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Evaluation of the Social Motivation Hypothesis of Autism
A Systematic Review and Meta-analysis

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Supplemental content

IMPORTANCE The social motivation hypothesis posits that individuals with autism spectrum disorder (ASD) find social stimuli less rewarding than do people with neurotypical activity. However, functional magnetic resonance imaging (fMRI) studies of reward processing have yielded mixed results.

OBJECTIVES To examine whether individuals with ASD process rewarding stimuli differently than typically developing individuals (controls), whether differences are limited to social rewards, and whether contradictory findings in the literature might be due to sample characteristics.

DATA SOURCES Articles were identified in PubMed, Embase, and PsycINFO from database inception until June 1, 2017. Functional MRI data from these articles were provided by most authors.

STUDY SELECTION Publications were included that provided brain activation contrasts between a sample with ASD and controls on a reward task, determined by multiple reviewer consensus.

DATA EXTRACTION AND SYNTHESIS When fMRI data were not provided by authors, multiple reviewers extracted peak coordinates and effect sizes from articles to recreate statistical maps using seed-based *d* mapping software. Random-effects meta-analyses of responses to social, nonsocial, and restricted interest stimuli, as well as all of these domains together, were performed. Secondary analyses included meta-analyses of wanting and liking, meta-regression with age, and correlations with ASD severity. All procedures were conducted in accordance with Meta-analysis of Observational Studies in Epidemiology guidelines.

MAIN OUTCOMES AND MEASURES Brain activation differences between groups with ASD and typically developing controls while processing rewards. All analyses except the domain-general meta-analysis were planned before data collection.

RESULTS The meta-analysis included 13 studies (30 total fMRI contrasts) from 259 individuals with ASD and 246 controls. Autism spectrum disorder was associated with aberrant processing of both social and nonsocial rewards in striatal regions and increased activation in response to restricted interests (social reward, caudate cluster: $d = -0.25$ [95% CI, −0.41 to −0.08]; nonsocial reward, caudate and anterior cingulate cluster: $d = -0.22$ [95% CI, −0.42 to −0.02]; restricted interests, caudate and nucleus accumbens cluster: $d = 0.42$ [95% CI, 0.07 to 0.78]).

CONCLUSIONS AND RELEVANCE Individuals with ASD show atypical processing of social and nonsocial rewards. Findings support a broader interpretation of the social motivation hypothesis of ASD whereby general atypical reward processing encompasses social reward, nonsocial reward, and perhaps restricted interests. This meta-analysis also suggests that prior mixed results could be driven by sample age differences, warranting further study of the developmental trajectory for reward processing in ASD.

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Social deficits characterize autism spectrum disorder (ASD). The social motivation hypothesis argues that ASD stems from diminished social motivation that occurs because individuals with ASD find social stimuli less rewarding compared with people with neurotypical function.[1-6] The social motivation hypothesis offers a developmental perspective on how aberrant reward processing might ultimately manifest as social deficits in ASD. The hypothesis posits that, from an early age, children with ASD attend less to social information, such as faces and gaze direction, and thus have decreased opportunities for social learning (eg, decreased engagement in joint attention, collaborative play, friendships), which in turn blunts social skill development. The social motivation hypothesis explains 2 core diagnostic features of ASD: diminished social approach and engagement.

Key Points

Question Does the literature on reward processing in autism spectrum disorder support the hypothesis that individuals with autism spectrum disorder show deficits in social motivation because they find social stimuli less rewarding?

Findings In this meta-analysis of 13 functional magnetic resonance imaging studies, 259 participants with autism spectrum disorder showed aberrant reward circuitry activation to both social and nonsocial rewards and increased activation to stimuli associated with their restricted interest.

Meaning Autism spectrum disorder may arise from an early neurobiological difference in response to rewarding social input, which in turn may lead to diminished social motivation; aberrant processing of rewards extends to nonsocial stimuli and might underlie increased motivation for restricted interests.

Psychological Studies of the Social Motivation Hypothesis

Much behavioral evidence for the social motivation hypothesis exists.[1] Infants with ASD attend less to people than to background objects in videos,[7] which is also true of adults with ASD.[8] Children with ASD fail to show the typical preference for social over nonsocial sounds.[9] They also demonstrate poorer friendship quality,[10] often develop theory of mind skills later than those without ASD, and continue to demonstrate related social cognition deficits into adulthood.[11] Neurocognitive evidence for the social motivation hypothesis, however, is less clear.

Functional Magnetic Resonance Imaging Studies on Reward Processing in ASD

Functional magnetic resonance imaging (fMRI) studies of the social motivation hypothesis have adopted paradigms from the reward literature, which partitions reward into wanting and liking subprocesses (ie, pursuit and consumption of reward, as in the incentive delay task). Monetary reward studies dominate the human fMRI reward literature, but ASD researchers incorporated social (eg, faces, people) and restricted interest (eg, trains) rewards, reflecting key features of ASD. Reward circuitry includes the ventral striatum/accumbens, dorsal striatum/caudate, anterior cingulate cortex, ventromedial prefrontal cortex, orbital frontal cortex, insula, amygdala, and putamen.[12] The ASD literature on reward processing includes small samples and contradictory results, with evidence for hyperactivation[13] and hypoactivation[14-16] of reward structures while viewing faces, and opposing results for other types of rewards (eg, monetary). Contradictory results with fMRI are not uncommon in clinical populations, potentially owing to inadequate statistical power[17] and inherent heterogeneity in taxometric conceptualizations (eg, opposing amygdala findings in ASD were later explained by comorbid anxiety[18]). However, findings from multiple small studies can be combined for increased power by leveraging recent advances in meta-analytic methodology.

Previous fMRI Meta-analyses of ASD

Previous meta-analyses of fMRI findings in ASD[19-25] usually collapsed across studies in broad domains (eg, social cognition) owing to small numbers of studies at that time. Facilitated by the recent increase of fMRI reports and new meta-analytic methodology, the field is now positioned to benefit from a meta-analysis focused on reward processing. Most previous fMRI meta-analyses in ASD[19-22,26] could not include covariates, effect sizes, statistical maps, or opposing findings, but these analyses are now possible with seed-based *d* mapping (SDM; http://www.sdmproject.com).[27] To our knowledge, the present study represents 1 of the first efforts to apply this new method to ASD.

This article quantitatively synthesizes the fMRI evidence for and against impairment in the reward neural circuitry in ASD using case-control studies, offers potential explanations for heterogeneity in past findings, and relates meta-analytic findings to the social motivation hypothesis of ASD. We meta-analyzed the response to social reward, restricted interests, and other types of nonsocial rewards. We hypothesized that, with the statistical power afforded by multiple studies, the ASD group would show hypoactivation to social stimuli in reward circuitry surviving whole-brain correction, despite no such single study findings that we located in the current literature.

Methods

Inclusion of Studies

Search Strategy

A literature review was conducted with university librarian assistance in PubMed, PsycINFO, and Embase databases from their inception until June 1, 2017. The search included an ASD term (*autis** or *asperger**) and functional neuroimaging term (*fMRI*, *functional MRI*, or *functional magnetic resonance imaging*), which identified 836 unique articles. Additional articles[13,28,29] were identified by reviewing article references[13,29] or author provision of unpublished data.[28] In accordance with MOOSE guidelines, search terms are described in the eMethods in the Supplement.[30]

Study Selection

Abstracts were screened in 2 rounds (eFigure 1 in the Supplement). Round 1 excluded 452 abstracts that were not original empirical fMRI reports comparing a sample with ASD with a

control sample. The remaining 384 abstracts were screened in round 2 by an independent rater (C.C.C. or A.R.Z.) and also subjected to an automated search for the term *reward* in the title, abstract, or key words. Abstracts not containing the term *reward* were excluded and classified into other domains, providing a description of the current state of fMRI ASD research. The 27 full-text articles meeting reward criteria were reviewed; 14 of these were excluded because their task did not involve participants receiving a reward in a domain of interest, relevant contrasts between full ASD and control groups were not available, or participants overlapped with other included articles (eMethods in the Supplement identifies excluded articles and reasons). Included studies used a variety of paradigms to interrogate rewards, including passively viewing rewards, reward-based decision making, implicit learning, or rewarded performance on incentive delay, go/no-go, domino, and auditory discrimination tasks (**Table 1**). For the purpose of this meta-analysis, data were pooled across all paradigms.

Data Extraction

For the eligible 13 articles, we requested data from authors for between-group contrasts of rewarded conditions compared with baseline (Table 1). We received statistical parametric maps from 9 studies (69%); this rate of more than 10% substantially increases the sensitivity to detect activation.[27] From the remaining 4 articles, coordinates and effect sizes of significant between-group activation peaks were extracted, and voxel-level maps of effect sizes and variances were recreated in SDM[27] (eMethods in the Supplement). Two individuals (C.C.C. and A.R.Z. or L.D.Y.) independently extracted data, and discrepancies were handled by consensus and an independent third party (R.T.S. or J.D.H.).

Meta-analysis

Statistical Analysis

SDM, version 5.141 software[27] was used because it offers several advantages over other fMRI meta-analytic methods (eMethods in the Supplement).[39] SDM converts *t* statistical maps to Cohen *d* effect size, then combines original and recreated study maps using a random-effects model. The model weights studies by their sample size and intrastudy variance, accounting for between-study variance. We report meta-analytic effect sizes as Cohen *d* for ease of interpretation in figures and the text; SDM-Z statistics and additional figures are available in the Supplement. Statistical significance was assessed using thresholding and permutation tests, following recommendations demonstrated to limit false-positives[27] used in previous meta-analyses.[32,40] Specifically, we applied the recommended thresholds (clusters with $z>1.00$, minimum cluster size of 10 voxels, uncorrected $P < .005$, and 20 permutations) within a whole-brain mask. Spatial smoothing (full width at half maximum, 20 mm) was applied for optimal control of true positives and true negatives.[27] Additional jackknife (leave one out) analyses were conducted to assess reproducibility of results. We localized activations using the Harvard-Oxford cortical and subcortical probabilistic atlases implemented in FSLEyes v0.15.0 (Oxford Centre for Functional Magnetic Resonance Imaging of the Brain). Between-study heterogeneity was addressed via a random-effects model, and voxel effects were assumed to vary randomly between studies. All additional analyses were conducted using the *metafor* package[41] in R.[42]

Data Analytic Strategy

Our data analytic strategy comprised 3 phases. First, we conducted a domain-general meta-analysis comparing activation between groups with ASD and typically developing controls using 30 contrasts from 13 studies, regardless of reward domain. Multiple contrasts from 1 study were combined into 1 reduced-variance map using previously described methods (eMethods in the Supplement).[32]

Next, we conducted 2 domain-specific meta-analyses (eTable 1 in the Supplement) comparing activation from baseline to either social stimuli (n = 7), such as photographs of a person smiling, or nonsocial stimuli (n = 10), such as money or game-relevant reinforcement. Finally, we conducted an exploratory meta-analysis with stimuli related to restricted interests (n = 3), such as videos of trains. For domain-specific analyses, when a study included both wanting and liking results, we selected contrasts from the wanting epoch (Table 1).

We conducted secondary meta-analyses to explore differences between reward wanting and liking paradigm phases. Analyses included only studies designed to allow for deconvolution of wanting and liking within brain signals (ie, studies using event-related designs; n = 6 of nonsocial and n = 3 of social stimuli).

Secondary Analysis

Exploratory Meta-regression With Sample Characteristics

Meta-regression with age explored whether reward-processing deficits occur independently of age and whether meta-analytic results are robust to between-study variation in sample age. Most studies matched participants on age, IQ, and sex, or reported that results did not change significantly when these variables were included as covariates (Table 1). However, differences between samples in age, IQ, or sex could contribute to varying results. Sex and IQ could not be examined in meta-regressions because the included studies showed little variance in mean sample IQ (range, 104-113; <1 SD) and sex (76.9%-100% male; 7 of 13 studies included only males). We conducted post hoc analyses of the correlation between age and mean cluster activation when at least 5 studies in a domain showed activation after removing outliers.

Post Hoc Correlation With ASD Symptom Severity

We assessed the association between ASD symptom severity and aberrant brain activation through correlations between the mean effect size in the primary striatal cluster and the mean score of the ASD group on the Social Responsiveness Scale, a commonly reported severity measure (high scores indicate more severe ASD symptoms and low scores indicate the absence of ASD symptoms).[43] This analysis could be conducted only in the social domain meta-analysis because half of the studies in the nonsocial domain did not provide Social Responsiveness Scale scores.

Table 1. Study Characteristics[a]

Source	ASD		TDC		Group Matching	Task	Contrasts Analyzed	Map	Wanting or Liking	Domain
	No. (Male)	IQ; Age, Mean (SD), y	No. (Male)	IQ; Age Mean (SD), y						
Assaf et al,[31] 2013	13 (10)	110.9 (21.2); 17.5 (3.3)	14 (11)	122.3 (12.8); 17.4 (3.6)	Age, sex; maps analyzed did not include covariates	Gain or loss of domino chips for performance each round in domino game with human or computer opponent; monetary reward at game end for losing (playing) all chips	Anticipation of rewarded outcome > baseline, collapsed across human and computer opponents (unpublished ASD vs TDC contrast)	Yes	Want	Nonsocial[b]
							Response to rewarded outcome > baseline, collapsed across human and computer opponents (unpublished ASD vs TDC contrast)	Yes	Like	Nonsocial
Carlisi et al,[32] 2017	20 (20)	113.2 (13.1); 14.7 (1.8)	29 (29)	118.9 (11.9); 15.3 (1.8)	Age, sex, IQ	Temporal discounting: receive future large or immediate small hypothetical monetary reward	Immediate monetary reward > delayed monetary reward (unpublished ASD vs TDC contrast)	Yes[c]	Combined	Nonsocial[b]
Cascio et al,[33] 2014	21 (21)	109.5 (14.0); 12.6 (2.5)	23 (23)	104.2 (12.5); 13.1 (3.4)	No matching; no significant group differences on age, sex, IQ	Passively view photos of own and others' special interests	Own interest > others' interests	Yes	Combined	Interest[b]
Choi et al,[34] 2015	27 (23)[d]	105.9 (14.7); 9.9 (2.5)	12 (10)[d]	103.7 (10.2); 9.1 (1.6)	Matching and covariates not reported	Receive social reward or punishment for auditory task performance (face with positive affect and thumbs up, or negative affect and thumbs down)	Feedback (positive or negative) > baseline (unpublished ASD vs TDC contrast)	Yes	Combined	Social[b]
Damiano et al,[35] 2015	24 (23)	107.0 (16.4); 14.7 (3.2)	21 (17)	110.8 (13.5); 14.3 (3.0)	No matching; no significant group differences on sex, IQ	Incentive delay to avoid monetary or social punishment (monetary loss or picture of sad face)	Anticipation of social loss > baseline	Yes	Want	Social[b]
							Outcome of social loss > baseline	No	Like	Social
							Anticipation of monetary loss > baseline	Yes	Want	Nonsocial[b]
							Outcome of monetary loss > baseline	No	Like	Nonsocial
Delmonte et al,[16] 2012	21 (21)	109.4 (16.0); 17.6 (3.5)	21 (21)	110.0 (12.5); 17.0 (3.4)	Age and IQ	Incentive delay for monetary or social reward (monetary gain or picture of smiling face)	Anticipation of social gain > baseline	Yes	Want	Social[b]
							Outcome of social gain > baseline	Yes	Like	Social
							Anticipation of monetary gain > baseline	Yes	Want	Nonsocial[b]
							Outcome of monetary gain > baseline	Yes	Like	Nonsocial
Dichter et al,[13] 2012	16 (14)	109.9 (20.3); 26.0 (9.1)	20 (14)	127.0 (8.1); 25.4 (7.0)	No; IQ as covariate in model	Incentive delay for monetary or social reward (monetary gain or picture of smiling face)	Anticipation of social gain > baseline	No	Want	Social[b]
							Outcome social gain > baseline	No	Like	Social
							Anticipation of monetary gain > baseline	No	Want	Nonsocial[b]
							Outcome of monetary gain > baseline	No	Like	Nonsocial

(continued)

Table 1. Study Characteristics[a] (continued)

Source	ASD		TDC		Group Matching	Task	Contrasts Analyzed	Map	Wanting or Liking	Domain
	No. (Male)	IQ; Age, Mean (SD), y	No. (Male)	IQ; Age Mean (SD), y						
Dichter al,[36] 2012	15 (15)	111.9 (22.7); 30.1 (11.6)	16 (16)	122.2 (10.7); 27.5 (7.5)	No; IQ as covariate in model	Incentive delay for monetary or preferred interest reward (monetary gain or picture of preferred interest)	Anticipation of interest object > baseline	No	Want	Interest[b]
							Outcome of interest object > baseline	No	Like	Interest
							Anticipation of monetary gain > baseline	No	Want	Nonsocial[b]
							Outcome of monetary gain > baseline	No	Like	Nonsocial
Kohls et al,[15] 2013	15 (15)	109.8 (12.1); 14.6 (3.3)	17 (17)	112.9 (12.6); 13.9 (3.0)	Age, sex, IQ	Go/no-go task with monetary or social reward	Go condition social > no reward condition	Yes	Combined	Social[b]
							Go condition monetary > no reward condition	Yes	Combined	Nonsocial[b]
Kohls et al,[28] 2018	39 (29)	103.6 (15.7); 12.6 (2.4)	22 (17)	112.0 (18.0) 12.9 (2.1)	No; no change in results when IQ covariate included	Incentive delay task for social or preferred interest reward (thumbs up and smiling video or personalized video of preferred interest)	Interest reward > no reward (unpublished ASD vs TDC contrast)	Yes	Combined	Interest[b]
							Social reward > no reward (unpublished ASD vs TDC contrast)	Yes	Combined	Social[b]
Schmitz et al,[37] 2008	10 (10)	107 (9); 37.8 (7)	10 (10)	106 (13); 38.2 (6)	Age, sex, IQ	Continuous performance task with monetary reward for performance	Monetary reward > no reward	No	Like	Nonsocial[b]
Scott-Van Zeeland et al,[14] 2010	16 (16)	112.3 (13.6); 12.4 (2.1)	16 (16)	119.0 (8.4); 12.3 (186)	Age, IQ	Implicit learning task; social or monetary reward or punishment for performance	Positive social deterministic > rest	No	Combined	Social[b]
							Positive monetary deterministic > rest	No	Combined	Nonsocial[b]
Solomon et al,[38] 2015	22 (18)	112.6 (12.4); 23.0 (5.1)	25 (20)	114.2 (11.5); 23.4 (4.2)	Age, sex, IQ	Implicit learning task with probabilistic reinforcement for performance	Anticipation of reward > baseline	Yes	Want	Nonsocial[b]
							Outcome of reward > baseline	Yes	Like	Nonsocial

Abbreviations: ASD, autism spectrum disorder; TDC, typically developing controls.

[a] Domains indicate which contrasts were included in which domain-specific meta-analysis and include social (n = 7), nonsocial (n = 10), and restricted interest (n = 3). Wanting refers to the time period preceding the reward, during which the individual anticipates the reward (eg, moving toward a piece of desirable chocolate). Liking refers to the period during which the individual is receiving and consuming the reward (eg, eating the chocolate). In functional magnetic resonance imaging study design and analysis, these 2 periods cannot always be reliably distinguished; such studies are described here as neither wanting nor liking, but combined. Studies with event-related designs usually analyzed wanting and liking results separately, with exceptions of Carlisi et al,[32] Choi et al,[34] and Scott-Van Zeeland et al.[14] This distinction could not be made in studies with block designs (combined), and these results were excluded from the supplemental analyses of wanting and liking.

[b] Contrast included in domain-specific meta-analysis presented in main text. All 30 contrasts in the table were included in domain-general meta-analysis; multiple contrasts from 1 study were combined using previously described methods implemented in seed-based *d* mapping.[32]

[c] Unpublished map provided in XBAM software format (as opposed to the more common FSL and SPM software formats); peak coordinates were extracted from XBAM map (eMethods in the Supplement provides details).

[d] Sex not reported; when contacted, authors noted sex ratio for whole sample only, so females were divided proportionately between ASD and TDC samples

Table 2. Significant Peak Activations Across All Reward Domains in 13 Studies

Region	Hemisphere	MNI Coordinates	SDM-Z Value	*P* Value	Voxels
ASD<TDC					
Anterior cingulate gyrus, caudate (L)	R, L	6, 6, 20	−2.143	<.00005	197
Caudate	R	22, 24, 12	−1.526	<.005	18
Central opercular cortex, insula	R	42, −6, 18	−1.756	<.0005	80
Cerebellum	R	32, −52, −26	−1.690	<.001	23
Cerebellum	L	−34, −84, −36	−1.470	<.005	13
Frontal pole	R	26, 54, −4	−1.721	<.0005	45
Inferior frontal gyrus, pars triangularis	R	34, 28, 18	−1.547	<.005	11
Lateral occipital cortex (inferior)	L	−42, −86, −18	−1.642	<.001	54
Middle frontal gyrus	R	24, 14, 34	−1.678	<.001	61
Nucleus accumbens, subcallosal cortex	L	−2, 6, −10	−1.630	<.001	24
Occipital fusiform gyrus, occipital pole, cerebellum	L	−10, −88, −28	−1.772	<.0005	58
Occipital pole, lingual gyrus, cerebellum	R	2, −90, −20	−1.722	<.0005	237
Parietal operculum cortex	R	30, −40, 16	−1.569	<.005	10
Precentral gyrus	R	52, −2, 30	−1.954	<.0005	149
Precentral gyrus	L	−58, −4, 36	−1.674	<.001	16
Precuneus cortex	L	−22, −42, 10	−1.476	<.005	38
Subcallosal cortex	R, L	2, 16, −6	−1.560	<.005	16
Thalamus	R	2, −26, 16	−1.632	<.001	42
Thalamus	L	−12, −34, 16	−1.605	<.001	34
ASD>TDC					
Anterior cingulate gyrus	R	6, 30, 8	1.961	<.005	11
Frontal pole	L	−22, 52, 18	2.236	<.0005	136
Insula	R	34, 14, −10	2.086	<.005	12
Lateral occipital cortex (inferior)	R	58, −66, 12	1.973	<.005	14
Lateral occipital cortex (inferior), angular gyrus	R	52, −66, 16	2.090	<.005	48
Lateral occipital cortex (superior)	R	16, −80, 40	1.998	<.005	24
Occipital fusiform gyrus, temporal occipital fusiform cortex	R	36, −58, −10	2.197	<.001	37
Parahippocampal gyrus (anterior)	R	28, −6, −30	2.187	<.001	49
Planum temporale, central opercular cortex	R	60, −16, 10	2.129	<.001	18
Planum temporale, superior temporal gyrus	L	−56, −26, 6	2.083	<.005	12
Precuneus cortex	L	−2, −72, 42	1.979	<.005	15
Putamen, amygdala	R	24, −2, −10	2.446	<.0005	107
Putamen, insula	L	−30, 0, 10	1.970	<.005	13
Superior frontal gyrus	L	−12, 28, 58	1.960	<.005	10
Superior temporal gyrus	L	−48, −22, −4	2.024	<.005	13
Superior temporal gyrus (posterior)	L	−36, −34, 4	2.100	<.001	14

Abbreviations: ASD, autism spectrum disorder; L, left; MNI, Montreal Neurological Institute; R, right; SDM-Z, seed-based *d* mapping *z*-statistic; TDC, typically developing controls.

Publication Bias

We assessed publication bias with the Egger test[44] implemented in SDM and visual inspection of funnel plots for significant meta-analysis clusters, using the mean effect size in the cluster from each study. This approach offers only an exploratory assessment of publication bias because, for contrasts without available maps, effect sizes for unreported brain data are unknown and conservatively assumed to be 0, consistent with standard fMRI meta-analytic practice.

Results

Characteristics of Included Studies

Thirteen studies reporting 30 results met inclusion criteria (eFigure 1 and eTable 1 in the Supplement) and included a total of 259 individuals (male, 233 [90%]) with ASD and 246 typically developing children (male, 221 [90%] serving as controls. The studies described several reward paradigms (Table 1). All null results were included in analysis as null (0) statistical maps.

Reward Processing in Autism

Activation Differences Across Reward Types

A meta-analysis of 13 studies revealed domain-general activation differences between the ASD group and controls (**Table 2**). However, opposing results of similar strength resulted in null meta-analytic findings (eg, left insular hypoactivation to nonsocial and hyperactivation to social stimuli), so we focus on the more interpretable results of domain-specific meta-analyses, for which complete results and figures depicting additional regions (hippocampus, amygdala,

superior frontal gyrus, insula, putamen, and frontal pole) are available in supplemental materials (eTables 2-4 and eFigures 3-6 in the Supplement).

Decreased Activation to Social Rewards

As predicted by the social motivation hypothesis, a meta-analysis of 7 studies with social stimuli revealed significant large clusters of reward circuitry hypoactivation in the ASD group in bilateral caudate (−12, 12, 16; d = −0.25; 95% CI, −0.41 to −0.08; P < .00001) and anterior cingulate cortex (0, 22, 34; d = −0.23; 95% CI, −0.39 to −0.06; P < .001) (**Figure 1** and **Figure 2**B). Reward circuitry hyperactivation was observed in the right insula and putamen (60, −16, 10; d = 0.24; 95% CI, 0.07 to 0.40; P < .0001) (eFigure 5 in the Supplement). Other areas with significant hypoactivation included the right hippocampus (eFigure 3 in the Supplement), lateral occipital cortex, and inferior frontal gyrus. Hyperactivation was observed in the right temporal occipital fusiform cortex and the left superior temporal gyrus/planum temporale (eTable 2 in the Supplement). Jackknife sensitivity analysis showed robustness of all striatal findings and most other regions; several smaller clusters were no longer significant after removing 1 of 2 studies[16,28] (eTable 2 in the Supplement). The Egger test (bias = −2.11, t_5 = −0.23; P = .41) and funnel plots (eFigures 3-6 in the Supplement) gave no evidence of publication bias.

Decreased Activation to Nonsocial Rewards

A meta-analysis of 10 studies with nonsocial stimuli revealed reward circuitry hypoactivation in the ASD group in bilateral caudate (−8, 2, 26; d = −0.22; 95% CI, −0.42 to −0.02; P < .0001), bilateral nucleus accumbens (−2, 16, −4; d = −0.21; 95% CI, −0.40 to −0.02; P < .0001), anterior cingulate cortex (−8, 2, 26; d = −0.22; 95% CI, −0.42 to −0.02; P < .0001), and right insula (38, −4, 16; d = −0.19; 95% CI, −0.33 to −0.04; P < .001) (Figure 1, Figure 2B, eFigure 5 in the Supplement). Reward circuitry hyperactivation was observed in 2 small clusters in the left caudate (−16, −12, 26; d = 0.20; 95% CI, 0.03 to 0.37; P < .0001) and the left insula (−34, 6, 6; d = 0.16; 95% CI, −0.03 to 0.36; P < .001), suggesting diversity within these structures. Other areas with significant hypoactivation included the left temporal occipital fusiform cortex, bilateral lingual gyrus, right occipital pole, and fusiform gyrus (eTable 3 in the Supplement). Hyperactivation was observed in the right hippocampus, left frontal pole, and left superior frontal gyrus (eFigures 3, 4, 6 in the Supplement). Jackknife sensitivity analysis showed robustness of all striatal findings and most other regions (eTable 3 in the Supplement). The Egger test (bias = −0.56; t_8 = −0.23; P = .83) and funnel plots (eFigures 3-6 in the Supplement) gave no evidence of publication bias.

Increased Activation to Restricted Interests

An exploratory meta-analysis of 3 studies of restricted interests revealed reward circuitry hypoactivation in the ASD group in the left nucleus accumbens (−4, 6, −12; d = −0.31; 95% CI, −0.55 to −0.07; P < .005) and anterior cingulate cortex (4, 4, 42; d = −0.30; 95% CI, −0.54 to −0.05; P < .005). Reward circuitry hyperactivation was observed in the right caudate and nucleus accumbens (14, 12, 2; d = 0.42; 95% CI, 0.07 to 0.78; P < .005) (Figure 2), left insula and putamen (−34, 20, −2; d = 0.44; 95% CI, 0.14 to 0.73; P < .001) (eFigure 5 in the Supplement), and, after controlling for sample age, bilateral anterior cingulate (eTable 4 in the Supplement). The nucleus accumbens showed both hypoactivation in the left hemisphere and hyperactivation in the right hemisphere, consistent with findings from both Cascio et al[33] and Kohls et al[28]; the third study in this meta-analysis reported no significant results in this region.[36] Other areas with significant hypoactivation included the left hippocampus, central opercular cortex, and parietal operculum cortex (eTable 4 and eFigure 3 in the Supplement). Hyperactivation was observed in the right thalamus, left frontal pole (eFigure 6 in the Supplement), and left precuneus cortex (eTable 4 in the Supplement). Jackknife sensitivity analyses reflected the small number of studies included; most significant clusters did not survive leaving out either Cascio et al[33] or Kohls et al,[28] indicating that these 2 studies largely drove the results, as expected due to samples twice as large[28] and availability of maps (eTable 4 in the Supplement). The Egger test (bias = −7.05; t_1 = −2.40; P < .25) and funnel plots (eFigures 3-6 in the Supplement) gave no evidence of publication bias.

Reward Disruption During Wanting and Liking Epochs

Secondary meta-analyses showed qualitative differences between wanting and liking of both social and nonsocial rewards (eTables 5-8 in the Supplement). Two notable findings include striatal regions demonstrating opposing findings during wanting and liking, and several hyperactivations during social liking. First, we observed social wanting hypoactivation differences that disappeared during liking in the bilateral caudate, anterior cingulate cortex, left hippocampus, and left frontal pole. We also observed nonsocial wanting hyperactivation differences that disappeared or changed to hypoactivation during liking in the putamen, insula, hippocampus, thalamus, and frontal pole. Second, we observed social liking hyperactivation in the accumbens, amygdala, insula, putamen, amygdala, caudate, frontal orbital cortex, and superior temporal gyrus.

Exploratory Meta-regression With Sample Characteristics

When ASD sample age was included as a covariate, a large, hyperactive cluster emerged in the hippocampus and amygdala for both social and nonsocial domains. Other results did not change meaningfully in the nonsocial domain, but all striatal clusters in the social domain were no longer significant. To understand this result, we explored the original caudate hypoactivation finding and observed a large, nonsignificant post hoc correlation with age (r = 0.63; P = .13), such that the ASD group showed greater hypoactivation in younger samples for social stimuli. We observed no correlation for nonsocial stimuli (r = −0.03; P = .94).

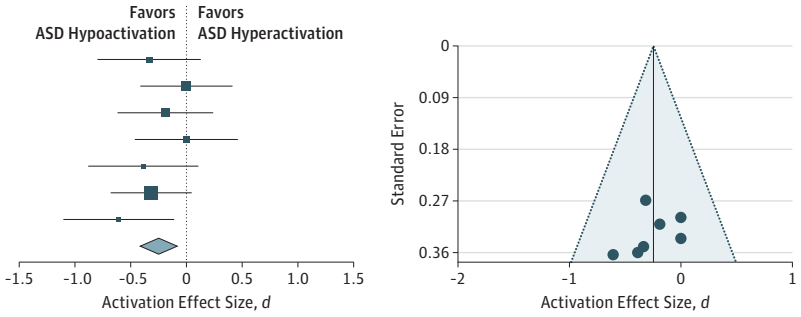
Post Hoc Correlation With ASD Symptom Severity

We observed a large, nonsignificant correlation between Social Responsiveness Scale score and activation in the

Figure 1. Significant Activation Differences Between Autism Spectrum Disorder (ASD) and Typically Developing Control (TDC) Samples in Response to Social and Nonsocial Stimuli

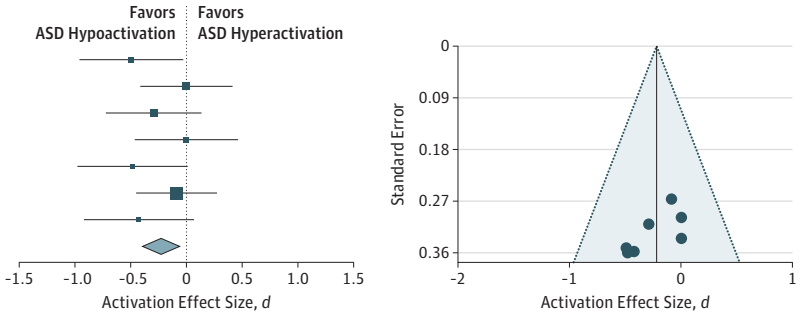
A Social reward, caudate 260 voxels (-12, 12, 6)

Source	*d* (95% CI)
Choi et al,[34] 2015	-0.33 (-0.80 to 0.13)
Damiano et al,[35] 2015	0.00 (-0.41 to 0.41)
Delmonte et al,[16] 2012	-0.19 (-0.62 to 0.24)
Dichter et al,[13] 2012	0.00 (-0.46 to 0.46)
Kohls et al,[15] 2013	-0.39 (-0.88 to 0.11)
Kohls et al,[28] 2018	-0.32 (-0.68 to 0.05)
Scott-Van Zeeland et al,[14] 2010	-0.61 (-1.10 to -0.11)
RE Model	-0.25 (-0.41 to -0.08)



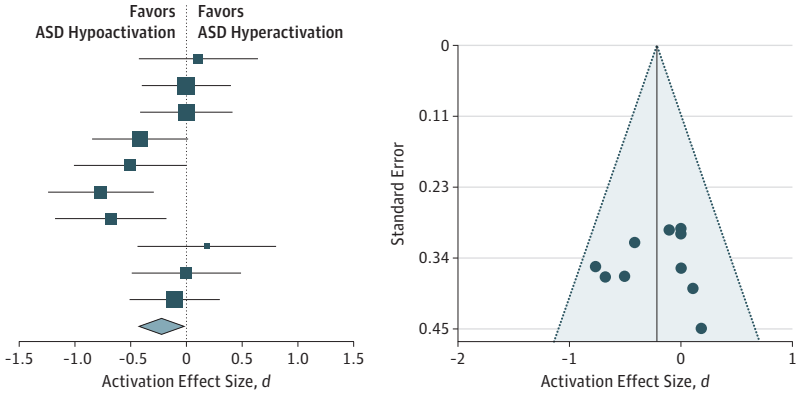
B Social reward, anterior cingulate 76 voxels (0, 22, 34)

Source	*d* (95% CI)
Choi et al,[34] 2015	-0.49 (-0.96 to -0.03)
Damiano et al,[35] 2015	0.00 (-0.41 to 0.41)
Delmonte et al,[16] 2012	-0.29 (-0.72 to 0.14)
Dichter et al,[13] 2012	0.00 (-0.46 to 0.46)
Kohls et al,[15] 2013	-0.48 (-0.98 to 0.01)
Kohls et al,[28] 2018	-0.09 (-0.45 to 0.27)
Scott-Van Zeeland et al,[14] 2010	-0.43 (-0.92 to 0.07)
RE Model	-0.23 (-0.39 to -0.06)



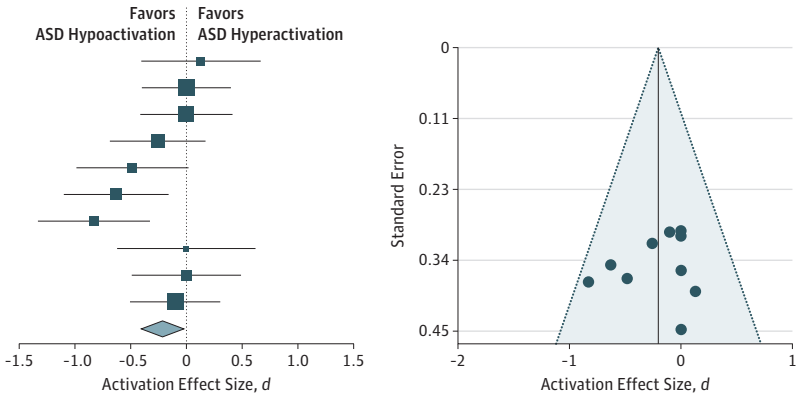
C Nonsocial reward, caudate and anterior cingulate 582 voxels (-8, 2, 26)

Source	*d* (95% CI)
Assaf et al,[31] 2013	0.11 (-0.43 to 0.64)
Carlisi et al,[45] 2017	0.00 (-0.40 to 0.40)
Damiano et al,[35] 2015	0.00 (-0.41 to 0.41)
Delmonte et al,[16] 2012	-0.41 (-0.85 to 0.02)
Dichter et al,[36] 2012	-0.51 (-1.01 to 0.00)
Dichter et al,[13] 2012	-0.77 (-1.24 to -0.29)
Kohls et al,[15] 2013	-0.68 (-1.18 to -0.18)
Schmitz et al,[37] 2008	0.18 (-0.44 to 0.80)
Scott-Van Zeeland et al,[14] 2010	0.00 (-0.49 to 0.49)
Solomon et al,[38] 2015	-0.11 (-0.51 to 0.30)
RE Model	-0.22 (-0.42 to -0.02)



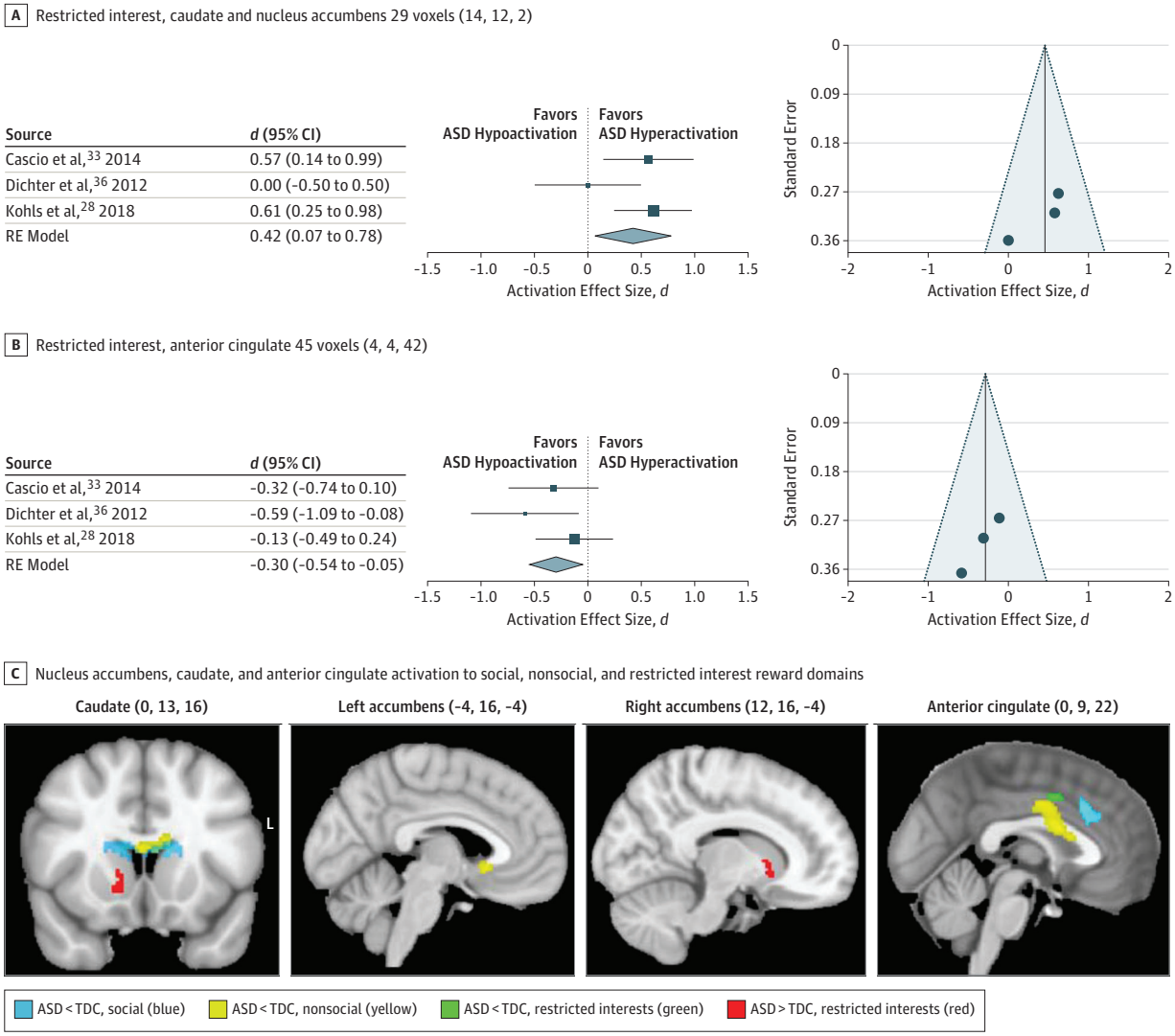
D Nonsocial reward, nucleus accumbens 102 voxels (-2, 16,-4)

Source	*d* (95% CI)
Assaf et al,[31] 2013	0.13 (-0.40 to 0.66)
Carlisi et al,[45] 2017	0.00 (-0.40 to 0.40)
Damiano et al,[35] 2015	0.00 (-0.41 to 0.41)
Delmonte et al,[16] 2012	-0.26 (-0.69 to 0.17)
Dichter et al,[36] 2012	-0.48 (-0.99 to 0.02)
Dichter et al,[13] 2012	-0.63 (-1.10 to -0.16)
Kohls et al,[15] 2013	-0.83 (-1.33 to -0.33)
Schmitz et al,[37] 2008	0.00 (-0.62 to 0.62)
Scott-Van Zeeland et al,[14] 2010	0.00 (-0.49 to 0.49)
Solomon et al,[38] 2015	-0.10 (-0.51 to 0.30)
RE Model	-0.21 (-0.40 to 0.02)



Differences in the caudate, nucleus accumbens, and anterior cingulate shown for social (A and B) and nonsocial (C and D) rewards. Forest and funnel plots reflect the average effect size of voxels in the significant meta-analytic cluster. These 4 results were among the most robust; findings replicated in every jackknife sensitivity analysis (eTables 2-4 in the Supplement). Forest plots depict the contribution of each study to the meta-analytic result. Funnel plots show no evidence of publication bias. Voxels not near a reported peak are conservatively estimated as 0 in studies with unavailable maps.[13,14,37,38] RE indicates random effects.

Figure 2. Significant Activation Differences Between Autism Spectrum Disorder (ASD) and Typically Developing Control (TDC) Samples With Aggregated Results Across Domains



A, Differences in the caudate and nucleus accumbens for the restricted interests domain shown. B, Differences in the anterior cingulate for the restricted interests domain shown. The forest and funnel plots reflect the average effect size of voxels in the significant meta-analytic cluster. Forest plots depict the contribution of each individual study to the meta-analytic result. Funnel plots show no evidence of publication bias. Voxels not near a reported peak are conservatively estimated as 0 in studies with unavailable maps.[36] C, Results from Figure 1 and Figure 2A and B aggregated across domains. In the caudate, individuals with ASD showed hypoactivation to social stimuli (blue), nonsocial stimuli (yellow), and hyperactivation to restricted interest stimuli (red) compared with controls. In the nucleus accumbens, individuals with ASD showed hypoactivation in the right hemisphere to nonsocial stimuli (yellow) and hyperactivation in the left to restricted interests (red). No significant cluster involving the accumbens was observed in the social meta-analytic results. In the anterior cingulate cortex, individuals with ASD showed hypoactivation to social stimuli, nonsocial stimuli, and restricted interest stimuli, compared with controls. RE indicates random effects.

caudate among 7 studies in the social meta-analysis (r = −0.72; P = .07), such that higher ASD severity correlated with greater hypoactivation.

Discussion

The social motivation hypothesis posits deficits in processing social rewards among individuals with ASD. Our meta-analysis reveals that individuals with ASD show neural differences in processing not only social, but also nonsocial and potentially restricted interest, rewards. Our results resolve prior inconsistencies in the fMRI literature and suggest that reward-processing differences extend beyond the social domain, potentially leading to domain-general motivation differences. These 2 contributions pave the way for future studies of reward processing in ASD.

This meta-analysis provides what we believe to be the strongest current fMRI evidence evaluating the social motivation hypothesis of ASD. We augmented the existing litera-

ture with unreported relevant data from publications on related disorders or tasks.[31,34,45] The existing literature included conflicting results that were difficult to compare owing to varied sample age, different correction methods, and region of interest analyses, which inherently introduce bias.[46] This meta-analysis addressed these issues and revealed that ASD groups showed reward circuitry hypoactivation for both social and nonsocial rewards. The caudate, accumbens, and anterior cingulate gyrus demonstrated the most robust hypoactivation, as reported by approximately half of the contributing studies (caudate,[14-16,28,35,36] anterior cingulate,[13-16,35-38] and accumbens[13,15,35,36]). No clear similarities among these studies emerged in paradigms or sample characteristics, suggesting that the association may be robust to different paradigms and sample characteristics.

Extending the Social Motivation Hypothesis

Early formulations of the social motivation hypothesis focused on differences in reward processing in the social domain.[2,47] Social impairments are cardinal features of ASD, but it is possible that atypical reward processing contributes to the development of restricted interests, sensory interests, and other symptoms encompassed by the ASD phenotype, as described in more recent conceptualizations of the social motivation hypothesis.[5,6,36,48,49] Early research characterized children with ASD as hyperfocused on objects,[50] and children as young as 12 months who later develop ASD already show atypical object exploration, with more attention to interesting sensory components.[51] Increased attention to objects may lead to increased object motivation and, given the competition between objects and social stimuli for attention in the everyday environment, to decreased social motivation in line with the social motivation hypothesis. The early developmental trajectory toward decreased social motivation may mirror trajectories toward other atypical motivations: restricted interests elicited hyperactivation of reward circuitry in this meta-analysis, other types of nonsocial rewards also showed hypoactivation, and there is preliminary evidence of altered processing of primary rewards, such as images of food.[29]

Based on previous publications[5,6,36] and our current evidence, we suggest that the field adopt a broader view of the social motivation hypothesis that includes altered processing of social and nonsocial rewards. We hope that this perspective will spark research on the differences between approach and avoidance motivation for appetitive or aversive stimuli; how processing differs across types of nonsocial rewards, including restricted interests; how reward processing impairments mediate gains in reward-based therapies, such as applied behavior analysis; and the role of motivation in individual differences observed in clinics (eg, aloof vs active but odd[52]). It remains unlikely that a single cognitive or neural mechanism could explain development and maintenance of all ASD symptoms[53] in all individuals.

Wanting and Liking

Reward is not a unitary construct, psychologically or neurobiologically.[54] It consists of a wanting phase (also called *anticipatory drive*) and a liking phase (related to the pleasurable effect of reward consumption[54]), with the former being most strongly tied to social motivation deficits in ASD.[4] Disentangling these phases with fMRI requires event-related designs. Our exploratory meta-analysis of the 6 studies using such designs suggested striatal hypoactivation during wanting and hyperactivation during liking of social stimuli. Additional studies are needed to fully understand differences between social wanting and liking.

Moderators

After controlling for age across studies, some striatal hypoactivation for individuals with ASD in the social domain was no longer significant. Post hoc correlations suggest that younger people with ASD may show greater differences in striatal activation during reward tasks, but this result requires replication and is presented to spark further study. This finding aligns with other fMRI,[55,56] behavioral,[57] and event-related potential[58] studies suggesting age,[59,60] pubertal,[61] and paradigm-dependent[62] differences in reward processing in typical development. Longitudinal or large cross-sectional studies are needed to disentangle how age and puberty affect reward processing in individuals with ASD.

Sex and IQ likely moderate reward processing as well. Unfortunately, this meta-analysis could not evaluate these effects owing to predominantly male samples with average IQ. IQ correlates with caudate reward response in adults without ASD.[63] Inclusion of lower functioning individuals in fMRI studies[64] would facilitate examination of the influence of IQ on reward processing in ASD. With regard to sex, prior incentive delay task studies report that neurotypical males show greater reward responsivity than females to monetary reward,[65] but few differences from baseline activation to social rewards.[66] Thus, inconsistent findings in previous ASD social reward processing studies of males may be attributable to use of paradigms that do not detect activation differences among males.

Limitations

Domain-specific meta-analyses would have benefited from larger sample sizes. However, most authors that we contacted provided original statistical maps, rendering us sufficiently powered to assess differences with as few as 4 or 5 studies.[27,67] With more than 500 study participants, to our knowledge, this meta-analysis currently stands as the largest fMRI analysis of reward processing in ASD.

We were restricted to qualitative comparisons between social and nonsocial reward domains because imaging meta-analytic methods do not yet allow for quantitative comparisons between meta-analyses using studies as subjects, owing to missing study variance data. However, results in most regions were sufficiently clear to enable qualitative comparisons across domains.

Another limitation concerns between-study heterogeneity owing to differences in paradigms, which is often underestimated in meta-analysis. Ideally, this meta-analysis would include only studies using the same experimental paradigm (ie, incentive delay task[13,16,28,35,36]). However, the literature is too small to offer large sets of similar, replicated stud-

ies. Thus, we combined studies that used different paradigms (Table 1). The included studies also differed in the salience of the reward, with some using static photos and strangers, others providing videos and familiar people or personalized restricted interests, and some using aversive stimuli.[35] Despite paradigm heterogeneity, we believe that using broader inclusion criteria to increase statistical power contributes meaningful fMRI results to reward-processing literature that often must compare results across different modalities (eg, fMRI, electroencephalographic, and behavioral).

Finally, many authors provided statistical maps, but some maps were unavailable. For these contrasts, we needed to estimate SDs of activation effect sizes, thereby limiting precision of meta-analytic study weights and usefulness of forest plots. This estimation should be considered when reviewing the results; however, it is unlikely to introduce bias because there was no apparent association between provision of maps and the study's results. Most prior ASD meta-analyses relied entirely on estimation of SDs, among other necessary approximations, and this image-based meta-analysis represents a step forward in meta-analysis of ASD fMRI data.

Conclusions

Our meta-analysis synthesizes a growing literature and shows aberrant neural processing of social, nonsocial, and potentially restricted interest rewards in individuals with ASD. These results offer what we believe to be the first fMRI evidence of domain general reward processing deficits in ASD, supporting a broader interpretation of the social motivation hypothesis. We also suggest that the literature's heterogeneity might be addressed by study of the effects of age, sex, and IQ on reward processing in ASD.

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Study concept and design: Clements, Schultz, Herrington.
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