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RESEARCH ARTICLE

WILEY AGGRESSIVE BEHAVIOR

Aggression-related brain function assessed with the Point Subtraction Aggression Paradigm in fMRI

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The Point Subtraction Aggression Paradigm (PSAP) measures aggressive behavior in response to provocations. The aim of the study was to implement the PSAP in a functional neuroimaging environment (fMRI) and evaluate aggression-related brain reactivity including response to provocations and associations with aggression within the paradigm. Twenty healthy participants completed two 12-min PSAP sessions within the scanner. We evaluated brain responses to aggressive behavior (removing points from an opponent), provocations (point subtractions by the opponent), and winning points. Our results showed significant ventral and dorsal striatal reactivity when participants won a point and removed one from the opponent. Provocations significantly activated the amygdala, dorsal striatum, insula, and prefrontal areas. Task-related aggressive behavior was positively correlated with neural reactivity to provocations in the insula, the dorsal striatum, and prefrontal areas. Our findings suggest the PSAP within an fMRI environment may be a useful tool for probing aggression-related neural pathways. Activity in the amygdala, dorsal striatum, insula, and prefrontal areas during provocations is consistent with the involvement of these brain regions in emotional and impulsive behavior. Striatal reactivity may suggest an involvement of reward during winning and stealing points.

KEYWORDS
aggression, amygdala, fMRI, prefrontal cortex, PSAP

1 | INTRODUCTION

Violent acts are a worldwide problem with great costs to society and victims (Waters, Hyder, Rajkotia, Basu, & Butchart, 2005). In humans, aggression is operationally defined as behavior directed toward another individual with the intent to cause harm while the target is motivated to avoid it (Bushman & Anderson, 2001). Aggression is typically divided into two subcategories: (i) impulsive/reactive aggression, which is often driven by strong emotions and occurs in reaction to a perceived threat/provocation and (ii) instrumental/proactive aggression, which is goal-oriented and purposeful (Barratt, Stanford, Dowdy, Liebman, & Kent, 1999; Nelson & Trainor, 2007; Siever, 2008). Although aggressive behavior can have survival advantages, reactive aggression is thought to account for most societal problems related to aggression (Nelson & Trainor, 2007). Thus, developing our understanding of the neurobiological pathways associated with reactive aggressive behavior would benefit our ability to develop more effective preventative and intervention strategies for reducing harmful and costly aggressive behavior.

Prevailing theory of the neural circuits underlying aggressive behavior posits that the orbitofrontal cortex (OFC) and the anterior cingulate cortex (ACC) regulate the intensity of negative emotions by inhibiting structures such as the insula and amygdala (Siever, 2008; Strüber, Lück, & Roth, 2008). This neural circuitry may be structurally

and functionally impaired in aggressive individuals as supported by studies of various patient groups (Yang & Raine, 2009). For example, patients with ventromedial prefrontal cortex damage are at higher risk of being reactively aggressive (Grafman et al., 1996). Aggressive psychiatric patients show orbital and prefrontal circuit dysfunction (Best, Williams, & Coccaro, 2002; Blair, Peschardt, Budhani, Mitchell, & Pine, 2006) as well as amygdala hyper-reactivity to angry facial expressions (Coccaro, McCloskey, Fitzgerald, & Phan, 2007). Psychological constructs linked to reactive aggression are positively correlated with amygdala reactivity to angry faces (Beaver, Lawrence, Passamonti, & Calder, 2008; Carré, Fisher, Manuck, & Hariri, 2012; Carré, Hyde, Neumann, Viding, & Hariri, 2012). The amygdala is critically involved in identifying and responding to indices of threat including fear and anger (Strüber, Lück, & Roth, 2008). In economic/social exchange paradigms, the dorsal striatum is activated when punishing someone perceived as unfair, which correlates positively with punishment level, suggesting a role for the dorsal striatum in human aggression (De Quervain et al., 2004; White, Brislin, Sinclair, & Blair, 2014). Together with the insula, these structures are critical for detecting the emotional significance of a stimulus and producing an affective state that could produce aggressive behavior (Nelson & Trainor, 2007; Phillips, Drevets, Rauch, & Lane, 2003). The above suggests that dysfunction in the circuit responsible for regulating emotions, including the OFC/PFC, ACC, amygdala, and the insula, heightens the risk of impulsive aggressive behavior (Siever, 2008; Strüber, Lück, & Roth, 2008).

Aggression-related circuits have been studied with functional neuroimaging (fMRI) and emotional faces paradigms, and have shown activity in the amygdala, ACC, OFC, and ventrolateral PFC in response to angry faces (Coccaro, McCloskey, Fitzgerald, & Phan, 2007; Passamonti et al., 2012). However, a paradigm simulating social interactions may better probe the neurobiological mechanisms associated with the response to and initiation of aggressive behavior in a social context. The Taylor Aggression Paradigm (TAP) represents the most commonly used paradigm for measuring aggressive behavior with fMRI (Beyer, Münte, Göttlich, & Krämer, 2014; Dambacher et al., 2014; Krämer, Jansma, Tempelmann, & Münte, 2007; Lotze, Veit, Anders, & Birbaumer, 2007). The TAP is a competitive reaction task where the winner punishes the loser with an optional level of noxious stimuli (e.g., noise blast or electrical shock: Taylor, 1967). TAP fMRI studies with healthy participants have found reactivity in the mediofrontal gyrus to provocations (i.e., receipt of noxious stimulus: Krämer, Jansma, Tempelmann, & Münte, 2007; Lotze, Veit, Anders, & Birbaumer, 2007). Additionally, increased activity was observed when participants responded aggressively (i.e., delivery of noxious stimulus) in the dorsal ACC, dorsal striatum (Dambacher et al., 2014; Krämer, Jansma, Tempelmann, & Münte, 2007), dorsomedial prefrontal cortex (dmPFC) (Lotze, Veit, Anders, & Birbaumer, 2007), and insula (Dambacher et al., 2014). Krämer et al. (2007) reported ventral striatum reactivity to winning a trial, consistent with its role in reward processing. However, the TAP is not without limitations, including fixed time points, when an aggressive response can be administered, the inability to refrain from administering punishment and a more direct relation to physical aggression than to non-violent forms of aggression. These limitations precipitate a need for alternative paradigms that can be used in an fMRI environment.

The Point Subtraction Aggression Paradigm (PSAP) is a commonly used behavioral aggression paradigm wherein participants earn points (i.e., money) and can steal points from (i.e., aggressive behavior) or have points stolen by an opponent (i.e., provocation), reflecting a more social/non-violent form of reactive aggression (Cherek, 1981). The PSAP has proved useful for probing behavioral responses related to reactive aggression (Cherek, Tcheremissine, & Lane, 2006). It has been demonstrated that criminally-violent individuals (Cherek, Moeller, Schnapp, & Dougherty, 1997; Cherek, Lane, Dougherty, Moeller, & White, 2000; da Cunha-Bang et al., 2017) and patients diagnosed with borderline personality and intermitted explosive disorder (New et al., 2009) respond more aggressively during the PSAP than healthy, non-violent individuals. Thus, the PSAP represents a potentially useful probe for aggression-related brain function.

Recently, Kose et al. (2015) published a study using a modified version of the PSAP in an fMRI environment, comparing brain responses in alcohol-dependent individuals and healthy controls. Healthy controls showed higher activity in the left dorsolateral PFC, left inferior frontal gyrus, right thalamus, and right hippocampus during post-provocation than alcohol-dependent individuals. Across healthy controls and alcohol-dependent individuals, the authors reported a negative correlation between aggression rate (i.e., aggressive responses per monetary response) and activity in lateral OFC, left caudate, and left thalamus during post-provocation.

The aim of the present study was to implement the PSAP in an fMRI environment and evaluate its effectiveness as a probe for aggression-related brain activity. Based on previous studies, we predicted that task-related responses would include brain regions centrally involved in emotion processing and aggression, i.e., the ACC, vmPFC, OFC, amygdala, insula, and both dorsal and ventral striatum. We also performed exploratory whole-brain analyses. Finally, we evaluated the extent to which brain responses to provocations were associated with aggressive behavior within the paradigm and personality measures of aggression. Thus, our study reflects the first description of brain responses in healthy individuals to the commonly used and well-validated version of the PSAP.

2 | MATERIALS AND METHODS

2.1 | Participants

Twenty participants (eight males) were recruited through ongoing studies (H-3-2013-100, H-4-2012-105, H-1-2010-085) at The Neurobiology Research Unit, Copenhagen, Denmark. Participants were healthy according to medical and psychiatric history, physical examination, blood biochemistry, and had unremarkable structural brain scans. All participants tested negative for drug urine screen and had no current/prior drug/alcohol abuse. No participants used any medication during the course of the experiment, except contraceptives.

One participant was excluded for not believing in the deception of the paradigm, leaving 19 participants (eight males) eligible for data analysis. Written informed consent was obtained prior to the study, which was approved by the Ethics Committee of Copenhagen, Denmark and conducted in accordance with the Declaration of Helsinki (H-3-2013-100).

2.2 | Questionnaires

Trait aggression was evaluated using the Buss-Perry Aggression Questionnaire (BPAQ: Buss & Perry, 1992). The Anger-Hostility subscale of the Profile of Mood States (POMS: McNair, Lorr, & Droppleman, 1971) was used as a state measure of aggression. Educational level was self-reported using a score ranging from 1 to 5 where 1 represents primary school education and 5 represents university-level education.

2.3 | Procedure

Instructions were read aloud to participants before the scan. Participants were told that they would be paired with another participant whom they were not allowed to meet, and thereby deceived into believing that they were not playing against a computer. The PSAP is a paradigm wherein participants press one of three buttons (Option 1, 2, and 3) a set number of times to achieve a particular outcome. Pressing the button for Option 1, 100 consecutive times resulted in the participant earning 1 point (5 DKK/0.67 EUR). Pressing the button for Option 2, 10 consecutive times resulted in the opponent having a point taken away (aggressive behavior). Pressing the button for Option 3, 10 consecutive times protected the participant from the opponent stealing a point. Participants responded using a five-finger button-box on the right hand. Options 1, 2, and 3 corresponded to the index, middle, and ring finger keys, respectively. After starting an option, participants were required to finish that option before choosing a new option. There was a minimum of 170 ms between button presses to regulate how quickly participants pressed the buttons. Participants were told that they were randomly assigned to the group that did not keep the points taken from their opponent (i.e., Option 2). Thus, Option 2 is aggressive behavior without direct monetary reward. Participants were told that their opponent was given alternative instructions and, among other things, the opponent player could keep the points they stole from the participant. While in the scanner, participants were reminded of the instructions and completed a 1-min training session immediately before playing two 12-min sessions of the PSAP.

The status of the game, including participant score total, presses and options were projected onto a screen viewed by the participant while lying in the scanner (Figure 1). The paradigm was programmed in E-prime v2.0 (Psychological Software Tools, Pittsburgh, PA). During the task, participants were provoked by having a point stolen every 6-60 s, in the absence of using Option 2 or Option 3 (inter-provocation interval). Due to technical issues, six participants had an IPI of 6–120 s, resulting in fewer provocations (group mean: 15 provocations when

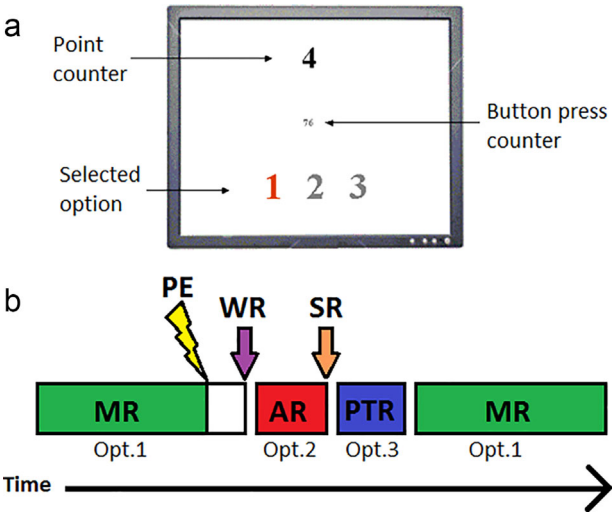

FIGURE 1 (a) Screen displaying what participants viewed while completing the PSAP paradigm, Here the participant is currently in Option 1 (earning-point mode, noted by red-colored digit). (b) Timeline with schematic representation of the task conditions. Conditions modeled as blocks or events are indicated as blocks or arrows, respectively. MR, Monetary Response; AR, Aggressive Response; PTR, Protective Response; PE, Provocation Event; WR, Winning Reward; SR, Stealing Reward, pt., Option

inter-provocation interval = 6–120 s and 20 when inter-provocation interval = 6–60 s). This difference was accounted for when determining aggressive behavior (see below). After completing Option 2 or 3, a provocation free interval of 60 s was initiated. Participants were explicitly aware of the protective effect of Option 3 but not Option 2. The provocation-free interval could only be initiated after the participant had received at least one provocation, ensuring that participants could not avoid provocations throughout the test. Participants were provoked immediately if they did not use Option 2 or 3 for 5 min.

We defined "PSAP aggressive behavior" as the number of Option 2 presses divided by the total number of button presses and the number of provocations received, scaled by 1,000 (i.e., [1000 × No. Option 2]/[No. of total button presses × No. of provocations]). Previous studies have used various measures of aggressive behavior (Carré, Campbell, Lozoya, Goetz, & Welker, 2013); Cherek, Lane, Dougherty, Moeller, & White, 2000; Geniole, Cunningham, Keyes, Busseri, & McCormick, 2015). Our metric adjusts aggressive behavior with respect to both individual differences in button-press rate and received provocations.

We administered a questionnaire after the scan where participants were asked to describe their opponent. Participants were excluded if they clearly indicated that they did not believe they played against a real person (e.g., writing, "I think I played against a computer").

2.4 | Imaging acquisition and fMRI set-up

Scans were acquired on a 3T MRI scanner (mMR Biograph, Siemens, Erlangen, Germany) with a twelve-channel head coil. Blood oxygen level dependent (BOLD) fMRI T2*-weighted gradient echo-planar

imaging (EPI) images were acquired (repetition time, TR = 2150 ms, echo time, TE = 26 ms, flip angle = 78°, 42 slices, slice thickness = 3 mm (no gap), voxel size = 3 × 3 × 3 mm). A total of 335 whole-brain volumes were acquired in each of the two 12-min PSAP sessions. For high-resolution whole-brain three-dimensional structural imaging, we acquired a T1-weighted, gradient-echo sequence (TR/TE = 1900/2.32 ms, inversion time, TI = 900 ms, flip angle = 9°, in-plane matrix = 256 × 256, 192 slices, slice thickness = 0.9 (no gap), voxel-size = 0.9 × 0.9 × 0.9 mm, acquisition time = 4.26 min).

2.5 | Data analysis

Functional neuroimaging data were analyzed with SPM8 (http://www.fil.ion.ucl.ac.uk/spm). The two PSAP runs were pre-processed separately. Single subject functional images were unwarped based on B0 field map images and spatially realigned to the first image. The T1-weighted structural image was then co-registered to the first functional image and the origin was reset to the anterior commissure using acpcdetect (https://www.nitrc.org/projects/art). The co-registered T1-weighted image was normalized into Montreal Neurological Institute (MNI) stereotactic space and the normalization parameters were applied to the functional images. Normalized functional images were smoothed using an 8 mm full-width half-maximum Gaussian kernel. Artifact Detection Tools (http://www.nitrc.org/projects/artifact_detect) was used to identify individual functional volumes that deviated significantly from the subject-specific dataset in terms of motion or signal variability. We used a motion threshold of 2 mm and signal variability threshold of four standard deviations. Flagged volumes were censored when estimating task-related effects.

We defined the following conditions: monetary response (block, from beginning of Option 1 until either a provocation or until the end of Option 1), aggressive response (block, duration of Option 2), protective response (block, duration of Option 3), provocation event (event, at time of provocation), winning reward (event, at end of Option 1), and stealing reward (event, at end of Option 2). See Figure 1 for additional condition details.

We used monetary response as the "baseline condition" and estimated the following contrasts: provocation event > monetary response, aggressive response > monetary response, winning reward > monetary response and stealing reward > monetary response. Single-subject design matrices were estimated using the general linear model in SPM8 to determine condition-specific BOLD responses. Individual contrast images (i.e., weighted sum of beta images) were included in the group level analyses to determine task-related brain responses using one-sample *t*-tests.

Bilateral a priori ROIs for brain regions associated with aggression were defined using WFU PickAtlas toolbox (Lancaster et al., 2000; Maldjian, Laurienti, Kraft, & Burdette, 2003). We defined a PFC region including the OFC as Brodmann Areas (BA) 10, 11, and 47 and an ACC region as BA 24, 25, and 32 (dilation 2D = 1 for both ROIs). Additionally, the amygdala, insula, and striatum (i.e., putamen and caudate) ROIs were defined by the Automated Anatomical Labeling (AAL: Tzourio-Mazoyer et al., 2002).

Cluster size for correction for multiple comparisons was estimated using 3dClustSim (compile date: July 8, 2016), an AFNI program (http://afni.nimh.nih/gov/afni) that uses a Monte Carlo simulation method, to determine cluster extent thresholds for specific ROIs unlikely to have occurred by chance (alpha <0.05) (Forman et al., 1995). A voxel-level statistical threshold of $p < 0.001$, uncorrected, was used for each ROI and whole-brain analyses. Clusters within the amygdala, ACC, PFC, insula, and striatum (both dorsal and ventral) were considered statistically significant with a voxel extent of $k \geq 1$, 27, 27, 22, and 25 voxels, respectively. Whole-brain clusters were considered statistically significant with a voxel extent of $k \geq 173$ voxels. Anatomical areas included in whole-brain clusters were determined with xjview (http://www.alivelearn.net/xjview).

Descriptive statistics of PSAP behavioral data and questionnaire data were analyzed using IBM®SPSS® Statistics, v20. To ensure that consistent, task-responsive brain areas were evaluated against personality and behavioral measures, mean contrast estimates from statistically significant task-responsive clusters within ROIs were extracted from SPM, and included in regression analyses. Linear regression analyses were performed to evaluate the association between PSAP aggressive behavior and trait aggression and task-response in the five ROIs. Sex was included as a covariate considering evidence for differences in aggressive behavior (Zeichner, Parrott, & Frey, 2003). $p \leq 0.05$ was considered statistically significant.

3 | RESULTS

3.1 | Participant characteristics

Demographic, questionnaire, and behavioral data are listed in Table 1. A histogram of the frequency of aggressive responses is provided as supplementary material (Supplementary Figure S1). Two participants did not use the aggressive response and were excluded from aggression and stealing reward contrasts. Two participants used the aggressive response only during the second PSAP session. All

TABLE 1 Demographic, personality, and PSAP behavioral information

	Mean	S.D.	Range
Age (years)	24.6	2.9	20–31
Educational score	3.8	1.6	1–5
BPAQ	56.5	15.6	40–87
POMS anger/hostility	3.5	3.6	0–14
No. of Points	25.1	5.0	15–33
No. of Provocations	18.3	4.1	13–29
PSAP Aggressive Behavior	3.5	3.1	0–13.8
Option 1 presses	4,381	489	3,300–4,991
Option 2 presses	328	295	0–1,360
Option 3 presses	541	182	190–881

BPAQ, Buss–Perry aggression questionnaire; POMS, profile of mood state.

participants used the protective response. Participant behavioral responses were similar to previous PSAP studies using similar settings. Participants selected the aggressive option approximately twice as often as they received provocations (mean instances choosing option 2: 32.8; mean number of provocations: 18.3) and selected the aggressive response on average 1.3 times per minute, within the range of previous reports (0.6–2.2 times per minute: Carré & McCormick, 2008; Cote, McCormick, Geniole, Renn, & MacAulay, 2013; Geniole, Carré, & McCormick, 2011; McCloskey, Berman, & Coccaro, 2005; New et al., 2009).

3.2 | Functional imaging data

Brain responses to provocations, aggressive behavior, winning, and stealing reward within each ROI are available in Supplementary Table S1, and whole-brain responses are available in Supplementary Table S2 and in Supplementary Figure S2.

3.2.1 | Provocation event > monetary response

We found statistically significant brain reactivity in each of our five ROIs (ACC, PFC, dorsal striatum, insula, and amygdala) when participants received provocations (Figure 2 and Supplementary Table S1).

3.2.2 | Aggressive response > monetary response

We observed no statistically significant reactivity in our ROIs during aggressive responding (Figure 2 and Supplementary Table S1).

3.2.3 | Stealing reward > monetary response

Within our ROIs, we observed statistically significant reactivity bilaterally in the dorsal striatum (i.e., caudate) in response to removing a point from the opponent's total (Figure 2 and Supplementary Table S1).

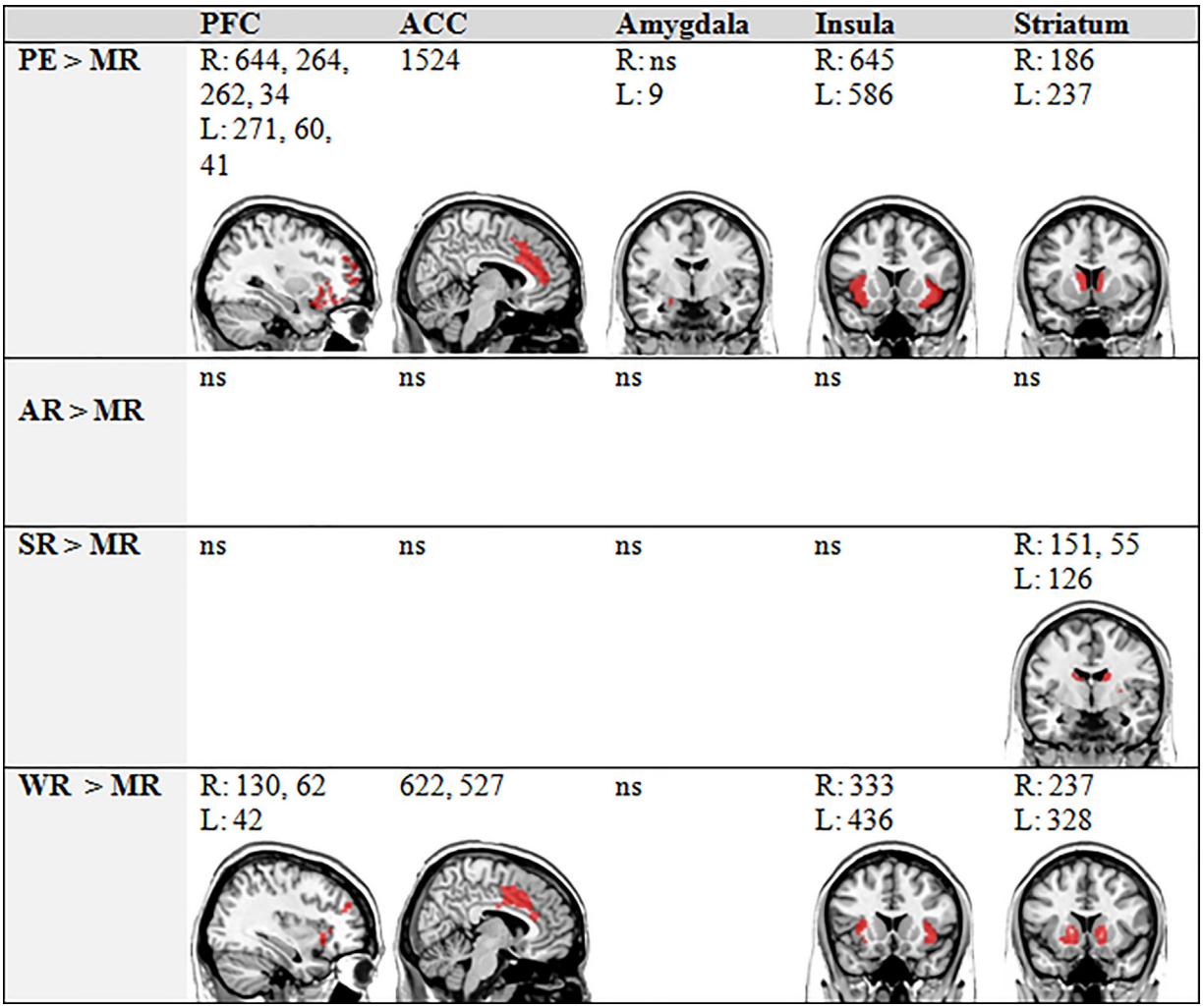

FIGURE 2 Task-related reactivity within regions of interest. PFC, Prefrontal cortex including orbitofrontal cortex. ACC, Anterior cingulate cortex. MR, Monetary Response, PE, Provocation Event, AR, Aggressive Response, SR, Stealing Reward, WR, Winning Reward, L, left, R, right, and ns, not significant. Clusters reflect a voxel-level significance threshold of $p < 0.001$, uncorrected, with region specific cluster extent thresholds

3.2.4 | Winning reward > monetary response

When participants won a point, we found increased bilateral reactivity in the PFC, ACC, insula, and ventral striatum (Figure 2 and Supplementary Table S1).

3.3 | Task aggression, trait aggression, and brain responses to provocations

Aggressive behavior in the PSAP was significantly positively associated with reactivity of the PFC, ACC, dorsal striatum, and insula to provocations (i.e., provocation events > monetary response), but not significantly associated with amygdala reactivity (Table 2). Trait aggression, measured by the BPAQ, was not significantly associated with brain reactivity for any ROI or PSAP aggressive behavior.

3.4 | Striatal response to stealing versus winning: Post hoc analysis

Following our observation of significant striatal reactivity to both the stealing and winning reward conditions, we compared these responses as a post hoc analysis. We observed greater reactivity in the ventral striatum/nucleus accumbens to winning a point than to stealing a point. Conversely, we observed greater reactivity in the dorsal striatum/caudate to stealing a point than to winning a point.

3.5 | Paradigm length: Post hoc analysis

We compared brain response patterns from both 12-min PSAP sessions to the first PSAP session to determine whether only one run of the paradigm provided informative neuroimaging results. We observed very similar task-related brain responses based on data from only the first PSAP session, as compared to both sessions (Supplementary Figure S3). Notably, amygdala reactivity to provocations increased and reactivity in the ACC during aggressive responding became significant. Striatal response to stealing reward > monetary response was similar but no longer statistically significant. This contrast included only 15 participants because four did not use Option 2 during the first PSAP session.

4 | DISCUSSION

We implemented and validated the use of the PSAP within an fMRI environment and demonstrated for the first-time fMRI outcomes in healthy individuals. Consistent with engaging aggression-related neural pathways, we observed distributed responses in brain regions centrally involved in aggressive behavior. We observed significant responses to provocation in the amygdala, PFC, ACC, and insula. We observed responses in the ventral striatum to winning (winning reward > monetary response) and in the dorsal striatum to stealing (stealing reward > monetary response). Evaluation of the association between brain responses and behavior and personality measures indicated a positive correlation between neural responses to provocations and PSAP aggressive behavior, supporting the behavioral relevance of these aggression-related reactivity measures. Here, we also discuss paradigm limitations and opportunities for improvement when used in the fMRI setting. Taken together, these data provide support for the use of the PSAP within an fMRI setting for probing neural processes underlying aggressive behavior.

4.1 | Functional imaging results

We observed provocation-related brain activity in the PFC (including the OFC), ACC, insula, amygdala, and dorsal striatum, possibly reflecting the complex neural response to a salient stimulus, evaluating potential behavioral responses and controlling immediate impulses. Participants cannot respond immediately to a provocation but must finish the current option. This requires participants inhibit immediate impulses to respond, possibly reflected by increased PFC (especially OFC), and ACC activity, areas known to regulate and inhibit behavioral impulses (Siever, 2008). Activity in the PFC has also been linked to monetary wins and losses (Kringelbach & Rolls, 2004) and decision-making (Wood & Grafman, 2003), consistent with the provocation

TABLE 2 Associations between regional brain responses to provocations, PSAP aggressive behavior, and trait aggression

Outcome	Region	Estimate	S.E.	95%C.I.	*p*-value	R^2
PSAP aggressive behavior	Amygdala	0.64	1.24	−0.42; 1.72	0.22	0.15
	PFC	1.26	0.60	−0.01; 2.54	0.05	0.27
	ACC	1.09	0.52	−0.01; 2.18	0.05	0.27
	Striatum	1.44	0.41	0.57; 2.31	0.003	0.47
	Insula	1.17	0.51	0.10; 2.24	0.03	0.30
BPAQ total score	Amygdala	2.84	2.32	−2.07; 7.77	0.24	0.27
	PFC	−2.41	3.06	−8.88; 4.06	0.44	0.23
	ACC	0.31	2.67	−5.34; 5.96	0.91	0.20
	Striatum	1.04	2.43	−3.22; 7.11	0.44	0.23
	Insula	−0.31	2.66	−5.96; 5.33	0.90	0.20

BPAQ, Buss-Perry Aggression Questionnaire; S.E., Standard Error; C.I., Confidence Interval.

event including the loss of a point (money) and a subsequent decision about how to respond. In previous studies using the TAP, provocation increased activity in the mediofrontal gyrus (Krämer, Jansma, Tempelmann, & Münte, 2007; Lotze, Veit, Anders, & Birbaumer, 2007) and in the recent PSAP fMRI study (Kose et al., 2015) healthy controls showed greater activity in the left dorsolateral PFC, left inferior frontal gyrus, right thalamus, and right hippocampus during post-provocation than alcohol-dependent subjects: these were all areas responsive to provocations in the current study (see Supplementary Table S2 for whole brain clusters). In the present study, prefrontal activity was more prominent in the right hemisphere, consistent with studies of inhibitory processing demonstrating a particular role for right inferior frontal cortex (Aron, Robbins, & Poldrack, 2004; Aron, Robbins, & Poldrack, 2014). Thus, our PSAP results in response to provocation are consistent with the existing literature, supporting PSAP as a useful tool for probing prefrontal regulatory processes.

The amygdala, ACC, dorsal, and ventral striatum and insula are centrally involved in detecting salient stimuli and producing appropriate affective states and behavioral responses (Phillips, Drevets, Rauch, & Lane, 2003; Strüber, Lück, & Roth, 2008). Additionally, the amygdala is responsive to stimuli signaling threat/provocations (Strüber, Lück, & Roth, 2008; White, Brislin, Sinclair, & Blair, 2014). Similar structures, including mPFC, are responsive to anticipation of aversive stimuli (Pohlack, Nees, Ruttorf, Schad, & Flor, 2012). As such, activity in these areas following provocation may reflect the processing of a salient/aversive/threat stimulus.

We observed significant ACC activity while participants behaved aggressively, but only when considering the first run of the paradigm, possibly reflecting a sensitivity of this measure to habituation. During stealing reward (stealing reward > monetary response) we observed increased reactivity bilaterally in the dorsal striatum. Activity in dorsal striatum and the ACC has also been reported during aggressive responding in the TAP (Krämer, Jansma, Tempelmann, & Münte, 2007; Lotze, Veit, Anders, & Birbaumer, 2007). Consistent with TAP fMRI studies (Dambacher et al., 2014; Lotze, Veit, Anders, & Birbaumer, 2007), we did not observe increased amygdala activity during aggressive responses. This may reflect the amygdala's function more as a threat or salience detector, responding to provocations or threatening faces (Coccaro, McCloskey, Fitzgerald, & Phan, 2007) rather than facilitating performance of aggressive acts.

Consistent with its role in reward processing, winning a point (winning reward > monetary response) resulted in a response within the ventral striatum (Breiter, Aharon, Kahneman, Dale, & Shizgal, 2001; Knutson, Westdorp, Kaiser, & Hommer, 2000; Krämer, Jansma, Tempelmann, & Münte, 2007). Participants also showed increased striatal reactivity to stealing a point. This response was located more dorsally than the striatal response to winning reward. Caudate activity is increased when actively punishing someone perceived as unfair, which has been interpreted as reflecting a rewarding feeling (De Quervain et al., 2004; Krämer, Jansma, Tempelmann, & Münte, 2007), but also the coordination of motor responses (White, Brislin, Sinclair, & Blair, 2014). Additionally, the caudate is critical for reward-based behavioral learning (Haruno et al., 2004). Thus, activity in this region when stealing might reflect a desire to "teach the opponent a lesson" and the expectation of a reward in the form of fewer provocations. Notably, there is no direct incentive to steal as participants do not keep the point stolen from their opponent and participants do not see the opponent's score or receive visual feedback to this action. More salient feedback following this action is a modification to the PSAP that may further motivate aggressive behavior in participants. Indeed, previous work using the PSAP found that aggressive behavior on the task was positively correlated with the extent to which participants enjoyed the task (Carré, Gilchrist, Morrissey, & McCormick, 2010), supporting the idea that the intrinsic reward value of aggression may outweigh the costs of aggressive behavior on the PSAP. Collectively, these findings support the theory that reward-related activity when punishing or hurting someone perceived as aggressive may contribute to reactive aggression (Krämer, Jansma, Tempelmann, & Münte, 2007).

Aggressive behavior in the PSAP was positively associated with brain reactivity to provocations in the PFC, ACC, insula, and dorsal striatum, suggesting a link between neural reactivity or sensitivity to provocations and aggressive behavior. In contrast, Kose et al. (2015) reported a negative correlation between aggression rate (i.e., aggressive responses per monetary response) and activity in lateral OFC, left caudate, and left thalamus during post-provocation, across alcohol-dependent, and healthy controls. These authors used a modified version of the PSAP, including several methodological differences from our study, making direct comparison between studies difficult. For example, Kose et al., (2015) only allowed button-presses while a blue dot flashed on the screen, did not include a protective option and only data from one out of three sessions were evaluated based on a minimum of aggressive responses more evenly spread over time. The lack of a protective option obviously restricts behavioral options for the participant and may confound the aggressive behavior due to fewer non-aggressive behavioral options (McCloskey, Berman, & Coccaro, 2005; Tedeschi & Quigley, 2000). This highlights methodological variability of the PSAP that must be considered carefully to maximize its usefulness for probing aggression-related neural correlates.

Trait aggression (BPAQ) was not correlated with PSAP aggressive behavior, which may reflect that we are underpowered to identify such effects, given our current sample size. Alternatively, this may be due in part to a culture norm, where aggressiveness is particularly unacceptable and therefore misrepresented in self-reports, undermining its relation to measured behavior. Mean BPAQ in our sample (Table 1) is low relative to previously reported normative data (women: 68.2 ± 17, men: 77.8 ± 16.5: Buss & Perry, 1992). However, our data showing that brain responses to provocations are related to task-related behavior suggests that the PSAP may be useful in studies probing neural processes underlying excessive or pathological aggression.

Implementing the PSAP in an fMRI environment presented practical constraints. The original paradigm included six 25-min sessions (Cherek, 1981), subsequently reduced to one 25-min session (Golomb, Cortez-Perez, Jaworski, Mednick, & Dimsdale, 2007). We collected data over two 12-min sessions. This task length may result in participants

disengaging from the task, experiencing physical fatigue in the hands/fingers, and/or habituation in the BOLD response. As such, it is notable and promising that brain responses during the first 12-min session were similar to the two sessions combined. This supports the use of a single, 12-min session in future studies. Indeed, neuroendocrine studies find similar positive correlations between competition-induced fluctuations in testosterone and subsequent aggressive behavior measured using either a single 10-min session of the PSAP or three 7 min sessions of the PSAP (Norman, Moreau, Welker, & Carré, 2015).

4.2 | Considerations and limitations

Our sample size is limited, reflecting a preliminary evaluation of this paradigm, hindering the ability to test for sex-specific effects. Future studies seeking to reproduce our observed task-response estimates and associations with aggressive behavior and trait aggressiveness should aim to include larger samples to more strongly support behavioral relevance of brain response measures from this paradigm.

Our implementation of the PSAP closely follows its well-assessed and widely used form for laboratory-provoked aggression. A limitation is that participants are not required to use the aggressive response and therefore there is no guarantee that aggressive behavior can be modeled. Two participants did not use the aggressive response and two more did not use it during the first session. It might be informative to model instances where participants choose the aggressive option immediately following a provocation. We observed too few such "post-provocation aggressive responses" and suggest that modifications to the PSAP that facilitate such aggressive behavior would improve its utility.

Although not all participants receive the same number of provocations, this is consistent with how the PSAP is commonly used and we found that adjusting for the variable number of provocations and total button presses did not substantively affect observed neural responses. Similarly, the number of provocations and the BOLD response to provocations were not correlated.

We cannot exclude the possibility that our use of MR as a baseline condition may be confounded by reward-related activity. Our results were effectively unchanged when modeling only the first 10 s of the MR condition in an effort to limit potential reward-related confounds. Future studies should consider incorporating alternative baseline conditions (e.g., inter-leaved blocks of only basic finger pressing).

The non-significant AR > MR contrast may stem from reward-related activity during MR and reward-related brain responses to aggressive behavior described above. It may also be related to the constraint that participants complete an option before choosing another. As such, there is a temporal disconnect between when a provocation occurs and when a participant can choose to behave aggressively. Allowing participants to change options before one is completed, perhaps at a small cost, may facilitate a more reactive form of aggression.

Although our inferences of cognitive and affective processes underlying observed brain responses are based in part on previous studies, we note that we cannot directly verify these links.

The PSAP offers advantages over the TAP, a commonly used aggression fMRI paradigm. With the PSAP, participants are free to initiate aggressive responses at any time. They can also refrain from behaving aggressively and pursue earning points. Thus, the PSAP may more accurately reflect reactive aggression—including non-violent forms. Conversely, aggression-related neural responses cannot be modeled if participants do not behave aggressively. Unlike the TAP, the PSAP does not involve the receipt/administration of a painful stimulus, which may discourage potential participants and raises ethical issues in youth populations. The PSAP circumvents the need to determine participant pain threshold and use special equipment for delivering pain stimuli (Dambacher et al., 2014; Giancola & Parrott, 2008; Taylor, 1967). Lastly, participants may quickly become aware that the TAP aims to study aggression, which can introduce behavioral biases less transparent in the PSAP. Taken together, we think the PSAP represents a valuable paradigm for studying aggression-related brain function with fMRI.

5 | CONCLUSION

In summary, our results suggest the PSAP can be implemented within an fMRI environment using a single 12-min session to evaluate aggression-related brain function. We observed significant reactivity across aggression-related brain areas including amygdala, PFC, ACC, and dorsal striatum when participants were provoked. Behavioral relevance of PFC, ACC, and striatal reactivity to provocations was supported by a positive association with aggressive behavior during the paradigm. Ventral and dorsal striatal reactivity to respectively earning a point and stealing from the opponent support that rewarding aspects of aggression may also be probed using this paradigm. Our results support this paradigm as a novel tool for evaluating neurobiological mechanisms underlying reactive aggressive behavior. Future studies applying this paradigm in pathologically aggressive individuals may provide novel insight into underlying neurobiological mechanisms and potential targets for novel treatment strategies.

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CONFLICTS OF INTEREST

The authors declare no competing financial interests.

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