Functional magnetic resonance imaging of autism spectrum disorders

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Introduction

Autism was first described by Leo Kanner[1] and Hans Asperger[2] in a series of clinical case studies. Both clinicians suggested that the conditions now referred to as autism spectrum disorders (ASDs) may have a neurobiological basis. With the relatively recent advent of modern brain imaging techniques, translational psychiatric research has embraced the systematic study of

This review presents an overview of functional magnetic resonance imaging findings in autism spectrum disorders (ASDs). Although there is considerable heterogeneity with respect to results across studies, common themes have emerged, including: (i) hypoactivation in nodes of the "social brain" during social processing tasks, including regions within the prefrontal cortex, the posterior superior temporal sulcus, the amygdala, and the fusiform gyrus; (ii) aberrant frontostriatal activation during cognitive control tasks relevant to restricted and repetitive behaviors and interests, including regions within the dorsal prefrontal cortex and the basal ganglia; (iii) differential lateralization and activation of language processing and production regions during communication tasks; (iv) anomalous mesolimbic responses to social and nonsocial rewards; (v) task-based long-range functional hypoconnectivity and short-range hyper-connectivity; and (vi) decreased anterior-posterior functional connectivity during resting states. These findings provide mechanistic accounts of ASD pathophysiology and suggest directions for future research aimed at elucidating etiologic models and developing rationally derived and targeted treatments.

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ASDs using these measurement tools to gain insight into the pathophysiology and possible etiology of ASDs. The ultimate promise of these approaches is to improve mechanistic accounts of ASDs as well as provide targets for novel intervention approaches.

ASDs emerge early in life and are generally associated with lifelong disability.[3] The defining symptoms of the disorder include social and communicative deficits and restricted and repetitive behaviors and interests.[4] Individuals with milder constellations of symptoms are classified as having an ASD, a term that reflects the highly heterogenous array of symptom presentations and that will likely be adopted to characterize individuals with a range of intellectual functioning in the next version of the *Diagnostic and Statistical Manual of Mental Disorders*.[5] Geschwind and Levitt[6] illustrated the complexity inherent to understanding the neurobiology of ASDs by suggesting that there are likely many "autisms," each with non-overlapping etiologies and presentations. Given the highly heterogenous nature of ASDs, it is perhaps not surprising that brain imaging studies have yielded a wide array of candidate brain circuits affected by the disorder. This range of brain endophenotypes is consistent with the challenges associated with identifying genes that cause ASDs: although ASDs have a very strong genetic component, with an estimated heritability as high as 90%,[7] the identification of reliable genetic markers remains elusive.

Functional magnetic resonance imaging (fMRI) has proven to be a useful tool to investigate aberrant neurobiological function in ASDs because of its excellent contrast properties, spatial resolution, and temporal resolution. fMRI uses specialized pulse sequences to localize metabolic correlates of neural activity linked to relevant neurocognitive processes. Additionally, unlike positron emission tomography (PET) and single-photon emission computed tomography (SPECT), fMRI does not rely on radiotracers and is noninvasive. The past two decades have witnessed a surge in fMRI research in ASDs, and the goal of this review is to provide an overview of the questions addressed by these studies, to identify consistent patterns across investigations, and to suggest directions for future research.

Task-based functional magnetic resonance imaging

Likely due at least in part to the heterogeneity of symptom expression in ASDs, there is no unifying account of brain dysfunction that explains all the core symptoms of ASDs. Instead, the triad of defining ASDs symptoms (ie, impaired social functioning, impaired communication, and restricted and repetitive behaviors and interests) suggests distinct neural systems. Additionally, it is common for some cognitive systems to be spared in individuals with ASDs (eg, even severe cases of ASDs may be accompanied by high intelligence and other so-called "islets of ability"[8]), suggesting that brain dysfunction in ASDs may be domain-specific. Likewise, task-based fMRI studies of ASDs have taken the piecemeal approach of investigating neurocognitive processes linked to specific symptom domains in relative isolation. Therefore, in this review studies are grouped based on these distinct neurocognitive processes. The clear majority of studies have used tasks that map onto the triad of defining ASD symptoms, and thus studies are first presented based on this trichotomy. However, emerging fMRI data addressing reward processing and resting-state functional connectivity do not clearly fit within these three domains, as thus are given separate sections in this review.

Social cognition

Most functional neuroimaging investigations in ASDs have addressed social perception (the automatic and preconscious processing of social information) and social cognition (processing meaning from emotional and social cues). Task-related fMRI studies addressing social functioning in ASDs have focused on nodes of the so-called "social brain," including the medial prefrontal cortex, implicated in making inferences about others' intentions, the temporoparietal junction, mediating mentalizing, the posterior superior temporal sulcus, activated by biological motion, the inferior frontal gyrus, involved in emotional judgments, the interparietal sulcus, which guides spatial attention in social contexts, the amygdala, involved in recognizing emotions from facial expressions, the fusiform gyrus, critical for face processing, and the anterior insula, involved in understanding internal states and mimicking social expressions (see ref 9 for a review).

Face processing

Perhaps the richest area of inquiry into social cognition deficits in ASDs has been studies of face processing *(Table I)*. Faces are perhaps the quintessential social

stimulus, and infants attend to and recognize faces from very early infancy.[10] Studies of face processing in ASDs are theoretically grounded by behavioral evidence of impaired joint attention, eye contact, and face recognition and discrimination in ASDs, as well as impaired social emotional judgments about faces, reduced face emotion recognition and perception, and abnormal eye scanpaths when viewing faces.[11,12]

In neurotypical participants, the medial-lateral fusiform gyrus (FG) as well as the superior temporal sulcus, amygdala, and orbitofrontal cortex, activate in response to faces.[13] The majority of fMRI studies in ASDs indicate FG hypoactivity to faces[14-22] and to facial expressions.[15,20,23-25] However, other reports suggest no differences in FG activation to familiar faces,[26-29] stranger faces in the presence of an attentional cue,[30] or when matching upright with inverted faces.[31]

These apparently inconsistent findings may be reconciled in a number of ways.[32,33] The degree of visual attention to faces appears to be a critical factor moderating FG activation to faces in ASDs, with tasks that guide visual attention to faces or analytic approaches that account for point-of-regard resulting in relatively less FG hypoactivation in ASDs.[21,30] This conclusion is supported by research indicating that face familiarity moderates FG responses to faces in ASDs[28] and that impaired social cognition in ASDs may be mediated, at least in part, by attention to social cues, rather than by deficits in social cue processing per se.[34,35] Similarly, lifelong amotivation to interact with faces may result in reduced perceptual skill when processing faces, and, in turn, cause FG hypoactivation to faces in ASDs that is perhaps a downstream consequence of reduced social experience rather than pathognomonic to ASDs.[36] Moreover, the FG encodes not only face percepts, but social knowledge as well,[37] suggesting that the FG may mediate: (i) the attribution of social meaning to stimuli; (ii) the retrieval of social semantic information; and (iii) self-referential experiences.[28] Thus, the disparate results of the face processing literature in ASDs likely reflect the diverse and subtle social processes mediated by the FG and recruited by diverse fMRI tasks.

Amygdala response to faces in ASDs has also been extensively studied, and results in this area are decidedly mixed. There is evidence of no differences in amygdala activation to faces,[18] of amygdala hypoactivation during face viewing[15,16,26,31,38] and face matching,[16] as well as evidence of amygdala hyperactivation to faces[39,40] in ASDs, particularly when accounting for gaze time to faces[21] (but see ref 41 for an exception). One study reported decreased amygdala habituation to the repeated presentation of faces, suggesting that social deficits in ASDs may be influenced by hyperarousal to faces due to protracted amygdala activation.[42]

Theory of mind

Theory of mind and mental inferences have been examine in ASDs via fMRI studies that address the ability to infer feeling states and/or intentions *(Table II)*, skills that typically develop during the first 4 or 5 years of life and that are critical for the development of social skills and for successful navigation of the social world.[43] Such tasks include images, stories, and animations designed to elicit the attribution of mental states. Results from typically developing individuals indicate with remarkable consistency that theory of mind is mediated by the posterior superior temporal sulcus at the temporoparietal junction, the temporal poles, the amygdala, and dorsal medial and ventrolateral prefrontal cortex.[44]

The amygdala plays a critical role in multiple aspects of mentalizing, including determining emotional states of others from facial expressions,[45] and a number of studies have reported aberrant amygdala activation in ASDs during tasks requiring inferring mental states from pictures of eyes[46,47] and judging facial expressions,[23] suggesting that the amygdala may fail to assign emotional relevance to social stimuli in ASDs. Other studies, however, have reported that ASDs are characterized by amygdala hyperactivity during face viewing[48] and anticipation,[49] suggesting that the so-called "amygdala theory of autism" may reflect impaired amygdala modulation rather than simply hypoactivation in social contexts.

Another brain region that has received scrutiny in fMRI studies of theory of mind in ASDs is the posterior superior temporal sulcus, a region recruited during tasks that involve interpreting other's mental states from biological motion cues.[50] There are reports of posterior superior temporal sulcus hypoactivation while processing incongruent eye gaze shifts,[51] while viewing direct and averted gaze,[52] during intentional attribution to animated sequences of geometric figures,[53] and during speech perception.[54] A recent study of children with ASDs and their unaffected siblings found that activation in posterior superior temporal sulcus (as well as the amygdala and ventromedial prefrontal cortex) during biological motion perception differentiated children with ASDs

both from their unaffected siblings and from matched control participants, suggesting that activation of this region may be related to phenotypic expression of social deficits in ASDs rather than genetic liability.[55]

Another area of inquiry has been functioning of the mirror neuron system (including, in humans, the pars opercularis in the inferior frontal gyrus). This system is active during imitation, action observation, intention understanding, and understanding emotional states of others.[56] The inferior frontal gyrus has been reported to be relatively less active in ASDs during imitation and observation of faces[57-59] and during imitation and observation of emotional expressions in ASDs,[48,60] suggesting that mirror neuron dysfunction may account for social deficits in ASDs, though this contention has been questioned.[61] Additionally, a recent meta-analysis of fMRI studies of social processing in ASDs revealed hypoactivation of the right anterior insula across studies (but see ref 62 for an exception), a region that is believed to be a relay station for projections from the IFG to the amygdala.[63]

Cognitive control

Restricted and repetitive behaviors and interests constitute a multifaceted symptom domain in ASDs that comprises both lower-order motoric repetitive behaviors (eg, body rocking, hand flapping) as well as higher-order cognitive manifestations (eg, a need for predictability).[64] Because fMRI requires minimal motion from research subjects, cognitive manifestations of restricted and repetitive behaviors have been the focus of fMRI research. Such studies have mostly relied on tasks requiring cognitive control because of linkages between deficits on neuropsychological cognitive control tasks and symptoms of restricted and repetitive behaviors and interests in ASDs.[65]

Animal lesion and nonclinical human neuroimaging studies indicate that cognitive control is mediated by frontostriatal brain systems, including the lateral prefrontal cortex, the inferior frontal cortex (including the insular cortex), the anterior cingulate cortex, the intraparietal sulcus, and the striatum.[66] Functional MRI studies of cognitive control in ASDs have revealed anomalous activation in frontostriatal brain regions *(Table III)*, including inferior and middle frontal gyri, dorsal anterior cingulate cortex, and the basal ganglia during cognitive control tasks. Such findings have been reported using go/no-go, Stroop, and switching tasks,[67] tasks that require interference inhibition,[68-72] response monitoring,[73] novelty detection,[74,75] spatial attention,[68] working memory,[76,77] and saccadic eye movements.[78] These findings have been interpreted to reflect deficits in behavioral inhibition and/or generation of adaptive behaviors linked to the expression of restricted and repetitive behavior and interests. Although the direction of effects has varied across studies (ie, frontostriatal hyperactivation vs hypoactivation), likely due to task demands and analysis methods, anomalous frontostriatal activation during tasks requiring cognitive control has been a consistent result in ASD samples, with the majority of findings indicating frontostriatal hyperactivation that has been interpreted to reflect a neurofunctional compensatory mechanisms to overcome cortical inefficiency.[70]

Communication

Investigations of communication deficits in ASDs have focused predominantly on brain regions mediating language perception, comprehension, and generation. The left hemisphere is typically language-dominant, and speech production is mediated by Broca's area at the junction of the frontal, parietal, and temporal lobes, whereas speech comprehension is mediated by Wernicke's area in the posterior temporal lobe.[79] Heschl's gyrus, in the dorsal temporal lobe, contains primary auditory cortex as well as the angular gyrus, involved in higher-order language comprehension and cross-modal integration, and the inferior parietal lobule, involved in processing semantic content.[80]

fMRI studies of communication functions in ASDs have used tasks requiring listening to speech sounds,[54,81,82] sentence comprehension,[83-85] verbal fluency,[86] pragmatic language comprehension,[87] semantic judgments,[88] response-naming,[89] and viewing body gestures[90-91] *(Table IV)*. Overall, findings indicate differential lateralization patterns in ASDs (ie, reduced left > right lateralization),[82,84,86,87,89] decreased synchrony of brain regions processing language,[83,92] decreased automaticity of language processing,[93] greater neurofunctional deficits for speech than songs,[94] and recruitment of brain regions that do not typically process language.[83,95-97] A recent methodological innovation in the domain of language-based fMRI studies in ASDs has been to present speech stimuli to very young children with ASDs (as young as 12 months old) while asleep.[82,98] Although the diagnostic stability of ASDs for children in this age range must be considered, this approach has the potential to leverage task-based fMRI

in far younger children with ASDs to examine altered developmental trajectories associated with impaired receptive language skills. Additionally, sleep fMRI would appear to be well suited to studying early emerging functional brain activation properties linked to speech processing in infant high-risk paradigms.

Reward processing

The social-communication deficits that characterize ASDs may reflect decreased motivation to engage in social behaviors in early childhood. This decreased motivation may result in fewer experiences with the social environment,[99] further compounding social-communicative deficits.[100] Reward processing is mediated primarily by dopaminergic projections from the ventral tegmental area to the striatum, orbitofrontal cortex, ventromedial prefrontal cortex, and the anterior cingulate cortex, forming a mesolimbic dopamine reward pathway.[101] Emerging evidence suggests that the neural circuits that mediate reward processing may have evolved, at least in part, to facilitate social attachment,[102] and reward mechanisms serve to encode and consolidate positive memories of social experiences, facilitating social functioning abilities hypothesized to be impaired in ASDs.[103]

Reward processing deficits in ASDs have been assessed in six fMRI studies to date *(Table V)*. Schmitz and colleagues[104] reported decreased left anterior cingulate gyrus and left midfrontal gyrus activation to rewarded trials during a sustained attention task in ASDs and that anterior cingulate gyrus activation predicted social symptom severity. Scott-Van Zeeland and colleagues[105] reported ventral striatal hypoactivation during social and nonsocial learning in ASDs. During a rewarded go/no-go paradigm, Kohls and colleagues[106] found ventral striatal hypoactivation to monetary rewards and amygdala and anterior cingulate cortex hypoactivation to monetary and social rewards in children with ASDs. Cascio and colleagues[107] reported increased bilateral insula and anterior cingulate cortex activation to images of food in children with ASDs who had fasted for at least 4 hours. Two studies by Dichter and colleagues,[49,108] using incentive delay tasks, found decreased nucleus accumbens activation during monetary anticipation, bilateral amygdala hyperactivation during face anticipation that predicted social symptom severity *(Figure 1)*, insular cortex hyperactivation during face outcomes, and

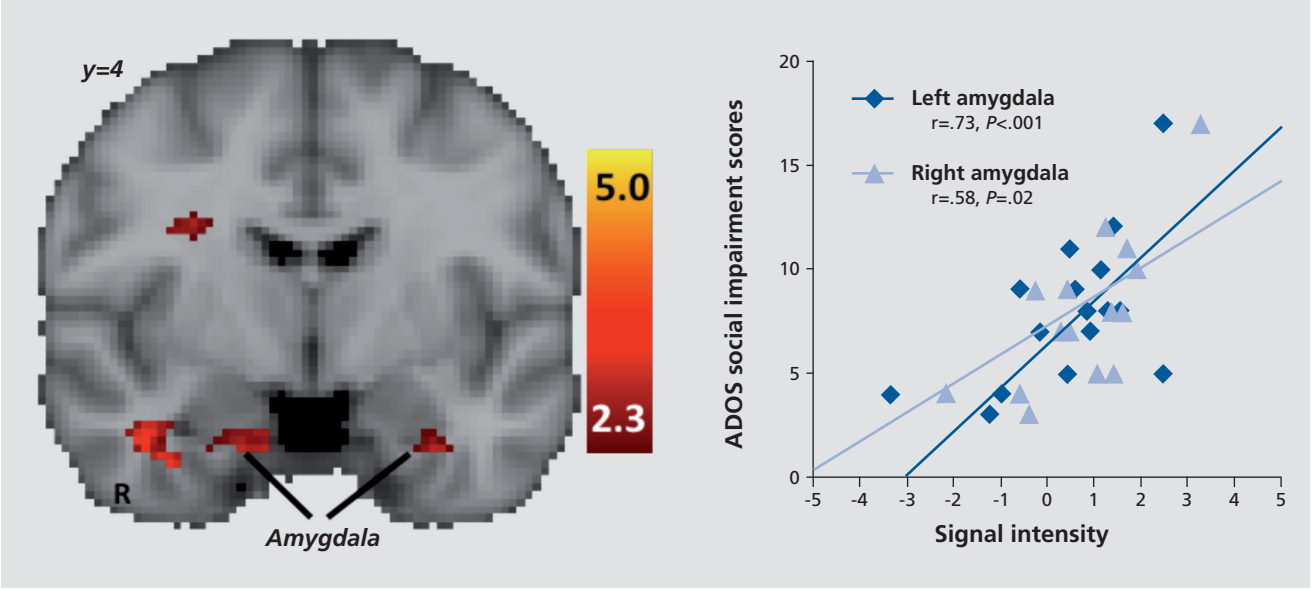

Figure 1. Individuals with autism spectrum disorders demonstrated bilateral amygdala hyperactivation during the anticipation of social rewards (left), and activation magnitude predicted social impairments (right). This pattern was not evident during the actual presentation of social rewards, or in response to other types of rewards. This and related findings suggest that the functional integrity of brain reward systems in autism spectrum disorders is contingent on both the type of reward processed and the temporal phase of the reward response. ADOS, Autism Diagnostic Observation Schedule

Adapted from ref 49: Dichter GS, Richey JA, Rittenberg AM, Sabatino A, Bodfish JW. Reward circuitry function in autism during face anticipation and outcomes. *J Autism Dev Disord*. 2012;42:147-160. Copyright © Springer 2012

ventromedial prefrontal cortex *hyper*activation while viewing images related to circumscribed interests in ASDs. Taken together, these results suggest that reward network dysfunction in ASDs may not be constrained to responses to social rewards, but rather may be characterized by anomalous responsivity that is contingent on the type of reward processed. When considered in light of empirical findings of dysfunctional reward circuitry in a number of psychiatric conditions, including substance use disorders, schizophrenia, affective disorders, and attention deficit/hyperactivity disorder, abnormal mesolimbic responses to rewards appears to be a common endophenotype that may cut across diagnostic boundaries.[109]

Functional connectivity

Whereas task-based fMRI studies focus on activity within specific brain regions evoked by cognitive tasks, studies of functional connectivity speak to the temporal dynamics of brain network activity. The integrity of brain connections affects integration and synchronization of information processing, and the study of functional connectivity in ASDs addresses circuitry-level questions believed to be central to dysfunction in ASDs.[6] There is a confluence of evidence that ASDs are characterized by decreased connectivity, in particular between frontal and posterior-temporal cortical systems that play key roles in processing social-affective information.[110] Although initial studies highlighted cortical underconnectivity in ASDs, more recent data suggests that ASDs may be characterized by both local overconnectivity and long-distance underconnectivity. It has been suggested that a cortical underconnectivity account of ASDs may address heterogeneity as well as broad information processing deficits in general, rather than the expression of specific core symptoms.[111]

Task-based functional connectivity

The majority of task-based studies in ASDs have documented reduced functional connectivity between frontal and parietal regions[75,83,112] as well as between frontal and temporal and/or occipital regions.[69,113] Tasks have included language comprehension,[83,88,97] cognitive control,[69,75,114] mentalizing,[53,113,115] social processing,[113] working memory,[116] and visuospatial processing.[112] A number of these studies have also indicated smaller and less synchronized cortical networks in ASDs.[116-117] It should be noted, however, that some task-based studies have found long-range over-connectivity between subcortical and cortical regions[118-119] as well as between frontal and temporal regions.[120-122] Other studies have examined connectivity during task-related paradigms by filtering out task-related activity to examine connectivity patterns that are task-independent, and found evidence of decreased[123-124] and increased[118-121] functional connectivity.

Resting-state functional connectivity

Relatively fewer studies have examined brain connectivity in ASDs during resting state fMRI scans *(Table VI)*. Cherkassky and colleagues[125] reported decreased frontal-posterior default network connectivity during task-based inter-trail intervals (see also refs 126-128) while others have found lower default-mode network connectivity at rest[125,128-131] in ASDs. There are also reports of decreased connectivity between the anterior and posterior insula and a number of social processing brain regions in ASDs[75,114,116] and less coherent endogenous low-frequency oscillations across multiple cortical and subcortical regions in ASDs.[132] von dem Hagen and colleagues[133] reported reduced functional connectivity within and between resting state networks incorporating "social brain regions" including the insula and amygdala within the default-mode and salience networks, respectively, and Di Martino and colleagues[134] reported increased connectivity between multiple striatal regions and striatal hyperconnectivity with the pons. Monk and colleagues[127] reported positive correlations between repetitive behavior symptoms and resting state connectivity between posterior cingulate cortex and the right parahippocampal gyrus in adults with ASDs, despite increased connectivity between the posterior cingulate cortex, the right temporal lobe, and the right parahippocampal gyrus, although Weng and collegues[128] found correlations between social and repetitive behavior symptoms and a number of resting connectivity metrics in adolescents with ASDs.

Structural MRI

Functional MRI results should ultimately be considered within a broader neuroimaging literature addressing brain structure and white matter connectivity in ASDs. Structural MRI yields information about brain anatomy, including gray- and white-matter volumes as well as

gyrus and sulcus development, and this approach is well-suited for studies seeking to predict future ASDs diagnoses in infants. Very briefly, the structural MRI literature indicates accelerated brain growth during early development in ASDs.[135,136] There are reports of significantly large head circumference[137] and brain volume in children with autism.[138] Longitudinal studies indicate that ASDs are characterized by an early transient period of postnatal brain overgrowth evident in 70% of children with ASDs before age 2 that is not present in adolescence and adulthood.[139-140] Evidence of enlarged total brain size in ASDs is accompanied by studies showing smaller cerebellar vermis,[141,142] amygdala, and hippocampus.[138] Increased brain size in young children with ASDs has also been linked to increased frontal lobe white matter[143] followed by reduced white matter in early and late adolescence and adulthood.[144,145]

Diffusion tensor imaging

Because the contrast properties of structural MRI are suboptimal for differentiating still-myelinating white matter from surrounding gray matter in children,[146] diffusion tensor imaging (DTI), a measure of microstructural properties of white matter fibers, has emerged as a valuable tool to assess white-matter structure in very young samples.[147] There is evidence of widespread abnormalities in white-matter fiber tract integrity in ASDs, but the extent and developmental course of these differences remains unclear.[148-151] Two- to three-year-old children with ASDs are characterized by increased fractional anisotropy (an index of white matter fiber density) in the frontal lobes and in the corpus callosum,[152] but in 5-year-old children with ASDs fractional anisotropy was reduced in frontal lobe tracts and no different from controls in tracts connecting frontal and posterior regions.[153] In 10- to 18-year-old children with ASDs, there is evidence of reduced fractional anisotropy in frontal-posterior tracts[154] and in hemispheric fractional anisotropy lateralization in the arcuate fasciculus,[155,156] but fractional anisotropy was found to be reduced in adolescents with ASDs in prefrontal cortex and tempoparietal junction.[157] It thus appears that young children with ASDs are characterized by increased fractional anisotropy in brain areas mediating social communication, whereas adolescents and adults with ASDs are characterized by generally lower fractional anisotropy, a pattern that recapitulates patterns of brain overgrowth discussed earlier. Finally, a prospective DTI study of 6- to 24-month-old infants at high-risk of developing ASDs found that fractional anisotropy trajectories for 12 of 15 fiber tracts examined differed between infants who later were identified as having an ASDs and those who did not. Infants who went on to have a diagnosis of an ASD had fiber tracts characterized by higher fractional anisotropy at 6 months of age, slower change between 6 and 24 months of age, and lower fractional anisotropy at 24 months of age.[158]

Summary

The goal of this review is to highlight consistencies in the ASD fMRI literature. Given the array of imaging tasks reviewed, it is perhaps not surprising that findings are heterogenous. Despite variations in findings, there is a sufficient degree of consistency to draw a number of substantive conclusions. Studies of social processes have generally found evidence of hypoactivation in nodes of the "social brain," including the medial prefrontal cortex, the inferior frontal gyrus and the anterior insula, the posterior superior temporal sulcus, the interparietal sulcus, the amygdala, and the fusiform gyrus. Studies addressing cognitive control, designed to address neural mechanisms underlying restricted and repetitive behaviors and interests, have converged on aberrant frontostriatal functioning in ASDs, specifically in inferior and middle frontal gyri, anterior cingulate cortex, and the basal ganglia. Communication impairments in ASDs have been linked to differential patterns of language function lateralization, decreased synchrony of brain regions processing language, and recruitment of brain regions that do not typically processing language. Reward processing studies have highlighted mesolimbic and mesocortical impairments when processing both social and nonsocial incentives in ASDs. Finally, task-based functional connectivity studies in ASDs have reported local overconnectivity and long-distance (ie, between frontal and posterior regions) underconnectivity, whereas resting state connectivity studies indicate decreased anterior-posterior connectivity and less coherent endogenous low-frequency oscillations across multiple regions.

Future directions

Most studies reviewed here focus on adulthood or adolescence, yet ASDs are present from very early child-

hood. It will be critical to address developmental profiles in children with ASDs to disambiguate proximal effects of altered brain function from downstream effects on learning and motivation. There also may be critical periods during early development when brain dysfunction creates a predisposition to develop a number of disorders, and understanding factors that influence these processes will be essential for the prevention of symptom onset. Indeed, emerging techniques allow for functional brain imaging in children as young as 12 months old, and future studies that focus on young samples are needed. Additionally, most studies reviewed here contain small samples, and larger samples will be needed to identify meaningful subgroups and track developmental profiles. Given the high costs associated with brain imaging and challenges recruiting large pediatric patient samples, it will be critical to leverage available bioinformatics tools to facilitate data sharing across research groups. Such tools are under development[159] and the National Institutes of Health recently established a database for sharing ASDs neuroimaging data.[160]

There is also a need to move to designs that incorporate psychiatric comparisons to delineate brain activation patterns in ASDs that diverge and converge with other disorders characterized by social communication impairments and repetitive behaviors. Similarly, ASDs are commonly comorbid with other psychiatric and neurodevelopmental conditions,[161] possibly due to shared genetic etiology and common socioenvironmental determinants, and thus it will be important to examine ASD samples with and without comorbid conditions to refine our understanding of neural endophenotypes in ASDs. Finally, the literature reviewed here is cross-sectional. Though these studies have elucidated aberrant patterns of brain activation in ASDs, these paradigms have rarely been applied to longitudinal treatment outcome studies aimed at understanding mechanisms of action of treatment response in ASDs. As neuroimaging and data-sharing techniques evolve, functional brain imaging will continue to improve our understanding of the pathophysiology of ASDs, with the ultimate goal of improved ASD identification and treatment.[162] ❑

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La resonancia magnética funcional en los trastornos del espectro autista

Esta revisión entrega una panorámica acerca de los hallazgos de la resonancia magnética funcional en los trastornos del espectro autista (TEA). Aunque existe bastante heterogeneidad en los resultados de los estudios han aparecido aspectos comunes que incluyen: 1) hipoactivación en los nodos del "cerebro social" durante las tareas de procesamiento social, que incluyen regiones dentro de la corteza prefrontal, el sulcus temporal superior posterior, la amígdala y el giro fusiforme, 2) activación frontoestriatal aberrante durante las tareas de control cognitivo, relacionadas con los intereses y las conductas restringidas y repetitivas, y que incluyen regiones dentro de la corteza prefrontal dorsal y los ganglios basales, 3) lateralización y activación diferencial de las regiones relacionadas con el procesamiento y la producción del lenguaje durante las tareas de comunicación, 4) respuestas mesolímbicas anómalas a las recompensas sociales y no sociales, 5) hipoconectividad funcional a largo plazo e hiperconectividad a corto plazo frente a tareas y 6) disminución de la conectividad funcional antero-posterior durante los estados de reposo. Estos hallazgos aportan razones mecanicistas para la fisiopatología de los TEA y sugieren orientaciones para las futuras investigaciones encaminadas a aclarar los modelos etiológicos y desarrollar tratamientos que puedan ser específicos y obtenerse racionalmente.

Imagerie par résonance magnétique fonctionnelle dans les troubles autistiques

Cet article présente une synthèse des résultats de l'imagerie par résonance magnétique fonctionnelle dans les troubles autistiques (TA). En dépit d'une grande hétérogénéité due aux résultats des études, des thèmes communs ressortent comme : 1) une hypoactivation des nœuds du « cerveau social » au cours des tâches sociales, qui concerne les régions du cortex préfrontal, du sillon temporal postéro-supérieur, de l'amygdale, et du gyrus fusiforme ; 2) une activation frontostriatale aberrante du cortex dorsal préfrontal et des noyaux gris centraux lors des tâches de contrôle cognitif se rapportant à des intérêts et à des comportements restreints et répétitifs ; 3) une activation et une latéralisation différentielles des régions de production et de traitement du langage au cours des tâches de communication ; 4) des réponses mésolimbiques anormales aux récompenses sociales et non sociales ; 5) une hypoconnectivité fonctionnelle à longue distance et une hyperconnectivité de courte distance basées sur les tâches ; 6) une connectivité fonctionnelle antéropostérieure diminuée pendant les états de repos. Ces résultats donnent un aperçu mécaniste de la physiopathologie des TA et suggèrent des directions pour la recherche future afin d'élaborer des modèles étiologiques et de développer de façon rationnelle des traitements ciblés et dérivés.

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TABLES I-VI

Notes for tables:

ASD: Autism Spectrum Disorder; TYP: Neurotypical; †ASD refers to the entire autism sample in a particular study, including high functioning autism, Asperger's syndrome, and pervasive developmental disorder not otherwise specified; *Total number of participants is presented first followed by the number of females in parentheses, if reported; **Not specified; ↓: decreased activation; ↑: increased activation

Abbreviations used in tables:

ACC	anterior cingulate cortex
ACG	anterior cingulate gyrus
AG	angular gyrus
AI	anterior insula
AMY	amygdala
ATL	anterior temporal lobe
BA	Broca's area
BG	basal ganglia
CN	caudate nucleus
DAC	dorsal anterior cingulate
DLPFC	dorsolateral prefrontal cortex
DMPFC	dorsomedial prefrontal cortex
DN	dentate nucleus
FFA	fusiform face area
FG	fusiform gyrus
IC	insular cortex
IFA	inferior frontal area
IFC	inferior frontal cortex
IFG	inferior frontal gyrus
IPL	inferior parietal lobe
IPS	intraparietal cortex
ITG	inferior temporal gyrus
LG	lingual gyrus
LSTG	left superior temporal gyrus
MCG	middle cingulate gyrus
MFC	midfrontal cortex
MFG	midfrontal gryus
MFL	medial frontal lobes
NAC	nucleus accumbens
OFC	orbitofrontal cortex
OFG	orbitofrontal gyrus
MPFC	medial prefrontal cortex
MTG	medial temporal gyrus
PO	pars opercularis
PCC	posterior cingulate cortex
PFC	prefrontal cortex
PHG	parahippocampal gyrus
PL	parietal lobe
PMC	premotor cortex
PVC	primary visual cortex
RPVC	right primary visual cortex
SFG	superior frontal gyrus
SPL	superior parietal lobe
STG	superior temporal gyrus
STS	superior temporal sulcus
THAL	thalamus
TL	temporal lobe
TPJ	temporoparietal junction
VS	ventral striatium
VLPFC	ventrolateral prefrontal cortex
VOC	ventral occipital cortex
VMPFC	ventromedial prefrontal cortex
WA	Wernicke's Area

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Citation	ASD *†	TYP*†	ASD age	TYP age	Task(s)
Ashwin, Baron-Cohen, Wheelwright, O'Riordan, Bullmore, 2007 [1]	13 (13)	13 (13)	31.2 + 9.1	25.6 + 5.1	Viewed facial stimuli known to activate AMY in healthy controls
Bird, Catmur, Silani, Frith, Frith, 2006 [2]	16 (14)	16 (14)	33.3 ± 11.5	35.3 + 12.1	Viewed pairs of stimuli (face/ house) in attended /unattended locations
Bookheimer, Wang, Scott, Sigman, Dapretto, 2008 [3]	12 (12)	12 (12)	11.3 ± 4.0	11.9 ± 2.4	Inverted or upright face matching
Corbett, Carmean, Ravizza, et al, 2009 [4]	12 (12)	15 (13)	9.01 ± 13.82	9.17 ±1.44	Face identify and expression matching
Coutanche, Thompson-Schill, Schultz, 2011 [5]	12 (12)	12 (12)	13.9 ± 4.48	13.6 ± 3.87	Recognition of emotional facial expressions
Dalton, Nacewicz, Johnstoner, et al, 2005 [6]	Task 1: 14 (14) Task 2: 16 (16)	Task 1:12 (12) Task 2:16 (16)	15.9 ± 4.71	17.1 ± 2.78	(1) Facial emotion discrimination (2) Face recognition
Deeley, Daly, Surguladze, et al, 2007 [7]	18 (18)	9 (9)	34 + 10	27 ±5	Viewed face stimuli with variable emotional expressions
Greimel, Schulte-Ruther, Kircher, et al, 2010 [8]	15 (15), 11 (11) (adolescents, fathers)	15 (15), 9 (9) (adolescents, fathers)	14.9 ± 1.6, 47.7 ±5.3 (adolescents, fathers)	15.0 ± 1.4, 43.9 ± 5.1 (adolescents, fathers)	Emotion identification in facial stimuli and in self
Hadjikhani, Joseph, Snyder, et al, 2004 [9]	11**	10**	36 ± 12	26 ± 6	Viewed faces, objects, and scrambled images
Hadjikhani, Joseph, Snyder, Tager-Flusberg, 2007 [10]	10**	7**	34 ± 11	35 ± 12	Viewed unemotional faces
Hall, Szechtman, Nahmias, 2003 [11]	8(8)	8(8)	**	**	Emotion and gender recognition tasks
Hall, Doyle, Goldberg, West, Szatmari, 2010 [12]	12 (12)	12 (12)	31.8**	32**	Identified gender of subliminally presented images of anxious faces
Hubl, Bolte, Feineis-Matthews, et al, 2003 [13]	10 (10)	10 (10)	25.3 ± 6.9	27.7 ± 7.8	Viewed faces and complex patterns

Table I. Studies investigating face processing in autism spectrum disorders.

Core findings in ASD group (relative to controls)	Conclusions
Differential activation to faces; ↑ACG, superior temporal cortex; No difference in AMY activation between angry and frightened faces	Different activation of social brain during face processing; Absence of response to varying emotional intensity of facial stimuli
Attention modulation present only to house images (rather than to both houses and faces)	Social stimuli less salient for individuals with ASD
↓Frontal cortex across all conditions, particularly left hemisphere, dorsal IFG (i.e. mirror neurons); ↓AMY; ↑Precuneus	Faces processed as objects; Behavioral differences in processing upright vs inverted faces implicates a social rather that visual processing impairment
↓AMY during expression matching; ↓FG during identity matching	ASD recruits frontal and parietal lobes, but not AMY, for face expression matching; ASD processes faces less efficiently and less effectively; AMY fails to provide socioemotional context during social interactions
Multi-voxel pattern analysis classification negatively correlated with symptom severity (activation levels did not); Searchlight analysis across the ventral TL identified regions with relationships between classification performance and symptom severity	Clinical severity was more classifiable from MVPA than from FG patterns; MVPA can identify regions not found using mean activation; ITG may play a role in ASD face processing
↓Bilateral FG, occipital gyri, MFG; ↑Left AMY, OFG; FG and AMY activation correlated with time fixating on eye regions in the ASD group	Diminished gaze fixation may account for FFG hypoactivation results in the literature
Fusiform, extrastriate hyporesponsiveness across emotion and intensity levels	While fusiform and extrastriate regions are activated to social stimuli in ASD, it is less so than in typical development
↓FG correlated with social deficits; ↓IFG during self-task; Fathers of ASD performed similarly to fathers of controls, but showed ↓FG	FG impairment shared between first-degree relatives is a fundamental feature of ASD; FG impairment during face processing related to empathy deficits
No FFA activation differences when viewing faces	Face processing abnormalities not due to dysfunction in the FFA, but to abnormalities in surrounding networks involved in social cognition
No differences in FFA, inferior occipital gyrus activation; ↓Right AMY, IFC, STS, somatosensory cortex, PMC	Atypical activation in a broader face-processing network outside of FFA and inferior occipital gyrus; Suggests mirror neuron system disturbance during face-processing in ASD
↓IFA, FG; ↑right ATL, ACG, THAL	Recognition of emotions in ASD achieved through recruitment of brain regions concerned with attention, perceptual knowledge, and categorization
↓FFA; No AMY differences between groups	Transmission of social information along subcortical pathways intact, but signaling to downstream structures as well as the mechanisms of subsequent processing are impaired
↓FG, esp. during face processing; ↑Medial occipital gyrus, superior parietal lobule, medial frontal gyrus	Deficits in face-specific regions, but overdevelopment in areas of visual search; Predisposed for local processing, rather than global

Table I. Continued

Citation	ASD *†	TYP*†	ASD age	TYP age	Task(s)
Humphreys, Hasson, Avidan, Minshew, Behrmann, 2008 [14]	13 (13)	15 (15)	27 ± 10	29 ± 10	Viewed faces, buildings, objects and patterns in controlled and naturalistic settings
Kleinhans, Richards, Sterling, et al, 2008 [15]	19**	21**	23.5 ± 7.8	25.1 ±7.6	Viewed familiar faces, houses
Kleinhans, Johnson, Richards, et al, 2009 [16]	19**	20**	**	**	Viewed neutral faces
Kleinhans, Richards, Weaver, et al, 2010 [17]	31 (29)	25 (23)	23.57 ± 6.6	23.32 ± 5.15	Matched facial expressions of fear or anger
Kleinhans, Richards, Johnson, et al, 2011 [18]	31 (29)	25 (23)	23.57 ± 6.6	23.32 ± 5.15	Viewed images of faces and houses
Koshino, Kana, Keller, et al, 2008 [19]	11 (11)	11 (10)	24.5 ± 10.2	28.7 ± 10.9	Working memory tasks using faces
Loveland, Steinberg, Pearson, Mansour, Reddoch, 2008 [20]	5 (4)	4 (3)	18 ± 1.3	17 + 1.1	Auditory and visual emotional congruence task
Monk, Weng, Wiggins, et al, 2010 [21]	12**	12**	26 ± 6	27 ± 6	Probe detection with different emotional expressions
Morita, Kosaka, Saito, et al, 2011 [22]	15 (14)	15 (13)	23.7 ± 4.3	23.3 ± 3.6	Rated photogenicity of faces
Ogai, Matsumoto, Suzuki, et al, 2003 [23]	5**	9**	21.8 ± 5.9	23.0 ± 5.2	Facial expression recognition
Pelphrey, Morris, McCarthy, Labar, 2007 [24]	8 (6)	8 (6)	24.5 ± 11.5	24.1 ± 5.6	Dynamic and static face processing
Perlman, Hudac, Pegors, Minshew, Pelphrey, 2011 [25]	12 (11)	7 (7)	25.5 ± 7.47	28.57 ±5.74	Viewed faces while compelled to look at eyes
Pierce, Muller, Ambrose, Allen, Courchesne, 2001 [26]	6 (6)	8 (8)	29.5 ± 8	28.3**	Face perception with gender identification
Pierce, Haist, Sedaghat, Courchesne, 2004 [27]	7 (7)	9 (9)	27.1 ± 9.2	**	Familiar versus unfamiliar face processing
Pierce Redcay, 2008 [28]	11 (9)	11 (9)	9.9 ± 2.1	9.8 ± 1.8	Matched faces of mothers, other children, adult strangers
Pinkham, Hopfinger, Pelphrey, Piven, Penn, 2008 [29]	12**	12**	24.08 ± 5.71	27.08 ± 3.99	Free-viewing face processing

Table I. Continued

Core findings in ASD group (relative to controls)	Conclusions
↓FFA, occipital face area, STS in response to faces; No group differences in place-related or object-related processing	Differential organization of ventral visual cortex; Developmental effects of lower functional connectivity have a more pronounced effect on later-developing systems, like face-processing, than for early-developing systems, like object- and place-processing
Reduced functional connectivity FFA-AMY, FFA-PCC, FFA-THAL; Greater social impairment correlated with worse connectivity FFA-AMY, FFA-right IFC	Abnormal connectivity in limbic system underlies social deficits in ASD
Reduced bilateral AMY habituation; No group differences in FG habituation	AMY hyperarousal to socially relevant stimuli; Sustained AMY arousal may contribute to social deficits
↓Left PFC; ↑Occipital lobe; Social anxiety correlated with ↑right AMY, ↑left middle temporal gyrus, ↓FFA	Social anxiety mediates emotional face perception
No activation in right AMY, right pulvinar, or bilateral superior colliculi to faces;	Rapid face identification but failure to engage subcortical brain regions involved in face detection and automatic emotional face processing.
↓Inferior left PFC, right posterior temporal; Activation in a different FFA location; Lower FFA-frontal connectivity	Faces processed as objects; Working memory of faces not mediated by typical frontal regions
During emotion trials, ↓OFC, STG, PHG, posterior cingulate gyrus, occipital gyrus	Fronto-limbic and superior temporal activity differences during integration of auditory and visual emotional stimuli
↑Right AMY to emotional faces; Greater right AMY and VMPFC coupling; Weaker positive right AMY and TL coupling	Attention must be factored into any model of neural circuitry in ASD; Overconnectivity may underlie greater emotional responses in ASD
↓Self-related activity in PCC; ↓Right IC and lateral OFC to embarrassment; ↓IC activity to self-face images associated with weak coupling between cognitive evaluation and emotional responses to self-face	Decoupling between evaluation of self-face images and emotional response; Dysfunction in PCC and IC contributes to lack of self-conscious behaviors in response to self-reflection
↓Left insula, left IFG, left putamen during recognition of disgust and fear	Difficulty understanding facial expressions in others and, therefore, in manipulating social information
↓AMY, STS, FG to dynamic faces	Dysfunctions in these component areas may contribute to problems in social and emotional processing
Right FG activity normalized by following predetermined scan paths to eyes, but AMY response unaffected	Rather than an underdeveloped FFA as a result of not focusing on faces during development, FFA appears functional; Impaired mechanism of appropriately directing gaze
↓Bilateral FG, left AMY; 50% of group showed atypical FG activation to faces	ASD is associated with aberrant locations of maximal activations to faces
No group difference in extent of FFA activation to faces; ↑FFA to familiar faces; Right hemisphere dominance to both types of faces; Limited response in the posterior cingulate, AMY, MFL	FFA hypoactivation to faces in ASD may be specific to unfamiliar faces; ASD may be characterized by anomalous FFA modulation by faces, rather than hypoactivation
Normal FG response to face of mother or other children; ↓FG to stranger adult faces	Selective reduction in FG activity in response to strangers may be a result to reduced attention and interest in those conditions
↓Right AMY, FFA; ↓Left VLPFC compared to non-paranoid individuals with schizophrenia	Potential common substrates of impaired social cognition in ASD and schizophrenia

Table I. Continued

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Citation	ASD *†	TYP*†	ASD age	TYP age	Task(s)
Rudie, Shehzad, Hernandez, et al, 2011 [30]	23 (21)	25 (22)	12.6 ± 2.83	13.3 ±.96	Emotional face processing
Scherf, Luna, Minshew, Behrmann, 2010 [31]	10 (10)	10 (10)	12.2 ± 1.1	11.2 ± 1.3	Vignettes of faces, common objects, houses and scenes of navigation
Schultz, Gauthier, Klin, et al, 2000 [32]	14 (14)	28 (28) (2 groups of 14)	24.08 ± 5.71	27.08 ± 3.99	Face discrimination
Uddin, Davies, Scott, et al, 2008 [33]	18 (18)	12 (12)	13.19 ± 2.61	12.23 ±2.10	Judged "self" or "other" for morphed face images
Wang, Dapretto, Hariri, Sigman, Bookheimer, 2004 [34]	12 (12)	12 (12)	13.91 ± 2.61	12.23 + 2.10	Emotion matching naming
Welchew, Ashwin, Berkouk, et al, 2005 [35]	13 (13)	13 (13)	31.2 +9.1	25.6 ±5.1	Face processing
Weng, Carrasco, Swartz, et al, 2011 [36]	22 (17)	20 (19)	14.36 ± 1.7	14.97 ± 1.95	Emotional face processing

Table I. Continued

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Core findings in ASD group (relative to controls)	Conclusions
Reduced functional integration: AMY-secondary visual areas, PO-parietal cortex; Reduced segregation: AMY-DLPFC, PO-VMPFC; Reduced integration: PO-FC, within right NAC	Reduced functional integration and segregation of large-scale brain networks during face viewing
↓FG, occipital face area, STS to faces; ↑Ventral posterior FG to faces	Selective ventral visual pathway disruption;Face-processing alteration present in early adolescence; Face perception in ASD akin to object perception in typical development
↓Right FG; ↑Right ITG	Brain activation in the ASD group during face discrimination was consistent with feature-based strategies
↓Right premotor/prefrontal during presentation of "other" faces	Functional dissociation between the representation of self versus others suggests a neural substrate of self-focus and decreased social understanding
↓FG and ↑precuneus during matching facial expressions; Lack of modulation by task demands in the AMY	Recruited different neural networks and relied on different strategies when processing facial emotion
Abnormal AMY—parahippocampal connectivity	Difficulty in grasping facial expressions in others and, therefore, in manipulating interpersonally derived information
↑AMY, ventral PFC and striatum, particularly to sad faces; Negative correlation between age, pubertal status, and AMY activation	Greater activation in social-emotional processing regions when viewing faces

Table I. Continued

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Citation	ASD *†	TYP*†	ASD age	TYP age	Task(s)
Baron-Cohen, Ring, Wheelwright, et al, 1999 [37]	6 (4)	12 (6)	26.3 ± 2.1	25.5 ± 2.8	Inferred mental states from images of eyes
Castelli, Frith, Happe, Frith, 2002 [38]	10**	10**	33 ± 7.6	25 ± 4.8	Viewed animated sequence of geometric shapes
Dapretto, Davies, Pfeifer, et al, 2006 [39]	10 (9)	9 (9)	12.05 ± 2.5	12.38 ± 2.22	Imitation and observation of emotional expressions
Kaiser, Hudac, Shultz, et al, 2010 [40]	25 (20)	17 (12) (no sibling with ASD); 20 (9) (sibling with ASD)	11.8 ± 3.6	10.9 ± 3.1 (no sibling with ASD); 11.3 ± 2.8 (sibling with ASD)	Viewed biological motion clips and scrambled motion clips
Hadjikhani, Joseph, Manoach, et al, 2009 [41]	9**	11 (8)	30 ± 11	31 ± 14	Emotion processing of body expressions
Pitskel, Bolling, Hudac et al, 2011 [42]	15 (15)	14 (13)	23.4 ± 6.9	24.2 ± 7.4	Viewed direct and averted gaze of virtual human face
Konishi, Nakajima, Uchida, et al, 1999 [43]	18 (12)	18 (12)	35.6 ± 12.4	33.0 ± 10.7	Imitation inhibition task
Pelphrey, Morris, McCarthy, 2005 [44]	10 (9)	9 (8)	23.2 ± 9.9	23.4 ± 5.8	Viewing congruent and incongruent eye gaze shifts
Silani, Bird, Brindley, et al, 2008 [45]	15 (13)	15 (13)	36.6 ± 11.7	33.7 ± 10.3	Emotion introspection task
Wang, Lee, Sigman, Dapretto, 2007 [46]	18 (18)	18 (18)	12.4 ± 2.9	11.8 ± 1.9	Processed potentially ironic remarks
Wicker, Fonlupt, Hubert et al, 2008 [47]	12 (11)	14 (14)	27 ± 11	23.4 ± 10	Emotion and age discrimination

Table II. Studies investigating theory of mind and mental inference-making in autism spectrum disorders.

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Core findings in ASD group (relative to controls)	Conclusions
↑Frontal-temporal regions; ↓AMY	Supports amygdala theory of autism
↓MPFC, STS, temporal poles; Decreased extrastriate functional connectivity	Possible neurofunctional explanation for impaired mentalizing
↓IFG; Mirror neuron activity inversely related to social symptom severity	Dysfunctional mirror neuron system may underlie social deficits in autism
Differed in right AMY, VMPFC, left VLPFC, right posterior STS, bilateral FG; Controls without ASD sibling differed from other two groups in left DLPFC, right ITG, bilateral FG; Controls with ASD sibling differed from other two groups in right posterior STS, VMPFC	Identifies non-overlapping regions associated with ASD phenotypes and ASD genetic vulnerability in the absence of ASD symptoms
No differential brain activation to bodies expressing fear compared with neutral bodies; ↓IFC, AI to emotionally neutral bodies	Emotion perception deficits in ASD may be due to compromised processing of the emotional component of observed actions
↓Right TPJ, right AI, left lateral OC; ↑Left DLPFC	Brain mechanisms underlying processing gaze direction in ASD
Imitation scores correlated with ↓medial PFC, TPJ	Highlights contribution of hyperimitation to reduced social cognition
↓STS on incongruent trials	Lack of STS modulation to congruent and incongruent gaze shifts contributes to eye gaze processing deficits
↓Self-reflection/ mentalizing regions (MPFC, ACC, precuneus, inferior OFC, temporal poles, cerebellum) during self introspection; AI activity predicted alexithymia and empathy in both groups	Alexithymia and empathy deficits linked to anomalous AI activity
↓MPFC, right STG to irony; MPFC activity in ASD modulated by instructions to attend to faces and tones of voice; MPFC activity inversely related to symptom severity in ASD group	MPFC mediates understanding the intentions of others
↓DMPFC, right VLPFC, right STG; Abnormal connectivity between AMY, VLPFC, DLPFC, posterior occipital-temporal regions	Abnormal connectivity between structures of the social brain could explain social deficits in ASD

Table II. Continued

Citation	ASD *†	TYP*†	ASD age	TYP age	Task(s)
Allen Courchesne, 2003 [48]	8 (7)	8 (7)	26.89 ± 8.59	26.77 ± 8.22	Motor control and attentional control
Allen, Muller, Courchesne, 2004 [49]	8 (7)	8 (7)	26.89 ± 8.59	26.77 ± 8.22	Repeated button pressing
Agam, Joseph, Barton, Manoach, 2010 [50]	11**	14**	28 ± 10	27 ± 8	Antisaccade task
Belmonte Yurgelun-Todd, 2003 [51]	6 (5)	6 (5)	32.7 ± 9.8	27.2 ± 4.4	Bilateral visual spatial attention task
Damarla, Keller, Kana, et al, 2010 [52]	13 (11)	13 (13)	19 ± 5.5	22.1 ± 4.25	Embedded figures task
Dichter Belger, 2007 [53]	17 (16)	15 (14)	22.9 ± 5.2	24.6 ± 6.5	Flanker task (interference inhibition)
Dichter Belger, 2008 [54]	12 (12)	22 (22)	23.2 ± 5.8	25.1 ± 6.0	Flanker task intermixed with high and low arousal images
Dichter, Felder, Bodfish, 2009 [55]	15 (14)	19 (18)	23.3 + 11.1	28.0 + 7.9	Oddball target detection task with social and non-social targets
Gilbert, Bird, Brindley, Frith, Burgess, 2008 [56]	14 (11)	18 (13)	38 ± 13	32 ± 8	(1) Random response generation task (2) Selected stimulus-oriented vs stimulus-independent thought
Gilbert, Meuwese, Towgood, Frith, Burgess, 2009 [57]	16 (14)	16 (12)	32 ± 7.7	31 ± 5.7	(1) Stimulus-oriented spatial task (2) Stimulus-independent spatial task
Gomot, Belmonte, Bullmore, Bernard, Baron-Cohen, 2008 [58]	12 (12)	12 (12)	13.5 ± 1.6	13.8 ± 1	Auditory novelty detection
Haist, Adamo, Westerfield, Courchesne, Townsend, 2005 [59]	8 (8)	8 (8)	23.4 ± 11.4	25.6 ± 12.5	Spatial attention task
Just, Cherkassky, Keller, Kana, Minshew, 2007 [60]	18 (17)	18 (15)	27.1 ± 11.9	24.5 ± 9.9	Tower of London task
Kana, Keller, Minshew, Just, 2007 [61]	12 (11)	12 (11)	26.8 ± 7.7	22.5 ± 3.2	Go/No-go task
Keehn, Brenner, Palmer, Lincoln, Muller, 2008 [62]	9 (9)	13 (13)	15.1 ± 2.6	14.1 ± 2.1	Visual search task
Kennedy, Redcay, Courchesne, 2006 [63]	12**	14**	25.49 ± 9.61	26.07 ± 7.95	Counting Stroop task
Lee, Yerys, Della Rosa, et al, 2009 [64]	12 (9)	12 (8)	10.17 ± 1.57	11.01 ± 1.78	Go/No-go task
Lee, Foss-Feig, Henderson et al, 2007 [65]	17 (12)	14 (11)	10.37 ± 1.52	10.85 ± 1.47	Embedded figures task
Liu, Cherkassky, Minshew, Just, 2011 [66]	15 (14)	15 (15)	25.2 ± 7.6	26.3 ± 8.2	(1) Line-counting task (2) Judged whether a 3D object was possible

Table III. Studies investigating cognitive control in autism spectrum disorders.

Core findings in ASD group (relative to controls)	Conclusions
↑Motor regions; ↓Cerebellar attention	Developmental cerebellar abnormality has differential functional implications for cognitive and motor systems
↑Ipsilateral anterior cereballar hemisphere	Cerebellar dysfunction that is a reflection of abnormal anatomy
↓Frontal eye field, dorsal ACC; Decreased frontal eye field—dorsal ACC connectivity; Both findings associated with repetitive behavior symptoms	Functional neural abnormalities in volitional ocular-motor control linked to repetitive behaviors
↓Left VOC; ↑Left IPS	Neurofunctional basis of impaired selective attention
↓Left DLPFC, inferior parietal areas; ↑Visuospatial areas; Decreased frontal—visuospatial connectivity	Cortical underconnectivity despite preserved visuospatial performance
↓Prefrontal, parietal regions during the incongruent social condition only	Social stimuli interfere with brain regions mediating cognitive control
↓Right MFG on conflict trials preceded by high arousal images only	Abnormal modulation of regions mediating cognitive control in context of high arousal
↑Right IFG, DMPFC to social targets; DMPFC activation to social targets predicted severity of social impairments	DMPFC hyperactivation during cognitive control of social stimuli contributes to expression of social deficits
Task 1: ↓Cerebellum, left lateral temporal cortex; Task 2: ↑Medial rostral PFC	Impaired cognitive control in is associated with task-specific functional changes
Similar activation patterns; Multi-voxel similarity analyses revealed found abnormal functional specialization within medial rostral PFC	Abnormal functional specialization within medial rostral PFC
↑Right PFC-premotor, left inferior parietal regions	Cognitive control associated with activation of a more widespread network of regions
↓Frontal, parietal, occipital, within the IPL; ↑SPL and extrastriate cortex	Deficit in automatic spatial attention abilities and aberrant voluntary spatial attention skills
Similar activation in DLPFC between groups; Lower frontal—parietal connectivity	Cognitive control deficits may be preferentially linked to lower cortical integration of information
↓Left ACG, left precuneus, right AG, premotor areas; Lower connectivity between ACG, MCG, right MFG, IFG, inferior parietal regions	Inhibition circuitry is activated atypically and is less synchronized, leaving inhibition to be accomplished by strategic control rather than automatically
↑Occipital and frontoparietal regions	Enhanced discrimination and increased top-down modulation of attentional processes
Decreased deactivation of resting network regions (MPFC/rostral ACC, PCC)	Lack of deactivation indicates abnormal internally directed processes at rest and may be compensatory
Age-moderated decreased connectivity in IFC, motor planning regions	Atypical developmental connectivity trajectories for IFC with other neural regions supporting response inhibition
↑Dorsomedial premotor, left superior parietal, right occipital cortex	Reduced cortical activation suggests that disembedded visual processing is performed sparingly
↓Medial frontal to possibility task; Decreased frontal—posterior connectivity	Less effort for lower-level processing; Reduced global-to-local interferences

Table III. Continued

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Citation	ASD *†	TYP*†	ASD age	TYP age	Task(s)
Luna, Minshew, Garver, et al, 2002 [67]	11 (9)	6 (6)	32.3 ± 9.3	30.3 ± 11.8	(1): Spatial working memory task (2) Guided saccade task
Manjaly, Bruning, Neufang et al, 2007 [68]	12**	12**	14.4 ± 2.7	14.3 ± 2.7	Embedded figures task
Mizuno, Villalobos, Davies, Dahl, Muller, 2006 [69]	8 (8)	8 (8)	28.4 ± 8.9	28.1 ± 8.3	Visuomotor coordination task
Muller, Kleinhans, Kemmotsu, Pierce, Courchesne, 2003 [70]	8 (8)	8 (8)	28.4 ± 8.9	28.1 ± 8.3	6-digit sequence learning
Muller, Cauich, Rubio, Mizuno, Courchesne, 2004 [71]	8 (8)	8(8)	28.4 ± 8.9	28.1 ± 8.3	8-digit sequence learning
Muller, Pierce, Ambrose, Allen, Courchesne, 2001 [72]	8 (8)	8 (8)	28.4 ± 8.9	28.1 ± 8.3	Visual stimulation using finger movements
Noonan, Haist, Muller, 2009 [73]	10 (10)	10 (10)	23 ± 9.9	25.8 ± 9.9	Source recognition task
Ring, Baron-Cohen, Wheelwright, et al, 1999 [74]	6 (4)	12 (6)	26.3 ± 2.1	25.5 ± 2.8	Embedded figures task
Solomon, Ozonoff, Ursu, et al, 2009 [75]	22 (17)	23 (18)	15.2 ± 1.7	16.0 ± 2.0	Preparing to overcome prepotency task
Schmitz, Rubia, Daly, et al, 2006 [76]	10 (10)	12 (12)	38 ± 9	39 ± 6	(1) Go/No-go task (2) Stroop task (3) Cognitive set shifting
Shafritz, Dichter, Baranek, Belger, 2008 [77]	18 (16)	15 (13)	22.3 ± 8.7	24.3 ± 6.2	Oddball target detection task
Silk, Rinehart, Bradshaw et al, 2006 [78]	7 (7)	9 (9)	14.7 ± 2.9	15.0 ± 1.8	Mental rotation task
Takarae, Minshew, Luna, Sweeney, 2007 [79]	13**	14**	24.5 ± 7.7	26.6 ± 7.8	Saccadic eye movement paradigms
Thakkar, Polli, Joseph, et al, 2008 [80]	12 (10)	14 (8)	30 ± 11	27 ± 8	Anti-saccade task

Table III. Continued

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Core findings in ASD group (relative to controls)	Conclusions
Task 1:↓DLPFC, PCC; Task 2: no differences	Neurofunctional basis of impaired working memory
↑Right PVC, bilateral extrastriate areas	Enhanced local processing in early visual areas rather than impaired global processing
Increased functional connectivity in left insula, right postcentral gyrus, MFG	Underconnectivity hypothesis unsupported; Subcortico-cortical connectivity may be hyperfunctional, potentially compensating for reduced cortico-cortical connectivity
↑PFC, posterior parietal cortex	Disturbances in cerebello-thalamocortical pathways
↑Right pericentral and PMC; Delayed activation of BA 3, 4, 6	Atypical use of the primary sensory and premotor cortices during learning
↓Contralateral periolandic cortex, BG, THAL, bilateral supplementary motor area, ipsilateral cerebellum, bilateral DLPFC; ↑Posterior cortex, PFC, extrastriate regions	Abnormal functional variability and less distinct regional activation patterns
Increased connectivity between left MFG—left superior parietal regions	An inefficiency in optimizing network connections during task performance
↓Right DLPFC, bilateral parietal cortex; ↑Right ventral occipitotemporal cortex	Object feature analysis, rather than working memory systems, are used for local processing and visual search in autism
↓Anterior frontal, parietal occipital regions; Decreased frontal/ parietal/occipital connectivity related to ADHD symptoms	Fronto-parietal connectivity deficits contribute to ADHD symptoms in autism
Task 1: ↑left IFG, OFG; Task 2: ↑left insula, AMY-hippocampal junction; Task 3: ↑PL	Cognitive control associated with increased brain activity in multiple regions
↓Frontal, striatal, and parietal regions; ACC activation correlated with repetitive behavior symptoms	Cognitive control deficits and repetitive behaviors might be associated with dysfunctions in neural circuitry
↓lateral and medial PMC, DLPFC, ACG, CN	Dysfunctional frontostriatal networks during cognitive control
↑DLPFC, CN, medial THAL, ACC, PCC, right DN	Cognitive control regions may compensate for lower-level processing difficulties
↑Rostral ACC; Reduced fractional anisotropy in white matter underlying rostral ACC; Repetitive behaviors correlated with rostral ACC activation	Rostral ACC abnormalities contribute to repetitive behaviors

Table III. Continued

Citation	ASD *†	TYP*†	ASD age	TYP age	Task(s)
Anderson, Lange, Froehlich, et al, 2010 [81]	26 (26)	15 (15)	21.7 ± 6.4	22.5 ± 6.3	(1) Thought about a described word (2) Filled in missing word in a sentence
Boddaert, Belin, Chabane, et al, 2003 [82]	5 (4)	8 (8)	19.1 ± 4.5	21.9 ± 3.3	Listened to speech-like sounds
Catarino, Luke, Waldman, et al, 2011 [83]	12 (12)	12 (12)	27.0 ± 10	34.0 ± 13	Detected semantic incongruities within written sentences
Eigsti, Schuh, Mencl, Schultz, Paul, 2011 [84]	16**	11**	**	**	Processed linguistic stimuli that varied in emotional and semantic content
Eyler, Pierce, Courchesne, 2012 [85]	40 (40)	40 (40)	32.0 mo ± 10.2	25.6 mo ± 9.6	Listened to story with complex, simple, or backward speech during sleep
Grezes, Wicker, Berthoz, de Gelder, 2009 [86]	12 (10)	12 (12)	26.6 ± 10.4	21.0 ± 1.6	Viewed fearful or neutral body language
Groen, Tesink, Petersson, et al, 2010 [87]	16 (12)	26 (21)	15.3 ± 1.6	15.7 ± 1.7	Sentences congruent or incongruent to speaker
Hadjikhani et al, 2009 [41]	12 (9)	11 (11)	30 ± 11	35 ± 12	Recognition of emotional bodies
Harris, Chabris, Clark, et al, 2006 [88]	14 (14)	22 (22)	36 ± 12	31 ± 9	Semantic and perceptual word processing
Hesling, Dilharreguy, Peppe, et al, 2010 [89]	8 (8)	8 (8)	23.38 ± 2.10	23.05 ± 2.02	Listened to speech stimulus involving variable intonation, rhythm, focus and affect
Just, Cherkassky, Keller, Minshew, 2004 [90]	17 (13)	17 (12)	28.0 ± 13.3	28.6 ± 10.7	Identified agent or object in each sentence
Kana, Keller, Cherkassky, Minshew, Just, 2006 [91]	12 (11)	13 (12)	22.5 ± 8.8	20.3 ± 4.0	Processed sentences with high or low imagery content
Kana Wadsworth, 2012 [92]	16 (16)	16 (16)	20.0 ± 6.43	21.6 ± 2.70	Processed sentences with puns
Kleinhans, Muller, Cohen, Courchesne, 2008 [93]	14 (14)	14**	23.79 ± 9.58	22.41 + 8.67	(1) Letter fluency task; (2) Category fluency task
Knaus, Silver, Lindgren, Hadjikhani, Tager-Flusberg, 2008 [94]	12 (12)	12 (12)	15.46 ± 2.48	14.94 ± 2.71	Reading version of response-naming task
Knaus, Silver, Kennedy, et al, 2010 [95]	14 (14)	20 (20)	16.83 ± 2.35	14.43 ± 2.47	(1) Response-naming task; (2) Control letter-judgment task
Lai, Schneider, Schwarzenberger, Hirsch, 2011 [96]	39 (35)	15 (10)	12.4 + 4.7	12.13 ± 4.34	Listened to speech

Table IV. Studies investigating communication in autism spectrum disorders.

Core findings in ASD group (relative to controls)	Conclusions
↓Left posterior insula, bilateral receptive language areas; Receptive language correlated with activation of posterior left WA; Verbal IQ correlated with activation of bilateral BA, PFC, lateral PMC	Posterior insula implicated in receptive language impairments
↑Right MFG	Abnormal auditory cortical processing implicated in language impairments
More spatially restricted activation pattern (only left IFG, left ACC, right FG)	Impaired integration of multiple neural networks related to difficulties in use of context
Affective and grammatical prosodic cues prompted more generalized activation	Language processing less automatic; Linkages between ToM and language processing deficits; Increased reliance on executive control regions for speech processing
↓Left hemisphere to speech sounds (worsens with age); Abnormally right-lateralized temporal cortex to language (worsens with age)	Lateralized abnormalities of temporal cortex processing of language in toddlers with autism
↓AMY, IFG, PMC to fearful gestures	Dysfunction in this network may impact the communication deficits present in autism
↓Left IFG for sentences requiring integration of speaker information; No difference for semantic- and world-knowledge sentences	ASD recruits left IFG atypically in language tasks that demand integration of social information
↓IFC, AI in response to emotionally neutral gestures	Identifies neural mechanisms of impaired affect communication
During semantic processing, ↓BA, ↑WA; Diminished activation difference between concrete and abstract words	Abnormal Broca's area development that may be linked with language deficits
Abnormal neural network for prosodic speech perception in left supra marginal gyrus; Absence of deactivation patterns in default mode	Prosodic impairments could not only result from activation pattern abnormalities, but also from an inability to inhibit default network
↑WA; ↓BA; Decreased functional connectivity between contributing cortical areas	Decreased information synchronization across the language processing network
Language and spatial centers not as synchronized; ↑Parietal and occipital regions during low-imagery sentences	Under-integration of language and imagery; Reliance on visualization to support language comprehension
↑Overall, particularly in right hemisphere and posterior areas during pun comprehension; ↓Left hemisphere	Altered neural route in language comprehension in general, and figurative language in particular
↑Right frontal and right superior TL during letter fluency task; Decreased lateralization of activation patterns during letter fluency, but not to category	Reduced hemispheric differentiation for certain verbal fluency tasks; abnormal functional organization may contribute to the language impairments
↑BA; Reduced BA left lateralization	Decreased efficiency of semantic processing
Atypical language laterality more prevalent in the ASD group	Language laterality may be a novel way to subdivide samples, resulting in more homogenous groups
↓Mean amplitude and spread of activity in STG	Possible neurofunctional correlate of language impairment

Table IV. Continued

Citation	ASD *†	TYP*†	ASD age	TYP age	Task(s)
Lai, Pantazatos, Schneider, Hirsch, 2012 [97]	36 (32)	21 (14)	9.61 ± 4.04	10.72 ± 4.42	Listened to speech and songs
Mizuno, Liu, Williams, et al, 2011 [98]	15 (14)	15 (15)	24.7 ± 7.8	24.7 ± 7.7	Linguistic perspective-taking task requiring deictic shifting
Redcay Courchesne, 2008 [99]	12 (12)	23 (17)	34.9 mo ± 7.4	19.6 mo ± 4.2	Listened to forward and backward speech
Redcay, Dodell-Feder, Mavros, et al, 2012 [100]	13 (10)	14 (11)	28.0 ± 7.05	27.0 ± 5.68	Interactive face-to-face joint attention game
Sahyoun, Belliveau, Soulieres, Schwartz, Mody, 2010 [101]	12 (10)	12 (9)	13.3 ± 2.45	13.3 ± 2.07	Pictorial reasoning with visuospatial processing, semantic processing, or both
Scott-Van Zeeland, McNealy, Wang, et al, 2010 [102]	18 (18)	18 (18)	12.62 ± 2.5	11.64 ± 1.58	Listened to two artificial languages and a random speech stream
Tesink, Buitelaar, Petersson, et al, 2009 [103]	24 (16)	24 (16)	26.3 ± 6.3	26.2 ± 6.0	Speaker inference task
Tesink, Buitelaar, Petersson, et al, 2011 [104]	24 (16)	24 (16)	26.3 ± 6.3	26.2 ± 6.0	Integrated contextual information during auditory language comprehension
Vaidya, Foss-Feig, Shook, et al, 2011 [105]	15 (11)	18 (14)	10.78 ± 1.29	10.96 ± 1.26	Responded to target word in presence of congruent or incongruent arrow or averted gaze

Table IV. Continued

Core findings in ASD group (relative to controls)	Conclusions
↓Left IFG during speech; ↑Left IFG during songs; Increased left IFG-STG connectivity for songs; Increased frontal—posterior connectivity	Functional systems that process speech and song more effectively engaged for song than for speech
↑Right AI, precuneus; Decreased right AI—precuneus connectivity	Higher activation compensates for decreased connectivity during deictic shifting
↓Extended network recruited in typical early language acquisition; ↑Medial, right GC; ↑Right hemisphere to forward speech	Children with ASDs may be on a deviant developmental trajectory characterized by greater recruitment of right hemisphere regions during speech perception
↓Left posterior STS, DMPFC during joint attention; ↑Posterior STS during solo attention	Failure of developmental neural specialization in STS and DMPFC during joint attention
↑Occipito-parietal, ventral temporal areas; Reduced inferior frontal - ventral temporal and middle temporal connectivity	Greater visual mediation of language processing
↑Fronto-temporal-parietal, as number of cues to word boundaries increased; No learning-related increases for artificial languages in BG, left temporoparietal cortex; Communicative impairment correlated with signal increases in these regions to artificial languages	Abnormalities in neural regions subserving language-related learning; Communicative impairments linked to decreased sensitivity to the statistical and speech cues in language
↑Right IFG for speaker-incongruent sentences; Absence of VMPFC modulation to incongruent sentences	Compensatory mechanisms during implicit low-level inferential processes in spoken language
↓Left, right IFG for sentences with world knowledge anomaly	Reduced integrative capacity of stored knowledge; Difficulties with exception handling
Congruent: regions associated with attention to gaze (left STS, PMC) activated to arrows; Incongruent: regions associated with arrows (ACC, left DLPFC, right CN) activated to gaze	Atypical functional anatomy to social and nonsocial communicative cues

Table IV. Continued

Citation	ASD *†	TYP*†	ASD age	TYP age	Task(s)
Cascio, Foss-Feig, Heacock, et al, 2012 [106]	17 (17)	23**	12.8 ± 2.5	13.2 ± 3.4	Viewed images of high-calorie foods after fasting
Dichter, Richey, Rittenberg, , 2012 [107]	16 (14)	20 (14)	26.0 ± 9.1	25.4 ± 7.0	Incentive delay task with monetary and social rewards
Dichter, Felder, Green, et al, 2012 [108]	15 (15)	16 (16)	30.1 ± 11.6	27.5 ± 7.5	Incentive delay task with monetary rewards and rewards related to circumscribed interests
Kohls, Schulte-Ruther, Nehrkorn, et al, 2012 [109]	15 (15)	17 (17)	14.6 ± 3.3	13.9 ± 3.0	Go/no-go task with social vs. monetary rewards
Schmitz, Rubia, van Amelsvoort, et al, 2008 [110]	10 (10)	10 (10)	37.8 ± 7	38.2 ± 6	Rewarded continuous performance task
Scott-Van Zeeland, Dapretto, Ghahremani, 2010 [111]	16 (16)	16 (16)	12.4 ± 2.14	12.3 ± 1.76	Implicit learning task with social vs. monetary rewards

Table V. Studies investigating reward processing in autism spectrum disorders.

Core findings in ASD group (relative to controls)	Conclusions
↑Bilateral insula along anterior-posterior gradient; ↑ACC to food cues	Abnormally enhanced neural response to primary rewards in ASD
↓NAC, OFC during monetary anticipation; ↑Right insula to face incentives; ↑Bilateral AMY during face anticipation that correlated with social symptoms	Domain-general reward circuitry dysfunction; atypical amygdala activation to social rewards may contribute to social symptom severity in ASD
↓NAC during monetary anticipation and outcomes; ↑VMPFC to circumscribed interests incentives	Reward circuitry hypoactivation to monetary incentives but hyperactivation to circumscribed interests in ASD. Possible neural mechanism of circumscribed interests in ASD
↓Midbrain, THAL, AMY, striatium, ACC to both rewards; ↓NAC to monetary reward, but not social reward	Domain-general reward system dysfunction in ASD
↑Left ACG during reward trials that correlated with social symptom severity;	Reward achievement associated with abnormal activation in areas responsible for attention and arousal in ASD
↓VS to both social and monetary rewards (more pronounced to social rewards.	Diminished neural responses during social reward learning may contribute to social learning impairments in ASD

Table V. Continued

Citation	ASD *†	TYP*†	ASD age	TYP age	Task(s)
Anderson, Nielsen, Froehlich, et al, 2011 [112]	40 (40)	40 (40)	22.7 ± 7.4	21.6 ± 7.4	8′ resting scan with eyes open
Cherkassky, Kana, Keller, Just, 2006 [113]	57 (53)	57 (52)	24.0 ± 10.6	24.0 ± 9	Periods of rest during task-based scans (duration not specified).
Di Martino, Kelly, Grzadzinski, et al, 2011 [114]	20 (17)	20 (14)	10.4 ± 1.7	10.9 ± 1.6	6′ 38″ resting scan with eyes open
Kennedy Courchesne, 2008 [115]	13 (13)	12 (12)	26.9 ± 12.3	27.5 ± 10.9	7′ 10″ resting scan with eyes open
Lai, Lombardo, Chakrabarti, et al, 2010 [116]	18 (18)	33 (33)	26.9 ± 7.4	28.4 ± 6.1	13′ 39″ resting scan with eyes closed (only last 512 of 625 volumes analyzed).
Monk, Peltier, Wiggins, et al, 2009 [117]	12 (11)	12 (10)	26 ± 5.93	27 ± 6.1	10′ resting scan with eyes open.
Paakki, Rahko, Long et al, 2010 [118]	28 (20)	27 (18)	14.58 ± 1.62	14.49 ± 1.51	7′ 36″ resting scan with eyes open.
von dem Hagen, Stoyanova, Baron-Cohen, Calder, 2012 [119]	18 (18)	25 (25)	30 ± 8	25 ± 6	10′ resting scan with eyes open.
Weng, Wiggins, Peltier, et al, 2010 [120]	16 (14)	15 (14)	15.0 ± 1.45	16.0 ± 1.44	10′ resting scan with eyes open.
Wiggins, Peltier, Ashinoff et al, 2011 [121]	39 (32)	41 (33)	14.0 ± 2.08	15.3 ± 2.4	10′ resting scan with eyes open.

Table VI. Studies investigating resting state connectivity in autism spectrum disorders.

Core findings in ASD group (relative to controls)	Conclusions
Negatively correlated ROI pairs showed decreased anticorrelation in ASD; Greatest connectivity differences in default mode network, superior parietal lobule, FG and AI	Weaker inhibitory connections, particularly for long connections; Resting state fMRI may be feasible as a diagnostic classifier for ASD
Decreased connectivity in resting-state networks despite similar volume and organization; Decreased posterior—anterior connectivity	Resting state underconnectivity in ASD
Increased connectivity between striatal subregions and heteromodal associative and limbic cortex; Increased pons-striatum and pons-insula connectivity	Increased connectivity in ectopic circuits reflects alternate trajectory of development, rather than immaturity of circuits
Reduced default mode network connectivity	Altered functional organization of the network involved in social and emotional processing
More randomness in midline structures, medial temporal structures, lateral temporal and parietal structures, insula, AMY, BG, THAL, IFG; Social symptoms negatively correlated with randomness in retrosplenial and right anterior IC	ASD associated with small but significant shift towards randomness in endogenous brain oscillations
Decreased PCC-SFG connectivity; Increased connectivity between PCC and right TL and right PHG; Social symptoms correlated with PCC-SFG connectivity; repetitive behaviors correlated with PCC—right PHG connectivity	Altered intrinsic connectivity that was associated with core symptoms
Decreased regional homogeneity in right STS, right IFG, right MFG, bilateral cerebellum, right insula, right postcentral gyrus; Increased regional homogeneity in right THAL, left IFG, left anterior subcallosal gyrus, bilateral cerebellar lobule VIII	Right-dominant alterations of resting state activity
Decreased default mode network connectivity; Decreased connectivity in salience network (includes insula) and a medial TL network (includes AMY)	Reduced connectivity in networks involved with the "social brain"; May be implicated in difficulties with communication and information integration
Decreased connectivity in 9 of 11 default mode areas; Social and repetitive behavior symptoms correlated with decreased connectivity in parts of default mode network; Communication correlated with increased connectivity in parts of default mode network	Decreased default mode network connectivity in adolescents with ASDs than in adults with ASDs
Decreased connectivity between posterior hub of default network and right SFG; Less increase in connectivity with age	Different developmental trajectory of default mode network

Table VI. Continued