

Research paper

Let me in: The neural correlates of inclusion motivation in loneliness

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ABSTRACT

Background: While it is well-established that humans possess an innate need for social belonging, the neural mechanisms underlying motivation for connection are still largely unknown. We propose that inclusion motivation – measured through the effort that individuals are willing to invest to be included in social interactions – may serve as one of the basic building blocks of social behavior and may change in lonely individuals.

Methods: Following the screening of 303 participants, we scanned 30 low- and 28 high-loneliness individuals with functional magnetic resonance imaging while they performed the Active Inclusion Task (AIT). The AIT assesses the participants' levels of effort invested in influencing their inclusion during classic Cyberball conditions of fair play and exclusion.

Results: High- compared to low-loneliness individuals showed higher urgency for inclusion, specifically during fair play, which correlated with higher activity in the right thalamus. Furthermore, in high-loneliness individuals, we found increased functional connectivity between the thalamus and the temporoparietal junction, putamen, and insula.

Limitations: Participants interacted with computerized avatars, reducing ecological validity. Additionally, although increasing inclusion in the task required action, the physical demand was not high. Additional limitations are discussed.

Conclusions: Inclusion motivation in loneliness is heightened during fair but not exclusionary interactions, and is linked to activity in brain regions implicated in appetitive behavior and social cognition. The findings indicate that lonely individuals may view threat in inclusionary interactions, prompting them to take action to regain connection. This suggests that inclusion motivation may help explain social difficulties in loneliness.

1. Background

The idea that humans are fundamentally social and have a basic need to belong is supported by a substantial body of research on motivation (Leary & Baumeister, 1995; Williams & Nida, 2011). We are highly motivated to seek social interactions and to maintain satisfying relationships with others (Berridge & Kringelbach, 2008). We avoid situations of social exclusion (Baumeister et al., 2007), respond negatively when facing rejection (Eisenberger et al., 2003), and derive enjoyment from being included (Hay et al., 2023). While initial connections may be created in a spontaneous manner (Marton-Alper et al., 2020), further

interaction and the maintenance of social bonds require active participation and effort (Lang et al., 2013). Here we focus on inclusion motivation, defined as the drive of the individual to be included in social interactions, which is translating into effort investment (Kanterman et al., 2022). While belonging refers to the subjective feeling of being accepted by a group (family, friends, coworkers, religion) (Allen et al., 2022), inclusion motivation refers to the effort of individuals aimed at being included in an ongoing interaction (Kanterman et al., 2022), thus increasing the sense of belonging in that situation. Hence, while belonging is a wide construct and a need that is promoted by many behaviors (Allen et al., 2022), inclusion motivation focuses on one type

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of behavior, which can be measured directly in tasks that require effort.

When the desire for connection is not met, people may experience loneliness. Loneliness is the feeling that accompanies the perception that one's social needs are deficient in quality or in quantity (Hawley & Cacioppo, 2010). Loneliness may emerge from a variety of factors such as objective isolation, immigration (Tang et al., 2024), trauma, or bullying (Schäfer et al., 2004). However, people may feel subjectively lonely regardless of objective conditions, which is the focus of the current study. While loneliness can be situational and transient, it may also become prolonged and chronic (Saporta et al., 2021). Chronic subjective loneliness as measured with the UCLA loneliness scale (Russel, 1996), is associated with negative effects on sleep, cardiovascular and immune systems, and cognitive functioning (Hawley & Cacioppo, 2010). It was recently suggested that higher compared to lower levels of chronic loneliness correlate with diminished trust in others (Lieberz et al., 2021), difficulties in synchronization with others in a task of movement synchronization (Saporta et al., 2023), and greater preferred interpersonal distance (Saporta et al., 2021).

While these differences in behavior may explain the reduced quality of interactions reported by higher-loneliness individuals (Hawley et al., 2008), studies focusing on the motivation to connect in loneliness show conflicting results (see Lam et al., 2021). On the one hand, loneliness is correlated with lower positive affect and reduced response of the reward system when viewing positive social images (Cacioppo et al., 2009). On the other hand, loneliness is also associated with enhanced activation in the reward system when viewing images of close others, as opposed to strangers (Inagaki et al., 2016). Interestingly, Lucas et al. (2010) demonstrated that social approach, which is diminished in higher compared to lower loneliness, may be increased in lonely individuals when they are presented with acceptance cues in the form of vignettes depicting safe and positive social interactions. These results suggest that individuals with higher compared to lower loneliness levels may exhibit reduced or increased motivation for connection, depending on factors such as familiarity, safety, and certainty, indicating that social motivation fluctuates in these individuals. Moreover, the universal human experience of motivational conflict between approach and avoidance tendencies during social engagements (Barker et al., 2019) is particularly accentuated in individuals with elevated loneliness levels compared to their less lonely counterparts (Cacioppo & Cacioppo,

2018).

Given that individuals experiencing loneliness feel a constant lack in belonging, we previously sought to examine their intrinsic drive for social inclusion in an ecological task which simulates the dynamics of social interactions (Kanterman et al., 2022). To assess inclusion motivation, we developed the Active Inclusion Task (AIT) (Fig. 1). The AIT is based on the widely used Cyberball paradigm, a computerized ball-tossing game that allows manipulating levels of inclusion and exclusion (Williams et al., 2000). To measure the level of effort participants are willing to invest to be included, the AIT is designed to allow active influence on inclusion during classic Cyberball conditions of fair-play (equal number of tosses) and exclusion (few to no tosses to the participant), by waving a virtual hand controlled by key presses. In line with evolutionary accounts of loneliness, according to which loneliness evolved to motivate the individual to connect with others (Cacioppo et al., 2014), we found that higher loneliness was associated with increased effort invested in attempts to be included, when effort demand was low (Kanterman et al., 2022).

Building on these findings, here we sought to examine the neural correlates that are associated with inclusion motivation in loneliness. We expected to find specific patterns of neural activity associated with social inclusion, exclusion, and motivation, that would be influenced by loneliness. Neuroimaging studies show that inclusion recruits, among other regions, the parietal cortex and the orbitofrontal cortex (OFC) (Bolling et al., 2011), both strongly implicated in motivation (task-reward associations, reward value encoding in particular) and social cognition (Weinstein, 2023). In contrary, social exclusion recruits the salience network, including the insula and cingulate cortex (Masten and Eisenberger, 2009; Onoda et al., 2009). While most research uses fair-play as a control condition (Hartgerink et al., 2015), in the current study we treated both conditions as conditions of interest, as social difficulties in loneliness may emerge not only during unpleasant interactions but also during neutral or pleasant ones (Hawley & Cacioppo, 2010). Additionally, as the AIT allows increasing inclusion during fair-play as well, we expect that in this condition participants will be either equally included or make an effort to be over-included. Over-inclusion has been shown to effectively increase the sense of belonging, with stronger effect among individuals with high fear of negative social evaluation (Simard & Dandeneau, 2018).

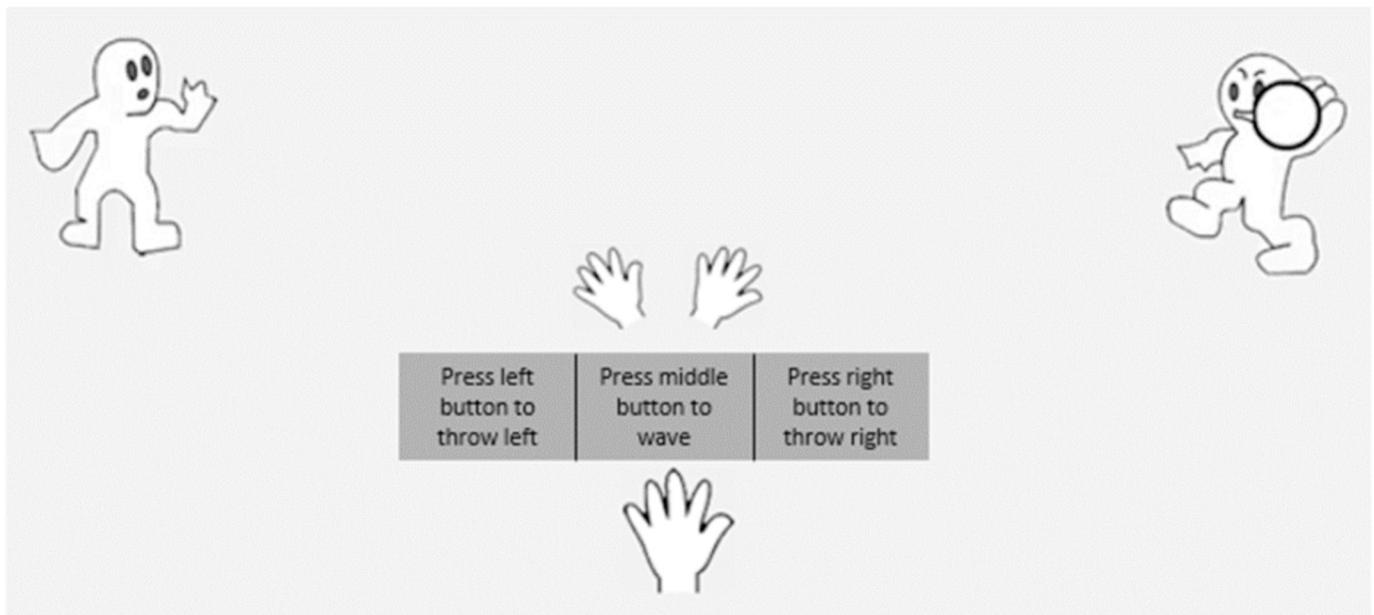


Fig. 1. Active Inclusion Task (AIT). The participant is represented by a virtual hand at the bottom of the screen with the programmed players depicted as avatars on the upper corners. The instructions were to press the left button on the response box to throw the ball to the left player; press the right button to throw it to the right player; and press the middle button to ‘wave the hand’ and thus signal to the other players the wish to receive the ball. All participants were right-handed.

As studies propose that loneliness is associated with negative affect and higher motivation to reconnect, we hypothesized that higher-compared to lower-loneliness individuals would (1) report lower positive affect and sense of belonging, and (2) would show higher inclusion motivation (reflected by effort) in the fair-play and exclusion conditions. We hypothesized that (3) across groups, fair-play compared to exclusion would yield increased activity in reward related regions, while higher activity during exclusion compared to fair-play will be observed in the salience network. However, as the current study focuses on the motivation to be included given the option to act, regions related to reward and effort investment, such as the ventral striatum (VS) and the thalamus, are also expected to be recruited (Cho et al., 2013; Oldham et al., 2018). The thalamus functions as a gateway to appetitive motivation and craving, plays a key role in modulating striatal activity (Millan et al., 2017; James et al., 2021), and is implicated in motivational competition which occurs when there is a potential for both reward and punishment (McNally, 2021). As higher-loneliness individuals experience greater uncertainty during social interactions (Nombro et al., 2022) and higher motivational conflict (Cacioppo & Cacioppo, 2018) compared to lower-loneliness individuals, we expected (4) to find increased recruitment of the thalamus in higher but not lower loneliness. Lastly, as studies suggest that loneliness is related to enhanced functional connectivity between brain regions implicated in social behavior during social tasks (Lam et al., 2021), we hypothesized that (5) lower- and higher-loneliness individuals would differ in functional connectivity between motivation and social cognition brain regions during the task, such that it would be stronger among higher-loneliness individuals.

2. Methods

2.1. Participants

The screening process of 303 participants is described in the *Supplementary materials*. 65 healthy students with no mental health history took part in the experiment. We used G*Power 3.1 (Faul et al., 2007) to determine the appropriate sample size. To examine the effect of loneliness on neural responses to social stimuli with effect size of 0.46 (Cohen's d ; Cacioppo et al., 2009), with $\alpha = 0.05$ and power = 0.95, a minimum of 52 participants was required for a between-subjects design (by comparing groups of individuals with lower and higher loneliness levels). We recruited a larger sample to ensure that all analyses could be conducted on a sufficient sample of participants with no missing data. We excluded two behavioral outliers (mean presses $>3SD$) and five additional participants due to unusable behavioral or neuroimaging data caused by technical issues. Our final sample included 58 participants, divided into two loneliness groups: lower ($n = 30$, 15 females, mean age = 24.3 ± 3.3 , mean UCLA score = 30.9 ± 4.6) and higher loneliness ($n = 28$, 18 females, mean age = 25.35 ± 3.9 , mean UCLA score = 53 ± 7.05). The study was conducted according to the Declaration of Helsinki and was approved by the ethics committee of the University of Haifa, Tel Aviv University, and Sheba Tel Hashomer Medical Center. All participants gave their written informed consent to participate in the study. As recent research indicates that the effects of loneliness on behavior and neural activity may be influenced by sex (Morr et al., 2022), we ran similar behavioral and neuroimaging analyses while including it as a covariate. No significant sex effects were found (all $p > .05$).

2.2. UCLA loneliness scale 3

To assess levels of loneliness, participants filled the University of California Los Angeles (UCLA) Loneliness Scale (Version 3) (Russell, 1996), designed to measure feelings of loneliness and social isolation. Participants rate 20 statements on a 4-point Likert scale, ranging from “never” to “often”, with final scores ranging from 20 (no loneliness) to 80 (extreme loneliness). Over a period of one year, the test-retest

reliability of the questionnaire was $r = 0.73$ (Russell, 1996) (see *Supplementary materials* for more information). The mean Cronbach's alpha of the UCLA-3 based on 13 samples ranges from 0.86 to 0.95 (Vassar & Crosby, 2008).

2.3. Active inclusion task (AIT)

The AIT (Kanterman et al., 2022) is based on the Cyberball paradigm (Williams et al., 2000). In the task, participants play a computerized interactive tossing game with two programmed players (Fig. 1). The game consists of two conditions: fair-play and exclusion. During fair-play participants have a 50 % probability of receiving the ball from each of the virtual players, while during exclusion the probability is 10 %. As in the original task, in both conditions participants are instructed that once the ball is received, they are to toss it to one of the players. In the AIT, however, they are also instructed to wave their hand by pressing a button on the response box whenever they want to receive more tosses. Each press increases the probability of receiving the ball by 75 % in both conditions. Inclusion probability returns to baseline as determined by condition type if the wave button is not pressed for 5 s. We used the exclusion condition to prompt action in all participants experimentally, and the fair-play condition to examine for the motivation for over-inclusion.

Participants were informed that they can affect the number of tosses they receive by waving a virtual hand controlled by the response box they hold inside the scanner. The more frequently and persistently they press, the more likely they are to influence the game and get more tosses. Participants completed 11 pseudorandomized blocks of fair-play (6) and exclusion (5) inside the scanner. Short pseudorandomized blocks were used to reduce expectancy violation and to simulate to a greater extent the dynamics of social interactions. The first, second and last blocks of the task were always fair-play. The first fair-play block was used as a training session and was discarded from the analysis. During the training block participants could learn and become accustomed to the contingency between the wave response and the increased probability of receiving the ball. The final block was set to fair-play as was done in a previous behavioral study using the AIT (Kanterman et al., 2022). Each block consisted of 21 tosses and lasted approximately 50–60 s, with a 5-s break between blocks. It took the programmed players 1 s to toss the ball once received, and it took an additional second for the ball to reach the recipient. We used a block design to avoid surprise effects in instances where events from one condition occur in the other, e.g., receiving tosses during exclusion or not during fair-play, for short periods of time, which may represent a potential confounding factor.

2.4. Self-report measures

Following scanning, participants received one of two sets of counterbalanced questionnaires, in which they were asked to think back on the games in which they received many tosses easily, or hardly any tosses. Half of the participants began with fair-play and half with exclusion. Participants rated their positive affect, and sense of belonging on a scale of 1 (low) to 9 (high).

2.5. Behavioral task measures

We used three behavioral task measures that were averaged per condition, resulting in 6 measurements for each participant: 1) average number of presses in each condition, 2) average duration of intervals between every two presses, measured in seconds, and 3) outcome, i.e., average number of received tosses. While the first measure represents general motivation for inclusion in absolute values, the second measure is more nuanced and represents urgency, assuming that short intervals between presses denote higher motivation. The wave response here is synonymous with behavioral responding, as button presses, and the intervals derived, were our primary measure of behavior. The final

measure of outcome was used to assess performance in the task.

2.6. Procedure

Participants were invited to the Strauss Imaging Center on the campus of Tel Aviv University to take part in the study. After signing an informed consent form, participants underwent a second medical debriefing (the first was during the screening phase as described in *Participants*) and were checked for metals by a professional technician to ensure safety. Prior to entering the scanner, participants received the instructions of the AIT (for more details see *Supplementary materials*) and were familiarized with the response box they had to use inside the scanner. The current experiment was a part of a larger study examining neural processing of social interactions in loneliness. Prior to the AIT, participants completed two additional tasks (one is reported in *Saporta et al., 2021*), such that the AIT was the final task in the study, after which participants exited the scanner. Then, participants rated their emotions with respect to each condition as described earlier. At the end of the experiment participants received a monetary compensation of 150 NIS (~\$50) for their participation.

2.7. fMRI data acquisition

Magnetic resonance imaging (MRI) data were acquired using a 3 T Siemens Magnetom Prisma Scanner (Siemens Medical Solutions, Erlangen, Germany) with a 64-channel head coil, at the Strauss Imaging Center on the campus of Tel Aviv University. Anatomical scans were acquired using a T1-weighted 3D MP2RAGE (TR—2.53 s; TE—2.99 ms; flip angle—7°, 176 sagittal slices; spatial resolution—1 × 1 × 1 mm³). While in the scanner, participants performed the task using a fiber optic response pad (Current Designs, Inc. PA, USA). Functional scans were acquired by multiband echo planar imaging (mb-EPI) pulse sequence for simultaneous excitation for multiple slices using TR—2 s; TE—30 ms; band factor—2; Ipat—2; isotropic spatial resolution—2 mm³.

Preprocessing and all analyses were carried out using the Statistical Parametric Mapping toolbox for MATLAB 2019 (SPM12; Wellcome Trust Center for Neuroimaging, University College London, <https://www.fil.ion.ucl.ac.uk/spm/software/>). Functional scans were pre-processed using quality assurance, slice timing correction, realignment, co-registration, normalization (to a standard T1 template, MNI), and finally 4 × 4 × 4 mm Gaussian smoothing. Head movements were examined and corrected or discarded when needed (>2.5 mm/°). Finally, anatomical regions were identified using the automated anatomical labeling atlas 3 (*Rolls et al., 2020*).

2.8. Behavioral analysis

We conducted two repeated-measures multivariate analyses of variance (MANOVA), with the first examining the effects of condition (fair-play, exclusion), group (lower, higher loneliness), and the interaction effect between the two, on self-reported emotion ratings. The second model examined the effects of condition and group on behavioral task measures. In both models, condition was used as within-subjects factors, while group was used as a between-subjects factor. The dependent variables (measure factor) were positive affect and sense of belonging combined in the first model, focusing on self-report measures, and the average number of presses, time intervals, and outcome combined in the second model, focusing on behavioral task measures. Finally, we conducted bivariate Pearson correlation analyses to test the relationships between emotion ratings and behavioral task measures, and with brain activity. For all behavioral analyses, $p < .05$ was considered significant, and effect sizes were estimated by using Cohen's d or Partial eta squared (η^2p). All behavioral analyses were performed using SPSS 25.0 and 27.0 while graphs were created using R version 4.2.2 (*R Core Team, 2021*).

2.9. Neuroimaging analysis

For our main analysis, we employed a 2 × 2 factorial design to investigate the effects of group (lower, higher loneliness) and condition (fair-play, exclusion) on brain activity. We conducted a whole-brain analysis with an initial voxel threshold of $p < .001$ uncorrected (*Gifuni et al., 2024*), with family wise (FWE) cluster correction set at $p < .05$. While our hypotheses were region-specific based on previous studies, we chose a whole-brain approach to allow for the discovery of other potential regions and networks that might underlie inclusion motivation. For the 1st-level analysis, we calculated 3D statistical parametric maps for each participant separately in each condition using a general linear model (GLM) in SPM12. At the 2nd-level, we carried out a flexible factorial analysis with condition as a within-subject factor and group as the between-subject factor. The following contrasts were examined: fair-play vs. exclusion and exclusion vs. fair-play across groups, and the interaction effect between condition and group.

Our first follow-up analysis aimed to disentangle significant interaction effects through post-hoc tests. We extracted parameter values of observed interaction effects using 6 mm spheres around the respective peak voxels and correlated them with behavioral measures selected based on the results of our behavioral and neuroimaging analyses. Building further on our brain activity analysis findings, we conducted a second follow-up analysis focusing on functional connectivity. Specifically, we performed a psychophysiological interaction analysis (PPI) using the same region which showed a significant interaction effect in our main analysis, to explore group-dependent differences in neural activity during the task. This data-driven approach allowed us to examine differences in functional connectivity between the two groups directly while avoiding multiple comparisons and remaining hypothesis-based (*Friston et al., 1997; McLaren et al., 2012*).

3. Results

3.1. Behavioral results

MANOVA was carried out, with condition as the within-subjects factor and group as the between-subjects factor. The dependent variables (measure factor) were positive affect and sense of belonging combined in a single model. We used MANOVA as the variables were positively correlated during fair-play [$r(58) = 0.61, p < .0001$], and during exclusion [$r(58) = 0.73, p < .0001$]. Multivariate tests revealed significant main effects for condition [$F(1,56) = 137.2, p < .0001, \eta^2p = 0.7$], such that during exclusion compared to fair-play, positive affect [$t(56) = 11.1, p < .0001, \text{Cohen's } d = 1.4$] and sense of belonging [$t(56) = 10.2, p < .0001, \text{Cohen's } d = 1.3$] were lower. Measure [$F(1,56) = 4.2, p = .007, \eta^2p = 0.12$], and importantly group [$F(1,56) = 7.7, p = .007, \eta^2p = 0.12$], were also significant. Higher- compared to lower-loneliness individuals had lower positive affect [$t(56) = 2.4, p = .018, \text{Cohen's } d = 0.64$] and sense of belonging [$t(56) = 3.6, p = .016, \text{Cohen's } d = 0.715$] in both conditions (*Fig. 2*). No other effects were found significant.

A second repeated-measures MANOVA was carried out using the same factors. The dependent variables were behavioral task measures: the average number of presses, intervals between presses, and outcome. In both conditions, presses were negatively correlated with intervals (fair-play: $r(58) = -0.33, p = .013$; exclusion: $r(58) = -0.67, p = .004$) and positively correlated with outcome (fair-play: $r(58) = 0.79, p = .000$; exclusion: $r(58) = 0.91, p < .0001$ across sample). Multivariate tests revealed a significant main effect for condition [$F(1,56) = 86.4, p < .0001, \eta^2p = 0.6$], measure [$F(1,56) = 570.7, p < .0001, \eta^2p = 0.9$], but not for group [$F(1,56) = 1.4, p = .234$]. Importantly, the interaction between condition, measure and group was significant [$F(2,55) = 6.04, p = .004, \eta^2p = 0.18$].

Univariate tests showed that all measures differed significantly between the two conditions, such that number of presses was higher [$F(1,56) = 163.7, p < .0001, \eta^2p = 0.75$] and time intervals were longer [F

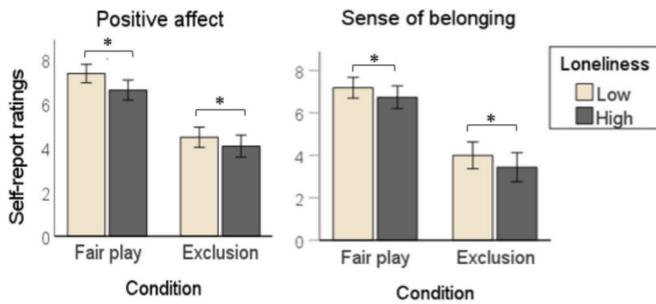


Fig. 2. Self-report measures results. Behavioral results focusing on emotions revealed significant main effects for condition and group such that positive affect and sense of belonging as reported by participants in retrospect, were higher during fair-play compared to exclusion. Moreover, higher- compared to lower-loneliness individuals reported lower positive affect and sense of belonging across conditions. Error bars: ± 2 SE. * $p < .05$.

(1,56) = 14.4, $p < .0001$, $\eta^2p = 0.2$] during exclusion compared to fair-play, while the outcome was lower [$F(1,56) = 795.7$, $p < .0001$, $\eta^2p = 0.9$]. Tests of within-subjects contrasts revealed that the interaction between condition and group was significant only when examining the measure of time intervals [$F(1,56) = 10.7$, $p = .003$, $\eta^2p = 0.16$; presses: $F(1,56) = 1.5$, $p = .192$; outcome: $F(1,56) = 3.9$, $p = .221$].

Paired t -tests conducted for each group separately revealed that the differences in intervals between the two conditions was significant in higher loneliness [$t(27) = -3.7$, $p = .001$, Cohen's $d = -0.69$] but not in lower loneliness [$t(29) = -1.5$, $p = .503$]. Furthermore, independent samples t -tests comparing the two groups revealed significantly shorter intervals in higher compared to lower loneliness during fair-play [$t(56) = 3.1$, $p = .001$, Cohen's $d = 0.87$], but not during exclusion [$t(56) = -1.3$, $p = .267$] (Fig. 3).

Note that an analysis of correlation across the entire sample (reported earlier) and within each group separately, revealed an inverse relationship between the number of presses and interval lengths (fair-play, lower loneliness: $r(30) = -0.492$, $p = .004$; fair-play, higher loneliness: $r(28) = -0.348$, $p = .05$; exclusion, lower loneliness: -0.703 , $p < .0001$; exclusion, higher loneliness: -0.589 , $p < .0001$). The significant difference in intervals between the two conditions was observed in higher but not lower loneliness levels, suggesting that this effect may have been masked in the current model.

3.2. Neuroimaging results

Our main analysis was a whole-brain analysis comparing fair-play vs. exclusion revealed increased blood-oxygen-level-dependent (BOLD) signal in the bilateral superior frontal sulcus (SFS) [$-26, -4, 60; 30, -2,$

58], bilateral superior parietal lobule (SPL) extending to the precuneus [$-18, -68, 60; 16, -68, 60$], and right inferior parietal lobule (IPL) [$44, -36, 54$]. The reversed contrast (exclusion vs. fair-play) initially yielded an increase in activation in the bilateral insula extending to the opercular part of the inferior frontal gyrus (IFG) [$44, 12, 6; -40, 20, -10$]. However, it was significant only at initial voxel threshold and did not survive FWE cluster level correction. Importantly, we found a significant condition by group interaction in the right thalamus [$12, -10, 8$], mainly covering medial and lateral parts, such that its recruitment was stronger during fair-play vs. exclusion in higher vs. lower loneliness (Table 1, Fig. 4). Note that there were no significant differences in activation of motor regions (precentral gyrus, supplementary motor area) in either condition or group.

To understand the interaction effect, we conducted our first follow-up analysis. We created a 6 mm sphere centered around peak activation [$12-10 8$] (without using anatomical ROIs) and extracted parameter estimates for each condition and group. Paired-samples t -test conducted in each group separately revealed that in both groups activation in the thalamus differed significantly between the two conditions, however in opposite directions: in lower loneliness, activity in the right thalamus was higher during exclusion vs. fair-play (mean activation 0.05 and -0.05 , respectively [$t(29) = -2.07$, $p = .047$, Cohen's $d = -0.36$]; in higher loneliness, on the other hand, activity was higher during fair-play (mean activity 0.14) vs. exclusion (mean activity -0.004 [$t(27) = 2.1$, $p = .04$, Cohen's $d = 0.42$]). Additionally, independent t -tests comparing the two groups in each condition separately, revealed that lower- compared to higher-loneliness individuals differed significantly in right thalamic activity specifically during fair-play [$t(56) = 2.2$, $p = .029$, Cohen's $d = -0.6$; exclusion: $t(56) = 0.51$, $p = .61$].

Next, bivariate Pearson correlation analyses between parameter estimates and behavioral measures in each group separately revealed a negative correlation between neural activity in the right thalamus and intervals during fair-play in higher [$r(28) = -0.39$, $p = .04$] but not in lower loneliness [$r(30) = -0.06$, $p = .7$], such that higher activity predicted shorter intervals. We focus here on the fair-play condition as this was the source of the behavioral and neural difference between the loneliness groups. Finally, we observed a difference in distribution such that the data points of higher-loneliness individuals were concentrated on the left, indicating shorter intervals, which could have contributed to the negative correlation. Lower-loneliness individuals' data were evenly distributed, showing no significant correlation (Fig. 5).

3.3. Psychophysiological interaction analysis results

Our second follow-up analysis was used to understand whether group differences in the neural activity of the right thalamus were accompanied by an altered interplay of this brain region with other

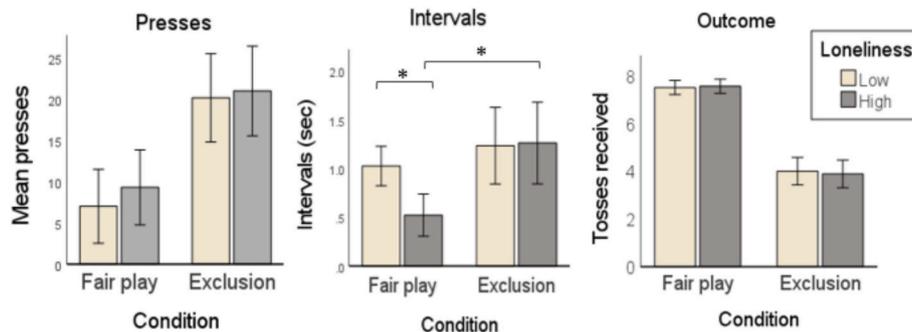


Fig. 3. Behavioral task measures. Behavioral results focusing on task measures (averaged per condition) revealed a significant main effect for condition, such that presses were higher, intervals were longer, and outcome was lower in exclusion compared to fair-play. Main effect of group was not significant. The interaction between condition and group was found significant in the measure of intervals, such that they were significantly shorter during fair-play compared to exclusion in higher but not lower loneliness, and shorter in higher compared to lower loneliness in the fair-play condition, explaining the longer intervals on average during exclusion. Error bars: ± 2 SE. * $p < .05$.

Table 1

Whole-brain analysis results. Whole-brain analysis comparing fair-play vs. exclusion and exclusion vs. fair-play across groups. Notes: BA = Brodmann area; Hemi = hemisphere; L = left; R = right, k = cluster size; t = peak t value. Initial voxel threshold set at $p < .001$ uncorrected, cluster level correction set at $p < .05$ FWE. * = significant at cluster level.

Contrast	Region	BA	Hemi	K	MNI coordinates			T	p
					x	Y	z		
Fair-play vs. Exclusion	Superior parietal lobule, Precuneus, Inferior parietal lobule	5, 7	L	530	-18	-68	60	6.7*	<0.0001
	Superior parietal lobule, Precuneus	5, 7	R	153	16	-60	60	4.9*	<0.0001
	Inferior parietal lobule	39, 40	R	492	44	-36	54	5.8*	<0.0001
	Superior frontal sulcus	8	L	232	-26	-4	60	5.4*	<0.0001
	Superior frontal sulcus	8	R	191	30	-2	58	4.9*	<0.0001
Exclusion vs. Fair-play	Inferior frontal gyrus opercular, Insula	13, 44	R	327	44	12	6	4.1	0.0001
	Insula, inferior frontal gyrus opercular	13, 44	L	190	-40	20	10	3.16	0.001
Condition × Group Interaction	Thalamus		R	30	12	-10	8	4.2*	0.010

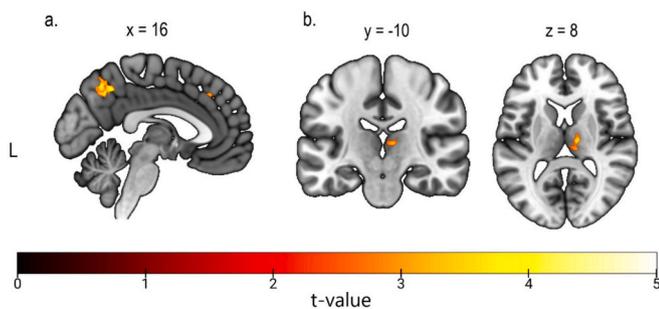


Fig. 4. Neuroimaging results. a. Whole-brain analysis comparing neural activity during fair-play versus exclusion across participants, yielded a significant increase in BOLD signal in the bilateral superior frontal sulcus, bilateral superior parietal lobule extending to the precuneus, and the right inferior parietal lobule. b. A significant condition by group interaction effect was found in the right thalamus such that it was more active in higher loneliness during fair-play. See MNI coordinates in Table 1.

regions involved in inclusion motivation in loneliness. Based on the results of our main analysis of brain activity, in which we found increased activation of the right thalamus in higher but not lower loneliness specifically during fair-play, we used the right thalamus as a

seed region in a PPI analysis [6 mm sphere centered around the peak voxel of the observed condition by group interaction: 12, -10, 8; initial voxel threshold $p < .001$ uncorrected, FWE cluster level corrected $p < .05$]. We compared higher and lower loneliness directly, first during fair-play and then during exclusion. Although the interaction effect that we observed was specific to fair-play, we tested for connectivity differences during exclusion as well, as there may be a discrepancy between differences in activation and differences in connectivity between lower and higher loneliness.

During fair-play, we found enhanced functional connectivity between the right thalamus and bilateral temporoparietal junction (TPJ), right insula, and bilateral putamen in higher loneliness compared to lower loneliness. During exclusion, higher loneliness was associated with enhanced functional connectivity between the right thalamus, the right TPJ and the left IPL, when compared to lower loneliness (Table 2, Fig. 6).

4. Discussion

The present study sought to investigate the neural basis underlying the motivation to be included in social interactions, and whether it differs with loneliness levels. Lower- and higher-loneliness individuals were scanned while they completed a task that allows participants to influence their inclusion in a ball toss game, by waving a virtual hand

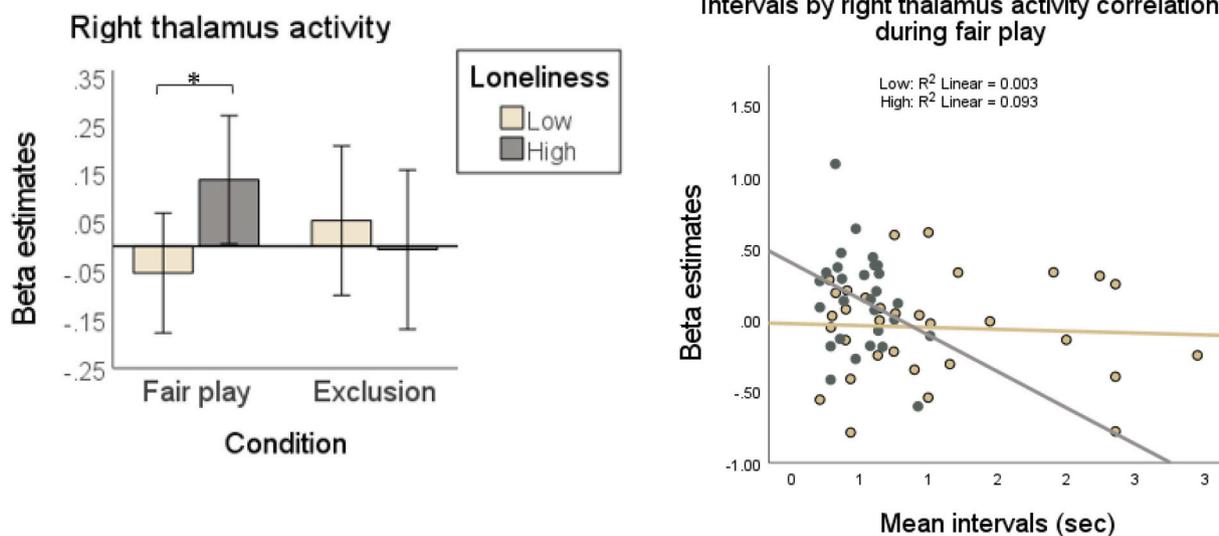


Fig. 5. Condition by group interaction. Significant condition by group interaction in the right thalamus is depicted on the left: lower and higher loneliness differed significantly during fair-play, such that higher loneliness exhibited higher thalamic activity specifically during fair-play. Pearson correlation, depicted on the right, showed that only higher loneliness exhibited an association between higher right thalamic activity and shorter intervals between presses during fair-play.

Table 2

Functional connectivity analysis results in higher- vs. lower-loneliness. Results of functional connectivity analysis comparing between lower and higher loneliness during fair-play and exclusion. Notes: BA = Brodmann area; Hemi = hemisphere; L = left; R = right, k = cluster size; t = peak t value. Initial voxel threshold set at $p < .001$ uncorrected, cluster level correction set at $p < .05$ FWE.

Contrast	Region	BA	Hemi	K	MNI coordinates			t	p
					x	Y	z		
<i>Higher vs. lower loneliness</i>									
<i>Fair-play</i>	Temporoparietal junction	39	R	357	50	-26	0	5.3*	<0.001
	Temporoparietal junction	39	L	543	-56	-38	28	5.4*	<0.001
	Insula	13	R	264	46	2	-8	5.3*	<0.001
	Putamen		L	244	-38	6	-4	5.3*	<0.001
	Putamen		R	88	38	2	36	5.2*	0.001
<i>Exclusion</i>	Temporoparietal junction	39	R	86	54	-40	22	5.1*	0.001
	Inferior parietal lobule	39,40	L	64	-30	-54	58	4.6*	0.008

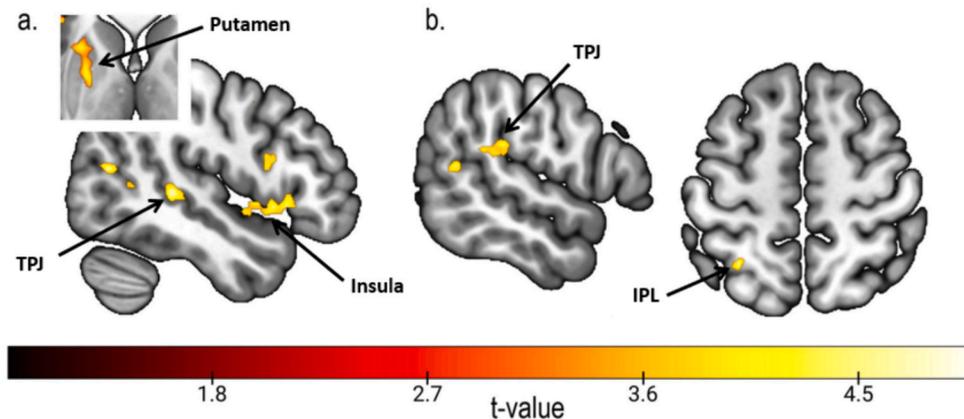


Fig. 6. Functional connectivity results. a. Fair-play vs. exclusion: enhanced functional connectivity between the right thalamus and bilateral temporoparietal junction, putamen, and right insula during fair-play compared to exclusion in higher compared to lower loneliness. b. Exclusion vs. fair-play: enhanced connectivity between the right thalamus, the right temporoparietal junction, and left inferior parietal lobule in higher loneliness. See MNI coordinates in Table 2.

controlled by button presses (i.e., exerting effort). As expected, all participants reported higher positive affect and sense of belonging, and received more tosses during games of fair-play compared to exclusion. During exclusion compared to fair-play all participants pressed more. However, all participants waved during fair-play too, and therefore reached over-inclusion on average (received 40 % of all tosses rather than 33 %).

While increasing the catch outcome by pressing the button could be a confounding factor, receiving more tosses as a result of one's actions is an intentional aspect of the design. During exclusion, catch outcomes are rarer and therefore unexpected, whereas during fair-play, they are frequent. Nonetheless, participants were aware that pressing the button could enhance their chances of inclusion, augmenting a sense of agency and control and making a toss not entirely surprising since achieving inclusion is the goal. Better outcomes are directly linked to the participants' engagement in the task. If participants discern that increased effort does not correlate with improved results, they may cease their efforts entirely (i.e., learned helplessness; Maier & Seligman, 2016).

At the neural level, across groups, fair-play relative to exclusion elicited increased activity in the parietal and frontal cortices. The reversed contrast yielded enhanced activation in the insula and IFG. However, these results did not remain significant following cluster level correction, possibly due to the participants reaching a 20 % inclusion rate in the exclusion condition by waving, thus reducing the aversiveness of the experience. Although wave responses were higher during exclusion, catch outcomes were higher during fair-play, which may have contributed to the lack of difference in motor responses between the two conditions.

The IPL is strongly implicated in observed action processing (Rizzolatti et al., 2006), empathy (Shamay-Tsoory, 2011), self-other discrimination (Uddin et al., 2006), and sensitivity to rejection (Radke

et al., 2021). The SPL and precuneus have been associated with social decision making and with effort that is exerted in order to obtain a social reward (Dubey et al., 2020). The SFS is located between the dorsomedial prefrontal cortex (dmPFC) and the dorsolateral prefrontal cortex (dlPFC), both implicated in social cognitive control (Kuss et al., 2015) and social decision making (Basten et al., 2010). We thus confirmed that fair-play vs. exclusion recruits brain regions that process reward. Contrary to our hypothesis, we did not find increased recruitment of the VS in either condition, which may indicate that the VS has a similar role in both conditions when action is possible, as some studies suggest that it has a universal role in reinforcement processing of diverse stimuli regardless of valence (Daniel & Pollmann, 2014). The neural findings suggest possible task engagement differences between blocks of fair-play and exclusion which may emerge from the study's design. While we consider this a plausible effect rather than a confounding factor, using other methods such as event-related designs could reveal more nuanced effects as separate blocks provide context and therefore set expectancy.

When examining the effects of loneliness, higher- compared to lower-loneliness individuals reported lower positive affect and sense of belonging across conditions, as hypothesized (1). These findings are in line with literature pointing to a negativity bias in loneliness, where individuals with higher levels of loneliness process social information in a way which is focused on the negative rather than the positive aspects of social stimuli, with research indicating that this bias occurs on all levels of processing, from perception to interpretation (Spithoven et al., 2017). Therefore, reduced sense of belonging may be independent of the task here, however the task still significantly impacts the behavior of higher-loneliness individuals.

Importantly, higher- compared to lower-loneliness individuals had significantly shorter intervals between presses (i.e., quicker waving) during fair-play but not during exclusion (2). First, this interaction

explains why we found overall longer intervals during exclusion across participants, against our prediction. Lower- vs. higher-loneliness individuals did not show significant differences in intervals between the two conditions. Moreover, lower- and higher-loneliness individuals did not differ significantly during exclusion, suggesting that the main effect of longer intervals during exclusion applies only to higher-loneliness. Second, although we did not find differences in the overall number of waves between the groups, the shorter intervals here represent quicker action, possibly pointing to higher craving and urgency for social inclusion among higher-loneliness individuals during this condition.

This result indicates that exclusion in the AIT may be processed similarly in both groups (i.e., as a threat), while fair-play may be perceived as less inclusive and therefore as more threatening in higher-compared to lower-loneliness individuals. Due to negativity bias (Spithoven et al., 2017), higher-loneliness individuals may be more sensitive to periods of micro-rejection that may occur during fair-play (when a toss is not received intermittently; Crowley et al., 2009). Moreover, recent research indicates that experimentally evoked social isolation (ten hours) leads to an increase in feelings of loneliness and in craving for social interaction, which correlates with increased midbrain activity similar to hunger (Tomova et al., 2020). Loneliness may therefore be conceptualized as chronic social hunger, and as such, even high inclusion, as in the current study, may not be sufficient to reduce the severity of subjective isolation.

At the neural level, while both groups showed increased activity in the parietal and frontal cortices during fair-play (3), only higher-loneliness individuals showed an additional recruitment of the right thalamus (4). Critically, the activity in the right thalamus correlated with the intervals between presses in the same condition, such that the more the thalamus was active, the shorter were the intervals in the fair-play condition. This relationship was not observed in the exclusion condition, further suggesting that lower- and higher-loneliness individuals differ in behavior and in the underlying neural correlates during inclusionary rather than exclusionary interactions. This finding is in line with research showing that loneliness is linked to a negative bias in the cognitive and neural processing of social and emotional stimuli, which influences social interactions. For example, individuals with higher compared to lower levels of loneliness exhibit shorter processing speed of negative social stimuli (Grennan et al., 2021).

Furthermore, we have previously observed that higher loneliness is associated with a reduced affective response to positive interactions (Lieberz et al., 2021). The thalamus is known to play a key role in the integration of emotional, cognitive, and motor inputs and in the modulation of behavior (Haber & Calzavara, 2009), and is highly involved in appetitive motivation, food intake, and addiction-related behaviors (Millan et al., 2017). Higher-loneliness individuals experience prolonged social deficiency while lower-loneliness individuals are socially satiated, thereby explaining the lack of a reward response in the latter. In the former, higher inclusion (over-inclusion) may be required in order to provide a sufficient sense of belonging and minimize the subjective experience of exclusion when there is none objectively. Additionally, as we did not find altered VS activity in higher- compared to lower-loneliness individuals in either condition, the possibility that it plays a universal role in motivation is strengthened (Daniel & Pollmann, 2014).

Finally, as our primary analysis revealed significant differences in activation between the two groups specifically in the right thalamus, we used this region as a seed in a follow-up functional connectivity analysis. The current study shows that loneliness is associated with enhanced functional connectivity between the right thalamus, a part of the reward system, and brain regions that are commonly associated with social cognition and motivation, in both conditions: TPJ, insula and putamen during fair-play, and the TPJ and IPL during exclusion (5). Thus, while differences in activation were not observed during exclusion, connectivity analysis revealed significant group differences during this condition too, suggesting that loneliness impacts thalamic connectivity in both conditions. The correlation between thalamic activity with activity

in the TPJ, insula and putamen during fair-play may underlie increased effort and engagement in higher compared to lower loneliness (Weinstein, 2023), whereas involvement of the TPJ and IPL during exclusion may represent higher aversiveness (Vitale & Smith, 2022). The lack of significant differences in thalamic activity between the two groups during exclusion may indicate that the effects of loneliness on the activity of the thalamus are condition-specific, however the connectivity of the thalamus with other regions is influenced by loneliness regardless of condition. Nonetheless, while the activity of the right thalamus was correlated with the activity of regions implicated in social cognition during both conditions, the connectivity with motivation-related regions was stronger during fair-play.

These findings indicate that higher-loneliness individuals exhibit a more pronounced interplay between regions of the reward and salience networks than lower-loneliness individuals when included, while the affective experience is more aversive. This, in turn, may prevent higher-loneliness individuals from reducing feelings of disconnection. However, the thalamus is involved in various processes other than motivation such as motor action (Haber & Calzavara, 2009) which could have contributed to the observed results. Nonetheless, the correlation of the activity of the thalamus with regions implicated in social cognition provides supporting evidence for the notion that the role of the thalamus here is motivational and social. We therefore posit that the effects observed in this study are social rather than non-social in nature. This conclusion is further supported by the absence of increased sensorimotor activity in the precentral and postcentral gyri, as well as the supplementary premotor cortex, across conditions. Furthermore, there was no evidence of enhanced activity in the anterior cingulate cortex (ACC), which is typically associated with surprise-related processes (Alexander & Brown, 2019).

Collectively, these results point towards the importance of focusing on inclusive and not only exclusive social experiences when studying social motivation in loneliness. While most Cyberball studies focus on exclusion and use fair-play as a control condition (Hartgerink et al., 2015), the current study supports the reinvestigation of the fair-play condition as a condition of interest, as it may reveal important differences in behavior between various populations. In the context of loneliness, this is the condition in which most effects were found. It is possible that social exclusion, an experience which is highly salient and aversive for most people, is processed as a clear social threat in both lower and higher loneliness. Social inclusion, on the other hand, allows for more subjective interpretation of the interaction. As loneliness is associated with negativity bias, a positive social interaction that entails high inclusion may still be experienced as less pleasant and therefore less rewarding, and possibly even as a threat which prompts taking action to regain connection among lonely individuals (Cacioppo et al., 2014).

Our results indicate that despite higher-loneliness individuals' strong need for affiliation, the experience of inclusion, and even over-inclusion, did not enhance their positive affect and sense of belonging. However, during exclusion, ratings did not decrease in higher compared to lower loneliness. Although the effects of the task were stronger than the effects of loneliness in this study, we posit that the behavior observed in the current experiment was influenced by the participants' extended period of loneliness, such that individuals who experience higher levels of loneliness showed higher social craving in the lab. As we focused on healthy students, the current sample did not include many extremely lonely participants. Moreover, our findings suggest that loneliness does not simply increase or decrease social motivation but rather dysregulates it, influencing behavior under different conditions. Notably, when participants had the option to act—unlike in classic Cyberball studies—those with higher loneliness did not exhibit a more negative response to exclusion. This finding raises critical questions about why lonely individuals may perceive positive social interactions negatively and how these perceptions might be changed, which merits further exploration in future studies.

4.1. Limitations

One potential limitation is that participants interacted with computerized avatars. While the task simulates the dynamics of social interaction by allowing real influence on the game, the use of programmed players may have reduced the ecological validity of the study. However, research indicates that Cyberball is highly effective in eliciting exclusion-related responses even when participants know that they play with a computer (Zadro et al., 2004). Additionally, although increasing inclusion in the task required action, the physical demand was not high, as participants only pressed a button. Button presses, however, are a widely accepted measure of motivation (Treadway et al., 2009). We therefore encourage future studies to manipulate effort demand by using more challenging conditions, and to investigate how variations in action-outcome contingencies and individual differences in reward sensitivity affect behavior (Kim et al., 2015). Furthermore, here we prioritized investigating loneliness as the main factor, which inherently encompasses aversive experiences in the past, to explain behavior and group differences in the task. However, future research should examine more in depth how trauma and other factors may influence the motivation to be included regardless of loneliness, or how it may influence differentially individuals who report similar levels of loneliness, who may have been exposed to different levels of these factors in the past. Lastly, while we previously demonstrated that the AIT differentiates between the effects of social and nonsocial factors (loneliness and behavioral inhibition and activation, respectively) on motivated behavior during the AIT task (Kanterman et al., 2022), this is the first study to use the task to study inclusion behavior while using fMRI. We therefore recommend that future research directly compare the neural mechanisms underlying social and non-social motivation using neuroimaging techniques.

4.2. Conclusions

The neural basis of inclusion motivation includes parietal and frontal regions. Granting the option to act during exclusion may reduce the recruitment of the salience network while increasing reward during fair-play. Furthermore, altered activity of the right thalamus and its functional connectivity with other regions may underlie increased craving for inclusion in loneliness, and may be evident specifically during fair interactions. The study demonstrates that alterations in social behavior in loneliness may be more prominent during pleasant versus unpleasant interactions.

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CRediT authorship contribution statement

- **Kanterman, A.** Conceptualization and task development, behavioral and neuroimaging data preparation, analysis, interpretation, writing and revisions.
- **Scheele, D.** Funding acquisition, multiple revisions, and suggestions (all parts of the article).
- **Nevat, M.** Task and behavioral measures conceptualization and development, programming, neuroimaging data preparation and analysis.
- **Saporta, N.** Screening of participants, behavioral and neuroimaging data acquisition, multiple revisions, and suggestions.
- **Lieberz, J.** Multiple revisions and suggestions (all parts of the article).
- **Hurlemann, R.** Funding acquisition and reviews.

- **Shamay-Tsoory, S.** Conceptualization and task development, funding acquisition, main supervision, behavioral and neuroimaging data analysis, interpretation, writing and revisions.

Declaration of competing interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jad.2024.06.049>.

References

- Alexander, W.H., Brown, J.W., 2019. The role of the anterior cingulate cortex in prediction error and signaling surprise. *Top. Cogn. Sci.* 11 (1), 119–135.
- Allen, K.A., Gray, D.L., Baumeister, R.F., Leary, M.R., 2022. The need to belong: a deep dive into the origins, implications, and future of a foundational construct. *Educ. Psychol. Rev.* 34 (2), 1133–1156.
- Barker, T.V., Buzzell, G.A., Fox, N.A., 2019. Approach, avoidance, and the detection of conflict in the development of behavioral inhibition. *New Ideas Psychol.* 53, 2–12.
- Basten, U., Biele, G., Heekeren, H.R., Fiebach, C.J., 2010. How the brain integrates costs and benefits during decision making. *Proc. Natl. Acad. Sci.* 107 (50), 21767–21772.
- Baumeister, R.F., Brewer, L.E., Tice, D.M., Twenge, J.M., 2007. Thwarting the need to belong: understanding the interpersonal and inner effects of social exclusion. *Soc. Personal. Psychol. Compass* 1 (1), 506–520.
- Berridge, K.C., Kringelbach, M.L., 2008. Affective neuroscience of pleasure: reward in humans and animals. *Psychopharmacology* 199, 457–480.
- Bolling, D.Z., Pitskel, N.B., Deen, B., Crowley, M.J., McPartland, J.C., Mayes, L.C., Pelphrey, K.A., 2011. Dissociable brain mechanisms for processing social exclusion and rule violation. *NeuroImage* 54 (3), 2462–2471.
- Cacioppo, J.T., Norris, C.J., Decety, J., Monteleone, G., Nusbaum, H., 2009. In the eye of the beholder: individual differences in perceived social isolation predict regional brain activation to social stimuli. *J. Cogn. Neurosci.* 21 (1), 83–92.
- Cacioppo, J.T., Cacioppo, S., Boomsma, D.I., 2014. Evolutionary mechanisms for loneliness. *Cognit. Emot.* 28 (1), 3–21.
- Cacioppo, J.T., Cacioppo, S., 2018. Loneliness in the modern age: An evolutionary theory of loneliness (ETL). In: *Advances in Experimental Social Psychology*, vol. 58. Academic press, pp. 127–197.
- Cho, Y.T., Ernst, M., Fudge, J.L., 2013. Cortico-amygdala-striatal circuits are organized as hierarchical subsystems through the primate amygdala. *J. Neurosci.* 33 (35), 14017–14030.
- Crowley, M.J., Wu, J., McCarty, E.R., David, D.H., Bailey, C.A., Mayes, L.C., 2009. Exclusion and micro-rejection: event-related potential response predicts mitigated distress. *Neuroreport* 20 (17), 1518.
- Daniel, R., Pollmann, S., 2014. A universal role of the ventral striatum in reward-based learning: evidence from human studies. *Neurobiol. Learn. Mem.* 114, 90–100.
- Dubey, I., Georgescu, A.L., Hommelsen, M., Vogele, K., Ropar, D., Hamilton, A.F.D.C., 2020. Distinct neural correlates of social and object reward seeking motivation. *Eur. J. Neurosci.* 52 (9), 4214–4229.
- Eisenberger, N.I., Lieberman, M.D., Williams, K.D., 2003. Does rejection hurt? An fMRI study of social exclusion. *Science* 302 (5643), 290–292.
- Faul, F., Erdfelder, E., Lang, A.G., Buchner, A., 2007. G* power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav. Res. Methods* 39 (2), 175–191.
- Friston, K.J., Buechel, C., Fink, G.R., Morris, J., Rolls, E., Dolan, R.J., 1997. Psychophysiological and modulatory interactions in neuroimaging. *NeuroImage* 6 (3), 218–229. <https://doi.org/10.1006/nimg.1997.0291>.
- Gifuni, A.J., Pereira, F., Chakravarty, M.M., Lepage, M., Chase, H.W., Geoffroy, M.C., Lacourse, E., Phillips, M.L., Turecki, G., Renaud, J., Jollant, F., 2024. Perception of social inclusion/exclusion and response inhibition in adolescents with past suicide attempt: a multidomain task-based fMRI study. *Mol. Psychiatry* 1–10.
- Grennan, G., Balasubramani, P.P., Alim, F., Zafar-Khan, M., Lee, E.E., Jeste, D.V., Mishra, J., 2021. Cognitive and neural correlates of loneliness and wisdom during emotional bias. *Cereb. Cortex* 31 (7), 3311–3322.
- Haber, S.N., Calzavara, R., 2009. The cortico-basal ganglia integrative network: the role of the thalamus. *Brain Res. Bull.* 78 (2–3), 69–74.
- Hartergerink, C.H., Van Beest, I., Wicherts, J.M., Williams, K.D., 2015. The ordinal effects of ostracism: a meta-analysis of 120 Cyberball studies. *PLoS One* 10 (5), e0127002.
- Hawley, L.C., Hughes, M.E., Waite, L.J., Masi, C.M., Thisted, R.A., Cacioppo, J.T., 2008. From social structural factors to perceptions of relationship quality and loneliness: the Chicago health, aging, and social relations study. *J. Gerontol. B Psychol. Sci. Soc. Sci.* 63 (6), S375–S384.

- Hagley, L.C., Cacioppo, J.T., 2010. Loneliness matters: a theoretical and empirical review of consequences and mechanisms. *Ann. Behav. Med.* 40 (2), 218–227.
- Hay, D.E., Bleicher, S., Azoulay, R., Kivity, Y., Gilboa-Schechtman, E., 2023. Affective and cognitive impact of social overinclusion: a meta-analytic review of cyberball studies. *Cognit. Emot.* 1–18.
- Inagaki, T.K., Muscatell, K.A., Moieni, M., Dutcher, J.M., Jevtic, I., Irwin, M.R., Eisenberger, N.I., 2016. Yearning for connection? Loneliness is associated with increased ventral striatum activity to close others. *Soc. Cogn. Affect. Neurosci.* 11 (7), 1096–1101.
- James, M.H., McNally, G.P., Li, X., 2021. Role of the thalamus in motivated behavior. *Frontiers in Behavioral Neuroscience* 15, 720592.
- Kanterman, A., Nevat, M., Shamay-Tsoory, S., 2022. Inclusion motivation: measuring the drive to be included in real time and how it is affected by loneliness. *Emotion* 22 (7), 1572.
- Kim, S.H., Yoon, H., Kim, H., Hamann, S., 2015. Individual differences in sensitivity to reward and punishment and neural activity during reward and avoidance learning. *Soc. Cogn. Affect. Neurosci.* 10 (9), 1219–1227.
- Kuss, K., Falk, A., Trautner, P., Montag, C., Weber, B., Fließbach, K., 2015. Neuronal correlates of social decision making are influenced by social value orientation—an fMRI study. *Frontiers in Behavioral Neuroscience* 9, 40.
- Lam, J.A., Murray, E.R., Yu, K.E., Ramsey, M., Nguyen, T.T., Mishra, J., Lee, E.E., 2021. Neurobiology of loneliness: a systematic review. *Neuropsychopharmacology* 46 (11), 1873–1887.
- Lang, F.R., Wagner, J., Wrzus, C., Neyer, F.J., 2013. Personal effort in social relationships across adulthood. *Psychol. Aging* 28 (2), 529.
- Leary, M.R., Baumeister, R.F., 1995. The need to belong. *Psychol. Bull.* 117 (3), 497–529.
- Lieberz, J., Shamay-Tsoory, S.G., Saporta, N., Esser, T., Kuskova, E., Stoffel-Wagner, B., Scheele, D., 2021. Loneliness and the social brain: how perceived social isolation impairs human interactions. *Adv. Sci.* 8 (21), 2102076.
- Lucas, G.M., Knowles, M.L., Gardner, W.L., Molden, D.C., Jefferis, V.E., 2010. Increasing social engagement among lonely individuals: the role of acceptance cues and promotion motivations. *Pers. Soc. Psychol. Bull.* 36 (10), 1346–1359.
- Maier, S.F., Seligman, M.E., 2016. Learned helplessness at fifty: insights from neuroscience. *Psychol. Rev.* 123 (4), 349.
- Marton-Alper, I.Z., Gvirts-Provolovski, H.Z., Nevat, M., Karklinsky, M., Shamay-Tsoory, S.G., 2020. Herding in human groups is related to high autistic traits. *Sci. Rep.* 10 (1), 17957.
- Masten, C.L., Eisenberger, N.I., 2009. Exploring the experience of social rejection in adults and adolescents: a social cognitive neuroscience perspective. Bullying, rejection, and peer victimization: A social cognitive neuroscience perspective 53–78.
- McNally, G.P., 2021. Motivational competition and the paraventricular thalamus. *Neurosci. Biobehav. Rev.* 125, 193–207.
- McLaren, D.G., Ries, M.L., Xu, G., Johnson, S.C., 2012. A generalized form of context-dependent psychophysiological interactions (gPPI): a comparison to standard approaches. *NeuroImage* 61 (4), 1277–1286. <https://doi.org/10.1016/j.neuroimage.2012.03.068>.
- Millan, E.Z., Ong, Z., McNally, G.P., 2017. Paraventricular thalamus: gateway to feeding, appetitive motivation, and drug addiction. *Prog. Brain Res.* 235, 113–137.
- Morr, M., Noell, J., Sassin, D., Daniels, J., Philipsen, A., Becker, B., Scheele, D., 2022. Lonely in the dark: trauma memory and sex-specific dysregulation of amygdala reactivity to fear signals. *Advanced Science* 9 (15), 2105336.
- Nombro, E., MacNeill, A.L., DiTommaso, E., 2022. Interpreting ambiguous situations: the role of loneliness. *Personal. Individ. Differ.* 199, 111862.
- Oldham, S., Murawski, C., Fornito, A., Youssef, G., Yücel, M., Lorenzetti, V., 2018. The anticipation and outcome phases of reward and loss processing: a neuroimaging meta-analysis of the monetary incentive delay task. *Hum. Brain Mapp.* 39 (8), 3398–3418.
- Onoda, K., Okamoto, Y., Nakashima, K.I., Nittono, H., Ura, M., Yamawaki, S., 2009. Decreased ventral anterior cingulate cortex activity is associated with reduced social pain during emotional support. *Soc. Neurosci.* 4 (5), 443–454.
- R Core Team, 2021. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna.
- Radke, S., Jankowiak, K., Tops, S., Abel, T., Habel, U., Derntl, B., 2021. Neurobiobehavioral responses to virtual social rejection in females—exploring the influence of oxytocin. *Soc. Cogn. Affect. Neurosci.* 16 (3), 326–333.
- Rizzolatti, G., Ferrari, P.F., Rozzi, S., & Fogassi, L. (2006, January). The inferior parietal lobule: Where action becomes perception. In *Percept, Decision, Action: Bridging the Gaps: Novartis Foundation Symposium 270* (pp. 129–145). Chichester, UK: John Wiley & Sons, Ltd.
- Rolls, E.T., Huang, C.C., Lin, C.P., Feng, J., Joliot, M., 2020. Automated anatomical labelling atlas 3. *Neuroimage* 206, 116189.
- Russell, D.W., 1996. UCLA loneliness scale (version 3): reliability, validity, and factor structure. *J. Pers. Assess.* 66 (1), 20–40.
- Saporta, N., Scheele, D., Lieberz, J., Stühr-Wulff, F., Hurlmann, R., Shamay-Tsoory, S.G., 2021. Opposing association of situational and chronic loneliness with interpersonal distance. *Brain Sci.* 11 (9), 1135.
- Saporta, N., Scheele, D., Lieberz, J., Nevat, M., Kanterman, A., Hurlmann, R., Shamay-Tsoory, S.G., 2023. Altered activation in the action observation system during synchronization in high loneliness individuals. *Cereb. Cortex* 33 (2), 385–402.
- Schäfer, M., Korn, S., Smith, P.K., Hunter, S.C., Mora-Merchán, J.A., Singer, M.M., Van der Meulen, K., 2004. Lonely in the crowd: recollections of bullying. *Br. J. Dev. Psychol.* 22 (3), 379–394.
- Shamay-Tsoory, S.G., 2011. The neural bases for empathy. *Neuroscientist* 17 (1), 18–24.
- Simard, V., Dandaneau, S., 2018. Revisiting the Cyberball inclusion condition: fortifying fundamental needs by making participants the target of specific inclusion. *J. Exp. Soc. Psychol.* 74, 38–42.
- Spithoven, A.W., Bijttebier, P., Goossens, L., 2017. It is all in their mind: a review on information processing bias in lonely individuals. *Clin. Psychol. Rev.* 58, 97–114.
- Tang, F., Li, K., Wang, Y., Zhu, Y., Jiang, Y., 2024. Social disconnectedness, perceived loneliness, and cognitive functioning: the role of neighborhood environment. *Innov. Aging*, igae009. <https://doi.org/10.1093/geroni/igae009>.
- Tomova, L., Wang, K.L., Thompson, T., Matthews, G.A., Takahashi, A., Tye, K.M., Saxe, R., 2020. Acute social isolation evokes midbrain craving responses similar to hunger. *Nat. Neurosci.* 23 (12), 1597–1605.
- Treadway, M.T., Buckholtz, J.W., Schwartzman, A.N., Lambert, W.E., Zald, D.H., 2009. Worth the ‘EEfRT’? The effort expenditure for rewards task as an objective measure of motivation and anhedonia. *PLoS One* 4 (8), e6598.
- Uddin, L.Q., Molnar-Szakacs, I., Zaidel, E., Iacoboni, M., 2006. rTMS to the right inferior parietal lobule disrupts self–other discrimination. *Soc. Cogn. Affect. Neurosci.* 1 (1), 65–71.
- Vassar, M., Crosby, J.W., 2008. A reliability generalization study of coefficient alpha for the UCLA loneliness scale. *J. Pers. Assess.* 90 (6), 601–607.
- Vitale, E.M., Smith, A.S., 2022. Neurobiology of loneliness, isolation, and loss: integrating human and animal perspectives. *Frontiers in Behavioral Neuroscience* 16, 846315.
- Weinstein, A.M., 2023. Reward, motivation and brain imaging in human healthy participants—a narrative review. *Front. Behav. Neurosci.* 17, 1123733.
- Williams, K.D., Cheung, C.K., Choi, W., 2000. Cyberostracism: effects of being ignored over the internet. *J. Pers. Soc. Psychol.* 79 (5), 748.
- Williams, K.D., Nida, S.A., 2011. Ostracism: consequences and coping. *Curr. Dir. Psychol. Sci.* 20 (2), 71–75.
- Zadro, L., Williams, K.D., Richardson, R., 2004. How low can you go? Ostracism by a computer is sufficient to lower self-reported levels of belonging, control, self-esteem, and meaningful existence. *J. Exp. Soc. Psychol.* 40 (4), 560–567.