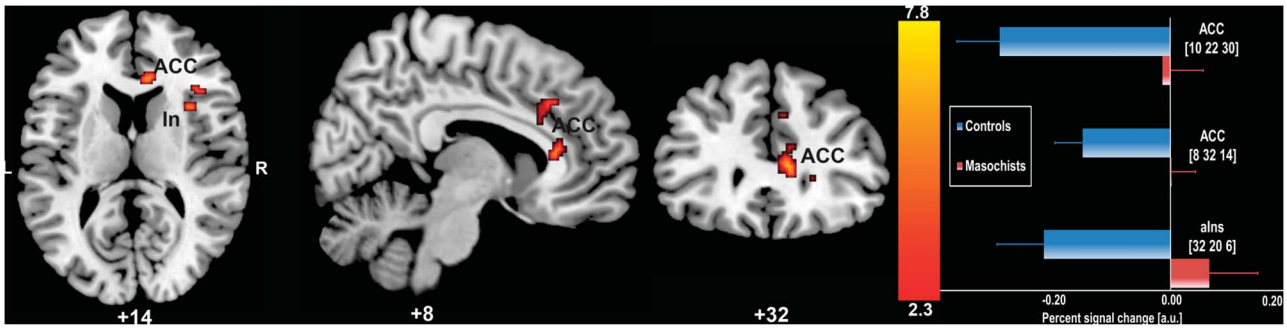

Figure 2. Imaging results of the masochistic picture trials. Areas of increased activation for masochists during the viewing of masochistic pictures compared with controls. Mean signal change (with SEM) is shown on the right side of the image. All results are whole brain family-wise error ($P < 0.05$) corrected. ACC, anterior cingulate cortex; aIn, anterior insula.

reveal any significant differences. The correlation of brain activation with picture valence (ie, pleasantness and unpleasantness of the masochistic pictures) showed a significant difference between masochists and controls in the left superior frontal gyrus (SFG). For masochists, more positive picture ratings were associated with less SFG activation (**Table 2**).

In regard to the other pictures, both groups showed comparable activation for neutral and positive picture trials. Masochists displayed significantly decreased activation of the left superior parietal lobe during viewing of negative pictures when compared with controls (SDC for more details, available online at http://links.lww.com/PAIN/A172).

3.3. Combined masochistic picture–pain condition

When painful stimuli were presented on a masochistic background, a significant difference between groups (masochists and controls) for pain intensity ratings during presentation of masochistic pictures ($F_{(1,30)} = 4.597$, $P = 0.040$) and pain unpleasantness ratings during presentation of masochistic pictures ($F_{(1,30)} = 6.373$, $P = 0.017$) emerged. Masochists indicated significantly lower pain intensity ratings during masochistic picture presentation (masochists: M = 2.18, SD = 1.47; controls: M = 3.52, SD = 2.00; t(30) = 2.14, $P = 0.04$) and pain unpleasantness ratings during masochistic picture presentation (masochists: M = 1.59, SD = 1.17; controls: 3.24, SD = 2.35, t(30) = 2.52, $P = 0.02$) than

Table 2

Imaging results: mean coordinates (millimeter) of brain areas activated for different contrasts and correlations.

Region	Brodmann area	MNI coordinates, mm			z-Stat	Cluster size (voxels)
		x	y	z		
Masochistic picture trials						
Masochists > controls						
Right ACC*	32	10	22	30	2.62	499
	32	8	32	14	2.56	
Right anterior insula	48	32	20	6	3.06	
Masochistic picture trials correlation of valence of masochistic pictures						
Masochists < controls						
Left SFG	9/32	−20	34	54	4.85	485
Masochistic picture–pain trials						
Masochists > controls						
Left M1†	6	−54	6	26	3.63	327
Left parietal operculum	48	−46	−32	24	3.03	
Left central operculum	42	−58	−22	18	3.38	
Right SFG‡	8	22	18	58	3.99	308
Right MFG	8	28	26	46	3.11	
Masochistic picture–pain trials correlation of valence of masochistic pictures						
Masochists > controls						
Right SMG	10	62	−36	32	3.71	444
Right superior parietal lobule§	5	12	−54	76	3.84	333
Left superior parietal lobule	5	−8	−54	72	3.09	
Left M1	5/6	−10	−44	72	3.20	
Masochistic picture–pain trials valence by unpleasantness ratings						
Masochists < controls						
ACC	24	0	12	34	3.39	318
MFG	48	−38	34	18	4.56	315
Right frontal pole	10	8	60	32	3.82	658
MTG	37	44	−32	−10	3.96	353
Masochistic picture–pain trials years of interest in masochistic activities						
Positive correlation						
Right angular gyrus	21	54	−54	22	4.4	683
Right lateral occipital cortex	7	36	−58	64	4.59	361
Negative correlation						
Left M1 or S1	6	−40	0	42	4.06	361
Right paracingulate gyrus‖	32	10	36	32	3.66	302
Right ACC	32	6	36	24	2.92	
Right MFG	6	34	6	42	4.72	300
Left PCC	23	−10	−52	28	3.23	311
Right lateral occipital cortex	39	50	−66	40	4.15	441
Right frontal pole	10	12	60	16	4.04	598
Left frontal pole	10	−20	52	14	3.87	387

* This large cluster consisted of 2 peaks, connected through white matter (possibly because of smoothing artefacts).

† The cluster listed under M1 encompasses the left parietal and central operculum.

‡ The cluster listed under SFG encompasses the MFG.

§ The cluster listed under superior parietal lobule encompasses the left M1.

‖ The cluster listed under paracingulate gyrus encompasses the ACC.

ACC, anterior cingulate cortex; M1, precentral gyrus; MFG, middle frontal gyrus; MTG, middle temporal gyrus; PCC, posterior cingulate cortex; S1, primary somatosensory cortex; SFG, superior frontal gyrus; SMG, supramarginal gyrus.

controls (**Fig. 1B**). We found significant correlations of pain intensity and pain unpleasantness ratings for controls ($r = 0.920$, $P < 0.001$) and masochists ($r = 0.916$, $P < 0.001$). For the emotional modulation of pain by negative, neutral, and positive pictures, we found main effects of EMOTION for pain intensity ($F_{(1,30)} = 765$, $P = 0.003$) and pain unpleasantness ($F_{(1,30)} = 12.499$, $P = 0.001$) but no interactions of EMOTION × GROUP (all $P > 0.231$), SDC for a more detailed analysis (available online at http://links.lww.com/PAIN/A172).

Group comparison revealed that masochists compared with controls showed significantly increased task-related activation in the left opercular cortex, including the parietal and central operculum, the precentral cortex (M1), and a cluster consisting of the right SFG and middle frontal gyrus (MFG) (**Fig. 3** and **Table 2**). The contrast in the other direction (controls > masochists) did not reveal any significant differences. See SDC Figures S3 and Table S4 for the separate task-related activation of the 2 groups (available online at http://links.lww.com/PAIN/A172).

Using the peak voxel of the parietal operculum from the group contrast for the masochistic picture–pain trials as a seed region, we found significantly decreased functional connectivity between the parietal operculum and the bilateral insula, central operculum, bilateral supramarginal gyrus (SMG), right inferior frontal gyrus, and left temporal pole for masochists compared with controls (**Fig. 4A** and **Table 2**). This was due to a large negative correlation of the parietal operculum with the right ACC, bilateral insula, bilateral primary motor cortex, and right thalamus, areas involved in the processing of pain and other salient cues for masochists (**Fig. 4B**), whereas controls did not show this negative connectivity (**Fig. 4C**; SDC Table S5 [available online at http://links.lww.com/PAIN/A172]). In addition, the SFG or MFG showed significantly increased connectivity with the right occipital cortex (x: 24, y: −90, z: 20; z: 3.19, cluster size: 972 voxels) for masochists compared with controls.

Correlation analyses between task-related activity during the masochistic picture–pain trials and picture valence (ie, pleasantness and unpleasantness of the masochistic pictures) showed significantly higher activation in the right SMG, bilateral superior parietal lobule, and left M1 in masochists compared with controls (**Table 2** and **Fig. 5A**). Masochists showed a positive correlation of activation of these areas with positive picture valence, whereas controls showed no significant correlation. Correlation analyses between task-related activity during the masochistic picture–pain trials and pain ratings did not show any significant differences between the 2 groups. Assuming that both masochistic context and pain stimuli need to be presented together to modulate pain perception in masochists, we calculated for each subject a normalization index for valence corrected by pain intensity (Val_{int} = valence or pain intensity) and for valence corrected by pain unpleasantness (Val_{unpl} = valence or pain unpleasantness) (the Materials and methods section). The correlation between task-related activity during masochistic pictures and Val_{int} was not significantly different between masochists and controls. However, the correlation between task-related activity during masochistic pictures and Val_{unp} was significantly decreased in the ACC, left MFG, right frontal pole, and left medial temporal gyrus in the masochists vs controls (**Table 2** and **Fig. 5B**). The slope of the correlation was significantly different between the 2 groups (**Fig. 5B** right). For masochists, a higher ratio (ie, pictures rated as highly pleasant with low pain unpleasantness during picture presentation) correlated positively with activation in these brain regions, whereas for controls a higher ratio (ie, pictures rated as highly pleasant with low pain unpleasantness during picture presentation) correlated negatively with activation in these brain regions.

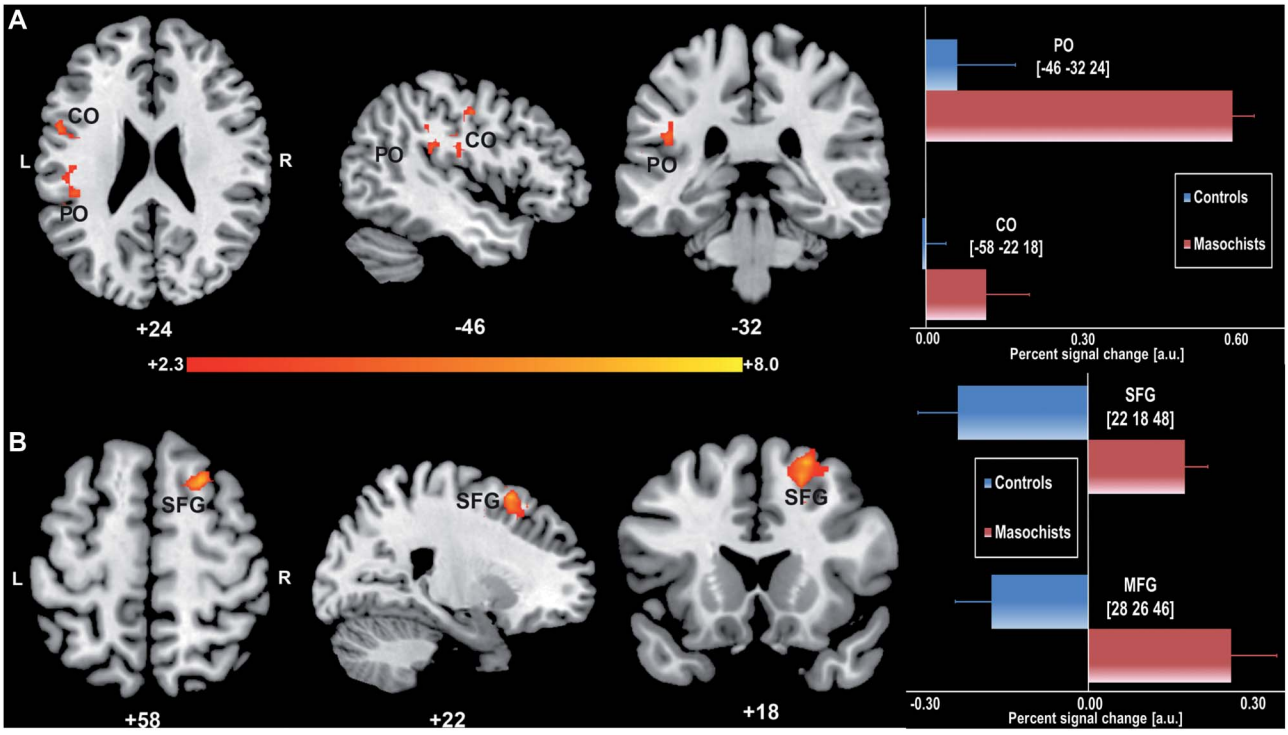

Figure 3. (A and B) Imaging results for the masochistic picture–pain condition. Areas of increased activation for masochists compared with control subjects (L and R). Mean signal change (with SEM) is shown on the right side of the image. All results are whole brain family-wise error ($P < 0.05$) corrected. CO, central operculum; L, left; MFG, middle frontal gyrus; PO, parietal operculum; R, right; SFG, superior frontal gyrus.

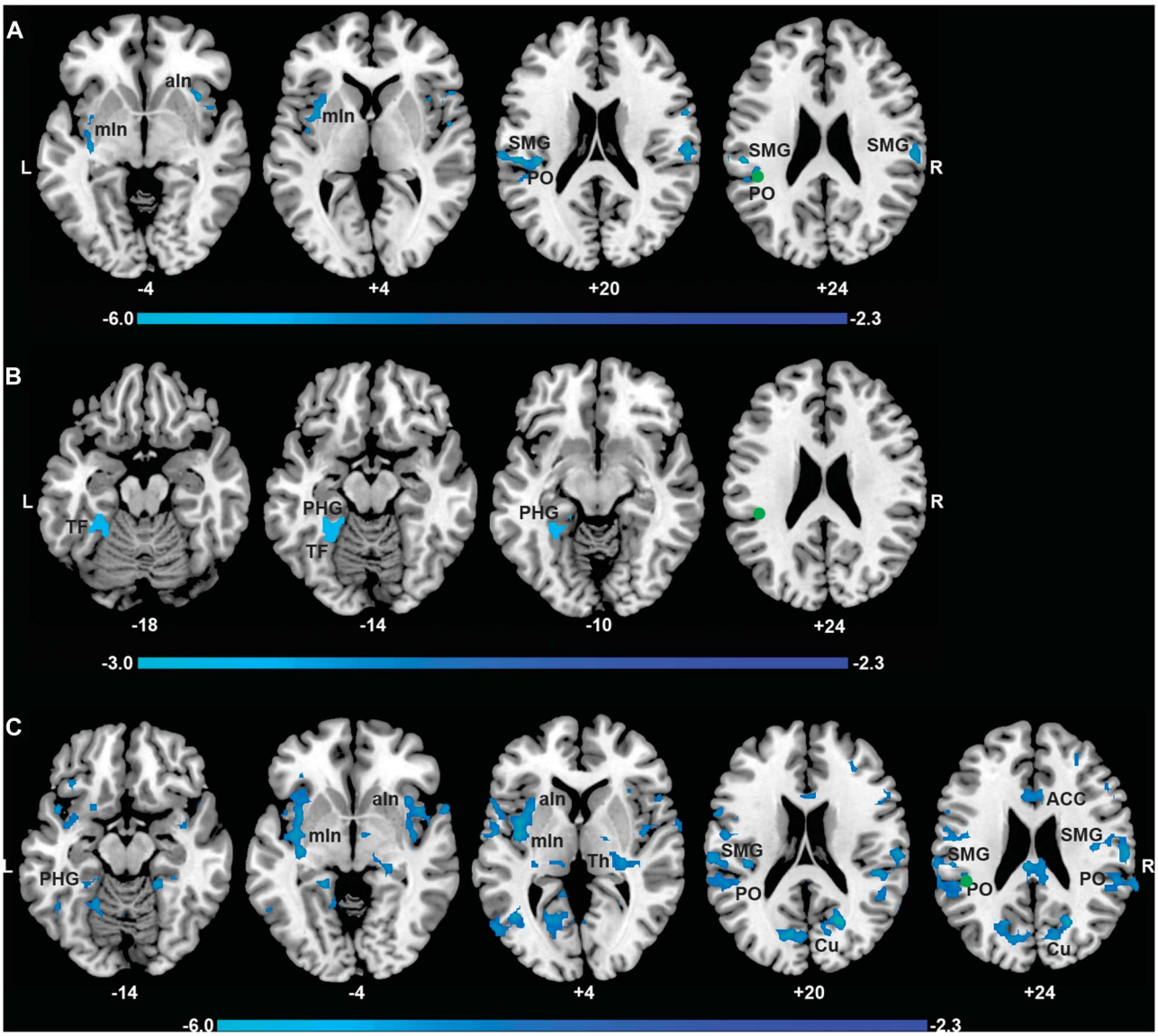

Figure 4. Functional connectivity using the seed region of interest of the left PO (−46, −32, 24) sketched as a stylized green dot for the masochistic picture–pain trials. (A) For masochists compared with controls (differential contrast), we found decreased functional connectivity with the right aIn, left mIn, bilateral PO, and bilateral SMG. (B) Decreased functional connectivity for only control subjects was observed with the right PHG and TF. (C) Decreased functional connectivity for only masochists was present with the PHG, mIn, aIn, SMG, PO, Th, ACC, and Cu. All results are whole brain family-wise error ($P < 0.05$) corrected. ACC, anterior cingulate cortex; aIn, anterior insula; Cu, cuneus; mIn, mid insula; PHG, parahippocampal gyrus; PO, parietal operculum; SMG, supramarginal gyrus; TF, temporal fusiform cortex; Th, thalamus.

The number of masochistic practices subjects engaged in and the ratio of picture valence divided by pain unpleasantness ratings (Val_{unpl}) correlated significantly ($r = 0.567$, $P = 0.043$). We found no significant correlations of duration of interest in masochistic practices with picture valence and pain intensity or pain unpleasantness ratings (all $P > 0.317$). Arousal ratings of masochistic pictures and duration of interest also showed no significant correlation ($r = 0.488$, $P = 0.091$). In the masochists, the duration of interest in masochistic activities correlated negatively and significantly with task-related activation during masochistic picture–pain trials in the left M1, right paracingulate gyrus and ACC, left MFG, left posterior parietal cortex, right lateral occipital cortex, and bilateral frontal pole (**Table 2** and **Fig. 6**), that is, the longer masochists practiced pain-related activities, the lower the activation in these regions. We found an additional, significant positive correlation with task-related activity in the right angular gyrus and right lateral occipital cortex.

3.4. Sex differences

Ratings of pain intensity and unpleasantness showed no significant interactions for SEX with EMOTION or GROUP (all $P > 0.096$).

4. Discussion

We examined the neuronal activation underlying body-related contextual modulation of pain in persons with masochistic behaviors. Masochists reported reduced pain intensity and pain unpleasantness when painful stimuli were presented in a masochistic context. Masochists also rated the pictures as more pleasant (similar to Ref. 53). Pain perception was not different from the nonmasochistic controls when another emotional or neutral or no context was present, suggesting that this difference was specific to the masochistic context. Another study found higher pressure pain thresholds in masochists.[10] However,

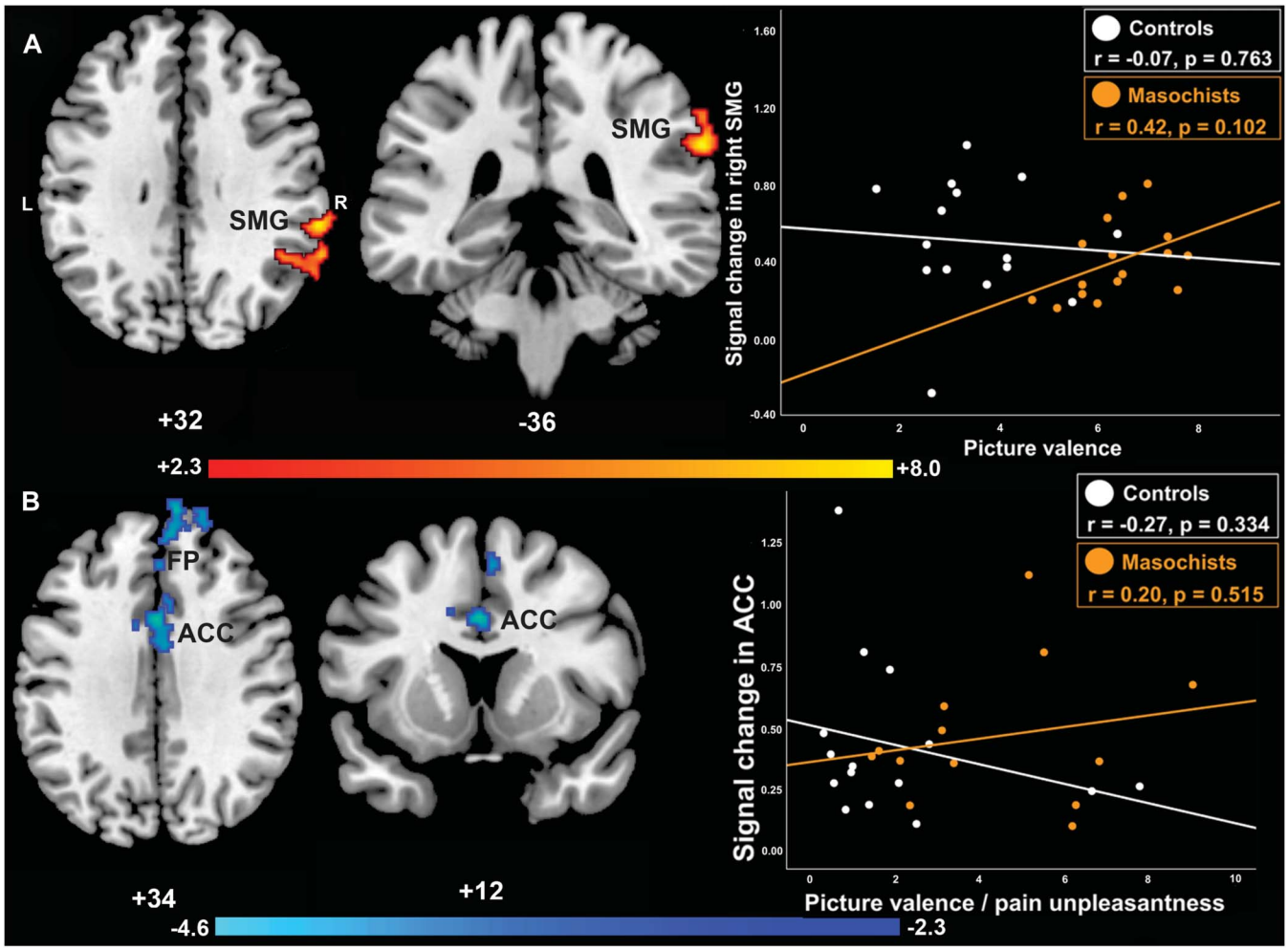

Figure 5. Correlations of brain activation with picture valence, and picture valence or pain unpleasantness. (A) There was a significant difference in the slope of the correlation between brain activation in the right SMG and valence of masochistic pictures between masochists and controls (masochists > controls); right panel: correlation of SMG signal change and picture valence for masochists (in orange) and controls (in white). (B) There was a significant difference in the slope of the correlation between brain activation in the ACC and the division of picture valence by pain unpleasantness between masochists and controls (masochists < controls); for display reasons, the x-coordinate was moved to x = 4 in this figure. Right panel: correlation of ACC signal change and the division of valence and pain unpleasantness ratings for masochists (in orange) and controls (in white). Two masochists were removed from this correlation because their division value was more than 2 SDs above the mean. All results are whole brain family-wise error ($P < 0.05$) corrected. ACC, anterior cingulate cortex; FP, frontal pole; SMG, supramarginal gyrus.

pressure pain stimuli activate different receptors and permit more fine-grained detection of pain thresholds. In our study, we observed reduced pain perception only in the presence of masochistic pictures with high effect sizes for both pain intensity (Cohen d = 0.72) and unpleasantness (Cohen d = 0.82) that are comparable with the effect sizes of opioids.[16] Brain activation patterns of the masochists to nociceptive stimuli outside a masochistic context did not differ from those of controls. However, painful stimuli in a masochistic context yielded increased activation for masochists in the left operculum, the right SFG, and MFG. More interestingly, the left operculum showed negative functional connectivity with the remainder of the activation related to pain and salience processing in masochists but not in controls.

4.1. The role of the opercular cortex

The masochistic picture–pain combination resulted in increased activation of the operculum. The parietal operculum can be cytoarchitectonically subdivided into 4 regions, of which 2 (OP1 and OP4) most closely correspond to the secondary somatosensory cortex,[13] where our activation peaks were located. The parietal operculum is not only involved in pain processing,[14,21,54] but also in somatosensory and visual (multisensory) integration, for example, during synesthesia or correlated visual and somatosensory stimulation,[4,34] related to back projections from higher integration areas.[35] The parietal operculum is active in associative pavlovian nociceptive conditioning and the formation and storage of associative memories,[10] specifically emotional memories.[48] When visual, auditory, and olfactory stimuli were paired with painful electric stimulation, modality-specific secondary sensory cortices were involved in storage and retrieval of the memory trace. The strength of the association between the 2 stimuli (painful stimuli and visual, auditory or olfactory stimuli) should thus be reflected in the activation of this area. We demonstrated that activation of the operculum in masochists was increased when they experienced painful stimuli on a visual masochistic background.

Additionally, masochists had a significantly higher negative correlation of activation in the parietal operculum with several regions involved in the processing of pain and other salient stimuli. An increase of activation in the parietal operculum, as

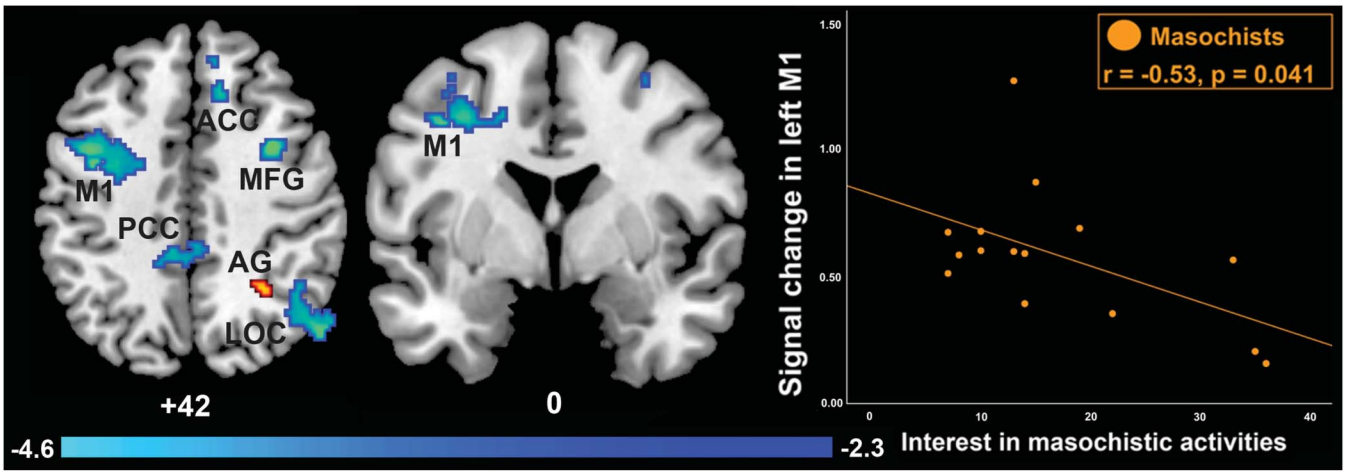

Figure 6. Correlations of brain activation with interest in masochistic activities. Masochists showed a significant positive correlation between years of interest in masochistic activities (in red) and activation of the right angular gyrus and a significant negative correlation (in blue) with activation of the left M1, ACC, and MFG; right panel: M1 signal change correlated with interest in masochistic activities for masochists. All results are whole brain family-wise error ($P < 0.05$) corrected. ACC, anterior cingulate cortex; AG, angular gyrus; LOC, lateral occipital cortex; M1, precentral gyrus; MFG, middle frontal gyrus; PCC, posterior cingulate cortex.

seen during the masochistic picture–pain trials, may functionally suppress activation in the left and right insulae, operculum, and SMG. Connections from the parietal operculum to the insula may act as a principal neural relay for conveying somatosensory input into the limbic system and thus provide a means for associating painful events with relevant affective states.[36] Moreover, lesions in the posterior operculum and the insula create a clinical syndrome called asymbolia for pain in which patients recognize pain but do not seem to suffer from the painful stimulation.[3]

Involvement of the parietal operculum might also point toward a more cognitive-evaluative appraisal of painful stimuli. Kong et al.[26] separated pain perception from its cognitive evaluation and found activation of the bilateral frontal operculum and anterior insula related to the enhanced cognitive evaluation. The subjects informed of pain habituation over time also showed increased activation of this area.[47] Masochists thus might have associated the masochistic context with pain reduction and a more positive cognitive evaluation. In a study of pain perception during the presentation of religious vs nonreligious pictures in religious and nonreligious subjects, decreased pain perception was reported by the religious group while viewing the religious picture. This contextual pain modulation was associated with increased activation of the ventrolateral prefrontal cortex and the pons.[56] We did not find such activation most likely due to the very different contextual modulation and the role of the ventrolateral prefrontal cortex in belief and morale.[2,50] Contrary to our prediction, we did not find increased activation areas involved in the processing of reward such as the ventral striatum in masochists. This further strengthens our assumption that there is an independent pain modulatory process, which involves multisensory integration in the parietal operculum.

4.2. Affective processing during masochistic picture viewing

During the viewing of masochistic pictures, the masochists showed significantly increased activation in the right ACC (BA 32) and anterior insula (BA 48) compared with controls. Although these areas are involved in the processing of sexual arousal,[15,17,24] we found only marginal overlap of our coordinates with those reported in the literature. The ACC activation reported by Ferretti et al. (2005) is more subgenual, whereas the activation reported by Karama et al. (2002) corresponds with our dorsal ACC (dACC) activation. Both studies also reported insula activation; however, that was either more posterior or more ventral. The ventral ACC (vACC), which is more involved in affective processing,[8,11] also seems to process positive memories of objects and experiences (area p32) and codes positive reward values that correlate with subjective pleasure.[20,55] Grabenhorst et al.[20a] also showed that the vACC displayed increased activation when subjects made decisions about the pleasantness or unpleasantness of sensory stimuli. It is possible that masochists ascribe a higher positive value to the depicted scenes and associate them with positive memories. Emotional awareness of one's own internal state[28] and the assessment of the salience of emotional information[11] also are related to activation of the vACC. Masochists furthermore can compare the masochistic pictures to their own emotional and physical experience. This comparison might involve memories of their own (positive) experiences and imagining themselves in the situation with the associated emotions, both involving the vACC.

Masochists also showed increased activation in the dACC during masochistic picture–pain trials. The dACC is more involved in cognitive processing[7,11] and plays a role in novelty, error detection, anticipation, and feedback-mediated decision making.[7,55] It is also involved in mediating the linkage of reinforcer-related information to motor areas involved in the expression of affective responses and goal-directed behavior (for a review, Ref. 49). The masochists might show increased activation in the dACC in response to a situation they experience as positive and strive to obtain. The anterior insula is involved in social-emotional processes[27] and is tightly anatomically linked to the vACC.[11] In sum, the higher ACC and anterior insula activation in masochists might be the result of enhanced affective processing.

4.3. Masochistic picture–pain stimulation and SFG or MFG activation

Masochists showed increased activation of the SFG or MFG in the masochistic picture–pain contrast compared with controls. The right SFG and also MFG have been implicated in declarative

memory processes,[25,32] specifically recollection-based and familiarity-based decisions.[51] The SFG is involved in source recollection, possibly indicating that masochists recall previous masochistic picture-related experiences. The results of our ratio of valence corrected for unpleasantness ratings support these assumptions; here again, the areas involved in memory retrieval showed higher activation for masochists (eg, medial temporal lobe). The enhanced activation of the masochistic group did not extend to areas commonly involved in the viewing of sadomasochistic pictures,[53] suggesting that the memories that were evoked may have been more related to the sensory stimulation and motor activity associated with masochistic activity rather than sexual pleasure. The increased connectivity of the SFG or MFG to the right occipital cortex is in line with more pronounced emotion induction in masochists.[37,38]

Taken together, our results show that masochists report reduced pain intensity and unpleasantness in a masochistic context compared with controls. We showed that the operculum is an important relay station involved in the attenuation of the affective-motivational aspects of the pain sensation in masochists. Masochists additionally engage areas involved in memory and cognitive reevaluation in a masochistic context. This dissociation between the sensory and affective aspects of pain can be linked to altered contextual and multisensory integrative processes in the operculum. Our data also suggest that this may be an acquired behavior learnt through years of masochistic practice. These novel mechanisms of contextual pain modulation might also be useful in treating clinical pain.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Appendix A. Supplemental Digital Content

Supplemental Digital Content associated with this article can be found online at http://links.lww.com/PAIN/A172.

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