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Imaging the “social brain” in schizophrenia: A systematic review of neuroimaging studies of social reward and punishment

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ABSTRACT

Decreased social functioning and high levels of loneliness and social isolation are common in schizophrenia spectrum disorders (SSD), contributing to reduced quality of life. One key contributor to social impairment is low social motivation, which may stem from aberrant neural processing of socially rewarding or punishing stimuli. To summarize research on the neurobiology of social motivation in SSD, we performed a systematic literature review of neuroimaging studies involving the presentation of social stimuli intended to elicit feelings of reward and/or punishment. Across 11 studies meeting criteria, people with SSD demonstrated weaker modulation of brain activity in regions within a proposed social interaction network, including prefrontal, cingulate, and striatal regions, as well as the amygdala and insula. Firm conclusions regarding neural differences in SSD in these regions, as well as connections within networks, are limited due to conceptual and methodological inconsistencies across the available studies. We conclude by making recommendations for the study of social reward and punishment processing in SSD in future research.

Schizophrenia spectrum disorders (SSD), including schizophrenia, schizoaffective disorder, and schizophreniform disorder, are characterized by impairments in social functioning. Available pharmacological and behavioral treatments are generally effective for positive symptoms, including hallucinations and delusions (Kirkpatrick et al., 2006). However, cognitive deficits (e.g., memory and decision-making impairments; Nuechterlein and Dawson, 1984) and negative symptoms (e.g., motivational impairment; Andreasen, 1982) remain key contributors to social functioning impairment and associated burden throughout the illness (Foussias and Remington, 2008; Fulford et al., 2018a). These symptoms are less responsive to intervention than positive symptoms (Kirkpatrick et al., 2006). It is thus critical to improve our mechanistic understanding of cognitive deficits and negative symptoms of SSD to inform the development of effective treatments for social impairment.

Social impairment is typically chronic and contributes to reduced quality of life in SSD (Fulford et al., 2013; Velthorst et al., 2017). People with SSD often report high levels of loneliness (Eglit et al., 2018), less connection with family, and fewer friends than people without SSD (Bellack et al., 1990; Corrigan and Phelan, 2004; Fulford et al., 2018a; Mueser and Bellack, 1998). In the general population, social isolation and loneliness contribute to poorer mental and physical health outcomes, including rates of early mortality on par with smoking and obesity (Holt-Lunstad et al., 2015; Steptoe et al., 2013), making it especially important to understand contributors to social impairment in SSD.

Many factors contribute to impaired social functioning in people with SSD. Social skill deficits, such as problems with conversational turn-taking, active listening, and appropriate eye contact and affective expression, have been well studied (Bellack et al., 1990; Mueser et al., 1991; Mueser and Bellack, 1998). These deficits are associated with lower subjective quality of life (Salokangas et al., 2006). General cognitive deficits, lack of meaningful relationships early in life, and limited opportunities for practice during critical developmental periods contribute to social skill deficits (Bellack et al., 1990). Other key contributors to social impairment in SSD include social cognitive deficits, including diminished Theory of Mind (ToM), facial affect recognition, and emotion recognition abilities (Penn et al., 2008). Positive symptoms, especially delusional thinking (viz. suspiciousness and paranoia), can also interfere with the development of trust critical for social connection (Gromann et al., 2013). It is worth noting that positive symptoms are effectively managed with medication and psychotherapy, and social skill and social cognition deficits can improve with existing cognitive and behavioral interventions (Kopelowicz et al., 2006; Kurtz and Richardson, 2011; Pinkham et al., 2007; Pinkham and Penn, 2006).

One area of research concerning social dysfunction in SSD that has

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received less attention is the role of social motivation. Reward and punishment learning are central components of motivation (Green et al., 2015; Salamone and Correa, 2012). Prior work suggests that people with SSD show deficits in initiating responses that are reinforced with rewards (i.e., positive reinforcement; Reinen et al., 2014) but demonstrate intact learning when rewards are removed, as well as avoidance of actions leading to loss (i.e., negative punishment; Strauss et al., 2013). Further, while responsivity to the receipt, removal, or absence of reward appears to be similar to people without SSD, there is evidence that those with SSD have difficulty processing the frequency with which rewards follow instrumental responses (Gold et al., 2008). Deficits in reward and punishment learning may be a consequence of memory deficits that impact recollection of high-arousal interactions (Herbener, 2008), or abnormalities in the value representation of rewarding or punishing stimuli (Gold et al., 2008).

Our understanding of motivational impairment in people with SSD is primarily based on research using nonsocial stimuli, such as monetary reward. Prior literature suggests both types of reward are associated with similar neural activation patterns (i.e., a "common neural currency"; see (Gu et al., 2019; Izuma et al., 2008; Wake and Izuma, 2017). However, social interactions are complex and dynamic, with high levels of ambiguity regarding potential for reward (e.g., acceptance) or punishment (e.g., rejection; FeldmanHall and Shenhav, 2019). For these reasons, nonsocial rewards as presented in existing paradigms (e.g., losing money) may not adequately capture the qualities of social interaction that contribute to impairment in social motivation (see Fulford et al., 2018a,b). Studies observing common neural representations of social and nonsocial reward have commonly used stimuli that are similarly static, and may therefore not have captured the full complexity involved in social processing (Gu et al., 2019; Izuma et al., 2008). It is also possible that social reward processing may both overlap with and extend beyond regions involved in processing nonsocial reward due to the additional complexities of social interactions.

Behavioral studies have explored social reward and punishment in SSD through game-like tasks, live interactions, and virtual reality. Findings from these studies suggest abnormalities in social reward and punishment valuation and reduced reward learning in SSD relative to controls (Catalano et al., 2018; Hanssen et al., 2019, 2018). Reward and punishment processing is also linked to social behavior in SSD. For instance, some prior literature has suggested that individuals with SSD perform worse on tasks while receiving praise (Berkowitz, 1964; Cavanaugh et al., 1960; Irwin and Renner, 1969). Conversely, a recent study found that praise improved effort expenditure in both SSD and controls, but higher levels of social withdrawal in participants with SSD were associated with lower effort expended with or without praise (Fulford et al., 2018b). Additionally, people with SSD appear to demonstrate abnormal social approach and avoidance behaviors associated with responses to social reward and punishment. In one study, individuals with SSD were found to show reductions in both approaching rewarding, or happy, faces, and avoiding punishing, or angry, faces (Radke et al., 2015). Another study found that compared with controls, those with SSD were faster to avoid rewarding (happy) faces with an averted gaze, and approached experimenters less in a personal space task (de la Asuncion et al., 2015). Nonetheless, the mechanisms underlying deficits in social motivation in SSD remain unclear. Understanding the neural mechanisms contributing to reduced social motivation in SSD, including the neural correlates of social reward and punishment, has the potential to inform treatment targets for social impairment (Ochsner, 2008; Rosenfeld et al., 2010).

Neural processing of social reward and punishment in humans has recently been proposed to be localized to three distinct systems, or networks (see Fig. 1; Redcay and Schilbach, 2019). The "mentalizing network," comprising the temporoparietal junction (TPJ), superior temporal sulcus (STS), inferior frontal gyrus (IFG), posterior cingulate cortex (PCC), precuneus, anterior temporal lobe (aTL), and dorsal and ventral medial prefrontal cortex (dmPFC, vmPFC), is typically more active during socially interactive cognitive tasks than equally complex non-social or non-interactive tasks (e.g., ToM; Alkire et al., 2018; Ciaramidaro et al., 2013). The "mirror neuron" network is comprised of the inferior parietal lobe (IPL), intraparietal sulcus (IPS), and ventral premotor cortex (vPMC); this network is generally more active while observing others' communicative actions than while observing non-communicative actions and is hypothesized to support preparation of movements that respond to such actions (Ciaramidaro et al., 2013). The third network, referred to as the "reward" or "affective network" and, alternately, the "social pain network," comprises the anterior cingulate cortex (ACC) and anterior insula (aINS) (Schmälzle et al., 2017), as well as the amygdala, orbitofrontal cortex (OFC), and ventral striatum (VS) (Gordon et al., 2013; Pfeiffer et al., 2014). This network is more active in the context of salient stimuli (e.g., social interactions), including both social reward and punishment, than during affectively neutral social interactions, relative to other networks; as such, we refer to this network as the affective network in this review. The mentalizing, mirror neuron, and affective networks together have been collectively referred to as the *social interaction network* (see Redcay and Schilbach, 2019). Of note, this system includes regions that are implicated in many different functions; as such, the aforementioned labels are not intended to serve as a complete description of each region's function, but rather to organize their potential role within the particular context of social interactions.

Structural differences in various regions implicated in the social interaction network have been identified in people with SSD, including smaller amygdala, left mPFC, bilateral ACC, bilateral STS, right insula, and precuneus volume than healthy controls (Kubota et al., 2012; Namiki et al., 2007; Yamada et al., 2007). Other studies have found enlarged grey matter volumes in the basal ganglia (encompassing the ventral striatum), possibly due to chronic use of typical (in contrast with atypical) antipsychotics (Scherk and Falkai, 2006), and reduced grey matter volume in frontal and temporal lobes (Schultz et al., 2010; Shenton et al., 2010) in SSD. Although these structural abnormalities have been observed in relation to other factors, such as development (i.e., volume is thought to decrease over time), antipsychotic medication, and ventricle size (i.e., larger ventricles are often observed alongside reduced grey matter), the actual causes of volume reductions in SSD remain largely unknown (Shenton et al., 2010). In all, there is evidence that regions involved in the mentalizing and affective networks are reduced in grey matter volume in people with SSD. It is thus also possible that people with SSD demonstrate abnormal function in these regions in addition to structure.

In this systematic review we qualitatively summarize published work examining social reward and punishment in functional neuroimaging studies of people with SSD. Due to the relative nascence of this line of research, including the limited number of studies and high variability among the tasks and analyses used, we determined that a meta-analysis would be premature at this time. For the purposes of this review, we define social reward and punishment as social stimuli designed to elicit the experience of acceptance (e.g., praise) or rejection (e.g., criticism) in the participant. We focus on studies that explicitly manipulated social reward and punishment within the context of a task administered during neuroimaging. In our synthesis of the existing studies, we address inconsistencies in the research, from the variability in operationalization of social reward and punishment, to the behavioral and neuroimaging methods used to measure these constructs. We conclude with recommending directions of future work.

1. Methods

We conducted a systematic review of the literature related to the functional neuroimaging of social reward and punishment in SSD. We structured our review according the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Moher et al., 2009) guidelines.

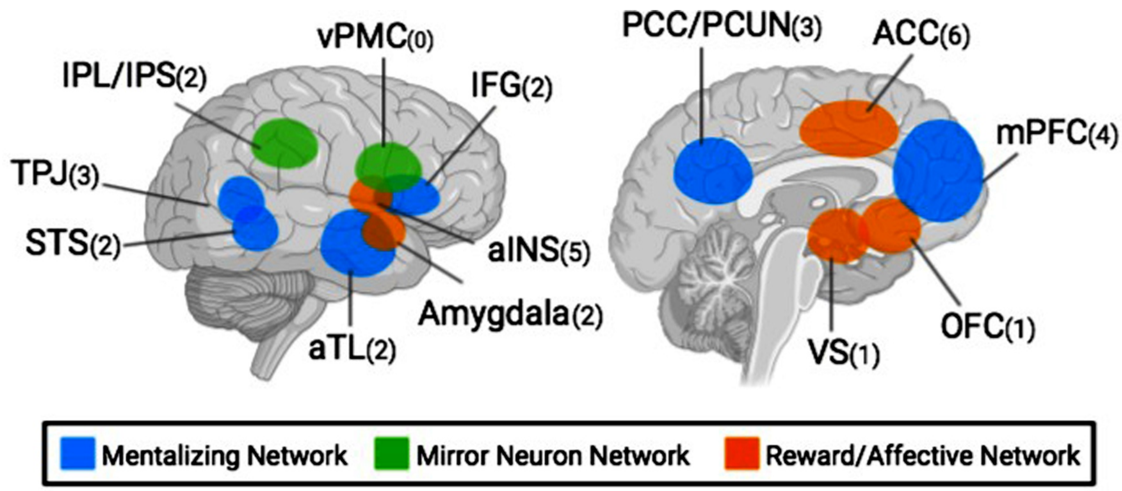


Fig. 1. Image adapted from Redcay and Schilbach (2019). Regions previously associated with affective, mentalizing, and mirror neuron systems, all comprising the social interaction system. Numbers in the image labels represent the number of reviewed studies reporting findings in the respective region. Regions depicted above: TPJ = temporoparietal junction, STS = superior temporal sulcus, aTL = anterior temporal lobe, PCC = posterior cingulate cortex, dmPFC = dorsomedial prefrontal cortex, vmPFC = ventromedial prefrontal cortex, IPL = inferior parietal lobe, IPS = intraparietal sulcus, vPMC = ventral premotor cortex, aINS = anterior insula, ACC = anterior cingulate cortex, OFC = orbitofrontal cortex, VS = ventral striatum. See Table 2 for findings within these regions.

1.1. Literature search strategy

Our search was conducted through three databases: PubMed, PsycINFO, and Web of Science. The search was restricted to “Title/Abstract” in PubMed, “Abstract” in PsycINFO, and “Topic” in Web of Science. Upon initial search, only two relevant studies before the year 2000 were identified, neither of which met inclusion criteria. As 2000 was the first year in which relevant studies were published, we used this as the starting year for our search. We used a comprehensive approach to defining our search terms to capture wide variation in the measurement of social reward and punishment. We selected search terms based on those identified in the existing literature and through discussion among the authors.

The final list of search terms included the following: (Neuroimaging OR MRI OR scanner OR imaging OR fMRI) AND Social* AND (Reward* OR reinforcement OR drive OR affiliati* OR trust OR "social inclusion" OR "social interaction" OR effort OR decision-making OR motivation OR pleasure OR friends* OR feedback OR “social orienting” OR “social exchange” OR “social evaluation” OR cooperati* OR praise OR communication OR approval OR acceptance OR prosocial OR “social valuation” OR peer* OR “social anhedonia” OR rejection OR “social punishment” OR “social comparison” OR criticism OR “social stress” OR exclusion) AND (Schizop* OR schizoa* OR psychosis OR psychotic). Additional articles were identified within the reference lists of the articles found from our database search. The search was performed on December 6, 2019.

1.2. Study inclusion criteria

We included studies that met the following eligibility criteria: 1) published between January 1, 2000 and December 31, 2019; 2) published as an empirical article in a peer-reviewed journal; 3) written or translated in English; 4) conducted in people with SSD (i.e., schizophrenia, schizoaffective disorder, schizophreniform disorder); 5) used neuroimaging (e.g., MRI, EEG, PET); 6) included a paradigm involving both the presentation of social stimuli (“social” being broadly defined as the appearance of or communication from another human in the stimulus) and a measurement of response (neural, behavioral, or both) to the social stimuli; 7) involved stimuli that were intended to elicit a positive (rewarding) or negative (punishing) emotional state; and 8) the reward or punishment experienced during the study was intended to be directly elicited by the social components of the stimuli.

Studies that measured social cognition (e.g., theory of mind or emotion recognition) but not emotional or motivational responses to social stimuli were not included. The distinction between these two concepts was determined from the following: 1) whether the authors explicitly defined a stimulus as rewarding or punishing, 2) whether the participants rated a stimulus as rewarding or punishing through self-report, or 3) whether participants’ behaviors in the task were interpreted as responsive to reward or punishment (e.g., choosing stimuli that were rewarded, demonstrating learning based on reward cues). Papers were excluded if they did not meet at least one of these three criteria. Studies including paradigms where reward or punishment was non-social (e.g., monetary or points-based), or that only examined correlations between neural structure or function and self-reported real-world social activity (i.e., quality of life questionnaires), were excluded. Furthermore, studies with individuals at clinical high risk for psychosis were not included. Some articles included stimuli with a social component along with nonsocial stimuli; if the authors did not analyze responses to the social and nonsocial stimuli separately, the paper was not considered to examine purely social reward and was thus excluded. No papers were excluded based on either regions of interest (ROIs) or the analytic approach. Because no studies were found that used a different modality and met all other seven criteria, we focus solely on task-based fMRI in this review.

2. Results

Our search returned a total of 761 publications, with 493 remaining after removing duplicates. Three of the 493 articles were found through additional sources (e.g., in the citations of another included article). A total of 461 articles were excluded after reviewing the title/abstract, leaving 31 articles remaining. Of these, 20 articles were excluded after the full text review (see Supplementary Materials for reasons for exclusion). A total of 11 articles were included after reviewing the full text (see Fig. 2). We begin by presenting general characteristics of these studies, then summarize the experimental results in relation to the aforementioned affective, mentalizing, and mirror neuron networks.

2.1. Study characteristics

Of the included studies, eight recruited people with schizophrenia, one with either schizophrenia or schizoaffective disorder, one with non-affective psychosis, and one with first-episode psychosis (FEP; see

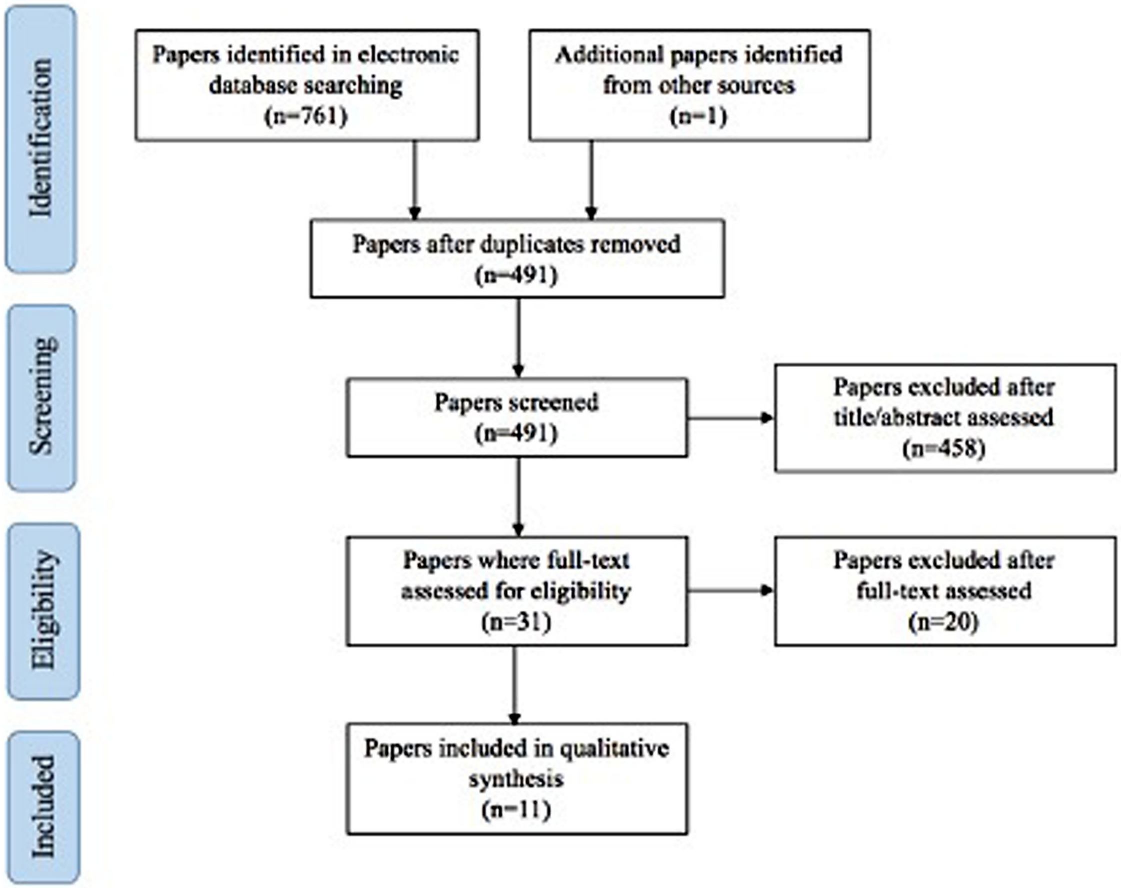


Fig. 2. Detailed overview of systematic selection of articles using the PRISMA guidelines.

Table 1). All but one study included a healthy control group, and one study included a third group of participants at clinical high risk for psychosis in addition to the SSD group. All studies had majority male participants in both psychosis and healthy control groups.

Studies used an array of experimental designs, falling into two general categories: 1) paradigms in which participants passively observed socially rewarding or punishing images (“passive observation”), or 2) interactive paradigms, in which participants received rewarding or punishing social feedback (“social engagement”). Passive observation and social engagement tasks have previously been described as “third person” and “second person” tasks, respectively (Redcay and Schilbach, 2019). Two studies involved passive observation of social feedback that was personalized to each participant. We considered these social engagement tasks because their personal nature required engagement with those giving social feedback from the participant prior to stimulus creation.

2.2. Neuroimaging methods

Studies varied in hardware used. Five studies used a General Electric Signa, two used a Siemens Trio, one used a Siemens Magnetom, and three used Philips scanners (Achieva, Gyroscan Intera, and one unspecified). Seven studies used a 3 T scanner, and four used 1.5 T. ROI and whole-brain analyses were used in all but one of the studies, which compared groups based on average complexity of the BOLD signal (see Table 2 for regions investigated in contrast analyses). Five studies performed only a whole-brain analysis, while four studies performed both whole-brain and a priori ROI analyses, one of which only reported whole brain results in supplementary materials due to a low threshold and thus are not discussed in this review. Only one study used predetermined ROIs and no exploratory whole-brain analysis. In addition to a whole-brain analysis, one study also measured functional connectivity from BOLD signal collected during the task. In total, among the 11 studies, nine reported between-group comparisons. Nine studies contributed to 16 within-group contrasts reported in this review; the remaining two did not report contrasts, but used correlation analyses instead. It should be noted that while regional activation was analyzed in these studies in temporal relation to the stimuli presented, no causal inferences can be drawn from the results.

2.3. Passive observation paradigms

Four studies used paradigms in which participants passively observed static social images. One of these studies presented rewarding images, one presented punishing images, and two presented both rewarding and punishing images in separate conditions.

Berger, Bitsch, Nagels, Straube, & Falkenberg (2018) showed 31 participants with SSD and 19 without SSD humorous (rewarding) and neutral cartoon images (Fig. 3A) and asked them to rate how funny each image was. Analyses involved a between-group contrast (SSD vs. controls), a within-group contrast (funny vs. neutral), and correlations between subjective funniness ratings and neural activity. While greater activation was present in response to humorous than neutral images across several brain regions in both groups, there were some notable group differences in which regions showed greater activation. In people with SSD (but not in controls), greater activation was found while viewing humorous than neutral images in the TPJ, IFG, left medial temporal gyrus (MTG), striatum, left midcingulate cortex (MCC), precuneus, cerebellum, right superior temporal gyrus (STG), and right temporal pole. Control participants showed greater activation in bilateral ACC, mPFC, dorsal striatum, insula, left amygdala, SFG, and middle frontal gyrus (MFG) during humor vs. neutral trials compared to

Table 1
Studies included in the current review, with respective qualities. Abbreviations are as follows: SSD = schizophrenia spectrum disorders; CN = controls; FEP = first episode psychosis; CHR = clinical high risk; NR = not reported; N/A = not applicable; MTG = medial temporal gyrus; STG = superior temporal gyrus; ACC = anterior cingulate cortex; SFG = superior frontal gyrus; MCC = medial cingulate cortex; SMA = supplementary motor area; AG = angular gyrus; IFG = inferior frontal gyrus; mPFC = medial prefrontal gyrus; OG = occipital gyrus; dlPFC = dorsolateral prefrontal cortex; dACC = dorsal ACC; pSTS = posterior superior temporal sulcus; SMG = supramarginal gyrus; TPJ = temporoparietal junction; SPG = superior parietal gyrus; IPG = inferior parietal gyrus; STP = superior temporal pole.

Sokunbi et al., 2014	Rylands et al., 2011	Makowski et al., 2016[d]	Lindner et al., 2014[c]	Lemmers-Janssen et al. 2018[b]	Lee et al., 2018	Lee et al., 2014	Gromann et al., 2013	Gradin et al., 2012	Bjorkquist et al. 2013	Berger et al., 2018[a]		**Reference**
UK	UK	Canada	Germany	Netherlands	USA	Korea	UK	UK	USA	Germany		**Location**
SSD, CN	SSD	SSD, CN	SSD, CN	FEP, CHR, CN	SSD, CN	SSD, CN	Non-affective psychosis, CN	SSD, CN	SSD or SAD, CN	SSD, CN		**Group(s)**
13	11	15	36	22	27	15	20	13	14	31	**n**	**SSD/Psychosis group description**
84.62	81.82	73.33	61.1	63.64	58	66.67	100	84.62	71	70.97	**% men**	
41.22 ± 11.78	33 ± 12.2	33.1 ± 7.7	30.8 ± 7.9	19.88 ± 1.54	45.8 ± 10.3	30.7 ± 6.6	33.7 ± 7.8	40.87 ± 11.72	31.57 ± 7.52	32.60 ± 10.02	**age**	
16	N/A	15	40	43	25	16	20	16	14	19	**n**	**CN group description**
43.75	N/A	60	67.5	51.16	68	56.25	100	43.75	64	47.37	**% men**	
41.56 ± 11.920	N/A	35.2 ± 9.8	29.5 ± 8.3	21.06 ± 2.74	47.2 ± 9.2	27.4 ± 6.9	32.2 ± 9.1	41.23 ± 11.78	31.36 ± 11.38	29.26 ± 5.15	**age**	
Social Engagement	Passive Observation	Social Engagement	Social Engagement	Social Engagement	Passive Observation	Social Engagement	Social Engagement	Social Engagement	Passive Observation	Passive Observation		**Type of Paradigm**
P	P	RP	P	RP	RP	RP	RP	P	RP	R		**Reward (R), Punishment (P), or Both (RP)**
[Correlation and group contrast only]	Relative Criticism (RC) vs. Relative Neutral (RN); Stranger Criticism (SC) vs. Stranger Neutral (SN); RC vs. SC; RN vs. SN; RC vs. SN; RN vs. SC	Self[HSR] vs. Other[HSR]; Self [LSR] vs. Other [LSR]; Self[HSR + LSR] vs. Other [HSR + LSR]	Happy vs. Neutral; Disgust vs. Neutral; Masked vs. Unmasked	Cooperative vs. Control; Unfair vs. Control; Cooperative vs. Unfair	High Payout vs. Low Payout; Social vs. Nonsocial	Acceptance vs. Refusal	[Correlation and group contrast only]	[Correlation and group contrast only]	Social vs. Nonsocial; Emotional vs. Neutral	Funny vs. Neutral		**Contrast(s) Reported**
Cyberball; computer game involving exclusion from passing a ball to other players.	Subjects passively heard neutral and critical statements made by key relative or stranger	Personality traits presented with picture of self or other as personality ratings; viewed and rated for desirability	Subjects passively viewed neutral and disgust faces presented for 33 ms before neutral face mask	Trust game involving cooperative and unfair repayments of investments from a "trustee"	Probabilistic reinforcement learning task with social and monetary rewards	Subjects raised hand to greet virtual avatar who either accepted or rejected handshake	Trust game involving cooperative and unfair repayments of investments from a "trustee"	Cyberball; computer game involving exclusion from passing a ball to other players.	Positive, negative, and neutral images with or without social component viewed and rated on valence	Humorous pictures viewed and rated on funniness		**Brief Description of Paradigm**
General Electric Signa, 1.5 T	Philips, 1.5 T	Siemens Magnetom, 3 T	Philips Gyroscan Intera, 3 T	Philips Achieva, 3 T	Siemens Trio, 3 T	General Electric Signa, 1.5 T	General Electric Signa, 3 T	General Electric Signa, 1.5 T	General Electric Signa, 3 T	Siemens MRT Trio, 3 T		**Scanner Type**
N/A	IFG, ACC, MFG, Temporal Pole, Insula, Precentral Gyrus, SFG	None	Amygdala, insula	Right Caudate, STS, Left Insula, mPFC	VS, vmPFC, ACC	None	Right Caudate, TPJ, mPFC	None	None	None		**Pre-determined ROIs**
N/A; SampEn and Hurst exponent calculated over whole brain	None (no whole-brain analysis)	Frontal, Cingulum, Lingual Gyrus, Calcarine	Only presented in supplementary material	TPJ	None	pSTS, Thalamus, Frontopolar Cortex, MFG, SFG, ACC,	Inferior Parietal Lobule, MTG	Occipital, Temporal, dlPFC, Superior	IFG, MTG, Middle OG, MCC, ACC, Thalamus	MTG, STG, ACC, Lingual Gyrus, Precuneus, SFG, MCC,		**Other Regions Found Through Whole-Brain Analysis**

(*continued on next page*)

Table 1 (*continued*)

Sokunbi et al., 2014	Rylands et al., 2011	Makowski et al., 2016[d]	Lindner et al., 2014[c]	Lemmers-Janssen et al. 2018[b]	Lee et al., 2018	Lee et al., 2014	Gromann et al., 2013	Gradin et al., 2012	Bjorkquist et al. 2013	Berger et al., 2018[a]	**Reference**
		[Fissure], OG, Precuneus, Temporal, Thalamus, Hippocampus, Caudate, Cerebellum, Rectus, Postcentral Gyrus, SMG, AG, SPG, IPG, Insula, STP, Amygdala, mPFC				Paracentral Lobule, Superior Parietal Lobule, Fusiform Gyrus, SMG, MCC, Insula, Cerebellum		Parietal, dACC, Superior Caudate, Fusiform Gyrus, Cerebellum, Parietal		Cerebellum, Putamen, SMA, Precentral Gyrus, Rolandic Operculum, Hippocampus, AG, IFG, Insula, mPFC	
Social Distress scale for Cyberball	N/A	Desirability ratings	Manipulation check	Initial investment amount, manipulation check	Rate of choosing optimal outcomes	Reaction time, manipulation check	Initial investment amount	Social Distress scale for Cyberball	Valence rating, reaction time	Funniness ratings	**Behavioral Measures Collected**
PANSS	PANSS, HEE (assessed from Camberwell Family Interview)	WASI, SERS, SDS, EQ, MCMI, AIHQ, SAS, PAS, IRI, TEPS	Multidimentional Loneliness Questionnaire, NEO-FFI, SANS, SAPS, BDI, STAI, Multiple Choice Vocabulary Intelligence Test	PANSS, WAIS, CAARMS	BPRS, CAINS, MAP, MATRICS/MCCB	Raven's Progressive Matrices, IAS, STAI, PANSS	PANSS, BDI, WAIS-III	BDI, Spielberger State Anxiety scale, Rosenberg Self-Esteem Scale, PANSS	PANSS, WRAT, WASI	SAPS/SANS, CDSS	**Questionnaires/ Interviews Collected**
Receiver Operating Characteristic analyses for mean whole brain sample entropy (SampEn) and H values. Independent t-tests and general linear model analyses.	Random effects model	One-sample and two-sample t-tests conducted for mean activation maps at subject and group level for each contrast. Mixed-design ANOVA with group as between-subjects variable and conditions as within-subjects variable.	Fixed-effects analyses at the individual level to generate individual contrast maps; random effect analyses at the group level.	Not specified	Repeated-measures ANOVA with group as between-subject factor and ROI and condition as within-subject factors	Paired sample t-tests between conditions for group-level contrast images; two-sample t-tests of condition-based activity differences between groups	Random effects general linear model analyses based on individual design matrices	Random effects analyses for within and between group differences	3-way mixed design ANOVA with within- and between-subjects variables included	Random effect analysis (one-sample t-test) within groups; two-sample t-tests between groups	**Type of Analysis**

[a] The data from healthy control participants reported in this paper were collected in a different, previous study.
[b] This study also included one more subject group of clinical high risk, which had an n of 17, 41.18 % male, and mean age of 23.78 ± 2.42.
[c] All studies above except one included 100 % right handed individuals, or did not report handedness. Lindner et al. (2014) was the only study that included left handed participants. 94.4 % of their SSD group was right handed, while 95 % of their control group was.
[d] More contrasts were analyzed in this paper, but only selected ones were reported (listed above).

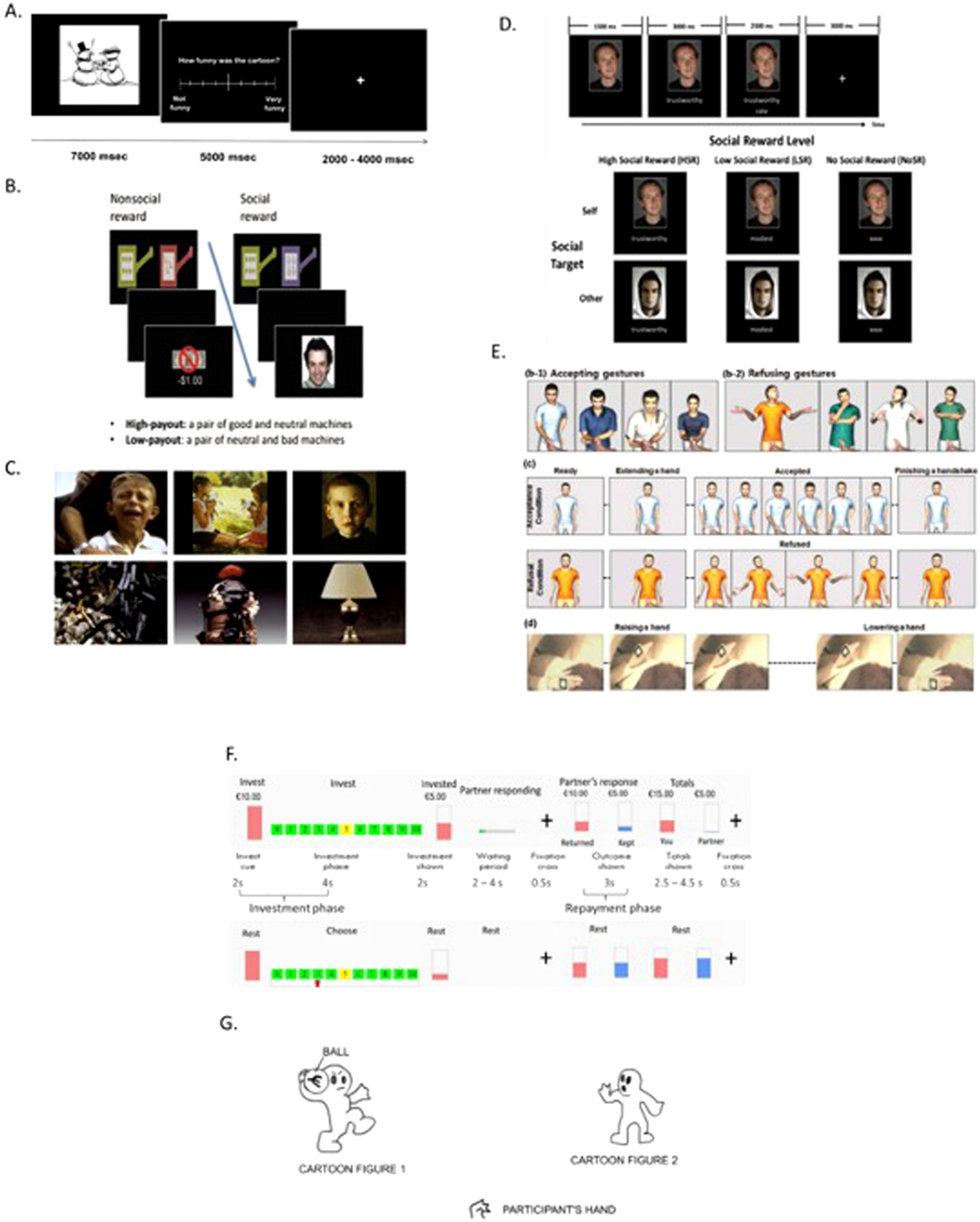
Table 2
Regions of interest demonstrating significant contrasts (group and condition) within the social interaction networks. Correlational analyses not included. SSD = schizophrenia spectrum disorders, CN = controls, ACC = anterior cingulate cortex, OFC = orbitofrontal cortex, VS = ventral striatum, aTL = anterior temporal lobe, IFG = inferior frontal gyrus, mPFC = medial prefrontal cortex, PCC = posterior cingulate cortex, TPJ = temporoparietal junction, IPL = inferior parietal lobe, IPS = intraparietal sulcus. See Fig. 1 for the location of each of these regions.

Network Involvement	Region	Study	Region Coordinates (x, y, z)	Type of Study	Between-Group Contrasts	Condition Contrasts	Group x Condition Interactions
Affective Network	ACC	Berger et al., 2018	6, 28, 2 (MNI)	Passive Observation	CN > SSD	Funny > Neutral cartoons	CN > SSD for Funny > Neutral
		Bjorkquist et al. 2013	−1.5, 4.5, 44.5 (Talairach)	Passive Observation	SSD > CN	Neutral > Affective pictures	SSD > CN for Neutral > Affective; Social > Nonsocial in HC only
		H. Lee et al., 2014	−11, 39, 6 (Talairach)	Social Engagement	SSD only	Rejection > Acceptance of handshake	Rejection > Acceptance in SSD only
		J. Lee et al., 2018	0, 44, 6 (MNI)	Passive Observation	CN > SSD	Social reward (smiles) only	CN > SSD for social reward
		Makowski et al., 2016	6, 24, 18; -4, 36, -10; 0, 36, -4 (MNI)	Social Engagement	CN and SSD	Reward and combined reward and punishment > neutral ("other"-related) personality traits	Reward > Neutral in both groups; Affective > Neutral in CN only
		Rylands et al., 2011	0, 27, 24 (MNI)	Social Engagement	SSD only (no CN group included)	Critical > Neutral statements from relatives	Criticism > neutral in SSD
	Insula	H. Lee et al., 2014	31, -7, 10 (Talairach)	Social Engagement	CN > SSD	Rejection > Acceptance of handshake	CN > SSD for Rejection > Acceptance
		Lemmers-Jansen et al., 2018	−33, 14, 0 (MNI)	Social Engagement	CN = SSD	Cooperation = Deception	No group or condition differences
		Lindner et al., 2014	−40, -16, 4 (L, SSD); 40, -10, 6 (R, SSD); -26, 18, -14 (L, CN); 30, 22, -20 (R, CN) (MNI)	Passive Observation	CN > SSD	Masked Disgust > Neutral faces	CN > SSD for disgust > neutral faces, and CN > SSD overall
		Makowski et al., 2016	−24, 22, -10; 30, 22, -18; 30, 12, -18 (MNI)	Social Engagement	CN > SSD	Reward and combined reward and punishment > neutral ("other"-related) personality traits	CN > SSD for Reward > Neutral; Affective > Neutral in CN only
		Rylands et al., 2011	−39, 12, 3 (MNI)	Social Engagement	SSD only (no CN group included)	Critical > Neutral statements from relatives	Criticism > neutral in SSD
	Amygdala	Lindner et al., 2014	Masked: SSD: -28, 4, -18 (L); 26, 2, -20 (R); CN: -22, 0, -26 (L); 26, -2, -28 (R). Unmasked: SSD: -24, 0, -26 (L); 26, -2, -28 (R); CN: -20, -2, -26 (L); 36, 0, -24 (R) (MNI)	Passive Observation	CN = SSD	Disgust = neutral faces	No group or condition differences
		Makowski et al., 2016	−14, -4, -14; 24, 2, -12 (MNI)	Social Engagement	CN > SSD	Reward and combined reward and punishment > neutral ("other"-related) personality traits	CN > SSD for Reward > Neutral; Affective > Neutral in CN only
	OFC	Makowski et al., 2016	4, 32, -10; 8, 46, 18 (MNI)	Social Engagement	CN and SSD	Reward and combined reward and punishment > neutral ("other"-related) personality traits	Reward > Neutral in SSD only; Affective > Neutral in CN only
	VS	J. Lee et al., 2018	+/-12, 12, -10 (MNI)	Passive Observation	CN > SSD	Social reward (smiles) only	CN > SSD for social reward

(*continued on next page*)

Table 2 (*continued*)

Network Involvement	Region	Study	Region Coordinates (x, y, z)	Type of Study	Between-Group Contrasts	Condition Contrasts	Group x Condition Interactions
Mentalizing Network	aTL	Makowski et al., 2016	−30, 16, -22; 36, 20, -24; 34, 18, -22; -34, 20, -18; 32, 20, -30; 30, 34, -14; -46, 18, -12 (MNI)	Social Engagement	CN and SSD	Reward and combined reward and punishment > neutral ("other"-related) personality traits	CN > SSD for Reward > Neutral; Affective > Neutral in both groups
		Rylands et al., 2011	−54, 12, -24 (MNI)	Social Engagement	SSD only (no CN group included)	Critical > Neutral statements from relatives	Criticism > neutral in SSD
	IFG	Makowski et al., 2016	Pars orbitalis: 28, 16, -22; -48, 28, -16; -30, 22, -14; 42, 22, -18; -26, 14, -22; 30, 34, -14; -46, 30, -16. Pars triangularis: 52, 38, 2; -40, 30, 0; -54, 20, 20. Pars opercularis: 56, 14, 10.	Social Engagement	CN = SSD	Reward > neutral; punishment > neutral; combined > neutral ("other"-related) personality traits	Any affective > neutral in both groups
		Rylands et al., 2011	−51, 27, -12	Social Engagement	SSD only (no CN group included)	Critical > Neutral statements from relatives	Criticism > neutral in SSD
	mPFC	Gromann et al., 2013	−3, 64, 20 (Talairach)	Social Engagement	CN = SSD	Cooperation > Deception	Cooperation > Deception in both groups
		J. Lee et al., 2018	2, 46, -8 (MNI)	Passive Observation	CN > SSD	Social reward (smiles) only	CN > SSD for social reward
		Lemmers-Jansen et al., 2018	−3, 65, 25 (MNI)	Social Engagement	CN = SSD	Deception > Cooperation	Deception > Cooperation in both groups
		Makowski et al., 2016	−28, 56, 24; 30, 24, 52; 6, 36, 40; −40, 12, 34 (MNI)	Social Engagement	CN and SSD	Reward and combined reward and punishment > neutral ("other"-related) personality traits	See OFC, MFG, and ACC
	PCC	Makowski et al., 2016	18, -44, 38; -24, -48, 24; -8, -54, 10 (MNI)	Social Engagement	Mixed findings	Reward and punishment > neutral ("other"-related) personality traits	CN > SSD for Reward > Neutral; Punishment > Neutral in SSD only
	Precuneus	Berger et al., 2018	0, -56, 32 (L/R); −4, -38, 56 (L) (MNI)	Passive Observation	SSD only	Funny > Neutral cartoons	Funny > Neutral in SSD only
		Makowski et al., 2016	10, -48, 40; -14, -46, 42; -14, -44, 58; 12, -54, 14; -6, -54, 14 (MNI)	Social Engagement	Mixed findings	Reward, punishment, and combined reward and punishment > neutral ("other"-related) personality traits	CN > SSD for Reward > Neutral; Punishment > Neutral in SSD only; Affective > Neutral in CN only
	TPJ	Berger et al., 2018	−58, -38, 2; −48, -32, 2 (MNI)	Passive Observation	SSD only	Funny > Neutral cartoons	Funny > Neutral in both groups
		Gromann et al., 2013	51, -54, 27 (Talairach)	Social Engagement	CN > SSD	Cooperation and Deception	CN > SSD for both conditions
		Lemmers-Jansen et al., 2018	51, -57, 26 (MNI)	Social Engagement	CN = SSD	Deception > Cooperation	Deception > Cooperation in both groups
Mirror Neuron Network	IPL/IPS	Gromann et al., 2013	44, -63, 48; 61, -43, -1 (Talairach)	Social Engagement	CN > SSD	Cooperation and Deception	CN > SSD for both conditions
		Makowski et al., 2016	40, -40, 54 (MNI)	Social Engagement	CN > SSD	Reward > neutral ("other"-related) personality traits	CN > SSD for Reward > Neutral



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people with SSD. No areas were significantly more associated with neutral compared to humorous stimuli, nor were any areas significantly more active overall in people with SSD than in healthy participants. In reference to the social interaction network, both the mentalizing and affective networks were represented in the regions demonstrating group differences in activation, including the ACC, insula, and amygdala (affective), and the mPFC (mentalizing), suggesting decreased affective processing of rewarding social information in SSD compared to controls. Activation of additional components of the mentalizing network (i.e., TPJ, IFG, and precuneus) during the humor condition in the SSD group only suggests abnormally increased processing during mentalizing or social engagement while viewing humorous images in SSD.

Fig. 3. Depictions of tasks from included papers: **Panel A:** Image captured from Berger et al. (2018): participants were presented with a cartoon, followed by a screen where they rated the cartoon's funniness, followed by a fixation cross; **Panel B:** Image captured from J. Lee et al. (2018): participants selected one of two presented slot machines, which resulted in monetary (left) or social (right) reward or punishment; **Panel C:** Image ccaptured from Bjorkquist and Herbener (2013): participants viewed pictures from the IAPS. From left to right, images display negative, positive, and neutral images. The top row are examples of social images, while the bottom row are examples of nonsocial images; **Panel D:** Image captured from Makowski et al. (2016): participants viewed their own image with various traits (top row of images and row labeled "self") in sequence. Participants also viewed images of others (row labeled "other"). Traits were "high social reward" or rewarding, "low social reward" or punishing/critical, or "no social reward" or neutral (images in order from left to right); **Panel E:** Image captured from H. Lee et al. (2014): participants viewed avatars (rows 1-3) that accepted or refused handshakes triggered by the participant raising their hand within the scanner (row 4); **Panel F:** Task used in Gromann et al. (2013) and Lemmers-Jansen et al. (2018) (image captured from Lemmers-Jansen et al., 2018): participants played a neuroeconomics game. Image displays examples of participants' response; **Panel G:** Task used in Gradin et al. (2012) and Sokunbi et al. (2014) (image captured from Sokunbi et al., 2014): Cyberball, in which participants virtually pass a ball back and forth between them and two other players. Participants are excluded when they are not passed the ball an equal number of times as the other players.

One study contrasted neural responses to socially punishing vs. neutral stimuli within and between groups of 36 people with SSD and 40 controls. Lindner et al. (2014) used images of faces expressing happiness (reward) and disgust (punishment) in unmasked and masked conditions (i.e., presented at speeds at which participants could or could not consciously perceive the faces, respectively). An additional contrast of neural activation during happy vs. neutral expressions was included as a control condition for further correlational analyses. Both groups of participants demonstrated higher activation in the insula, part of the affective network, during unmasked disgust vs. neutral expressions, and reduced insula activation in response to masked disgust vs. neutral expressions. Those with SSD also showed reduced insula activation compared to controls in response to the masked expressions only.

Lee et al. (2018) utilized an existing paradigm (Lin et al., 2011) that probabilistically presented monetary gain (reward), loss (punishment), and no gain or loss (neutral) in response to participants' choices between two images of slot machines with varying geometric shapes on the front (Fig. 3B). In a second condition, the authors replaced monetary stimuli with smiling (reward), angry (punishment), or neutral faces. Successful reward or punishment learning was operationalized as the proportion of optimal choices made over time. Data were collected in 27 people with SSD and 25 controls, and were analyzed using both ROI and whole-brain approaches. *A priori* ROIs were established in the VS, mPFC, and ACC. Analyses contrasted social vs. nonsocial reward stimuli within and between participants with and without SSD. A significant group by reward type interaction suggested that people with SSD, but not healthy participants, demonstrated less activation during social than non-social reward across all three ROIs, though activation was similar between groups in comparison to the neutral condition. Additional whole-brain analyses did not identify group or condition differences in any other regions. Activity within the VS and ACC, components of the affective network, was modulated by social and nonsocial reward, while the mPFC, a component of the mentalizing network, was also more associated with social than non-social stimuli. No group differences were found in neural processing of reward or punishment alone.

One study compared the experience of both reward and punishment to neutral stimuli. Bjorkquist and Herbener (2013) used International Affective Picture System (IAPS) stimuli to measure participants' emotional responses to both positive and negative social (having at least one human present in the picture; see Fig. 3C) and nonsocial images that were affective (including positively-valenced and negatively-valenced images; see Fig. 3C) or neutral. Data were collected in 14 people with SSD and 14 controls. Analyses contrasted neural responses between groups (SSD vs. controls), as well as to social vs. nonsocial images within groups, separately for affective and neutral images. In the analysis contrasting the affective and neutral stimuli, two spatially grouped clusters of regions showed significant between-group activation: the temporo-occipital cluster involved the inferior temporal gyrus (ITG), right MTG, and middle occipital gyri, and the cingulate cluster involved the right MCC and bilateral ACC. Control participants, but not participants with SSD, had greater activation during social than nonsocial images in the temporo-occipital cluster, and this effect was greater in the affective pictures. In contrast, participants with SSD showed greater activation during neutral than affective pictures (regardless of social content), and greater activation during social than nonsocial pictures (regardless of affective content), in the cingulate cluster. An additional post-hoc ROI analysis revealed increased thalamus activation during affective pictures over neutral pictures in both groups. Of these regions, only the ACC (in the cingulate cluster) is involved in the affective network; surprisingly, there was higher activity in this cluster during neutral than affective images.

2.3.1. Summary of studies using passive observation paradigms

In all, 4 of the 11 studies included in this review used paradigms in which participants passively observed socially rewarding or punishing stimuli. Of these, one study found evidence of diminished mentalizing network region activity during social stimulus viewing as well as evidence for greater mentalizing network region activity for salient compared to neutral social stimuli, in participants with SSD compared to controls (Berger et al., 2018). One study found no difference in mentalizing region activity between participants with SSD compared to controls within social reward conditions as compared to neutral conditions (Lee et al., 2018). All four studies demonstrated increased activity in affective network regions in the context of social stimuli. Of these, two studies found overall greater activation of regions in this network in controls compared to participants with SSD (Berger et al., 2018; Lindner et al., 2014) and one study found greater activation of regions in the network in controls as compared with participants with SSD while observing social, rather than nonsocial, stimuli (Lee et al., 2018). In addition, one study (Bjorkquist and Herbener, 2013) found greater activation during neutral compared to affective stimuli in people with SSD only, but grouped reward and punishment together in the same condition. None of the studies using passive observation of social stimuli found significant group differences or within-group contrasts in the mirror neuron network. These results, however, are limited by the passive quality of the stimuli. The interactive nature of social engagement paradigms may provide a more ecologically valid set of stimuli and reveal more complex patterns of neural activity.

2.4. Social engagement paradigms

In 7 of 11 studies included in this review, social stimuli were presented as feedback in a task or game. Of these, three studies used novel paradigms in which positive and/or negative social feedback (i.e., praise, criticism, or exclusion) was provided either after or during a condition in which participants also gave input to another person (or a representation of another person). Two studies used a cooperative trust game between participants and preprogrammed computer algorithms. The remaining two studies used Cyberball, a well-validated social exclusion paradigm (Williams et al., 2000).

Makowski et al. (2016) used a novel paradigm to examine rewarding vs. neutral, punishing vs. neutral, and affective (combining rewarding and punishing) vs. neutral feedback. Participants (15 with SSD, 15 controls) completed personality questionnaires during an initial visit and were told that their responses would be rated by clinicians. During an fMRI session two weeks later, participants viewed pictures of themselves and of strangers; words describing personality traits that ranged from positive (high social reward; e.g., “intelligent”) to negative (low social reward; e.g., “careless”) were presented below the image (see Fig. 3D). Participants were told that clinicians provided the ratings. Subjective reward or punishment was measured through participants’ report of how desirable they considered each trait. All analyses involved between-group contrasts. Reward vs. neutral contrasts compared high social reward trait ratings given to the participant (“self”) with high social reward trait ratings given to a stranger (“other”). People with SSD and healthy participants both demonstrated greater activation during self-related than other-related reward in frontal regions (mPFC, IFG, bilateral ACC, SFG, and MFG). The two groups differed in their activation of MCC, posterior cingulate cortex (PCC), AG, superior parietal gyrus (SPG), and inferior parietal gyrus (IPG), all of which were more active while receiving self-related than other-related reward in controls than participants with SSD. Frontal regions associated with self-related rewards in both groups included those involved in mentalizing (mPFC, IFG), affective (bilateral ACC), and mirror neuron (IPG) networks. The PCC, a region implicated in the mentalizing network, showed greater activation in controls than those with SSD while viewing self-related reward, consistent with group differences in mentalizing processes during social reward receipt.

Makowski et al. (2016) also examined the contrast between punishment (self-related low social reward traits) and neutral conditions (other-related low social reward traits). Participants with SSD demonstrated significantly increased activation during punishment in the right frontal cortex, precuneus, AG, left calcarine gyrus, and right fusiform gyrus, while control participants had increased activation only in the left IFG. Of these regions, the left IFG and precuneus are implicated in the mentalizing network, suggesting abnormal processing within mentalizing regions in people with SSD while receiving negative social feedback.

Makowski et al. (2016) reported a third contrast, in which conditions were combined to contrast all self-related (high and low social reward traits assigned to the participant, acting as an affective condition) and other-related (high and low social reward traits assigned to a stranger, acting as control/neutral trials) conditions. Controls and participants with SSD did not overlap in their neural activation during combined reward and punishment, and activation patterns for both groups were widely distributed throughout the brain. Control participants showed significant activation during self-related compared to other-related traits in bilateral medial prefrontal regions, hippocampus, amygdala, temporal regions, parietal areas, and occipital areas, encompassing regions in all three social interaction networks. Participants with SSD, however, showed activation in the right pre- and post-central gyri and parietal lobe during affective (self-related) compared to neutral (other-related) traits, possibly involving regions contributing to the mirror neuron network. Overall, findings suggest associations of activity in different social interaction network regions in SSD with interpretation of affective compared to neutral social feedback.

Three studies explored direct contrasts between rewarding and punishing social feedback. In a study by H. Lee and colleagues (2014), 15 participants with SSD and 16 participants without SSD viewed social interactions between themselves and individual avatars through a virtual reality (VR) headset during fMRI. Within the VR environment, a virtual avatar approached the participant, who was instructed to raise their hand for a handshake, at which point a signal was sent via a motion sensor attached to the participant’s hand. The avatar representing the participant in the VR environment would raise its hand simultaneously (see Fig. 3E). The approaching avatar would respond to this gesture by either accepting the handshake or rejecting it. Subjective reports of feeling disliked and rejected by avatars were collected from participants after each task condition. Analyses included between- (SSD vs. controls) and within- (acceptance vs. refusal of handshake) group contrasts. Regions that demonstrated significantly higher activity during punishment/rejection than reward/acceptance included the right posterior superior temporal sulcus (pSTS) and right thalamus in the control group, and the left frontopolar cortex, right MFG and SFG, and left ACC in those with SSD. In addition, the control group demonstrated higher activation than the SSD group during the punishment condition in the right pSTS, right supramarginal gyrus (SMG), left MCC, bilateral insula, and left cerebellum. Conversely, regions with significantly higher activity during reward included the right paracentral lobule, bilateral superior parietal lobule, and left fusiform gyrus, in the SSD group only. The mentalizing network was represented in this study by the pSTS, which was associated more with punishment than reward, and was more active in control participants than participants with SSD. The affective network showed different activation patterns between groups, with the ACC associated with punishment significantly more than reward in SSD participants only, and the insula associated more with punishment than reward in both groups, but with higher activation in controls.

Lemmers-Jansen, Fett, Hanssen, Veltman, & Krabbendam (2018) and Gromann et al. (2013) used a cooperative trust paradigm commonly used in neuroeconomics research (Berg et al., 1995; Fig. 3F). Participants are given variable amounts of money and instructed to invest a chosen amount that is given to another player (in reality, the computer). The trustee receives triple the investment amount, and can return as much or as little of their earnings to the participant. Conditions are considered cooperative (rewarding) when the trustee returns 100, 150, or 200 percent of their earnings; they are considered deceptive or unfair (punishing) when the trustee returns less than 100 percent (i.e., 50 or 75 percent). In both studies, change in the participant’s investment amount from their baseline amount for each trial was used as a measure of reward or punishment, as it reflected the level of trust the participant had developed in their partner. Lemmers-Jansen et al. (2018) reported the contrast between cooperative and unfair conditions, as well as between-group contrasts, using data from 22 participants with SSD and 43 controls. Though the TPJ and mPFC (both components of the mentalizing network) were more active during unfair compared to cooperative conditions, no differences in activation were found between participants with SSD and healthy controls.

It should be noted that the participants in this study by Lemmers-Jansen et al. (2018) were characterized as FEP. Those who have experienced a single episode of psychosis do not necessarily go on to develop SSD, and thus may display different patterns of neural functioning (Alvarez-Jiménez et al., 2011; Robinson et al., 1999) Results from this paper should be interpreted with caution in relation to the other studies reviewed here, which examined neural activity in people with more chronic forms of SSD; however, people with FEP have often demonstrated more similar neural structure and processing to people with chronic SSD than to controls (Wood et al., 2001; Woodward et al., 2009).

Gromann et al. (2013), using the same contrasts (cooperative vs. unfair; SSD vs. controls), also found condition differences in the mPFC; however, contrary to the results from Lemmers-Jansen et al. (2018), there was stronger activation in the mPFC during the cooperative compared to unfair condition, which was found in both control ($n = 20$) and SSD ($n = 20$) groups. In addition, activation in the TPJ (also a part of the mentalizing network) was greater in control participants than participants with SSD, in both conditions. This group difference was seen in the inferior parietal lobule (IPL) in both conditions, and was revealed during only the cooperative condition in the right caudate nucleus and MTG. The TPJ and mPFC are components of the mentalizing network, and the IPL is a component of the mirror neuron network, suggesting multiple roles of the social interaction network during cooperative interactions that differ in people with SSD and healthy individuals.

In a study examining neural responses to social punishment, 11 participants with SSD listened to short audio clips of critical and neutral statements spoken about them by relatives and unfamiliar speakers during fMRI (Rylands et al., 2011). Contrasts were reported as z-score differences between activation in response to audio (neutral and critical statements from both categories of speakers) compared to baseline (silence). Of the 11 studies included in this systematic review, this was the only one to not include an exploratory whole-brain analysis or a control group. Analyses using *a priori* ROIs revealed significantly more activation while listening to critical than neutral statements spoken by relatives in the left IFG, left temporal cortex, and MFG. The ACC and insula demonstrated significantly greater activation associated with critical vs. neutral comments, also only during relatives' speech. In addition, the right precentral gyrus was associated with criticism from relatives over baseline but no other conditions. Both the mentalizing network (represented by the left IFG) and the affective network (represented by the ACC and insula) showed similar patterns, suggesting both networks are more active during criticism than neutral statements in people with SSD.

Two additional studies modeled social punishment using the Cyberball task (Williams et al., 2000) to examine neural responses to social exclusion in SSD. Cyberball is a computer game in which the participant is instructed to pass a ball to two other players (see Fig. 3C). During the control condition, the participant receives the ball an equal amount of time (30 %) as the other two players. During the exclusion condition, however, the participant receives the ball only a small percentage of the time, or not at all. In both Gradin et al. (2012) and Sokunbi et al. (2014), exclusion rates were set at 0, 25, 50, 75, and 100 percent. Subjective levels of social punishment in both studies were determined from self-reported feelings of exclusion. Neither study reported within- or between-group contrasts. Gradin et al. (2012) collected data in 13 people with SSD and 16 people without SSD. They found positive correlations between exclusion rates and neural activity in mPFC, ventral ACC, and OFC in the control group only. For participants with SSD, activity in the dorsal ACC, superior caudate, posterior brain stem, fusiform gyrus, and cerebellum was negatively correlated with rates of exclusion; that is, more exclusion was associated with less regional activity. Rates of exclusion were also associated with less activity in the precuneus in both participant groups. Results showed that the part of the mentalizing network (mPFC) was active during control, but not SSD, participants' processing of social exclusion. The affective network was also more active during processing of social exclusion in the control group (within the ACC and OFC), yet was negatively correlated with rates of exclusion in the SSD group, suggesting abnormal emotional processing during exclusion in people with SSD. Sokunbi et al. (2014) did not analyze specific regions in the brain, but rather reported correlations between two measures of signal complexity (a measure of difficulty in describing or predicting a signal)—sample entropy and Hurst exponent—and social distress scores (defined as self-reported perceived exclusion) from 13 people with SSD and 16 people without SSD. Participants with SSD had significantly higher overall signal complexity than controls; however, signal complexity was unrelated to social distress across groups.

2.4.1. Summary of studies using social engagement paradigms

In 7 of the 11 studies included in this review, participants received social feedback from confederates (i.e., second-person tasks). In three of these studies, controls showed greater social interaction network activation compared to participants with SSD: one study showed higher activity in both mentalizing and affective networks in controls compared to those with SSD, particularly during social punishment (Lee et al., 2014), while two other studies found higher activity in controls compared to SSD participants in mentalizing network regions during rewarding conditions, but not during punishing conditions (Gromann et al., 2013; Makowski et al., 2016). Regional activation also varied between conditions across studies. In one study, regions in the affective and mentalizing networks showed greater activation during both reward and punishment compared to neutral conditions across groups (Makowski et al., 2016); however, mentalizing and affective network regions showed greater activation during punishment than reward or neutral conditions in healthy participants in two studies (Gradin et al., 2012; Lee et al., 2014), in both participant groups in two other studies (Lemmers-Jansen et al., 2018; Makowski et al., 2016), and in participants with SSD in one study that did not include a healthy control group (Rylands et al., 2011). Levels of social exclusion were also negatively correlated with processing in mentalizing and affective network regions in participants with SSD, yet were positively correlated in healthy participants (Gradin et al., 2012). Additionally, regions involved in the mirror neuron network were implicated during both reward and punishment in two of the studies using social engagement paradigms, in contrast with studies using passive observation paradigms, which did not find any group or condition differences in these regions (Gromann et al., 2013; Makowski et al., 2016).

2.5. Overall summary of reviewed studies

Studies using both passive and socially engaging stimuli consistently found increased activation during both rewarding and punishing, compared to neutral, social stimuli in the mentalizing network in both SSD and controls. Additionally, overall activation was reduced in certain areas of the network in some studies (e.g., in the mPFC) and increased in other areas (e.g., in the IFG and precuneus) in people with SSD compared to controls. Studies across paradigm types also consistently found increased activation during rewarding or punishing, compared to neutral, social stimuli in the affective network, with the exception of one study. Activation of the ACC was more often than not comparable during these conditions in people with SSD and controls, while activation of the insula was most often reduced in SSD compared to controls. Only two studies found significant activation differences between conditions within mirror neuron network regions. Both studies found increased activity during rewarding or punishing, compared to neutral, social stimuli, and that this activation was greater in controls than in people with SSD. Both studies also used tasks categorized as social engagement.

3. Discussion

In this systematic review of the published literature, we identified 11 studies examining neural activity in the context of social reward and punishment in SSD. These studies spanned a variety of passive and interactive paradigms in over 400 participants across 7 years. We summarized key brain structures implicated in within- and between-group differences in neural activity, highlighting those conceptualized as comprising the "social interaction" network, including mentalizing regions (TPJ, STS, IFG, PCC, precuneus, aTL, dmPFC, vmPFC), mirror neuron regions (IPL and IPS), and affective regions (ACC, aINS, amygdala, OFC, and VS) (see Fig. 1). In all, findings from the reviewed studies suggest different patterns of neural activation in people with SSD than in controls across all three networks; however, between-group findings varied depending on the type of paradigm used. We first clarify the role of each distinct region within the three networks involved in the social interaction network, then highlight potential contributors to the variability in findings among the studies reviewed.

3.1. Overall patterns of neural activation

Due to the predominant use of regional analyses in the included papers, we do not discuss analyses of functional connections among the social interaction networks. However, some patterns emerged regarding the activation of distinct regions within the networks, particularly in their response to stimuli observed passively compared to those involving social engagement.

3.1.1. Regions comprising the mentalizing network

Within the 11 studies included in this review, regions implicated in the mentalizing network played varying roles. The most common region to demonstrate differences in activation between conditions or groups was the mPFC (in four studies), followed by the IFG, TPJ, and precuneus (in three studies), and the STS (in one study). The mPFC demonstrated comparable or attenuated activity across conditions for participants with SSD as compared to controls (Table 2). Although only apparent in one study, activity in the STS was also attenuated in people with SSD compared to controls. In contrast, the IFG and precuneus were associated with elevated activity in response to either rewarding or punishing as compared to neutral stimuli in people with SSD. Findings in the TPJ were not consistent over studies, as activity was found to be equal, diminished, or inconclusive in people with SSD in one study each. These results suggest a possible pattern of differences in neural processing of social reward and punishment in SSD; that is, different regions within the mentalizing network play different functional roles, and only certain regions within the network may be relevant for understanding decreased social motivation in SSD. For example, decreased mPFC activity may suggest decreased executive control during social reward and punishment processing, while increased IFG and precuneus activity may reflect increased effort in understanding others' communicated intentions in relation to the self in people with SSD.

Across groups, more socially salient stimuli produced higher neural activation than neutral conditions in the mentalizing network. The only exception to this pattern was higher activation in the mPFC for reward than punishment in one study (Gromann et al., 2013), and higher activation in the mPFC and TPJ for punishment than reward in another study (Lemmers-Jansen et al., 2018). Differences in results may be due to different analytic approaches: while other studies included in this review contrasted response to reward or punishment with neutral stimuli, these two studies contrasted response to reward vs. punishment. The lack of a neutral condition in the latter studies precludes the ability to compare findings. Additionally, one of these conflicting studies examined social processing in people with FEP, a group who may be characterized by neural functioning that differs from people with multi-episode SSD (Lemmers-Jansen et al., 2018). However, this is less likely to contribute to disparities in findings, as the inconsistency described above was in within-group analyses and thus independent of group differences.

3.1.2. Regions comprising the affective network

Within the studies included in this review, the most commonly identified regions of the affective network were the ACC (in seven studies), the insula (in six studies), and the amygdala (in three studies). The VS and OFC were analyzed in one study each. Participants with SSD demonstrated overall reduced activation within these regions, most consistently in the insula, in four of the six studies (one study found equal activation in both participant groups, and one study only recruited people with SSD). The ACC most often showed similar between-group activation, though some studies found higher activation in participants with SSD and one study found higher activation in controls. All but one of the studies that analyzed regions in the affective network found generally higher activation throughout the network in response to socially rewarding or punishing stimuli in comparison to neutral stimuli across participant groups. The one study finding higher activation in response to neutral vs. affective stimuli used static images.

Despite consistency in patterns of activation in response to salience of social stimuli, there was less consistency across the 11 reviewed studies in terms of valence; that is, whether activation was elevated in response to social reward or punishment depended on study design and analytic contrast. Variation was largely determined by the contrasts used: most studies focused on analyses contrasting one valence (e.g., reward or punishment) with neutral conditions. The two exceptions to this were one study in which reward and punishment were combined into a single affective condition (Bjorkquist and Herbener, 2013), and one study in which reward and punishment were analyzed separately (Makowski et al., 2016). In the latter study, affective network regions were only found to be relevant to processing reward. Additionally, neither study that used the cooperative trust paradigm found any significant differences in processing within the affective network (Gromann et al., 2013; Lemmers-Jansen et al., 2018).

In general, controls showed greater affective network activation than those with SSD; however, activation within the ACC specifically may be sensitive to environmental context during social situations in people with SSD. For example, H. Lee et al. (2014) found greater contrast between socially punishing and rewarding stimuli in participants with SSD than controls using avatars in a virtual environment, which demonstrated eye contact, facial and body movements, and physical proximity. In contrast, Berger et al. (2018) and Gradin et al. (2012) found greater contrast between socially rewarding or punishing and neutral images in controls than participants with SSD using cartoons. It may be that face-to-face communication contributes more to affective neural responding in people with SSD compared to less interactive feedback. Paradigms with higher ecological validity may be required to accurately investigate ACC activation in people with SSD during social reward and punishment.

3.1.3. Regions comprising the mirror neuron network

Less evidence was provided for the activation of the mirror neuron network during social reward and punishment, appearing in only two studies, both of which used social engagement paradigms (Gromann et al., 2013; Makowski et al., 2016). These studies found increased parietal activation in response to both rewarding and punishing compared to neutral stimuli, though activation was higher overall in controls compared to participants with SSD in both studies. Due to the limited number of studies, findings regarding activation patterns are inconclusive, though it is notable that regions were more active during salient conditions in controls only, and only in the context of social engagement paradigms. In addition, both studies found significant activation contrasts in these regions through whole-brain analyses and not through a priori region of interest analyses. The mirror neuron network may be more active during social engagement paradigms than in passive observation paradigms, as interaction involves more direct social communication (e.g., real-time feedback), and therefore more opportunities for mirroring behavior (e.g., planning future behavioral responses to unfair or cooperative payments, or compliments or criticisms).

3.1.4. Regions outside the social interaction network

While several studies identified neural activity in response to socially rewarding or punishing stimuli in regions outside of the hypothesized social interaction network, these regions were most commonly discovered through whole-brain analyses. These analyses were exploratory in nature, and thus used liberal significance thresholds for activity contrasts. Others identified regions that may have been involved in processing stimuli features not necessarily implicated in social reward specifically. Nonetheless, we emphasize that while the social interaction network has been useful in interpreting neural activity in response to social stimuli, neural activation is undoubtedly widespread during social interactions. We encourage researchers to consider all regions found in whole-brain analyses, as well as the previously hypothesized role of each of these regions in processing stimuli, when examining activation in relation to social reward and punishment in people with SSD (see Supplementary Materials for a full list of regions outside these networks).

3.1.5. Regions implicated in social reward and punishment in broader psychopathology

Social reward and punishment have been examined in disorders other than SSD as well. Autism spectrum disorder (ASD), for example, has been characterized by aberrant social stimulus processing, including decreased responsivity to social reward. Findings from a recent meta-analysis suggest that people with ASD demonstrate decreased ACC and IFG activity and increased insula activity during social reward (Clements et al., 2018). The studies of SSD reviewed here suggest mixed findings in the ACC and IFG, and decreased activation in the insula across most studies; however, patterns were comparable to Clements et al. (2018) when considering the separation of social reward and social punishment. In SSD, ACC activity was more often attenuated compared to controls for contrasts involving rewarding vs. neutral stimuli, and decreased insula activity was most often found in contrasts of punishing vs. neutral stimuli.

Clements et al. (2018) also revealed hypoactivation in bilateral caudate, right hippocampus, and lateral occipital cortex, as well as hyperactivation in putamen, right temporal occipital fusiform cortex, and left STG in ASD. However, the most robust findings reported were in the dorsal striatum: the caudate was bilaterally hypoactive, while the putamen was hyperactive. While we did not discuss striatal regions in depth in the current review, we found that two studies reported overall decreased striatal activation in SSD during social reward, one study reported activity during social reward in controls only, and one study reported comparable activity levels between groups in both social reward and punishment (see Supplementary Table 1).

Social anxiety disorder is often studied in relation to responses to social punishment, as one of its defining features is a fear of rejection or judgment from others. Findings from a meta-analysis of neural activity during social punishment in social anxiety disorder report hyperactivation of the fear circuit, many regions of which overlap with those involved in the proposed social interaction network: amygdala, insula, ACC, and mPFC (Bruehl et al., 2014). Bruehl and colleagues (2014) also report hyperactivity in PCC, precuneus, and cuneus. Findings in the current review of SSD differ from those reported in social anxiety disorder: activity was most often reduced in the insula, and either reduced or comparable to controls in the amygdala, ACC, and mPFC.

Finally, reward processing has been studied in depression, though social reward in particular has not been examined extensively. In general, hypoactivation has been found in striatal regions (including nucleus accumbens, caudate, and putamen) and striatal-ACC connectivity during rewarding stimuli (Admon and Pizzagalli, 2015). Further exploration of neural activation during social reward and punishment may contribute to the field's knowledge of transdiagnostic abnormalities in social interaction processing.

3.2. Addressing the variability of social reward and punishment neuroimaging studies in SSD

Here we highlight potential contributors to the substantial variability in findings among the 11 studies reviewed. We start by addressing the variety of operational definitions of social reward and punishment and their impact on the design of paradigms used to measure and manipulate these phenomena. We then discuss the impact of paradigm design on behavioral and neuroimaging results. We end with providing suggestions for future research.

3.2.1. Defining social reward and punishment in SSD

While the study of nonsocial (e.g., monetary) reward and punishment is fairly standardized and structured, the study of social reward and punishment covers a wide array of methods and stimuli, from static pictures to interactive, real-time feedback. Standardization of social reward and punishment stimuli is critical to developing methods for measuring these constructs in laboratory settings.

A first step toward standardization involves the delineation of different constructs and subconstructs within the broader frameworks of social reward and punishment. For example, differentiating between the experience of reward and punishment in the context of a reciprocal interaction (second-person, or socially engaging stimuli), as opposed to that experienced while observing social stimuli that are not interactive (third-person, or passive stimuli), would help clarify the roles of regional brain activity. Neural responses to third-person social stimuli may be more similar to responses to non-social stimuli than second-person social stimuli, due to a lack of dynamic processes characteristic of real-life social interaction in third-person paradigms (Fulford et al., 2018a; Schilbach et al., 2013). To truly disentangle both the experience and neural correlates of social and non-social reward and punishment, it is crucial for researchers to use interactive, second-person social stimuli.

It is also important to measure subjective experiences in response to social stimuli to determine the extent of reward or punishment elicited. In three of the papers discussed in this review, participants' subjective experiences were not measured (Bjorkquist and Herbener, 2013; Lindner et al., 2014; Rylands et al., 2011); in three other studies, experiences of reward and punishment were determined by participants' behavior (Gromann et al., 2013; Lee et al., 2018; Lemmers-Jansen et al., 2018), discounting individual differences in subjective experiences of reward and punishment. Furthermore, behavior and subjective experience may diverge, such as when there is a mismatch between reward and goal congruency (Frömer et al., 2019; Rutledge et al., 2014). Thus, inferences drawn from approaches focused solely on behavior may be limited.

Another consideration is the method of delivering social punishment in particular. One common approach in the available literature is to deliver criticism or rejection (e.g., critical comments, angry faces, or blatant rejection of a friendly offer), with the goal of directly inducing an aversive response. Another approach frames social punishment as the absence of social reward or acceptance (e.g., exclusion in Cyberball, or lack of acceptance of a handshake). The conceptualization of social punishment is essential to understanding the role of ambiguity in social stimulus processing: in real-life social interactions, the clarity with which social feedback can be interpreted as a lack of acceptance vs. outright rejection or criticism is often limited. For this reason, it is essential for researchers to distinguish within their studies which type of social punishment their task delivers.

3.2.2. The effects of paradigm design on results

Each paradigm reviewed has strengths and weaknesses. Passively observed, static stimuli are often administered in the form of emotionally salient social images, delivering social reward in a method analogous to an image of a dollar bill representing monetary reward. In these paradigms, stimulus presentation is brief, allowing for simpler analysis using temporally imprecise fMRI, and making data easier to collect and interpret. Social interactions, however, are much more dynamic and fluctuate repeatedly between rewarding, punishing, and ambiguous outcomes (Fulford et al., 2018a; Heerey, 2015; Zhang and Ji, 2005). The use of static stimuli cannot substitute for interaction and may mimic more closely the delivery of nonsocial, nonmonetary reward (such as a flashing image in a video game).

In contrast, interactive social feedback is reciprocal and has more potential for ambiguous interpretation, two key components of real-life social interaction (Catalano et al., 2018; Fulford et al., 2018a; Niedenthal et al., 2010; Schilbach et al., 2013). For these reasons, second-person paradigms are preferable for use in studying naturalistic neural and behavioral responses during social interaction. However, social feedback paradigms often lack quantitative experimental control, with stimuli consisting of images or sounds that cannot be assigned objective, discrete values on the continuum between socially rewarding (e.g., a smile, a compliment) and socially punishing (e.g., a frown, a critical comment). The subjectivity of these stimuli poses challenges to the quantification of reward and punishment, limiting meaningful comparisons of neural reactivity across different conditions of social feedback. One notable exception is Cyberball, which quantifies levels of social punishment as the percentage of times the ball is passed to the participant; however, this paradigm only manipulates exclusion—the inclusion condition could be interpreted as either neutral or rewarding in valence; that is, it represents a lack of exclusion rather than the presence of rewarding behavior.

There is also the question of how the incorporation of non-social reward might affect behavior in ostensibly social paradigms. In the cooperative trust paradigm reviewed here (Gromann et al., 2013; Lemmers-Jansen et al., 2018), communication between participants and their investing counterparts is limited to the exchange of monetary value, devoid of explicitly social stimuli (e.g., facial affect or linguistic cues); as such, the extent to which this paradigm involves social reward and punishment is limited to the assumption that the exchange of money between parties is a social activity. In reality, monetary rewards are almost always received from other people (including the researcher), yet they are not classified as social within the literature given their static, unambiguous, and non-affiliative properties. It is likely that at least some behavior and other outcomes (e.g., neural activity) measured during cooperative trust paradigms are influenced by processes involved in the exchange of monetary reward. Future research could directly test this hypothesis by comparing outcomes of social exchange tasks that do and do not incorporate monetary reward.

3.2.3. Future directions and implications

Advances in theory development and methodology should serve to improve reliability and validity of neural markers of social reward and punishment broadly. Here, we cover some methods used in the adjacent literature and offer additional conceptual suggestions for improving the study of social reward and punishment in SSD.

Recent literature has moved toward using social engagement, or second-person, paradigms, with some studies using similar paradigms to those reviewed here. For example, Pelletier-Baldelli et al. (2018) studied social reward and punishment in healthy participants and participants at clinical high risk for psychosis in fMRI using a similar paradigm to Makowski et al. (2016), but involving feedback from peers. In a sample of people with depression, Oppenheimer et al. (2019) delivered real-time feedback during fMRI, in which confederate peers were given the choice to interact with the participant (reward/acceptance) or a different person of the same gender and age (punishment/exclusion). Kujawa et al. (2014) also developed a task for youth with depression that mimicked a game show; participants voted for confederate profiles to stay or leave an “island” on which a group of young people were located, then received feedback about whether these confederates voted for the participant to stay (reward/acceptance) or leave (punishment/exclusion). Other fMRI studies of social reward and punishment have featured hand-holding, shared experiences of social stimuli, and positive and critical feedback on essays written by the participant (Coan et al., 2006; Ma et al., 2018; Peters et al., 2018). The above studies use novel methods for investigating a wide range of definitions of social reward and punishment that could be applied to work in SSD.

Recent task iterations of social exclusion have capitalized on the increasing ecological validity of online interaction paradigms. For example, virtual chatrooms can allow participants to interact with preprogrammed confederates. In some designs, reward and punishment occurs through the number of messages received (e.g., high number of messages indicate reward through inclusion, low number indicates punishment through exclusion; Donate et al., 2017). Other designs deliver reward and punishment through the content of responses (e.g., praise or criticism; Jiang and Johnston, 2017). Social media paradigms allow participants to write brief profiles about themselves and receive quantifiable levels of reward or punishment through the use of number of “likes” that the participants’ output receives, mimicking platforms such as Facebook or Twitter (Wolf et al., 2015). These paradigms, used primarily in healthy samples, show consistent effects on subjective feelings of ostracism and mood (Donate et al., 2017; Wolf et al., 2015).

Examining neural correlates of social rewards through virtual chatroom and social media paradigms may be a fruitful area for further research, as the design of such paradigms offer a high degree of feasibility, ecological validity, and experimental control. Implementing such paradigms through neuroimaging methods would not compromise ecological validity, as online social interaction does not require face-to-face interaction, and people with SSD regularly engage in social media as a form of interpersonal communication (Miller et al., 2015). Social media paradigms also offer a high level of experimental control, allowing for quantifiable levels of social reward and punishment that may be useful for examining changes in neural activity.

Another potentially fruitful approach to paradigm design that has been introduced and improved upon in recent years is VR. In addition to Lee et al. (2014), various studies of social cognition have begun to use this innovative technology. Some have created social stress in virtual environments through the use of avatars that display varying levels of hostility through verbal or nonverbal cues; these studies have examined responses in the form of social distance maintained from avatars and self-reported levels of paranoia (Geraets et al., 2018; Hesse et al., 2017; Park et al., 2009; Veling et al., 2016). Other studies have used VR to assess social anxiety and emotion recognition ability in people with psychosis (Rus-Calafell et al., 2018). This area of literature has also investigated the efficacy of using VR for social skills training for SSD (Rus-Calafell et al., 2014). Future use of VR in studies of social reward and punishment has the potential to provide naturalistic, ecologically valid stimuli in a highly controlled and standardized manner. Though it is currently less commonly used due to cost and difficulty in paradigm design, VR may be adapted in more studies as the technology becomes cheaper, more accessible, and easier to use.

In addition to improvements in paradigm design, an increasing focus on how neural regions within a network interact (e.g., in task-based functional connectivity), rather than the strength of response within individual regions, can improve understanding of responses to social reward and punishment. Of the studies reviewed, Berger et al. (2018) examined functional connectivity during a social reward task. With the mPFC as a seed region, people with SSD showed diminished connectivity compared to controls in various frontal and subcortical areas (e.g., right caudate nucleus, right MCC, precuneus), and increased connectivity in the cerebellum and superior parietal lobe, while viewing funny images. This finding may help to explain how deficits in processing within a single region may extend to disrupted functioning overall; that is, reduced or abnormal mPFC (i.e., executive) functioning may affect connections with, for example, limbic regions responsible for the experience of affect. It may be that generally, while people with SSD have deficits within specific regions of the brain that are essential to processing social reward or punishment, impaired communication between these regions may be a stronger indicator of functioning. Alternately, dysfunction of one region may not directly lead to impairments in social motivation, but rather may indirectly lead to impairment through decreased input to other regions in the network. More recent studies have begun to follow suit, though they have not explicitly examined neural connectivity in the context of social reward and punishment (Bitsch et al., 2019; Schwarz et al., 2019).

To maximize the contribution of these novel methodologies, however, it is essential to ensure that the question of neural processing of social reward and punishment in SSD is approached from a perspective informed by theory. In particular, aberrant processing of neutral social stimuli may contribute more to deficits of social motivation than processing of social reward and punishment for people with SSD. Meta analytic findings of neuroimaging studies suggest that people with SSD demonstrate comparable processing of emotional, nonsocial stimuli (particularly negative stimuli) to healthy controls, but elevated neural responses to neutral nonsocial stimuli (Anticevic et al., 2010; Taylor et al., 2012; discussed in Kring and Barch, 2014). Indeed, across the included studies in this review, group differences were found in social interaction network responses to socially rewarding or punishing conditions, but findings were less consistent when reward and punishment were contrasted with each other (i.e., Gromann et al., 2013; Lee et al., 2014; Lemmers-Jansen et al., 2018). Within findings from contrasts between socially rewarding or punishing conditions and neutral social stimuli, it is possible that abnormal processing during neutral conditions could be driving some effects. Abnormal processing of neutral stimuli, in turn, may be influenced by a negative interpretation bias. Beck and Rector (2005) suggest that defeatist beliefs and social disinterest in people with SSD, stemming from neurocognitive difficulties and repeated failure experiences early in life, interact with social cognitive impairments to create low expectations and overall negative bias (Beck and Rector, 2005; Pelletier-Baldelli and Holt, 2019). This, in turn, would diminish social motivation, as future interpersonal interactions are expected to be less enjoyable (Gard et al., 2007; Green et al., 2012).

However, the direction and strength of the effect of neutral social stimuli processing in SSD is unknown due to a dearth of studies explicitly examining neutral social conditions in SSD using neuroimaging. Indeed, no studies in this review explicitly compared neural activity during processing of neutral stimuli between participant groups. It is essential that future studies examine group differences in processing of neutral conditions, in which socially interactive and engaging stimuli are present without reward or punishment, between people with SSD and healthy controls. Likewise, future research would benefit from examining responses to social ambiguity, in which social stimuli have both rewarding and punishing qualities within a given interaction. Neutral and ambiguous stimuli are similar in that there is no obvious interpretation of the social interaction, as there are equal amounts of evidence in favor of positive and negative interpretations. Strong negative biases and low expectations, along with impairments in social cognitive abilities and social skills, may drive those with SSD to react more negatively to social and nonsocial stimuli that do not explicitly deliver reward or punishment than those without these biases and expectations (see Fig. 4). These biases may translate into diminished motivation, as interactions that are typically considered neutral or ambiguous would be encoded as more punishing/rejecting in SSD, and therefore discourage further social behavior. Focusing on the study of neural reactions to ambiguous social stimuli in SSD will allow us to determine the extent to which negative bias affects interpretation of typical social interactions in real life.

4. Conclusions

In this review we summarized the current state of the literature examining the neural correlates of social reward and punishment processing in SSD. We described key findings, focusing on methodological differences across studies. We then summarized the patterns of neural activation within (e.g., reward vs. punishment) and between (SSD vs. control) groups. Finally, we made recommendations for future research focused on achieving balance between ecological validity and experimental control.

We emphasized the importance of considering three key factors in studying social reward and punishment in SSD using functional neuroimaging. First, social interactions are, by nature, reciprocal and ambiguous. To truly examine the neural processing of social reward and punishment, in comparison to nonsocial reward and punishment, researchers should design tasks to include neutral or ambiguous conditions in addition to social reward and punishment conditions, and use socially engaging tasks to mimic realistic social interactions. Further, researchers examining social punishment must distinguish between stimuli that are truly punishing, and stimuli that merely lack reward. Second, we recommended the use of paradigms that balance experimental control with ecological validity. Previous studies outside of the SSD and neuroimaging literature have used paradigms that manipulate social interactions through online environments. Adapting these paradigms to measure social reward and punishment in SSD in fMRI may improve both the reliability and ecological validity of this line of work. Third, we stressed the importance of considering the role of neutral stimuli in contrasting different conditions in statistical analyses. Previous research has suggested relatively intact processing of reward and punishment in people with SSD, as well as abnormal neural responses to neutral stimuli (i.e., that more closely mimic neural responses to punishment). Thus, neutral stimuli may not be appropriate as a control condition; rather, responses to neutral stimuli should be

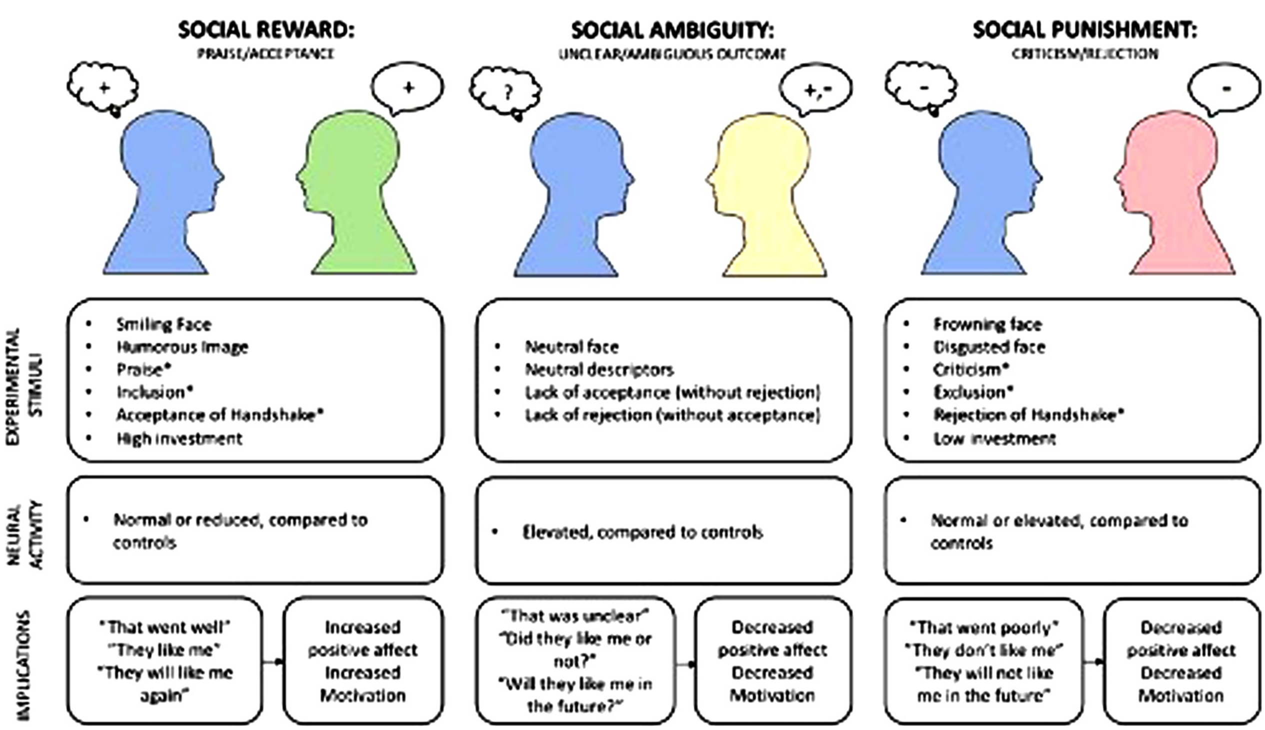

Fig. 4. Model of social reward, punishment, and ambiguity. Rewarding social interactions involve unambiguously positive social stimuli and may be processed normally in SSD. Likewise, punishing social interactions involve unambiguously negative social stimuli and may also be processed normally in SSD. Ambiguous interactions, which do not deliver explicit reward or punishment, may be processed in a manner that is more similar to social punishment in SSD than in healthy controls. * = Examples of socially engaging stimuli included in this review.

further compared between groups before making such conclusions.

People with SSD often experience social functioning deficits that contribute to a highly diminished quality of life. Understanding ways in which social motivation affects social functioning in this population is critical to developing effective treatments. One construct underlying motivation is the processing of social reward and punishment, as well as the processing of neutral, or ambiguous, social stimuli. Aberrant responses to these stimuli within regions and connections involved in the proposed social interaction network may contribute to abnormal processing of these stimuli in SSD. While findings thus far have been informative, additional research on processing of ambiguous interactions, using socially engaging stimuli, is required to draw conclusions that will inform development of treatments moving forward.

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Appendix A. Supplementary data

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References

Admon, R., Pizzagalli, D.A., 2015. Dysfunctional reward processing in depression. Curr. Opin. Psychol. 4, 114–118.

Alkire, D., Levitas, D., Warnell, K.R., Redcay, E., 2018. Social interaction recruits mentalizing and reward systems in middle childhood. Hum. Brain Mapp. 39, 3928–3942.

Alvarez-Jiménez, M., Parker, A.G., Hetrick, S.E., McGorry, P.D., Gleeson, J.F., 2011. Preventing the second episode: a systematic review and meta-analysis of psychosocial and pharmacological trials in first-episode psychosis. Schizophr. Bull. 37, 619–630. https://doi.org/10.1093/schbul/sbp129.

Andreasen, N.C., 1982. Negative symptoms in schizophrenia: definition and reliability. JAMA Psychiatry 39, 784–788. https://doi.org/10.1001/archpsyc.1982.04290070020005.

Anticevic, A., Van Snellenberg, J.X., Cohen, R.E., Repovs, G., Dowd, E.C., Barch, D.M., 2010. Amygdala recruitment in schizophrenia in response to aversive emotional material: a meta-analysis of neuroimaging studies. Schizophr. Bull. 38, 608–621. https://doi.org/10.1093/schbul/sbq131.

Beck, A.T., Rector, N.A., 2005. Cognitive approaches to schizophrenia: theory and therapy. Annu. Rev. Clin. Psychol. 1, 577–606.

Bellack, A.S., Morrison, R.L., Wixted, J.T., Mueser, K.T., 1990. An analysis of social competence in schizophrenia. Br. J. Psychiatry 156, 809–818.

Berg, J., Dickhaut, J., McCabe, K., 1995. Trust, reciprocity, and social history. Games Econ. Behav. 10, 122–142.

Berger, P., Bitsch, F., Nagels, A., Straube, B., Falkenberg, I., 2018. Frontal hypoactivation and alterations in the reward-system during humor processing in patients with schizophrenia spectrum disorders. Schizophr. Res. 202, 149–157. https://doi.org/10.1016/j.schres.2018.06.053.

Berkowitz, H., 1964. Effects of prior experimenter-subject relationships on reinforced reaction time of schizophrenics and normals. J. Abnorm. Soc. Psychol. https://doi.org/10.1037/h0040651.

Bitsch, F., Berger, P., Nagels, A., Falkenberg, I., Straube, B., 2019. Impaired right temporoparietal junction-hippocampus connectivity in schizophrenia and its relevance for generating representations of other minds. Schizophr. Bull. 45, 934–945. https://doi.org/10.1093/schbul/sby132.

Bjorkquist, O.A., Herbener, E.S., 2013. Social perception in schizophrenia: evidence of temporo-occipital and prefrontal dysfunction. Psychiatry Res. 212, 175–182. https://doi.org/10.1016/j.pscychresns.2012.12.002.

Bruehl, A.B., Delsignore, A., Komossa, K., Weidt, S., 2014. Neuroimaging in social anxiety disorder—a meta-analytic review resulting in a new neurofunctional model. Neurosci. Biobehav. Rev. 47, 260–280.

Catalano, L.T., Heerey, E.A., Gold, J.M., 2018. The valuation of social rewards in schizophrenia. J. Abnorm. Psychol. 127, 602–611. https://doi.org/10.1037/abn0000366.

Cavanaugh, D.K., Cohen, W., Lang, P.J., 1960. The effect of "social censure" and "social approval" on the psychomotor performance of schizophrenics. J. Abnorm. Soc. Psychol. https://doi.org/10.1037/h0045115.

Ciaramidaro, A., Becchio, C., Colle, L., Bara, B.G., Walter, H., 2013. Do you mean me? Communicative intentions recruit the mirror and the mentalizing system. Soc. Cogn. Affect. Neurosci. 9, 909–916. https://doi.org/10.1093/scan/nst062.

Clements, C.C., Zoltowski, A.R., Yankowitz, L.D., Yerys, B.E., Schultz, R.T., Herrington, J.D., 2018. Evaluation of the social motivation hypothesis of autism: a systematic review and meta-analysis. JAMA Psychiatry 75, 797–808.

Coan, J.A., Schaefer, H.S., Davidson, R.J., 2006. Lending a hand: social regulation of the neural response to threat. Psychol. Sci. 17, 1032–1039. https://doi.org/10.1111/j.1467-9280.2006.01832.x.

Corrigan, P.W., Phelan, S.M., 2004. Social support and recovery in people with serious mental illnesses. Community Ment. Health J. 40, 513–523.

de la Asuncion, J., Docx, L., Sabbe, B., Morrens, M., de Bruijn, E.R.A., 2015. Converging evidence of social avoidant behavior in schizophrenia from two approach-avoidance tasks. J. Psychiatr. Res. 69, 135–141. https://doi.org/10.1016/j.jpsychires.2015.08.008.

Donate, A.P.G., Marques, L.M., Lapenta, O.M., Asthana, M.K., Amodio, D., Boggio, P.S., 2017. Ostracism via virtual chat room—effects on basic needs, anger and pain. PLoS One 12, e0184215.

Eglit, G.M.L., Palmer, B.W., A'verria, S.M., Tu, X., Jeste, D.V., 2018. Loneliness in schizophrenia: construct clarification, measurement, and clinical relevance. PLoS One 13, e0194021.

FeldmanHall, O., Shenhav, A., 2019. Resolving uncertainty in a social world. Nat. Hum. Behav. 3, 426–435.

Foussias, G., Remington, G., 2008. Negative symptoms in schizophrenia: avolition and Occam's razor. Schizophr. Bull. 36, 359–369. https://doi.org/10.1093/schbul/sbn094.

Frömer, R., Dean Wolf, C.K., Shenhav, A., 2019. Goal congruency dominates reward value in accounting for behavioral and neural correlates of value-based decision-making. Nat. Commun. 10, 4926. https://doi.org/10.1038/s41467-019-12931-x.

Fulford, D., Niendam, T.A., Floyd, E.G., Carter, C.S., Mathalon, D.H., Vinogradov, S., Stuart, B.K., Loewy, R.L., 2013. Symptom dimensions and functional impairment in early psychosis: more to the story than just negative symptoms. Schizophr. Res. 147, 125–131.

Fulford, D., Campellone, T., Gard, D.E., 2018a. Social motivation in schizophrenia: how research on basic reward processes informs and limits our understanding. Clin. Psychol. Rev. 63, 12–24.

Fulford, D., Treadway, M., Woolley, J., 2018b. Social motivation in schizophrenia: the impact of oxytocin on vigor in the context of social and nonsocial reinforcement. J. Abnorm. Psychol. 127, 116.

Gard, D.E., Kring, A.M., Gard, M.G., Horan, W.P., Green, M.F., 2007. Anhedonia in schizophrenia: distinctions between anticipatory and consummatory pleasure. Schizophr. Res. 93, 253–260.

Geraets, C.N.W., van Beilen, M., Pot-Kolder, R., Counotte, J., van der Gaag, M., Veling, W., 2018. Social environments and interpersonal distance regulation in psychosis: a virtual reality study. Schizophr. Res. 192, 96–101. https://doi.org/10.1016/j.schres.2017.04.034.

Gold, J.M., Waltz, J.A., Prentice, K.J., Morris, S.E., Heerey, E.A., 2008. Reward processing in schizophrenia: a deficit in the representation of value. Schizophr. Bull. 34, 835–847.

Gordon, I., Eilbott, J.A., Feldman, R., Pelphrey, K.A., Vander Wyk, B.C., 2013. Social, reward, and attention brain networks are involved when online bids for joint attention are met with congruent versus incongruent responses. Soc. Neurosci. 8, 544–554.

Gradin, V.B., Waiter, G., Kumar, P., Stickle, C., Milders, M., Matthews, K., Reid, I., Hall, J., Steele, J.D., 2012. Abnormal neural responses to social exclusion in schizophrenia. PLoS One 7, e42608. https://doi.org/10.1371/journal.pone.0042608.

Green, M.F., Hellemann, G., Horan, W.P., Lee, J., Wynn, J.K., 2012. From perception to functional outcome in schizophrenia: modeling the role of ability and motivation. Arch. Gen. Psychiatry 69, 1216–1224.

Green, M.F., Horan, W.P., Barch, D.M., Gold, J.M., 2015. Effort-Based Decision Making: A Novel Approach for Assessing Motivation in Schizophrenia. Schizophr. Bull. 41, 1035–1044. https://doi.org/10.1093/schbul/sbv071.

Gromann, P.M., Heslenfeld, D.J., Fett, A.-K., Joyce, D.W., Shergill, S.S., Krabbendam, L., 2013. Trust versus paranoia: abnormal response to social reward in psychotic illness. Brain 136, 1968–1975. https://doi.org/10.1093/brain/awt076.

Gu, R., Huang, W., Camilleri, J., Xu, P., Wei, P., Eickhoff, S.B., Feng, C., 2019. Love is analogous to money in human brain: coordinate-based and functional connectivity meta-analyses of social and monetary reward anticipation. Neurosci. Biobehav. Rev. 100, 108–128. https://doi.org/10.1016/j.neubiorev.2019.02.017.

Hanssen, E., Fett, A.-K., White, T.P., Caddy, C., Reimers, S., Shergill, S.S., 2018. Cooperation and sensitivity to social feedback during group interactions in schizophrenia. Schizophr. Res. 202, 361–368. https://doi.org/10.1016/j.schres.2018.06.065.

Hanssen, E., Krabbendam, L., Robberegt, S., Fett, A.-K., 2019. Social and non-social reward learning reduced and related to a familial vulnerability in schizophrenia spectrum disorders. Schizophr. Res. https://doi.org/10.1016/j.schres.2019.10.019.

Heerey, E.A., 2015. Decoding the dyad: challenges in the study of individual differences in social behavior. Curr. Dir. Psychol. Sci. 24, 285–291.

Herbener, E.S., 2008. Emotional memory in schizophrenia. Schizophr. Bull. 34, 875–887.

Hesse, K., Schroeder, P.A., Scheeff, J., Klingberg, S., Plewnia, C., 2017. Experimental variation of social stress in virtual reality – feasibility and first results in patients with psychotic disorders. J. Behav. Ther. Exp. Psychiatry 56, 129–136. https://doi.org/10.1016/j.jbtep.2016.11.006.

Holt-Lunstad, J., Smith, T.B., Baker, M., Harris, T., Stephenson, D., 2015. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. Perspect. Psychol. Sci. 10, 227–237.

Irwin, L., Renner, K.E., 1969. Effect of praise and censure on the performance of schizophrenics. J. Abnorm. Psychol. https://doi.org/10.1037/h0027192.

Izuma, K., Saito, D.N., Sadato, N., 2008. Processing of social and monetary rewards in the human striatum. Neuron 58, 284–294. https://doi.org/10.1016/j.neuron.2008.03.020.

Jiang, Y., Johnston, C., 2017. Controlled social interaction tasks to measure self-

perceptions: No evidence of positive illusions in boys with ADHD. J. Abnorm. Child Psychol. 45, 1051–1062. https://doi.org/10.1007/s10802-016-0232-y.
Kirkpatrick, B., Fenton, W.S., Carpenter, W.T., Marder, S.R., 2006. The NIMH-MATRICS consensus statement on negative symptoms. Schizophr. Bull. 32, 214–219.
Kopelowicz, A., Liberman, R.P., Zarate, R., 2006. Recent advances in social skills training for schizophrenia. Schizophr. Bull. 32, S12–S23. https://doi.org/10.1093/schbul/sbl023.
Kring, A.M., Barch, D.M., 2014. The motivation and pleasure dimension of negative symptoms: neural substrates and behavioral outputs. Eur. Neuropsychopharmacol. 24, 725–736. https://doi.org/10.1016/j.euroneuro.2013.06.007.
Kubota, M., Miyata, J., Sasamoto, A., Kawada, R., Fujimoto, S., Tanaka, Y., Sawamoto, N., Fukuyama, H., Takahashi, H., Murai, T., 2012. Alexithymia and reduced white matter integrity in schizophrenia: a diffusion tensor imaging study on impaired emotional self-awareness. Schizophr. Res. 141, 137–143.
Kujawa, A., Arfer, K.B., Klein, D.N., Proudfit, G.H., 2014. Electrocortical reactivity to social feedback in youth: a pilot study of the Island Getaway task. Dev. Cogn. Neurosci. 10, 140–147. https://doi.org/10.1016/j.dcn.2014.08.008.
Kurtz, M.M., Richardson, C.L., 2011. Social cognitive training for schizophrenia: a meta-analytic investigation of controlled research. Schizophr. Bull. 38, 1092–1104. https://doi.org/10.1093/schbul/sbr036.
Lee, H., Ku, J., Kim, J., Jang, D.-P., Yoon, K.J., Kim, S.I., Kim, J.-J., 2014. Aberrant neural responses to social rejection in patients with schizophrenia. Soc. Neurosci. 9, 412–423. https://doi.org/10.1080/17470919.2014.907202.
Lee, J., Jimenez, A.M., Reavis, E.A., Horan, W.P., Wynn, J.K., Green, M.F., 2018. Reduced neural sensitivity to social vs nonsocial reward in schizophrenia. Schizophr. Bull. https://doi.org/10.1093/schbul/sby109.
Lemmers-Jansen, I.L.J., Fett, A.-K.J., Hanssen, E., Veltman, D.J., Krabbendam, L., 2018. Learning to trust: social feedback normalizes trust behavior in first-episode psychosis and clinical high risk. Psychol. Med. (Paris) 1–11. https://doi.org/10.1017/S003329171800140X.
Lin, A., Adolphs, R., Rangel, A., 2011. Social and monetary reward learning engage overlapping neural substrates. Soc. Cogn. Affect. Neurosci. 7, 274–281.
Lindner, C., Dannlowski, U., Walhofer, K., Rodiger, M., Maisch, B., Bauer, J., Ohrmann, P., Lencer, R., Zwitserlood, P., Kersting, A., Heindel, W., Arolt, V., Kugel, H., Suslow, T., 2014. Social alienation in schizophrenia patients: association with insula responsiveness to facial expressions of disgust. PLoS One 9, e85014. https://doi.org/10.1371/journal.pone.0085014.
Ma, X., Zhao, W., Luo, R., Zhou, F., Geng, Y., Xu, L., Gao, Z., Zheng, X., Becker, B., Kendrick, K.M., 2018. Sex-and context-dependent effects of oxytocin on social sharing. Neuroimage 183, 62–72.
Makowski, C.S., Lepage, M., Harvey, P.-O., 2016. Functional neural correlates of social approval in schizophrenia. Soc. Cogn. Affect. Neurosci. 11, 445–457. https://doi.org/10.1093/scan/nsv125.
Miller, B.J., Stewart, A., Schrimsher, J., Peeples, D., Buckley, P.F., 2015. How connected are people with schizophrenia? Cell phone, computer, email, and social media use. Psychiatry Res. 225, 458–463. https://doi.org/10.1016/J.PSYCHRES.2014.11.067.
Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann. Intern. Med. 151, 264–269.
Mueser, K.T., Bellack, A.S., 1998. Social Skills and Social Functioning.
Mueser, K.T., Bellack, A.S., Douglas, M.S., Morrison, R.L., 1991. Prevalence and stability of social skill deficits in schizophrenia. Schizophr. Res. 5, 167–176.
Namiki, C., Hirao, K., Yamada, M., Hanakawa, T., Fukuyama, H., Hayashi, T., Murai, T., 2007. Impaired facial emotion recognition and reduced amygdalar volume in schizophrenia. Psychiatry Res. Neuroimaging 156, 23–32.
Niedenthal, P.M., Mermillod, M., Maringer, M., Hess, U., 2010. The Simulation of Smiles (SIMS) model: embodied simulation and the meaning of facial expression. Behav. Brain Sci. 33, 417.
Nuechterlein, K.H., Dawson, M.E., 1984. A heuristic vulnerability/stress model of schizophrenic episodes. Schizophr. Bull. 10, 300.
Ochsner, K.N., 2008. The social-emotional processing stream: five core constructs and their translational potential for schizophrenia and beyond. Biol. Psychiatry 64, 48–61.
Oppenheimer, C.W., Silk, J.S., Lee, K.H., Dahl, R.E., Forbes, E., Ryan, N., Ladouceur, C.D., 2019. Suicidal ideation among anxious youth: a preliminary investigation of the role of neural processing of social rejection in interaction with real world negative social experiences. Child Psychiatry Hum. Dev. https://doi.org/10.1007/s10578-019-00920-6.
Park, S.-H., Ku, J., Kim, J.-J., Jang, H.J., Kim, S.Y., Kim, S.H., Kim, C.-H., Lee, H., Kim, I.Y., Kim, S.I., 2009. Increased personal space of patients with schizophrenia in a virtual social environment. Psychiatry Res. 169, 197–202. https://doi.org/10.1016/j.psychres.2008.06.039.
Pelletier-Baldelli, A., Holt, D.J., 2019. At Issue: Are Negative Symptoms Merely the “Real World” Consequences of Deficits in Social Cognition? Schizophr. Bull.
Pelletier-Baldelli, A., Orr, J.M., Bernard, J.A., Mittal, V.A., 2018. Social reward processing: a biomarker for predicting psychosis risk? Schizophr. Res.
Penn, D.L., Sanna, L.J., Roberts, D.L., 2008. Social cognition in schizophrenia: an overview. Schizophr. Bull. 34, 408–411. https://doi.org/10.1093/schbul/sbn014.
Peters, J.R., Chester, D.S., Walsh, E.C., DeWall, C.N., Baer, R.A., 2018. The rewarding nature of provocation-focused rumination in women with borderline personality disorder: a preliminary fMRI investigation. Borderline Personal. Disord. Emot. Dysregulation 5, 1. https://doi.org/10.1186/s40479-018-0079-7.
Pfeiffer, U.J., Schilbach, L., Timmermans, B., Kuzmanovic, B., Georgescu, A.L., Bente, G., Vogeley, K., 2014. Why we interact: on the functional role of the striatum in the subjective experience of social interaction. Neuroimage 101, 124–137.
Pinkham, A.E., Penn, D.L., 2006. Neurocognitive and social cognitive predictors of interpersonal skill in schizophrenia. Psychiatry Res. 143, 167–178. https://doi.org/10.1016/j.psychres.2005.09.005.
Pinkham, A.E., Penn, D.L., Perkins, D.O., Graham, K.A., Siegel, M., 2007. Emotion perception and social skill over the course of psychosis: a comparison of individuals “at-risk” for psychosis and individuals with early and chronic schizophrenia spectrum illness. Cogn. Neuropsychiatry 12, 198–212. https://doi.org/10.1080/13546800600985557.
Radke, S., Pfersmann, V., Derntl, B., 2015. The impact of emotional faces on social motivation in schizophrenia. Eur. Arch. Psychiatry Clin. Neurosci. 265, 613–622. https://doi.org/10.1007/s00406-015-0589-x.
Redcay, E., Schilbach, L., 2019. Using second-person neuroscience to elucidate the mechanisms of social interaction. Nat. Rev. Neurosci. 1.
Reinen, J., Smith, E.E., Insel, C., Kribs, R., Shohamy, D., Wager, T.D., Jarskog, L.F., 2014. Patients with Schizophrenia are Impaired When Learning in the Context of Pursuing Rewards.
Robinson, D., Woerner, M.G., Alvir, J.M.J., Bilder, R., Goldman, R., Geisler, S., Koreen, A., Sheitman, B., Chakos, M., Mayerhoff, D., Lieberman, J.A., 1999. Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. Arch. Gen. Psychiatry 56, 241–247. https://doi.org/10.1001/archpsyc.56.3.241.
Rosenfeld, A.J., Lieberman, J.A., Jarskog, L.F., 2010. Oxytocin, dopamine, and the amygdala: a neurofunctional model of social cognitive deficits in schizophrenia. Schizophr. Bull. 37, 1077–1087.
Rus-Calafell, M., Gutiérrez-Maldonado, J., Ribas-Sabaté, J., 2014. A virtual reality-integrated program for improving social skills in patients with schizophrenia: a pilot study. J. Behav. Ther. Exp. Psychiatry 45, 81–89.
Rus-Calafell, M., Garety, P., Sason, E., Craig, T.J.K., Valmaggia, L.R., 2018. Virtual reality in the assessment and treatment of psychosis: a systematic review of its utility, acceptability and effectiveness. Psychol. Med. 48, 362–391.
Rutledge, R.B., Skandali, N., Dayan, P., Dolan, R.J., 2014. A computational and neural model of momentary subjective well-being. Proc. Natl. Acad. Sci. 111, 12252–12257.
Rylands, A.J., McKie, S., Elliott, R., Deakin, J.F.W., Tarrier, N., 2011. A functional magnetic resonance imaging paradigm of expressed emotion in schizophrenia. J. Nerv. Ment. Dis. 199, 25–29. https://doi.org/10.1097/NMD.0b013e3182043b87.
Salamone, J.D., Correa, M., 2012. The mysterious motivational functions of mesolimbic dopamine. Neuron 76, 470–485. https://doi.org/10.1016/j.neuron.2012.10.021.
Salokangas, R.K.R., Honkonen, T., Stengård, E., Koivisto, A.-M., 2006. Subjective life satisfaction and living situations of persons in Finland with long-term schizophrenia. Psychiatr. Serv. 57, 373–381.
Scherk, H., Falkai, P., 2006. Effects of antipsychotics on brain structure. Curr. Opin. Psychiatry 19, 145–150.
Schilbach, L., Timmermans, B., Reddy, V., Costall, A., Bente, G., Schlicht, T., Vogeley, K., 2013. Toward a second-person neuroscience 1. Behav. Brain Sci. 36, 393–414.
Schmälzle, R., O'Donnell, M.B., Garcia, J.O., Cascio, C.N., Bayer, J., Bassett, D.S., Vettel, J.M., Falk, E.B., 2017. Brain connectivity dynamics during social interaction reflect social network structure. Proc. Natl. Acad. Sci. 114, 5153–5158.
Schultz, C.C., Koch, K., Wagner, G., Roebel, M., Schachtzabel, C., Gaser, C., Nenadic, I., Reichenbach, J.R., Sauer, H., Schlösser, R.G.M., 2010. Reduced cortical thickness in first episode schizophrenia. Schizophr. Res. 116, 204–209.
Schwarz, K., Moessnang, C., Schweiger, J.I., Baumeister, S., Plichta, M.M., Brandeis, D., Banaschewski, T., Wackerhagen, C., Erk, S., Walter, H., 2019. Transdiagnostic prediction of affective, cognitive, and social function through brain reward anticipation in schizophrenia, bipolar disorder, major depression, and autism Spectrum diagnoses. Schizophr. Bull.
Shenton, M.E., Whitford, T.J., Kubicki, M., 2010. Structural neuroimaging in schizophrenia from methods to insights to treatments. Dialogues Clin. Neurosci. 12, 317.
Sokunbi, M.O., Gradin, V.B., Waiter, G.D., Cameron, G.G., Ahearn, T.S., Murray, A.D., Steele, D.J., Staff, R.T., 2014. Nonlinear complexity analysis of brain FMRI signals in schizophrenia. PLoS One 9, e95146. https://doi.org/10.1371/journal.pone.0095146.
Steptoe, A., Shankar, A., Demakakos, P., Wardle, J., 2013. Social isolation, loneliness, and all-cause mortality in older men and women. Proc. Natl. Acad. Sci. 110, 5797–5801.
Strauss, G.P., Waltz, J.A., Gold, J.M., 2013. A review of reward processing and motivational impairment in schizophrenia. Schizophr. Bull. 40, S107–S116.
Taylor, S.F., Kang, J., Brege, I.S., Tso, I.F., Hosanagar, A., Johnson, T.D., 2012. Meta-analysis of functional neuroimaging studies of emotion perception and experience in schizophrenia. Biol. Psychiatry 71, 136–145. https://doi.org/10.1016/j.biopsych.2011.09.007.
Veling, W., Pot-Kolder, R., Counotte, J., van Os, J., van der Gaag, M., 2016. Environmental social stress, paranoia and psychosis liability: a virtual reality study. Schizophr. Bull. 42, 1363–1371. https://doi.org/10.1093/schbul/sbw031.
Velthorst, E., Fett, A.-K.J., Reichenberg, A., Perlman, G., van Os, J., Bromet, E.J., Kotov, R., 2017. The 20-Year longitudinal trajectories of social functioning in individuals with psychotic disorders. Am. J. Psychiatry 174, 1075–1085. https://doi.org/10.1176/appi.ajp.2016.15111419.
Wake, S.J., Izuma, K., 2017. A common neural code for social and monetary rewards in the human striatum. Soc. Cogn. Affect. Neurosci. 12, 1558–1564.
Williams, K.D., Cheung, C.K.T., Choi, W., 2000. Cyberostracism: effects of being ignored over the Internet. J. Pers. Soc. Psychol. 79, 748.
Wolf, W., Levordashka, A., Ruff, J.R., Kraaijeveld, S., Lueckmann, J.-M., Williams, K.D., 2015. Ostracism online: a social media ostracism paradigm. Behav. Res. Methods 47, 361–373. https://doi.org/10.3758/s13428-014-0475-x.
Wood, S.J., Velakoulis, D., Smith, D.J., Bond, D., Stuart, G.W., McGorry, P.D., Brewer, W.J., Bridle, N., Eritaia, J., Desmond, P., Singh, B., Copolov, D., Pantelis, C., 2001. A longitudinal study of hippocampal volume in first episode psychosis and chronic schizophrenia. Schizophr. Res. 52, 37–46. https://doi.org/10.1016/S0920-9964(01)00175-X.
Woodward, N.D., Waldie, B., Rogers, B., Tibbo, P., Seres, P., Purdon, S.E., 2009.

Abnormal prefrontal cortical activity and connectivity during response selection in first episode psychosis, chronic schizophrenia, and unaffected siblings of individuals with schizophrenia. Schizophr. Res. 109, 182–190. https://doi.org/10.1016/j.schres.2008.11.028.
Yamada, M., Hirao, K., Namiki, C., Hanakawa, T., Fukuyama, H., Hayashi, T., Murai, T., 2007. Social cognition and frontal lobe pathology in schizophrenia: a voxel-based morphometric study. Neuroimage 35, 292–298. https://doi.org/10.1016/j.neuroimage.2006.10.046.
Zhang, Y., Ji, Q., 2005. Active and dynamic information fusion for facial expression understanding from image sequences. IEEE Trans. Pattern Anal. Mach. Intell. 27, 699–714.