HHS Public Access

Author manuscript

J Neurosci Methods. Author manuscript; available in PMC 2022 April 13.

Published in final edited form as:

J Neurosci Methods. 2021 September 01; 361: 109271. doi:10.1016/j.jneumeth.2021.109271.

Brain imaging-based machine learning in autism spectrum disorder: methods and applications

Ming Xu[a,b], **Vince Calhoun**[c], **Rongtao Jiang**[a], **Weizheng Yan**[c], **Jing Sui**[d,*]

[a]Brainnetome Center and National Laboratory of Pattern Recognition, Institute of Automation, Chinese Academy of Sciences, Beijing, China 100190

[b]School of Artificial Intelligence, University of Chinese Academy of Sciences, Beijing, China 100049

[c]Tri-institutional Center for Translational Research in Neuroimaging and Data Science (TReNDS), Georgia State University, Georgia Institute of Technology, and Emory University, Atlanta, GA, USA 30303

[d]State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, Beijing, China 100088

Abstract

Autism spectrum disorder (ASD) is a neurodevelopmental condition with early childhood onset and high heterogeneity. As the pathogenesis is still elusive, ASD diagnosis is comprised of a constellation of behavioral symptoms. Non-invasive brain imaging techniques, such as magnetic resonance imaging (MRI), provide a valuable objective measurement of the brain. Many efforts have been devoted to developing imaging-based diagnostic tools for ASD based on machine learning (ML) technologies. In this survey, we review recent advances that utilize machine learning approaches to classify individuals with and without ASD. First, we provide a brief overview of neuroimaging-based ASD classification studies, including the analysis of publications and general classification pipeline. Next, representative studies are highlighted and discussed in detail regarding different imaging modalities, methods and sample sizes. Finally, we highlight several common challenges and provide recommendations on future directions. In summary, identifying discriminative biomarkers for ASD diagnosis is challenging, and further establishing more comprehensive datasets and dissecting the individual and group heterogeneity will be critical to achieve better ADS diagnosis performance. Machine learning methods will continue to be developed and are poised to help advance the field in this regard.

Keywords

Autism spectrum disorder (ASD); Machine learning; Classification; Prediction; fMRI; sMRI; dMRI

*Correspondence to: State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, Beijing, China. jsui@bnu.edu.cn (J. Sui).

Declaration

The authors declare no biomedical financial interests or potential conflicts of interest.

1. Introduction

Autism spectrum disorder (ASD) is a highly heritable and heterogeneous neurodevelopmental disorder, which encompasses a set of early-appearing social communication deficits and restricted, repetitive sensory-motor behaviors(Lord et al., 2020). ASD affects about 1% of the world population, and males are around 4 times more susceptible than females (Elsabbagh et al., 2012). As the social abilities of individuals with ASD are impaired to some degree, lifelong supports are usually necessary for most patients, which place huge extra burdens on families and societies (Lord et al., 2018). Precise and efficient diagnosis is important for the early interventions of ASD, which may significantly improve the daily living skills and social abilities of patients (Elder et al., 2017). However, due to the elusive pathogenesis and mechanisms, there is no objective biomarker for ASD diagnosis. Currently, the ASD diagnosis is primarily based on clinical interviews and direct behavior observations (Lord et al., 2018), which may often lead to misdiagnosis of children with ASD, thus miss the optimal intervention chances (Mazefsky and Oswald, 2006). Therefore, there is an urgent need to develop an objective, neuroimaging-based diagnosis system of ASD.

Magnetic resonance imaging (MRI) techniques have paved an exciting path towards non-invasive objective measurements of the human brain. Generally, MRI can be divided into structural MRI (sMRI), diffusion MRI (dMRI), and functional MRI (fMRI). sMRI can provide static anatomical information of the brain, includes T1-weighted (T1w) and T2-weighted imaging (T2w), usually with high spatial resolution in research. dMRI makes it possible to localize the subtle white matter fiber tract abnormalities through features like fractional anisotropy (FA), mean diffusivity (MD) *etc*. By contrast, fMRI, including resting-state fMRI (rsfMRI) and task fMRI, detects the dynamic physiological information, mainly reflecting the changes of blood oxygenation level (Ogawa et al., 1990), which can illustrate the metabolism of the brain at different states (resting-state or task-evoked), and reveal the abnormalities of functional network connectivity (Arbabshirani et al., 2017).

These non-invasive imaging techniques are promising tools for investigating the neurological underpinnings of ASD, which are essential for developing discriminative neuroimaging biomarkers for clinical diagnosis. By comparing the functional connectivity (FC) of ASD subjects with healthy controls using statistical methods, dysfunction of task-negative networks and task-positive networks in ASD have been revealed across many studies (Cherkassky et al., 2006; Kennedy and Courchesne, 2008; Kennedy and Courchesne, 2006; Nomi and Uddin, 2015). Other studies have found differences in gray matter volume (McAlonan et al., 2005; Rojas et al., 2006) and white matter volumes (Herbert et al., 2004). In recent years, various machine learning approaches have been applied in ASD classifications. Compared with traditional univariate group-level studies, machine learning approaches can extract more informative features in a data-driven manner, and facilitate exploring more complex abnormal imaging patterns for individual-level diagnosis (Sui et al., 2020).

In this survey, we concentrate on ASD classification methods and applications based on different modalities of MRI. First, by utilizing a specific screening method, 119 related

articles are selected, which are then summarized in several aspects, such as classification method, feature type, sample size and accuracy. Second, we highlight some representative studies to show the existing efforts in imaging-based diagnosis. Finally, the opinions on current challenges and future directions in ASD researches are provided. We hope the review will offer comprehensive views and developing trends of this field, and inspires the subsequent researchers to develop more robust and accurate ASD diagnosis tools.

2. Research overview

2.1. Screening method

Studies on identifying or predicting the ASD clinical diagnostic status either cross-sectionally or longitudinally based on MRI using machine-learning methods were included in this review. Fig. 1a shows the literature screening process. Relevant articles were collected by keyword searching in Web of Sciences and Pubmed covering publications between January 2010 and December 2020 based on the following formula: autis* AND (imaging OR MRI OR DTI) AND (machine Learning OR classif* OR predict*). 1146 articles were identified. By reviewing the title and abstract, we manually removed 954 articles focusing on other diseases, without imaging analysis, not classification studies, or based on non-human species. Review articles and conference articles were also excluded. We further reviewed the full text in detail, resulting in the exclusion of another 73 non-eligible articles. Totally 119 articles are included in this survey, and Table 1 lists all of these studies in terms of employed imaging modalities, demographic information of samples, classification methods and model performances.

2.2. Key aspects of the ASD survey

As we can see in Fig. 1c, the number of papers published on this topic every year from 2010 to 2020 is growing. Before 2015, most publications are based on structural imaging, whereas studies based on functional imaging are increasing more sharply in recent 5 years, as do classification combined with multimodal imaging. With the public data sharing, especially the Autism Brain Imaging Data Exchange (ABIDE, tinyurl.com/fcon1000-abide) dataset (Di Martino et al., 2014), recent ASD classifications incline to use relatively larger samples. However, the overall classification accuracy exhibits significant negative correlations with the sample sizes used in these studies (Fig. 1d). In terms of classification methods, SVM and neural network (NN) are the most prevalent choices (Fig 1e). Other ML methods, such as decision tree (DT), logistic regression classifier (LRC), linear discriminative analysis (LDA) and ensembled classifier, are also applied in some studies. Fig. 1f and g summarize the accuracy distributions based on different methods with different imaging modalities. On the whole, classification based on fMRI data can achieve relatively higher accuracy than other modalities.

2.3. Machine learning pipeline

In brain imaging studies, machine learning approaches can automatically extract representative multivariate patterns from the neuroimaging data and help make decisions. Fig. 1b presents a general pipeline for developing neuroimaging-based ASD diagnosis. Although detailed implementations of ASD classification vary across studies, these can be

grouped into four components which include: (a) feature extraction, selection/reduction, (b) model training, (c) model testing and (d) performance evaluation.

2.4. Feature extraction, selection/reduction

A feature refers to any measurable property with information about the class ownership extracted from raw data. Transforming the neuroimaging data into reliable and biologically relevant features plays an important role in the ASD diagnosis system and substantially determines the data separability (Wolfers et al., 2019). As different MRI modalities have unique advantages in assessing the biological states of brains, feature engineering should fully leverage the characteristics of different imaging modalities. For structural imaging-based diagnosis, anatomical features, such as gray matter volume (GM) and white matter volume (WM), cortical morphological features, such as cortical thickness and surface area, and geometric features such as convexity and curvature, are widely used to delineate the possible subtle structural changes of ASD (Ecker et al., 2010a, 2010b; Jiao et al., 2010; Uddin et al., 2011). Metrics that describe the white matter microstructure, such as fractional anisotropy (FA) and mean diffusivity (MD), are also applied in ASD classifications (Ingalhalikar et al., 2010; Lange et al., 2010). For functional imaging-based classification, FC is the most common feature used in machine learning studies (Anderson et al., 2011; Kazeminejad and Sotero, 2019; Plitt et al., 2015). Other temporal statistics, such as regional homogeneity (ReHo) and amplitude of low-frequency fluctuation (ALFF), network metrics, such as nodal degree and clustering coefficients, may also contribute to the ASD diagnosis (Thomas et al., 2020). Considering the spatial scale of features, feature construction approaches can be divided into three categories: voxel-based, region-based, and network-based. Voxel-based approaches calculate the feature at voxel level, while region-based approaches calculate the feature based on several predefined region-of-interests (ROIs). Network-based approaches extract interaction profiles of multiple voxels or regions as features. Independent component analysis (ICA) is one of the representative methods to construct network-based features (J. Zhao et al., 2020).

Feature reduction is a fundamental and critical step for neuroimaging studies, because of curse-of-dimensionality (Mwangi et al., 2014), where the feature dimensionality largely exceeds the number of samples, which is quite common in medical imaging analysis (Jiang et al., 2020b). Suitable feature reduction can not only reduce the feature redundancy and noise, but also facilitate the understanding of neural substrates of a disease, as the most group-discriminant feature can be retained, while improving model accuracy and generalizability (Plitt et al., 2015).

Feature reduction methods can be divided into two categories: supervised and unsupervised respectively. Supervised feature reduction methods require the training label to select informative and discriminative feature dimensions, and they can be further subdivided into three classes: filter, wrapper and embedded. Filter methods usually rank the features based on simple statistical measures, and each feature is treated independently (Zhang et al., 2020b). Although they are computationally efficient and robust, multiple comparison issues are often inevitable. Wrapper methods use greedy forward, backward or combined search strategies to find a feature subspace that can optimize a given objective function.

Representative wrapper methods include the recursive feature elimination (RFE) (Guyon et al., 2002; Ingalhalikar et al., 2010) and the searchlight method (Kriegeskorte et al., 2006; Uddin et al., 2011). Embedded methods, such as LASSO (least absolute shrinkage and selection operator) (Duchesnay et al., 2011; F. Zhao et al., 2020) and elastic net, unify the feature reduction and classification by plugging "penalties" to enforce the learning algorithm finding sparse feature representations. In contrast, unsupervised feature reduction methods typically construct low-dimensional feature representations based on linear or non-linear combinations of the original features, such as principal component analysis (PCA) and ICA, and the training label is not required.

2.5. Classifier training

During the training phase, the parameters of classifiers are optimized based on the training dataset to find better representations of the class boundary or decision rule. Various classifiers have been used in ASD diagnosis, and we provide a brief review of the most representative algorithms in the following.

A linear discriminative classifier (LDC) is a simple linear model to separate classes by maximizing the between-class to within-class variance ratio. LDC is sensitive to outliers, and it assumes that the data is normally distributed. A logistic regression classifier is close to LDC, but it models the log-odd ratio as a linear function.

Decision tree classifier (DTC) is another commonly used machine learning approach, in which class labels are modeled as leaves, and branches represent the subset of features that lead to the labels. DTC is capable to approximate complex decision regions by the collection of simpler decision rules, thus owning good interpretability. However, evidence has shown that the efficiency and accuracy of DTC cannot be optimized simultaneously (Safavian and Landgrebe, 1991). Applying pruning methods on DTC and ensembles of DTCs often gain better discriminative power, particularly in situations with relatively small sample sizes compared to the dimensions of features.

Support vector machine is a supervised machine learning algorithm with solid mathematical foundations, which aims at finding a decision boundary that could maximize the margin between two categories in a high dimensional space. SVM has good generalizability and robustness, as the final discriminant function of SVM only depends on the data points that are located nearest to the decision boundary, which is known as support vectors. By using kernel tricks, SVM can easily handle nonlinear classification problems. However, non-linear kernel functions often make the final SVM model lack interpretability. According to our survey, SVM is the most common classifier used in ASD diagnosis.

Deep learning classifiers are a family of classification algorithms that use a hierarchy of non-linear layers to automatically discover the representations with strong discriminating power from the input data, they have received considerable attention in recent years as it out-performs conventional methods in many fields (Abrol et al., 2021; LeCun et al., 2015; Plis et al., 2014). Deep learning methods applied in ASD diagnosis can be divided into three categories: autoencoder (AE)-based, convolutional-based, and recurrent neural network (RNN) -based methods (Zhang et al., 2020a). AE-based methods are able to

learn highly discriminative and low-dimensional feature representations, but the spatial structure of data is often discarded. Convolution-based methods, on the other hand, can better leverage the spatial information of MRI data. Three-dimensional convolutional neural network (3D-CNN) (Khosla et al., 2018) and graph convolutional network (GCN) (Parisot et al., 2018) are representative methods. Different from convolutional-based models which focus on embedding spatial information of MRI, RNN-based methods are proposed to leverage characteristic temporal patterns from the fMRI time-series data (Dvornek et al., 2017).

2.6. Classification and performance evaluation

One important aspect of classification is unbiased cross-validation (CV). Namely, after training, parameters of a classifier have been adjusted and can usually perform well on the training set, but whether it is generalizable should be further validated on a testing set. To avoid bias, the testing data should never appear in the training process, but the preprocessing procedures should keep consistent with the training set. As dividing an independent dataset from the limited samples for evaluation might lead to an insufficient-trained model, k-fold cross-validation is often performed for evaluation of the model effectiveness in neuroimaging analysis. The entire dataset is randomly divided into k nearly equal-size subsets, one of the subsets is picked as the testing set, and the rest k-1 subsets are treated as the training set. This process executes k times so that each of the subsets is used as a testing set once, and will guarantee that no overlap between the training set and the testing set at each run. Some variants of the conventional k-fold CV, including stratified k-fold CV and leave-one-out CV (LOOCV) are more suitable to handle special cases, such as imbalanced dataset and small-size dataset (Japkowicz and Shah, 2015).

To quantitively evaluate the model performance, confusion matrix-based metrics, including accuracy, sensitivity and specificity, are commonly utilized. Accuracy is the ratio of correctly identified samples to the total samples, which intuitively indicates the ability for classifying patients and controls. Sensitivity is the proportion of identified true positive samples to the total positive samples, and specificity is the proportion of true negative samples to the total negative samples, both of which describe different aspects of the discriminate ability of the model. The area under the receiver operating characteristic (ROC) curve is another commonly used metric to evaluate the overall performance of a model. ROC curve regards sensitivity as a function of 1-specificity, the closer the curve to the top-left corner, the better the performance of the classifier.

A lot of available data associated with model performance can be obtained by metrics calculation and CV method, thus statistical testing can be performed based on these data to give more convincing evidence of the model reliability and superiority. For example, McNemar’s test can compare the performance of two algorithms in one dataset, while Friedman’s test can compare the performance of multiple algorithms in multiple datasets (Japkowicz and Shah, 2015).

3. Highlighted research

Structural abnormal variations in frontal, parietal and limbic regions have been reported in many ASD studies (McAlonan et al., 2005; Waiter et al., 2004), which indicate the diagnosis value of brain morphology. Ecker and colleagues used linear kernel SVM to classify adult ASD patients based on morphological features derived from sMRI (Fig. 2a and b), and obtained promising accuracies (Ecker et al., 2010a, 2010b). They also found GM map and cortical thickness measures were more discriminative compared to the WM map. In terms of fMRI, Anderson et al. (2011) performed early explorations for classifying adolescent and young adult ASD patients based on whole-brain FC by using a data-driven method, and found the most discriminative connections mainly locate at DMN (default mode network), superior parietal lobule, fusiform gyrus and anterior insula (Fig. 2c). Uddin and colleagues further examined the functional and structural alterations on children with ASD (Fig. 2d), and gave a critical insight into the early neural signatures of ASD (Uddin et al., 2011, 2013). Studies based on dMRI are relatively small but are still noteworthy. Specifically, Ingalhalikar et al. (2011) extracted regional features from dMRI data, and created a classifier based on a dataset consisting of 45 ASD children and 30 healthy controls. They found several brain structures with altered FA and MD values contributed to ASD discrimination, showing the great potential of dMRI in ASD diagnosis.

At the early stage, the sample sizes of ASD diagnosis studies based on MRI are small, and mainly focused on a specific cohort, such as a specific age group or high-functioning patients (Ecker et al., 2010b). The manual stratification of patients based on demographic information to some extent dissects the heterogeneity of ASD, but may also sacrifice the generalizability for other cohorts (Ecker et al., 2010b). The establishments of large-scale datasets are critical for addressing these problems. However, later large sample classification studies utilized ABIDE have relatively lower classification accuracies. Sabuncu et al. (2015) constructed different structural feature sets and tested the performance of different classifiers on a subset comprising of 325 ASDs and 325 healthy controls from ABIDE, the highest accuracy was 60%. By performing extensive validations on different methods, Abraham et al. (2017) classified the patients from healthy controls selected from ABIDE dataset based on fMRI at an accuracy of 67%, and illustrated that different process pipelines would impact the model performances (Fig. 2e).

Based on large public datasets, some promising results for ASD classification have been obtained by employing DL algorithms. To minimize the impacts of some subjective prior hypothesis on feature selection, Heinsfeld et al. (2018) used two stacked denoising autoencoders for unsupervised feature extraction at the pre-training stage, and transferred the encoders wights to a multilayer perceptron (MLP) for supervised learning. They achieved 70% accuracy by 10-fold CV on the dataset composed of 530 healthy controls and 503 ASDs selected from ABIDE. Based on the same dataset, Z.-A. Huang et al. (2020) proposed a graph-based feature selection strategy to find more informative representations of the FC network, and then employed a three-layer deep belief network (DBN) model to perform classifications, achieving 76.4% accuracy.

Different modalities of MRI can provide distinct discriminative information for ASD identification, but only limited classification studies are based on multimodal imaging features. Deshpande et al. (2013) combined the features of fMRI and dMRI to classify 15 high-functioning ASD patients and 15 typical developing controls, and successfully uncovered some distinctive connectivity path abnormalities of adults with ASD. Zhou et al. (2014) analyzed the T1w MRI and fMRI collected from 127 children with ASD and 153 typically developing controls, and further generated multimodal features, including GM of local subcortical regions, FC of ROIs, and fALFF values. They trained RF and classified two groups at an accuracy of 70%. Sen et al. (2018) constructed two feature learners for sMRI and fMRI respectively, then combined the extracted features to train an SVM to classify 573 healthy controls and 538 ASDs selected from ABIDE, and obtained 64.3% accuracy.

On the other hand, compared to most ASD classification studies based on DSM labels, a few studies attempted to identify early brain metrics to predict the later ASD diagnosis longitudinally. As it is difficult to diagnose ASD 24 months ahead of the conventional DSM criteria, such studies show more translational medical impact. For example, Hazlett et al. (2017) used the longitudinal sMRI data comprising 318 infants, and systematically analyzed the timing of brain morphological aberrations. A deep neural network classifier was trained to use brain surface area information of individuals at 6- and 12-month-old to predict their risks to have ASD at 24 months old, suggesting that early, post-natal hyper-expansion of the cortical surface played an important role in ASD development (Fig. 2f). Another study (Fig. 2g) examined longitudinal fMRI data of 59 infants, similarly, the FC data in 6-month-old infants were used to predict the diagnosis at 24 months, with 96.6% accuracy achieved (Emerson et al., 2017).

3.1. Challenges in machine-learning-based ASD diagnosis

Despite that machine learning approaches are gaining more and more applications in automated ASD diagnosis, we must notice that great challenges still exist in the way of translating classification outcomes to clinical practice. Current large samples mainly come from retrospective data aggregation, and from prospective multicenter collections, such as ABIDE (Di Martino et al., 2017; Di Martino et al., 2014) and EU-AIMS LEAP (Charman et al., 2017), however, the biological diversity of patients is still not optimally reflected. Specifically, first, most ASD classification models are established based on male-biased samples. The male bias in ASD prevalence has been reported in many epidemiology studies (Lai et al., 2015), and indicates that the risk for ASD may be affected by factors related to gender, thus the disproportional representation of female individuals may hamper investigations of sex-related imaging differences. Second, considering the compliance requirements for data collection, less cognitively capable individuals and patients with severe ASD behaviors are often excluded, which may constrain the generalizability of findings. In addition, individuals with ASD often meet the criteria for diagnosis of other comorbid conditions, including attention-deficit/hyperactivity disorder and anxiety in various forms (Lord et al., 2018). On the one hand, co-occurring psychiatric disorders and a high degree of symptom overlaps increase the risk for misdiagnosis and thus hinder the improvement of model performance; on the other hand, delicately parsing the atypicality associated with different comorbid conditions may reveal the pathology underlying ASD

heterogeneity. However, most classification models are trained on binary samples, and individuals with comorbid conditions are generally excluded. In the future, developing data collection protocols that are applicable for all subjects and recruiting more female subjects are potential for reducing the sample bias, and will facilitate identifications of ASD biomarkers with high generalizability.

Additionally, data aggregation often induces domain shift problems (Li et al., 2020; J. Wang et al., 2020). For example, the scanners employed in different sites may be from various manufacturers, and the parameter configurations and data acquisition protocols may have huge differences, which will impact the data quality and result in nuisance noise for data analysis. Besides, the participant recruitment criteria and the status during the acquisition process may be also different. These above-mentioned issues are usually hard to control, and may lead to more heterogeneities in aggregated datasets.

Proper feature reduction methods are critical for improving the model performance. It is worth noting that any feature reduction should be implemented in a non-biased manner. Test data should not be involved in any steps of feature reduction, or the model performance will be manually amplified, and may induce overfitting (Arbabshirani et al., 2017). An effective feature reduction method should eliminate artifacts and retain reliable information as much as possible, and it usually runs inside the CV framework to find feature subset with relatively high generalizability. However, different feature subsets may be selected in each iteration of CV, which may impact the feature interpretation (Castellanos et al., 2013). Additionally, different feature subsets may be derived from different feature reduction methods, and the performances of feature reduction methods are usually not consistent across datasets (Wang et al., 2008), which induces a grand challenge for robust and reproducible feature identification.

3.2. Future directions

Classical binary classification assumes that both cases and controls are well-defined entities. However, it becomes problematic in ASD, where the diagnostic criteria are composed of behavioral symptoms that overlap with other mental disorders (Marquand et al., 2016), and the behavioral presentations of individuals with ASD manifest high variability. The current large-scale datasets manifest great gender bias, and are mainly composed of high-functioning patients, the comorbidity information is also missed. It would be potential to reveal the intrinsic heterogeneity of ASD by constructing a more comprehensive dataset. As the underlying heterogeneity of ASD is often ignored in traditional binary classification. Developing a new methodology that could achieve cutting across diagnostic classifications and identify biological homogeneous ASD subgroups based on imaging has been motivated, as the underlying heterogeneity of ASD is often ignored in traditional binary classification. Such methods are often named as stratification or subtyping (Hong et al., 2020; Wolfers et al., 2019), and are supposed to not only deepen the understanding of neurobiological heterogeneity in ASD, but also potentially facilitate the development of personalized therapies.

Furthermore, combining multimodal brain imaging data could give comprehensive views of brain organizations, and facilitate to reveal complex, cross-modal alterations associated with

the intrinsic pathology of disorders (Jiang et al., 2020a, 2020c; Qi et al., 2020a). However, in the surveyed articles, the number of studies using multimodal imaging is still very limited, and the performance improvements based on multimodal data are also not significant enough, especially in large datasets. One reason could be that most studies achieve multimodal classification by simply concatenating brain features extracted from different modalities or ensemble the results of different models, thereby the intrinsic complementary information among different modalities may not be fully utilized. By contrast, multimodal fusion techniques are effective tools for uncovering the joint information (Calhoun and Sui, 2016; Sui et al., 2012). By applying symptom-guided multimodal fusion methods, Qi et al. (2020b) evaluated ASD heterogeneity across ASD subtypes, suggesting that ASD has a common neural basis that is consistent with the core deficits, however, every different ASD subtype is also strongly linked to unique multimodal covarying brain systems. More interestingly, the identified subtype-specific patterns are only predictive for ASD symptoms particularly manifested in the corresponding subtype, but not the other subtypes. Considering the exciting advances in recent data fusion studies, we believe that the adoption of multimodal fusion in ASD classifications will further improve the performance and enable the identification of more robust diagnosis markers.

Moreover, researches of genetic disorder with high penetrance of ASD give a critical insight into the neural circuitry underlying behavior symptoms of autism, and hold significant potential in disentangling the heterogeneity of ASD (Sahin and Sur, 2015). Various genetically manipulated animal models have been employed to study the neurobiological foundations of aberrant connectivity observed in ASD (Cai et al., 2020; Liska et al., 2018; Pagani et al., 2019), but whether the brain dysfunction patterns captured in an animal model can direct the ASD diagnosis in human is rarely be investigated. A representative cross-species machine-learning study is performed by Zhang and colleagues (Zhan et al., 2020). They analyzed the fMRI of transgenic monkeys and identified nine core brain regions. Further, these regions were one-to-one mapped to the human brain and used as seeds to construct a sparse logistic regression classifier for patient classification. They achieved an accuracy of 82% in ABIDE I. The cross-species machine-learning framework provides an innovative way to build biomarkers for psychiatric disorders, and the identified cross-species markers may be potential for drug discovery and assessment.

To date, the majority of ASD classification studies are based on cross-sectional data. As a life-long neurodevelopmental condition, the symptoms of ASD are not static within individuals across development and the long-term outcomes are also varied (Lord et al., 2015; Szatmari et al., 2015). The heterogeneous trajectories of ASD underscore the need of a developmental perspective in imaging analysis. The classification model established on longitudinal datasets enables to the identification of biomarkers that present before symptom onset, which is critical for early interventions (Hazlett et al., 2017; Sui et al., 2020; H. Wang et al., 2020). In addition, longitudinal datasets allow researchers to assess the stability of the classifier over time, which is another essential dimension that should be encouraged to dissect the heterogeneity and further improve the clinical practice.

Finally, considering the strong capability to identify subtle and complex patterns from large data, deep learning has recently become a promising tool in ASD classification based on

brain imaging. Compared with traditional machine learning methods, deep learning can implement data-driven automatic feature learning without any prior knowledge, and the stacked nonlinear layers allow it to represent very complex decision rules (Arbabshirani et al., 2017; Rashid and Calhoun, 2020). Nevertheless, some limitations and challenges of deep learning should also be noticed. Generally, the performance of deep learning model highly depends on the data volume and quality. A small sample with high noise may result in overfitting and poor feature learning, whereas such conditions are quite common in neuroimaging data (Rashid and Calhoun, 2020; Zhang et al., 2020a). Moreover, deep learning models are often treated as a black-box system that lacks transparency, which may limit the interpretability in practical use, though there are methods to visualize deep learning models which should be further emphasized (Abrol et al., 2021; Zhang et al., 2020a).

4. Conclusion

To summarize, this review offers a comprehensive survey on ASD classification methods in the recent 10 years. Although various classification approaches have been widely applied in MRI researches of ASD, and have achieved improved accuracy while revealing multimodal brain impairments, more dedicated experimental design, training and validations are still required to construct a generalizable and reliable classification model, especially considering the high heterogeneity of ASD. Even though this field is still far from clinical use, we believe that with the development of new powerful mathematical tools and the closer interdisciplinary cooperation, imaging-based diagnosis of ASD is promising and will be eventually achieved.

Acknowledgments

This work is supported in part by the National Natural Science Foundation of China (No. 82022035, 61773380), Beijing Municipal Science and Technology Commission (Z181100001518005), China; the National Institute of Health (1R01MH117107, R01EB005846, and P20GM103472), USA. The authors declare no biomedical financial interests or potential conflicts of interest.

References

Abraham A, Milham MP, Di Martino A, Craddock RC, Samaras D, Thirion B, Varoquaux G, 2017. Deriving reproducible biomarkers from multi-site resting-state data: an Autism-based example. Neuroimage 147, 736–745. [PubMed: 27865923]

Abrol A, Fu Z, Salman M, Silva R, Du Y, Plis S, Calhoun V, 2021. Deep learning encodes robust discriminative neuroimaging representations to outperform standard machine learning. Nat. Commun 12, 353. [PubMed: 33441557]

Aghdam MA, Sharifi A, Pedram MM, 2018. Combination of rs-fMRI and sMRI data to discriminate autism spectrum disorders in young children using deep belief network. J. Digit. Imaging 31, 895–903. [PubMed: 29736781]

Aghdam MA, Sharifi A, Pedram MM, 2019. Diagnosis of autism spectrum disorders in young children based on resting-state functional magnetic resonance imaging data using convolutional neural networks. J. Digit. Imaging 32, 899–918. [PubMed: 30963340]

Ahmed MR, Zhang Y, Liu Y, Liao H, 2020. Single volume image generator and deep learning-based ASD classification. Ieee J. Biomed. Health 24, 3044–3054.

Alvarez-Jimenez C, Munera-Garzon N, Zuluaga MA, Velasco NF, Romero E, 2020. Autism spectrum disorder characterization in children by capturing local-regional brain changes in MRI. Med. Phys 47, 119–131. [PubMed: 31682019]

Anderson JS, Nielsen JA, Froehlich AL, DuBray MB, Druzgal TJ, Cariello AN, Cooperrider JR, Zielinski BA, Ravichandran C, Fletcher PT, Alexander AL, Bigler ED, Lange N, Lainhart JE, 2011. Functional connectivity magnetic resonance imaging classification of autism. Brain: J. Neurol 134, 3739–3751.

Arbabshirani MR, Plis S, Sui J, Calhoun VD, 2017. Single subject prediction of brain disorders in neuroimaging: promises and pitfalls. Neuroimage 145, 137–165. [PubMed: 27012503]

Ataei S, Attar N, Aliakbary S, Bakouie F, 2019. Graph theoretical approach for screening autism on brain complex networks. Sn Appl. Sci 1.

Barttfeld P, Wicker B, Cukier S, Navarta S, Lew S, Leiguarda R, Sigman M, 2012. State-dependent changes of connectivity patterns and functional brain network topology in autism spectrum disorder. Neuropsychologia 50, 3653–3662. [PubMed: 23044278]

Bernas A, Aldenkamp AP, Zinger S, 2018. Wavelet coherence-based classifier: a resting-state functional MRI study on neurodynamics in adolescents with high-functioning autism. Comput. Methods Prog. Biomed 154, 143–151.

Bhaumik R, Pradhan A, Das S, Bhaumik DK, 2018. Predicting autism spectrum disorder using domain-adaptive cross-site evaluation. Neuroinformatics 16, 197–205. [PubMed: 29455363]

Bi X.-a, Chen J, Sun Q, Liu Y, Wang Y, Luo X, 2018a. Analysis of asperger syndrome using genetic-evolutionary random support vector machine cluster. Front. Physiol 9.

Bi X.-a, Liu Y, Jiang Q, Shu Q, Sun Q, Dai J, 2018b. The diagnosis of autism spectrum disorder based on the random neural network cluster. Front. Human Neurosci 12.

Bi X-A, Liu Y, Sun Q, Lu X, Tan H, Chen J, Zeng N, 2019. The genetic-evolutionary random support vector machine cluster analysis in autism spectrum disorder. Ieee Access 7, 30527–30535.

Bi X.-a, Wang Y, Shu Q, Sun Q, Xu Q, 2018c. Classification of autism spectrum disorder using random support vector machine cluster. Front. Genet 9.

Brahim A, Farrugia N, 2020. Graph Fourier transform of fMRI temporal signals based on an averaged structural connectome for the classification of neuroimaging. Artif Intell. Med 106.

Cai D-C, Wang Z, Bo T, Yan S, Liu Y, Liu Z, Zeljic K, Chen X, Zhan Y, Xu X, Du Y, Wang Y, Cang J, Wang G-Z, Zhang J, Sun Q, Qiu Z, Ge S, Ye Z, Wang Z, 2020. MECP2 duplication causes aberrant GABA pathways, circuits and behaviors in transgenic monkeys: neural mappings to patients with autism. J. Neurosci 40, 3799–3814. [PubMed: 32269107]

Calderoni S, Retico A, Biagi L, Tancredi R, Muratori F, Tosetti M, 2012. Female children with autism spectrum disorder: an insight from mass-univariate and pattern classification analyses. Neuroimage 59, 1013–1022. [PubMed: 21896334]

Calhoun VD, Sui J, 2016. Multimodal fusion of brain imaging data: a key to finding the missing link(s) in complex mental illness. Biol. Psychiatry Cogn. Neurosci. Neuroimaging 1, 230–244. [PubMed: 27347565]

Castellanos FX, Di Martino A, Craddock RC, Mehta AD, Milham MP, 2013. Clinical applications of the functional connectome. NeuroImage 80, 527–540. [PubMed: 23631991]

Chaitra N, Vijaya PA, Deshpande G, 2020. Diagnostic prediction of autism spectrum disorder using complex network measures in a machine learning framework. Biomed. Signal. Process 62.

Chanel G, Pichon S, Conty L, Berthoz S, Chevallier C, Grezes J, 2016. Classification of autistic individuals and controls using cross-task characterization of fMRI activity. Neuroimage-Clinical 10, 78–88. [PubMed: 26793434]

Charman T, Loth E, Tillmann J, Autism DCJM, 2017. The EU-AIMS Longitudinal European Autism Project (LEAP): clinical characterisation. Mol. Autism 8, 24. [PubMed: 28649312]

Chen T, Chen Y, Yuan M, Gerstein M, Li T, Liang H, Froehlich T, Lu L, 2020. The development of a practical artificial intelligence tool for diagnosing and evaluating autism spectrum disorder: multicenter study. Jmir Med. Inf 8.

Chen H, Duan X, Liu F, Lu F, Ma X, Zhang Y, Uddin LQ, Chen H, 2016. Multivariate classification of autism spectrum disorder using frequency-specific resting-state functional connectivity – a multi-center study. Prog. Neuro-Psychopharmacol 64, 1–9.

Cherkassky VL, Kana RK, Keller TA, Just MAJN, 2006. Functional connectivity in a baseline resting-state network in autism. Neuroreport 17, 1687–1690. [PubMed: 17047454]

Dekhil O, Ali M, El-Nakieb Y, Shalaby A, Soliman A, Switala A, Mahmoud A, Ghazal M, Hajjdiab H, Casanova MF, Elmaghraby A, Keynton R, El-Baz A, Bames G, 2019. A personalized autism diagnosis CAD system using a fusion of structural MRI and resting-state functional MRI data. Front. Psychiatry 10.

Dekhil O, Ali M, Haweel R, Elnakib Y, Ghazal M, Hajjdiab H, Fraiwan L, Shalaby A, Soliman A, Mahmoud A, Keynton R, Casanova MF, Barnes G, El-Baz A, 2020. A comprehensive framework for differentiating autism spectrum disorder from neurotypicals by fusing structural MRI and resting state functional MRI. Semin. Pediatr. Neurol 34.

Dekhil O, Hajjdiab H, Shalaby A, Ali MT, Ayinde B, Switala A, Elshamekh A, Ghazal M, Keynton R, Barnes G, El-Baz A, 2018. Using resting state functional MRI to build a personalized autism diagnosis system. Plos One 13.

Demirhan A, 2018. The effect of feature selection on multivariate pattern analysis of structural brain MR images. Phys. Med 47, 103–111. [PubMed: 29609811]

Deshpande G, Libero LE, Sreenivasan KR, Deshpande HD, Kana RK, 2013. Identification of neural connectivity signatures of autism using machine learning. Front. Human Neurosci 7.

Duchesnay E, Cachia A, Boddaert N, Chabane N, Mangin J-F, Martinot J-L, Brunelle F, Zilbovicius M, 2011. Feature selection and classification of imbalanced datasets application to PET images of children with autistic spectrum disorders. Neuroimage 57, 1003–1014. [PubMed: 21600290]

Dvornek NC, Ventola P, Pelphrey KA, Duncan JS. Identifying Autism from Resting-State fMRI Using Long Short-Term Memory Networks. In Wang Q, Shi Y, Suk HI, Suzuki K, editors. Machine Learning in Medical Imaging, 2017: 362–70.

Ecker C, Marquand A, Mourao-Miranda J, Johnston P, Daly EM, Brammer MJ, Maltezos S, Murphy CM, Robertson D, Williams SC, Murphy DGM, 2010a. Describing the brain in autism in five dimensions-magnetic resonance imaging-assisted diagnosis of autism spectrum disorder using a multiparameter classification approach. J. Neurosci 30, 10612–10623. [PubMed: 20702694]

Ecker C, Rocha-Rego V, Johnston P, Mourao-Miranda J, Marquand A, Daly EM, Brammer MJ, Murphy C, Murphy DG, Consortium MA, 2010b. Investigating the predictive value of whole-brain structural MR scans in autism: a pattern classification approach. Neuroimage 49, 44–56. [PubMed: 19683584]

Eill A, Jahedi A, Gao Y, Kohli JS, Fong CH, Solders S, Carper RA, Valafar F, Bailey BA, Mueller R-A, 2019. Functional connectivities are more informative than anatomical variables in diagnostic classification of autism. Brain Connect. 9, 604–612. [PubMed: 31328535]

Elder JH, Kreider CM, Brasher SN, Ansell M, 2017. Clinical impact of early diagnosis of autism on the prognosis and parent-child relationships. Psychol. Res. Behav. Manag 10, 283–292. [PubMed: 28883746]

Elnakieb YA, Ali MT, Soliman A, Mahmoud AH, Shalaby AM, Alghamdi NS, Ghazal M, Khalil A, Switala A, Keynton RS, Barnes GN, El-Baz A, 2020. Computer aided autism diagnosis using diffusion tensor imaging. Ieee Access 8, 191298–191308.

Elsabbagh M, Divan G, Yun-Joo K, Kim YS, Kauchali S, Carlos M, Cecilia MN, Patel V, Paula CS, Wang C, 2012. Global prevalence of autism and other pervasive developmental disorders. Autism Res. 5.

Emerson RW, Adams C, Nishino T, Hazlett HC, Wolff JJ, Zwaigenbaum L, Constantino JN, Shen MD, Swanson MR, Elison JT, Kandala S, Estes AM, Botteron KN, Collins L, Dager SR, Evans AC, Gerig G, Gu H, McKinstry RC, Paterson S, Schultz RT, Styner M, Schlaggar BL, Pruett JR Jr., Piven J, Network I, 2017. Functional neuroimaging of high-risk 6-month-old infants predicts a diagnosis of autism at 24 months of age. Sci. Trans. Med 9.

Eslami T, Mirjalili V, Fong A, Laird AR, Saeed F, 2019. ASD-DiagNet: a hybrid learning approach for detection of autism spectrum disorder using fMRI data. Front. Neuroinform 13.

Fan G, Chen Y, Chen Y, Yang M, Wang J, Li C, Li Y, Liu T, 2020. Abnormal brain regions in two-group cross-location dynamics model of autism. Ieee Access 8, 94526–94534.

Ferrari E, Bosco P, Calderoni S, Oliva P, Palumbo L, Spera G, Fantacci ME, Retico A, 2020. Dealing with confounders and outliers in classification medical studies: the autism spectrum disorders case study. Artif. Intell. Med 108.

Georges N, Mhiri I, Rekik I, 2020. Alzheimers Dis Neuroimaging I. Identifying the best data-driven feature selection method for boosting reproducibility in classification tasks. Pattern Recognit. 101.

Ghiassian S, Greiner R, Jin P, Brown MRG, 2016. Using functional or structural magnetic resonance images and personal characteristic data to identify ADHD and autism. Plos One 11.

Gori I, Giuliano A, Muratori F, Saviozzi I, Oliva P, Tancredi R, Cosenza A, Tosetti M, Calderoni S, Retico A, 2015. Gray matter alterations in young children with autism spectrum disorders: comparing morphometry at the voxel and regional level. J. Neuroimaging 25, 866–874. [PubMed: 26214066]

Graa O, Rekik I, 2019. Multi-view learning-based data proliferator for boosting classification using highly imbalanced classes. J. Neurosci. Methods 327.

Guo X, Dominick KC, Minai AA, Li H, Erickson CA, Lu LJ, 2017. Diagnosing autism spectrum disorder from brain resting-state functional connectivity patterns using a deep neural network with a novel feature selection method. Front. Neurosci 11.

Gupta S, Rajapakse JC, Welsch RE, 2020. Alzheimer's Dis Neuroimaging I. Ambivert degree identifies crucial brain functional hubs and improves detection of Alzheimer's Disease and Autism Spectrum Disorder. Neuroimage-Clinical 25.

Guyon I, Weston J, Barnhill S, Vapnik V, 2002. Gene selection for cancer classification using support vector machines. Mach. Learn 46, 389–422.

Hazlett HC, Gu H, Munsell BC, Kim SH, Styner M, Wolff JJ, Elison JT, Swanson MR, Zhu H, Otteron KNB, Collins DL, Constantino JN, Dager SR, Estes AM, Evans AC, Fonov VS, Gerig G, Kostopoulos P, McKinstry RC, Pandey J, Paterson S, Pruett JR Jr., Schultz RT, Shaw DW, Zwaigenbaum L, Piven J, Network I, 2017. Early brain development in infants at high risk for autism spectrum disorder. Nature 542, 348-+. [PubMed: 28202961]

Heinsfeld AS, Franco AR, Cameron Craddock R, Buchweitz A, Meneguzzi F, 2018. Identification of autism spectrum disorder using deep learning and the ABIDE dataset. Neuroimage-Clinical 17, 16–23. [PubMed: 29034163]

Herbert MR, Ziegler DA, Makris N, Filipek PA, Kemper TL, Normandin JJ, Sanders HA, Kennedy DN, Caviness VS Jr, 2004. Localization of white matter volume increase in autism and developmental language disorder. Comp. Study 55, 530–540.

Hong S-J, Vogelstein JT, Gozzi A, Bernhardt BC, Yeo BTT, Milham MP, Di Martino A, 2020. Toward neurosubtypes in autism. Biol. Psychiatry 88, 111–128. [PubMed: 32553193]

Huang H, Liu X, Jin Y, Lee S-W, Wee C-Y, Shen D, 2019. Enhancing the representation of functional connectivity networks by fusing multi-view information for autism spectrum disorder diagnosis. Human Brain Mapping 40, 833–854. [PubMed: 30357998]

Huang F, Tan E-L, Yang P, Huang S, Ou-Yang L, Cao J, Wang T, Lei B, 2020a. Self-weighted adaptive structure learning for ASD diagnosis via multi-template multi-center representation. Med. Image Anal 63.

Huang Z-A, Zhu Z, Yau CH, Tan KC, 2020b. Identifying autism spectrum disorder from resting-state fMRI using deep belief network. Ieee Trans. Neural Netw. Learn PP.

Hui W, Chen C, Hsieh F, 2012. Extracting multiscale pattern information of fMRI based functional brain connectivity with application on classification of autism spectrum disorders. Plos One 7.

Hu J, Cao L, Li T, Liao B, Dong S, Li P, 2020. Interpretable learning approaches in resting-state functional connectivity analysis: the case of autism spectrum disorder. Comput. Math. Method Med 2020.

Iidaka T, 2015. Resting state functional magnetic resonance imaging and neural network classified autism and control. Cortex 63, 55–67. [PubMed: 25243989]

Ingalhalikar M, Kanterakis S, Gur R, Roberts TPL, Verma R, 2010, DTI based diagnostic prediction of a disease via pattern classification. In Jiang T, Navab N, Pluim JPW, Viegever MA, editors. Medical Image Computing and Computer-Assisted Intervention - Miccai 2010, Pt I: 558-+.

Ingalhalikar M, Parker D, Bloy L, Roberts TPL, Verma R, 2011. Diffusion based abnormality markers of pathology: toward learned diagnostic prediction of ASD. Neuroimage 57, 918–927. [PubMed: 21609768]

Jahedi A, Nasamran CA, Faires B, Fan J, Müller RA, 2017. Distributed intrinsic functional connectivity patterns predict diagnostic status in large autism cohort. Brain Connect. 7, 515–525. [PubMed: 28825309]

Japkowicz N, Shah M, 2015. Performance evaluation in machine learning. In: El Naqa I, Li R, Murphy MJ (Eds.), Machine Learning in Radiation Oncology: Theory and Applications. Springer International Publishing, Cham, pp. 41–56.

Jiang R, Calhoun VD, Cui Y, Qi S, Zhuo C, Li J, Jung R, Yang J, Du Y, Jiang T, Sui J, 2020b. Multimodal data revealed different neurobiological correlates of intelligence between males and females. Brain Imaging Behav. 14, 1979–1993. [PubMed: 31278651]

Jiang R, Calhoun VD, Fan L, Zuo N, Jung R, Qi S, Lin D, Li J, Zhuo C, Song M, Fu Z, Jiang T, Sui J, 2020c. Gender differences in connectome-based predictions of individualized intelligence quotient and sub-domain scores. Cereb Cortex 30, 888–900. [PubMed: 31364696]

Jiang H, Cao P, Xu M, Yang J, Zaiane O, 2020a. Hi-GCN: a hierarchical graph convolution network for graph embedding learning of brain network and brain disorders prediction. Comput. Biol. Med 127, 104096-. [PubMed: 33166800]

Jiang R, Zuo N, Ford JM, Qi S, Zhi D, Zhuo C, Xu Y, Fu Z, Bustillo J, Turner JA, Calhoun VD, Sui J, 2020d. Task-induced brain connectivity promotes the detection of individual differences in brain-behavior relationships. NeuroImage 207, 116370. [PubMed: 31751666]

Jiao Y, Chen R, Ke X, Chu K, Lu Z, Herskovits EH, 2010. Predictive models of autism spectrum disorder based on brain regional cortical thickness. Neuroimage 50, 589–599. [PubMed: 20026220]

Jung M, Tu Y, Park J, Jorgenson K, Lang C, Song W, Kong J, 2019. Surface-based shared and distinct resting functional connectivity in attention-deficit hyperactivity disorder and autism spectrum disorder. Br. J. Psychiatry 214, 339–344. [PubMed: 31088591]

Jun E, Kang E, Choi J, Suk H-I, 2019. Modeling regional dynamics in low-frequency fluctuation and its application to Autism spectrum disorder diagnosis. Neuroimage 184, 669–686. [PubMed: 30248456]

Just MA, Cherkassky VL, Buchweitz A, Keller TA, Mitchell TM, 2014. Identifying autism from neural representations of social interactions: neurocognitive markers of autism. Plos One 9.

Kam T-E, Suk H-I, Lee S-W, 2017. Multiple functional networks modeling for autism spectrum disorder diagnosis. Human Brain Mapping 38, 5804–5821. [PubMed: 28845892]

Kazeminejad A, Sotero RC, 2020. The importance of anti-correlations in graph theory based classification of autism spectrum disorder. Front. Neurosci 14.

Kazeminejad A, Sotero RC, 2019. Topological properties of resting-state fmri functional networks improve machine learning-based autism classification. Front. Neurosci 12.

Kennedy. Daniel P, R. E, 2006. Courchesne Eric Failing to deactivate: resting functional abnormalities in autism. Proc. Natl. Acad. Sci. U. S. A 103, 8275–8280. [PubMed: 16702548]

Kennedy DP, Courchesne E, 2008. The intrinsic functional organization of the brain is altered in autism. Neuroimage 39, 1877–1885. [PubMed: 18083565]

Kernbach JM, Satterthwaite TD, Bassett DS, Smallwood J, Margulies D, Krall S, Shaw P, Varoquaux G, Thirion B, Konrad K, Bzdok D, 2018. Shared endo-phenotypes of default mode dysfunction in attention deficit/hyperactivity disorder and autism spectrum disorder. Trans. Psychiatry 8.

Ke F, Choi S, Kang YH, Cheon K-A, Lee SW, 2020. Exploring the structural and strategic bases of autism spectrum disorders with deep learning. Ieee Access 8, 153341–153352.

Khan NA, Waheeb SA, Riaz A, Shang X, 2020. A three-stage teacher, student neural networks and sequential feed forward selection-based feature selection approach for the classification of autism spectrum disorder. Brain Sci. 10.

Khosla M, Jamison K, Kuceyeski A, Sabuncu MR, 2018, 3D convolutional neural networks for classification of functional connectomes. In Stoyanov D, Taylor Z, Carneiro G, SyedaMahmood T, editors. Deep Learning in Medical Image Analysis and Multimodal Learning for Clinical Decision Support, Dlmia 2018: 137–45.

Kong Y, Gao J, Xu Y, Pan Y, Wang J, Liu J, 2019. Classification of autism spectrum disorder by combining brain connectivity and deep neural network classifier. Neurocomputing 324, 63–68.

Kriegeskorte N, Goebel R, Bandettini P, 2006. Information-based functional brain mapping. Proc. Natl. Acad. Sci. U. S. A 103, 3863–3868. [PubMed: 16537458]

Ktena SI, Parisot S, Ferrante E, Rajchl M, Lee M, Glocker B, Rueckert D, 2018. Metric learning with spectral graph convolutions on brain connectivity networks. Neuroimage 169, 431–442. [PubMed: 29278772]

Lai M-C, Lombardo MV, Auyeung B, Chakrabarti B, Baron-Cohen S, 2015. Sex/gender differences and autism: setting the scene for future research. J. Am. Acad. Child Adolesc. Psychiatry 54, 11–24. [PubMed: 25524786]

Lange N, DuBray MB, Lee JE, Froimowitz MP, Froehlich A, Adluru N, Wright B, Ravichandran C, Fletcher PT, Bigler ED, Alexander AL, Lainhart JE, 2010. Atypical diffusion tensor hemispheric asymmetry in autism. Autism Res. 3, 350–358. [PubMed: 21182212]

Lanka P, Rangaprakash D, Dretsch MN, Katz JS, Denney TS Jr., Deshpande G, 2020. Supervised machine learning for diagnostic classification from large-scale neuroimaging datasets. Brain Imaging Behav. 14, 2378–2416. [PubMed: 31691160]

LeCun Y, Bengio Y, Hinton G, 2015. Deep learning. Nature 521, 436–444. [PubMed: 26017442]

Leming M, Manuel Gorriz J, Suckling J, 2020. Ensemble deep learning on large, mixed-site fMRI datasets in autism and other tasks. Int. J. Neural Syst 30.

Lim L, Marquand A, Cubillo AA, Smith AB, Chantiluke K, Simmons A, Mehta M, Rubia K, 2013. Disorder-specific predictive classification of adolescents with attention deficit hyperactivity disorder (ADHD) relative to autism using structural magnetic resonance imaging. PLoS One 8, e63660. [PubMed: 23696841]

Liska A, Bertero A, Gomolka R, Sabbioni M, Galbusera A, Barsotti N, Panzeri S, Scattoni ML, Pasqualetti M, Gozzi A, 2018. Homozygous loss of autism-risk gene CNTNAP2 results in reduced local and long-range prefrontal functional connectivity. Cereb. Cortex 28, 1141–1153. [PubMed: 28184409]

Liu J, Sheng Y, Lan W, Guo R, Wang Y, Wang J, 2020a. Improved ASD classification using dynamic functional connectivity and multi-task feature selection. Pattern Recogn. Lett 138, 82–87.

Liu Y, Xu L, Li J, Yu J, Yu X, 2020b. Attentional connectivity-based prediction of autism using heterogeneous rs-fMRI data from CC200 Atlas. Exp. Neurobiol 29, 23–37.

Li Q, Becker B, Jiang X, Zhao Z, Zhang Q, Yao S, Kendrick KM, 2019. Decreased interhemispheric functional connectivity rather than corpus callosum volume as a potential biomarker for autism spectrum disorder. Cortex 119, 258–266. [PubMed: 31167156]

Li X, Gu Y, Dvornek N, Staib LH, Ventola P, Duncan JS, 2020. Multi-site fMRI analysis using privacy-preserving fe derate d learning and domain adaptation: ABIDE results. Med. Image Anal 65.

Li H, Parikh NA, He L, 2018. A novel transfer learning approach to enhance deep neural network classification of brain functional connectomes. Front. Neurosci 12.

Lord C, Bishop S, Anderson D, 2015. Developmental trajectories as autism phenotypes. Am. J. Med. Genet. Pt C: Semin. Med. Genet 169, 198–208.

Lord C, Brugha TS, Charman T, Cusack J, Dumas G, Frazier T, Jones EJH, Jones RM, Pickles A, State MW, Taylor JL, Veenstra-VanderWeele J, 2020. Autism spectrum disorder. Nat. Rev. Dis. Primers 6, 5. [PubMed: 31949163]

Lord C, Elsabbagh M, Baird G, Veenstra-Vanderweele J, 2018. Autism spectrum disorder. Lancet 392, 508–520. [PubMed: 30078460]

Marquand AF, Rezek I, Buitelaar J, Beckmann CF, 2016. Understanding heterogeneity in clinical cohorts using normative models: beyond case-control studies. Biol. Psychiatry 80, 552–561. [PubMed: 26927419]

Di Martino A, O'Connor D, Chen B, Alaerts K, Anderson JS, Assaf M, Balsters JH, Baxter L, Beggiato A, Bernaerts S, Blanken LME, Bookheimer SY, Braden BB, Byrge L, Castellanos FX, Dapretto M, Delorme R, Fair DA, Fishman I, Fitzgerald J, Gallagher L, Keehn RJJ, Kennedy DP, Lainhart JE, Luna B, Mostofsky SH, Müller R-A, Nebel MB, Nigg JT, O'Hearn K, Solomon M, Toro R, Vaidya CJ, Wenderoth N, White T, Craddock RC, Lord C, Leventhal B, Milham MP, 2017. Enhancing studies of the connectome in autism using the autism brain imaging data exchange II. Sci. Data 4, 170010. [PubMed: 28291247]

Di Martino A, Yan CG, Li Q, Denio E, Castellanos FX, Alaerts K, Anderson JS, Assaf M, Bookheimer SY, Dapretto M, Deen B, Delmonte S, Dinstein I, Ertl-Wagner B, Fair DA, Gallagher L, Kennedy DP, Keown CL, Keysers C, Lainhart JE, Lord C, Luna B, Menon V, Minshew NJ, Monk CS, Mueller S, Müller RA, Nebel MB, Nigg JT, O'Hearn K, Pelphrey KA, Peltier SJ, Rudie JD, Sunaert S, Thioux M, Tyszka JM, Uddin LQ, Verhoeven JS, Wenderoth N, Wiggins JL, Mostofsky SH, Milham MP, 2014. The autism brain imaging data exchange: towards a large-scale evaluation of the intrinsic brain architecture in autism. Mol. Psychiatry 19, 659–667. [PubMed: 23774715]

Mazefsky CA, Oswald DP, 2006. The discriminative ability and diagnostic utility of the ADOS-G, ADI-R, and GARS for children in a clinical setting. Autism 10, 533–549. [PubMed: 17088271]

McAlonan GM, Cheung V, Cheung C, Suckling J, Lam GY, Tai KS, Yip L, Murphy DG, Chua SE, 2005. Mapping the brain in autism. A voxel-based MRI study of volumetric differences and intercorrelations in autism. Brain: J. Neurol 128, 268–276.

Mhiri I, Rekik I, 2020. Joint functional brain network atlas estimation and feature selection for neurological disorder diagnosis with application to autism. Med. Image Anal 60.

Mostafa S, Tang L, Wu F-X, 2019. Diagnosis of autism spectrum disorder based on eigenvalues of brain networks. Ieee Access 7, 128474–128486.

Murdaugh DL, Shinkareva SV, Deshpande HR, Wang J, Pennick MR, Kana RK, 2012. Differential deactivation during mentalizing and classification of autism based on default mode network connectivity. Plos One 7.

Mwangi B, Tian TS, Soares JC, 2014. A review of feature reduction techniques in neuroimaging. Neuroinformatics 12, 229–244. [PubMed: 24013948]

Nielsen JA, Zielinski BA, Fletcher PT, Alexander AL, Lange N, Bigler ED, Lainhart JE, Anderson JS, 2013. Multisite functional connectivity MRI classification of autism: ABIDE results. Front. Human Neurosci 7.

Niu K, Guo J, Pan Y, Gao X, Peng X, Li N, Li H, 2020. Multichannel deep attention neural networks for the classification of autism spectrum disorder using neuroimaging and personal characteristic data. Complexity 2020.

Nomi JS, Uddin LQ, 2015. Developmental changes in large-scale network connectivity in autism. Neuroimage Clin. 7, 732–741. [PubMed: 25844325]

Ogawa S, Lee TM, Tank ARKW, 1990. Brain magnetic resonance imaging with contrast dependent on blood oxygenation. Proc. Natl. Acad. Sci. U. S. A 87, 9868–9872. [PubMed: 2124706]

Pagani M, Bertero A, Liska A, Galbusera A, Sabbioni M, Barsotti N, Colenbier N, Marinazzo D, Scattoni ML, Pasqualetti M, Gozzi A, 2019. Deletion of autism risk gene Shank3 disrupts prefrontal connectivity. J. Neurosci 39, 5299–5310. [PubMed: 31061091]

Parisot S, Ktena SI, Ferrante E, Lee M, Guerrero R, Glocker B, Rueckert D, 2018. Disease prediction using graph convolutional networks: application to autism spectrum disorder and Alzheimer's disease. Med. Image Anal 48, 117–130. [PubMed: 29890408]

Payabvash S, Palacios EM, Owen JP, Wang MB, Tavassoli T, Gerdes M, Brandes-Aitken A, Cuneo D, Marco EJ, Mukherjee P, 2019. White matter connectome edge density in children with autism spectrum disorders: potential imaging biomarkers using machine-learning models. Brain Connect. 9, 209–220. [PubMed: 30661372]

Pinaya WHL, Mechelli A, Sato JR, 2019. Using deep autoencoders to identify abnormal brain structural patterns in neuropsychiatric disorders: a large-scale multi-sample study. Human Brain Mapping 40, 944–954. [PubMed: 30311316]

Plis SM, Hjelm DR, Salakhutdinov R, Allen EA, Bockholt HJ, Long JD, Johnson HJ, Paulsen JS, Turner JA, Calhoun VD, 2014. Deep learning for neuroimaging: a validation study. Front. Neurosci 8.

Plitt M, Barnes KA, Martin A, 2015. Functional connectivity classification of autism identifies highly predictive brain features but falls short of biomarker standards. Neuroimage-Clinical 7, 359–366. [PubMed: 25685703]

Qi S, Bustillo J, Turner JA, Jiang R, Zhi D, Fu Z, Deramus TP, Vergara V, Ma X, Yang X, Stevens M, Zhuo C, Xu Y, Calhoun VD, Sui J, 2020a. The relevance of transdiagnostic shared networks

to the severity of symptoms and cognitive deficits in schizophrenia: a multimodal brain imaging fusion study. Trans. Psychiatry 10, 149.

Qi S, Morris R, Turner JA, Fu Z, Jiang R, Deramus TP, Zhi D, Calhoun VD, Sui J, 2020b. Common and unique multimodal covarying patterns in autism spectrum disorder subtypes. Mol. Autism 11, 90. [PubMed: 33208189]

Rabany L, Brocke S, Calhoun VD, Pittman B, Corbera S, Wexler BE, Bell MD, Pelphrey K, Pearlson GD, Assaf M, 2019. Dynamic functional connectivity in schizophrenia and autism spectrum disorder: convergence, divergence and classification. Neuroimage-Clinical 24.

Rakhimberdina Z, Liu X, Murata T, 2020. Population graph-based multi-model ensemble method for diagnosing autism spectrum disorder. Sensors-Basel 20.

Rakic M, Cabezas M, Kushibar K, Oliver A, Liado X, 2020. Improving the detection of autism spectrum disorder by combining structural and functional MRI information. Neuroimage-Clinical 25.

Rashid B, Calhoun V, 2020. Towards a brain-based predictome of mental illness. Human Brain Mapping 41, 3468–3535. [PubMed: 32374075]

Reiter MA, Jahedi A, Fredo ARJ, Fishman I, Bailey B, Mueller R-A, 2020. Performance of machine learning classification models of autism using resting-state fMRI is contingent on sample heterogeneity. Neural Comput. Appl

Rojas DC, Peterson E, Winterrowd E, Reite ML, Rogers SJ, Tregellas JR, 2006. Regional gray matter volumetric changes in autism associated with social and repetitive behavior symptoms. Bmc Psychiatry 6, 56. [PubMed: 17166273]

Ronicko JFA, Thomas J, Thangavel P, Koneru V, Langs G, Dauwels J, 2020. Diagnostic classification of autism using resting-state fMRI data improves with full correlation functional brain connectivity compared to partial correlation. J. Neurosci. Methods 345.

Sabuncu MR, Konukoglu E, 2015. Clinical prediction from structural brain MRI scans: a large-scale empirical study. Neuroinformatics 13, 31–46. [PubMed: 25048627]

Sabuncu MR, Konukoglu E, Alzheimer's Dis N, 2015. Clinical prediction from structural brain MRI scans: a large-scale empirical study. Neuroinformatics 13, 31–46. [PubMed: 25048627]

Sadeghi M, Khosrowabadi R, Bakouie F, Mandavi H, Eslahchi C, Pouretemad H, 2017. Screening of autism based on task-free fMRI using graph theoretical approach. Psychiatry Res. Neuroimaging 263, 48–56. [PubMed: 28324694]

Safavian SR, Landgrebe D, 1991. A survey of decision tree classifier methodology. IEEE Trans. Syst. Man Cybern 21, 660–674.

Sahin M, Sur M, 2015. Genes, circuits, and precision therapies for autism and related neurodevelopmental disorders. Science.

Segovia F, Holt R, Spencer M, Gorriz JM, Ramirez J, Puntonet CG, Phillips C, Chura L, Baron-Cohen S, Suckling J, 2014. Identifying endophenotypes of autism: a multivariate approach. Front. Comput. Neurosci 8.

Sen B, Borle NC, Greiner R, Brown MRG, 2018. A general prediction model for the detection of ADHD and Autism using structural and functional MRI. Plos One 13.

Sewani H, Kashef R, 2020. An autoencoder-based deep learning classifier for efficient diagnosis of autism. Children-Basel 7.

Shahamat H, Abadeh MS, 2020. Brain MRI analysis using a deep learning based evolutionary approach. Neural Netw. 126, 218–234. [PubMed: 32259762]

Sherkatghanad Z, Akhondzadeh M, Salari S, Zomorodi-Moghadam M, Abdar M, Acharya UR, Khosrowabadi R, Solari V, 2020. Automated detection of autism spectrum disorder using a convolutional neural network. Front. Neurosci 13.

Song Y, Epalle TM, Lu H, 2019. Characterizing and predicting autism spectrum disorder by performing resting-state functional network community pattern analysis. frontiers in human. Neuroscience 13.

Soussia M, Rekik I, 2018. Unsupervised manifold learning using high-order morphological brain networks derived from T1-w MRI for autism diagnosis. Front. Neuroinform 12.

Spera G, Retico A, Bosco P, Ferrari E, Palumbo L, Oliva P, Muratori F, Calderoni S, 2019. Evaluation of altered functional connections in male children with autism spectrum disorders on multiple-site data optimized with machine learning. Front. Psychiatry 10.

Subbaraju V, Sundaram S, Narasimhan S, Suresh MB, 2015. Accurate detection of autism spectrum disorder from structural MRI using extended metacognitive radial basis function network. Expert Syst. Appl 42, 8775–8790.

Subbaraju V, Suresh MB, Sundaram S, Narasimhan S, 2017. Identifying differences in brain activities and an accurate detection of autism spectrum disorder using resting state functional-magnetic resonance imaging: a spatial filtering approach. Med. Image Anal. 35, 375–389. [PubMed: 27585835]

Sui J, Adali T, Yu Q, Chen J, Calhoun VD, 2012. A review of multivariate methods for multimodal fusion of brain imaging data. J. Neurosci. Methods 204, 68–81. [PubMed: 22108139]

Sui J, Jiang R, Bustillo J, Calhoun V, 2020. Neuroimaging-based individualized prediction of cognition and behavior for mental disorders and health: methods and promises. Biol. Psychiatry 88, 818–828. [PubMed: 32336400]

Szatmari P, Georgiades S, Duku E, Bennett TA, Bryson S, Fombonne E, Mirenda P, Roberts W, Smith IM, Vaillancourt T, Volden J, Waddell C, Zwaigenbaum L, Elsabbagh M, Thompson A, Team ftPiAS, 2015. Developmental trajectories of symptom severity and adaptive functioning in an inception cohort of preschool children with autism spectrum disorder. JAMA Psychiatry 72, 276–283. [PubMed: 25629657]

Tang L, Mostafa S, Liao B, Wu F-X, 2019. A network clustering based feature selection strategy for classifying autism spectrum disorder. Bmc Med. Genom 12.

Thomas RM, Gallo S, Cerliani L, Zhutovsky P, El-Gazzar A, van Wingen G, 2020. Classifying autism spectrum disorder using the temporal statistics of resting-state functional MRI data with 3D convolutional neural networks. Front. Psychiatry 11.

Uddin LQ, Menon V, Young CB, Ryali S, Chen T, Khouzam A, Minshew NJ, Hardan AY, 2011. Multivariate searchlight classification of structural magnetic resonance imaging in children and adolescents with autism. Biol. Psychiatry 70, 833–841. [PubMed: 21890111]

Uddin LQ, Supekar K, Lynch CJ, Khouzam A, Phillips J, Feinstein C, Ryali S, Menon V, 2013. Salience network-based classification and prediction of symptom severity in children with autism. Jama Psychiatry 70, 869–879. [PubMed: 23803651]

Waiter GD, Williams JH, Murray AD, Gilchrist A, Perrett DI, Whiten A, 2004. A voxel-based investigation of brain structure in male adolescents with autistic spectrum disorder. Neuroimage 22, 619–625. [PubMed: 15193590]

Wang H, Fan L, Song M, Liu B, Wu D, Jiang R, Li J, Li A, Banaschewski T, Bokde ALW, Quinlan EB, Desrivières S, Flor H, Grigis A, Garavan H, Chaarani B, Gowland P, Heinz A, Ittermann B, Martinot J-L, Martinot M-LP, Artiges E, Nees F, Orfanos DP, Poustka L, Millenet S, Fröhner JH, Smolka MN, Walter H, Whelan R, Schumann G, Jiang T, 2020a. Functional connectivity predicts individual development of inhibitory control during adolescence. Gereb. Cortex

Wang Y, Wang J, Wu F-X, Hayrat R, Liu J, 2020c. AIMAFE: autism spectrum disorder identification with multi-atlas deep feature representation and ensemble learning. J. Neurosci. Methods 343.

Wang J, Wang Q, Zhang H, Chen J, Wang S, Shen D, 2019c. Sparse multiview task-centralized ensemble learning for ASD diagnosis based on age- and sex-related functional connectivity patterns. Ieee Trans. Cybern 49, 3141–3154. [PubMed: 29994137]

Wang C, Xiao Z, Wang B, Wu J, 2019a. Identification of autism based on SVM-RFE and stacked sparse auto-encoder. Ieee Access 7, 118030–118036.

Wang C, Xiao Z, Wu J, 2019b. Functional connectivity-based classification of autism and control using SVM-RFECV on rs-fMRI data. Phys. Med 65, 99–105. [PubMed: 31446358]

Wang J, Zhang L, Wang Q, Chen L, Shi J, Chen X, Li Z, Shen D, Multi-Class ASD, 2020b. Classification based on functional connectivity and functional correlation tensor via multi-source domain adaptation and multi-view sparse representation. Ieee Trans. Med. Imaging 39, 3137–3147. [PubMed: 32305905]

Wang L, Zhu J, Zou H, 2008. Hybrid huberized support vector machines for microarray classification and gene selection. Bioinformatics 24, 412–419. [PubMed: 18175770]

Wee CY, Wang L, Shi F, Yap P-T, Shen D, 2014. Diagnosis of autism spectrum disorders using regional and interregional morphological features. Human Brain Mapping 35, 3414–3430. [PubMed: 25050428]

Wolfers T, Floris DL, Dinga R, van Rooij D, Isakoglou C, Kia SM, Zabihi M, Llera A, Chowdanayaka R, Kumar VJ, Peng H, Laidi C, Batalle D, Dimitrova R, Charman T, Loth E, Lai M-C, Jones E, Baumeister S, Moessnang C, Banaschewski T, Ecker C, Dumas G, O'Muircheartaigh J, Murphy D, Buitelaar JK, Marquand AF, Beckmann CF, 2019. From pattern classification to stratification: towards conceptualizing the heterogeneity of Autism Spectrum Disorder. Neurosci. Biobehav. Rev 104, 240–254. [PubMed: 31330196]

Xiao X, Fang H, Wu J, Xiao C, Xiao T, Qian L, Liang F, Xiao Z, Chu KK, Ke X, 2017. Diagnostic model generated by MRi-derived brain features in toddlers with autism spectrum disorder. Autism Res. 10, 620–630. [PubMed: 27874271]

Xiao Z, Wang C, Jia N, Wu J, 2018. SAE-based classification of school-aged children with autism spectrum disorders using functional magnetic resonance imaging. Multimedia Tools Appl. 77, 22809–22820.

Xiao Z, Wu J, Wang C, Jia N, Yang X, 2019. Computer-aided diagnosis of school-aged children with ASD using full frequency bands and enhanced SAE: a multi-institution study. Exp. Ther. Med 17, 4055–4063. [PubMed: 31007742]

Yahata N, Morimoto J, Hashimoto R, Lisi G, Shibata K, Kawakubo Y, Kuwabara H, Kuroda M, Yamada T, Megumi F, Imamizu H, Nanez JE Sr., Takahashi H, Okamoto Y, Kasai K, Kato N, Sasaki Y, Watanabe T, Kawato M, 2016. A small number of abnormal brain connections predicts adult autism spectrum disorder. Nat. Commun 7.

Yamagata B, Itahashi T, Fujino J, Ohta H, Nakamura M, Kato N, Mimura M, Hashimoto R.-i, Aoki Y, 2019. Machine learning approach to identify a resting-state functional connectivity pattern serving as an endophenotype of autism spectrum disorder. Brain Imaging Behav. 13, 1689–1698. [PubMed: 30280304]

Yang X, Schrader PT, Zhang N, 2020. A deep neural network study of the ABIDE repository on autism spectrum classification. Int. J. Adv. Comput. Sci. Appl 11, 1–6.

Yin W, Mostafa S, Wu F-X, 2020. Diagnosis of autism spectrum disorder based on functional brain networks with deep learning. J. Comput. Biol

Zhang F, Savadjiev P, Cai W, Song Y, Rathi Y, Tunc B, Parker D, Kapur T, Schultz RT, Makris N, Verma R, O'Donnell LJ, 2018. Whole brain white matter connectivity analysis using machine learning: an application to autism. Neuroimage 172, 826–837. [PubMed: 29079524]

Zhang L, Wang M, Liu M, Zhang D, 2020a. A survey on deep learning for neuroimaging-based brain disorder analysis. Front. Neurosci 14.

Zhang L, Wang X-H, Li L, 2020b. Diagnosing autism spectrum disorder using brain entropy: a fast entropy method. Comput. Methods Prog. Biomed 190.

Zhan Y, Wei J, Liang J, Xu X, He R, Robbins TW, Wang Z, 2020. Diagnostic classification for human autism and obsessive-compulsive disorder based on machine learning from a primate genetic model. Am. J. Psychiatry appiajp202019101091-appiajp.

Zhao F, Chen Z, Rekik I, Lee S-W, Shen D, 2020a. Diagnosis of autism spectrum disorder using central-moment features from low- and high-order dynamic resting-state functional connectivity networks. Front. Neurosci 14.

Zhao J, Huang J, Zhi D, Yan W, Ma X, Yang X, Li X, Ke Q, Jiang T, Calhoun VD, Sui J, 2020b. Functional network connectivity (FNC)-based generative adversarial network (GAN) and its applications in classification of mental disorders. J. Neurosci. Methods 341, 108756. [PubMed: 32380227]

Zhao F, Zhang H, Rekik I, An Z, Shen D, 2018. Diagnosis of autism spectrum disorders using multi-level high-order functional networks derived from resting-state functional MRI. Front. Human Neurosci 12.

Zhou Y, Yu F, Duong T, 2014. Multiparametric MRI characterization and prediction in autism spectrum disorder using graph theory and machine learning. PLOS One 9, e90405. [PubMed: 24922325]

Zu C, Gao Y, Munsell B, Kim M, Peng Z, Cohen JR, Zhang D, Wu G, 2019. Identifying disease-related subnetwork connectome biomarkers by sparse hypergraph learning. Brain Imaging Behav. 13, 879–892. [PubMed: 29948906]

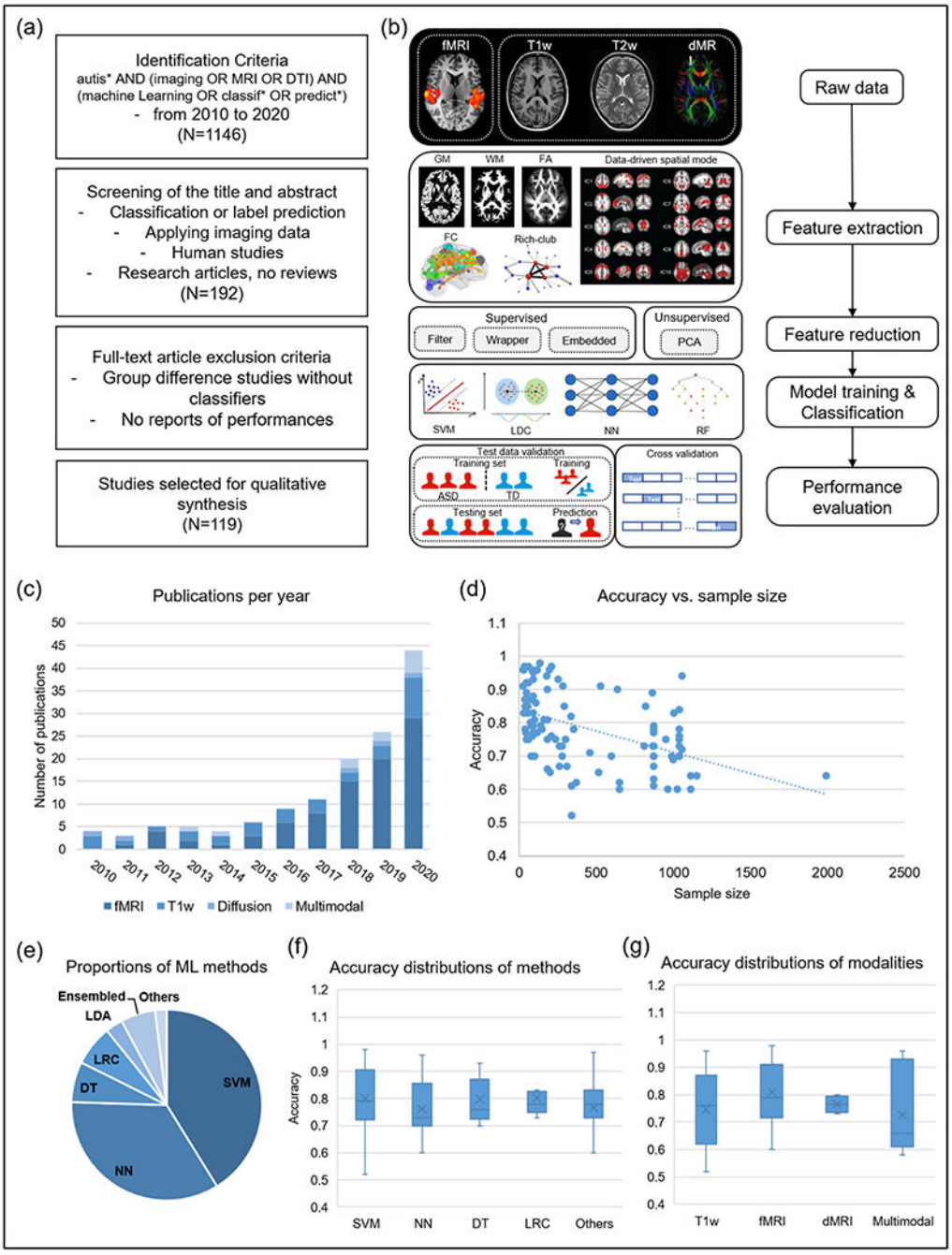

Fig. 1.

Literature search results and general machine-learning pipeline. (a) Literature search results for each step. (b) Summery of machine learning pipelines. (c) The number of publications based on different imaging modalities per year. (d) Scatter plot of the classification accuracy vs. sample size (articles without specific accuracy are excluded in Fig. 1d–g, resulting in 105 left papers). (e) Proportions of machine learning methods used for classification. Pie of other methods mainly includes sporadically used methods, such as Gaussian process classification and leave-one-out classifier *etc*. (f) Distributions of classification accuracy for

different methods. Box of other methods includes ensemble learning based methods and sporadically used methods. (g) Distributions of classification accuracy for different imaging modalities.

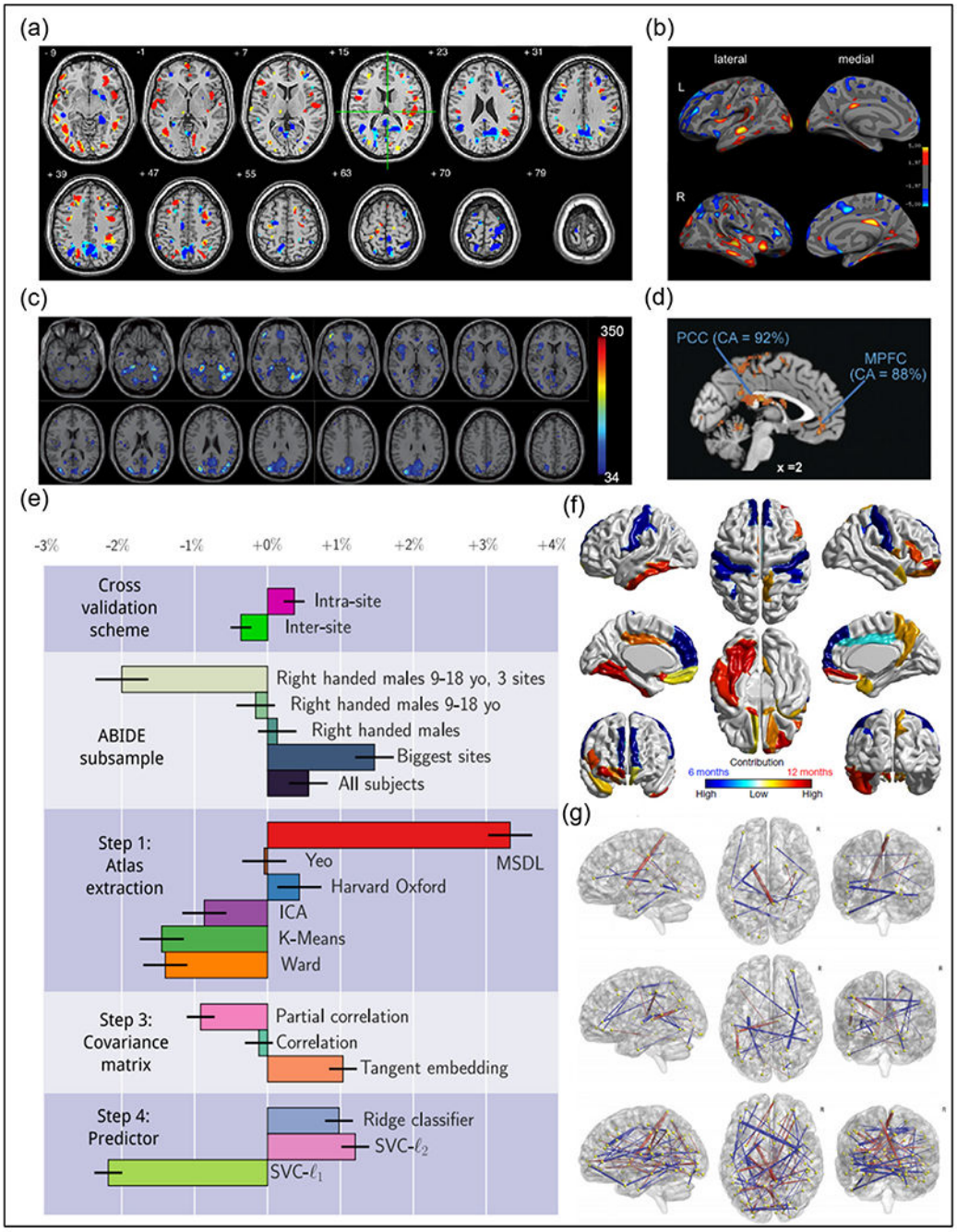

Fig. 2.

Representative classification studies in ASD. (a) Gray matter maps that carry out the most discriminative information for adult ASD classification (Ecker et al., 2010b), and most clusters are located in parietal-frontal regions. (b) The regions where cortical thickness has relatively high contributions to the adult ASD classification (Ecker et al., 2010a). (c) Brain regions that involve in discriminative connectivity for ASD classification (Anderson et al., 2011). (d) Relatively high classification accuracies for children with ASD were obtained from gray matter in PCC and MPFC (Uddin et al., 2011). (e) Impact of pipeline steps on

ASD classification based on ABIDE data (Abraham et al., 2017). (f) cortical regions with surface area measurements at 6 and 12 months contributing to the prediction of 24 months diagnosis (Hazlett et al., 2017). (g) FCs that show abnormal alterations in 6-month children who developed ASD at 24 months (Emerson et al., 2017).

Table 1

Summary of 119 ASD classification studies after screening.

Modality	Subjects	Age(years)	Sex-male	Feature	Classifier	Accuracy	Reference
T1w	HC=20 ASD=20	33±11	100%	Volumetric and geometric features of selected regions	SVM	85%	(Ecker et al., 2010a)
T1w	HC=22 ASD=22	27±7	100%	GM and WM maps of whole brain	SVM	77%	(Ecker et al., 2010b)
T1w	HC=16 ASD=22	9.2±2.1	84%	Regional cortical thickness measurements	Logistic model	87%	(Jiao et al., 2010)
fMRI	HC=40 ASD=40	22.7±7.4	100%	ROI-based FC	Leave-one-out classifier	79%	(Anderson et al., 2011)
T1w	HC=24 ASD=24	13.2±0.6	91%	GM and WM maps of whole brain	SVM	92%	(Uddin et al., 2011)
DTI	HC=45 ASD=30	10.5±2.5	75%	FA and MD of brain regions	SVM	80%	(Ingalhalikar et al., 2011)
fMRI	HC=29 ASD=29	n.s.	83%	Multi-scale FC pattern information	LRC	82.8%	(Hui et al., 2012)
fMRI	HC=14 ASD=13	21.4±3.9	100%	Whole-brain and seed-based connectivity patterns	LRC	96%	(Murdaugh et al., 2012)
fMRI	HC=12 ASD=12	23.7±7.1	71%	The degree of each ROI in functional networks	SVM	91%	(Barttfeld et al., 2012)
T1w	HC=38 ASD=38	4.4±1.5	0%	Whole-brain GM map	SVM	AUC=80%	(Calderoni et al., 2012)
fMRI dMRI	HC=15 ASD=15	21.1±0.9	n.s.	FC and FA value	SVM	95.9%	(Deshpande et al., 2013)
T1w	ADHD=29 ASD=29	14.9±1.9	n.s.	Whole-brain GM maps	GPC	85.2%	(Lim et al., 2013)
fMRI	HC=20 ASD=20	9.9±1.5	80%	ICA components	LRC	78%	(Uddin et al., 2013)
fMRI	HC=517 ASD=447	16.6±8.1	85.3%	ROI based FC	Leave-one-out classifier	60%	(Nielsen et al., 2013)
T1w	HC=59 ASD=58	10.8±4.0	76%	Regional and interregional morphological features	SVM	96.3%	(Wee et al., 2014)
T1w	HC=40 ASD=52	14.4±1.7	67%	GM map	SVM	77.2%	(Segovia et al., 2014)
fMRI	HC=17 ASD=17	25.6±6.7	94%	Voxels selected by factor analysis	Naïve bayes classifier	97%	(Just et al., 2014)
T1w fMRI	HC=153 ASD=127	13.5±6	86%	Integration of GM and FC of selected regions	Random tree classifier	70%	(Zhou et al., 2014)

Modality	Subjects	Age(years)	Sex-male	Feature	Classifier	Accuracy	Reference
T1w	HC=325 ASD=325	17.8±7.4	88%	Volumetric and thickness measurements of ROIs	SVM	60%	(Sabuncu and Konukoglu, 2015)
T1w	HC=20 ASD=21	4.1±0.8	n.s.	Regional morphological features	SVM	AUC=74%	(Gori et al., 2015)
fMRI	HC=328 ASD=312	13.2±3.1	84%	ROI based FC	PNN	90%	(Iidaka, 2015)
fMRI	HC=59 ASD=59	17.7±2.7	100%	ROI based FC	LRC/SVM	76.7%	(Plitt et al., 2015)
T1w	HC=546 ASD=508	n.s.	85.3%	Gray matter probability values of selected regions	NN	60%-98%	(Subbaraju et al., 2015)
fMRI	HC=14 ASD=15	28.6±1.9	86.2%	Beta maps of two tasks	SVM	82.8%	(Chanel et al., 2016)
fMRI	HC=128 ASD=112	14.8±1.7	85.4%	ROI based FC of different frequency bands	SVM	79.17%	(Chen et al., 2016)
T1w	HC=573 ASD=538	17.3±8.4	85.2%	Histogram of oriented gradients features	Ensembled classifiers	60%	(Ghiassian et al., 2016)
fMRI	HC=107 ASD=74	31.4±8.5	82%	Region based FC	LRC	75%	(Yahata et al., 2016)
fMRI	HC=55 ASD=55	12.7±2.4	76.4%	ROI-based FC	NN	86.36%	(Guo et al., 2017)
fMRI	HR=145 ASD=34	0.5, 1.0, 2.0	63%	Cortical thickness, regional surface area, sex, volume	NN	94%	(Hazlett et al., 2017)
fMRI	HC=144 ASD=119	<20	n.s.	ROI-based FC	DRBM	67.42%	(Kam et al., 2017)
fMRI	HC=31 ASD=29	20.5±6.2	100%	Nodal metrics of ROI-based FC network	SVM	92%	(Sadeghi et al., 2017)
fMRI	HC=126 ASD=126	17.3±6.0	80.6%	ROI-based FC	CRF	92.8%	(Jahedi et al., 2017)
fMRI	HC=530 ASD=505	6.5–58	85.2%	ROI-based FC	SVM	78%-95%	(Subbaraju et al., 2017)
T1w	HC=39 ASD=46	2.3±0.3	88.2%	Regional cortical thickness	RF	75.6%	(Xiao et al., 2017)
fMRI	HC=468 ASD=403	n.s.	83.5%	Connectivity measures between all pairs of regions	SVM	66.8%	(Abraham et al., 2017)
fMRI	HR=48 ASD=11	0.5, 2.0	69.5%	ROI-based FC	SVM	96.6%	(Emerson et al., 2017)
fMRI sMRI	HC=69 ASD=116	5-10	n.s.	Regional based mean time series, GM and WM	DBN	65.56%	(Aghdam et al., 2018)
fMRI	HC=30 ASD=24	15.5±1.0	87%	Time of in-phase coherence of pairs of networks	SVM	86.7%	(Bernas et al., 2018)

Modality	Subjects	Age(years)	Sex-male	Feature	Classifier	Accuracy	Reference
fMRI	HC=205 ASD=167	19.7±5.3	81.7%	ROI based FC	SVM	62%	(Bhaumik et al., 2018)
fMRI	HC=72 AS=63	13.6±5.5	82%	ROI based FC	GE-RSVM	97.5%	(Bi et al., 2018a)
fMRI	HC=42 ASD=50	13.3±2.4	88%	Graph metrics of ROI-based FC	NN	95%	(Bi et al., 2018b)
fMRI	HC=39 ASD=45	13.4±2.4	88.1%	Graph metrics of ROI-based FC	SVM	96.15%	(Bi et al., 2018c)
fMRI	HC=160 ASD=123	12.9±3	53.3%	Power spectral densities of ROIs	SVM	91%	(Dekhil et al., 2018)
T1w	HC=325 ASD=325	17.8±7.4	88.6%	Cortical thickness	NN	62%	(Demirhan, 2018)
fMRI	HC=530 ASD=505	Site specific	Site specific	ROI-based FC	NN	70%	(Heinsfeld et al., 2018)
fMRI	HC=652 ASD=369 ADHD=284	7-21	100%	Connectivity factors identified by hierarchical Bayesian modeling	SVM	67.33%	(Kernbach et al., 2018)
fMRI	HC=468 ASD=403	n.s.	n.s.	ROI-based FC	s-GCN	62.9%	(Ktena et al., 2018)
fMRI	HC=161 ASD=149	Site specific	Site specific	ROI-based FC	NN	67.1%	(Li et al., 2018)
fMRI	HC=468 ASD=403	n.s.	n.s.	ROI-based FC	GCN	70.4%	(Parisot et al., 2018)
fMRI T1w	HC=573 ASD=538	Site specific	Site specific	Texture features and network features	SVM	64.3%	(Sen et al., 2018)
T1w	HC=186 ASD=155	16.9±6.3	86.5%	Low-order and high-order morphological networks	Ensemble	61.2%	(Soussia and Rekik, 2018)
fMRI	HC=42 ASD=42	9.9±1.5	82.1%	Time courses of networks	NN	87.2%	(Xiao et al., 2018)
dMRI	HC=70 ASD=79	11.0±2.6	100%	FA and MD for fiber clusters	SVM	78.3%	(Zhang et al., 2018)
fMRI	HC=46 ASD=54	10.7±2.3	87%	Low-order and high-order FC	Ensemble	81%	(Zhao et al., 2018)
fMRI	HC=249 ASD=210	5-10	72.1%	Fast Fourier transformed fMRI around three axes	CNN	70.5%	(Aghdam et al., 2019)
fMRI	HC=37 ASD=42	13.0±2.0	84.8%	Graphlet-based network feature	Decision tree	69.81%	(Ataei et al., 2019)
fMRI	HC=106 ASD=103	14.2±3.3	88.5%	Graph metrics derived from FC	GE-RSVM	96.8%	(Bi et al., 2019)

Modality	Subjects	Age(years)	Sex-male	Feature	Classifier	Accuracy	Reference
fMRI T1w	HC=113 ASD=72	13.5±2.6	44.3%	ROI-based FC, geometric and volumetric features	RF	81%	(Dekhil et al., 2019)
fMRI sMRI	HC=47 ASD=46	13.6±2.8	82.8%	ROI-based FC and various anatomic features	CRF	92.5%	(Eill et al., 2019)
fMRI	HC=530 ASD=505	Site specific	Site specific	ROI-based FC	NN	70.3%	(Eslami et al., 2019)
T1w	HC=150 ASD=50	18.14	n.s.	Cortical curvature, thickness and sulcal depth	SVM	65%	(Graa and Rekik, 2019)
fMRI	HC=47 ASD=45	11.1±2.3	80.4%	Multiple group-sparse networks	SVM	79.4%	(Huang et al., 2019)
fMRI	HC=171 ASD=121	14.4±5.8	78.4%	Likelihood map based on trained region-wise HMM	SVM	84.6%	(Jun et al., 2019)
fMRI	HC=125 ASD=86	11.4±2.1	100%	ROI-based FC	SVM	76.3%	(Jung et al., 2019)
fMRI	Total 816	5-65	n.s.	Graph metrics of ROI-based FC	SVM	69%-95%	(Kazeminejad and Sotero, 2019)
T1w	HC=104 ASD=78	14.5±5.3	80.2%	ROI based morphological connectivity	NN	90.39%	(Kong et al., 2019)
fMRI	HC=455 ASD=409	17.4±8.6	86.2%	Interhemispheric connectivity	SVM	88.7%	(Li et al., 2019)
fMRI	HC=468 ASD=403	Site specific	Site specific	Eigenvalues of Laplacian matrix of networks, graphic metrics	LDA	77.7%	(Mostafa et al., 2019)
DTI	HC=33 ASD=14	8.9±2.7	100%	Edge-density map	RF	75.3%	(Payabvash et al., 2019)
T1w	HC=105 ASD=83	27.3±4.1	88.3%	ROI based volumetric measurements	DAE	AUC=63.9%	(Pinaya et al., 2019)
fMRI	HC=34 ASD=32 SZ=33	23.5±0.7	77.3%	Dynamic functional connectivity	LDA	Sensitivity=50.0%	(Rabany et al., 2019)
fMRI	HC=116 ASD=119	Site specific	Site specific	Community pattern descriptors of FC	LDA	75%	(Song et al., 2019)
fMRI	HC=88 ASD=102	Site specific	100%	ROI-based FC	SVM	AUC=75%	(Spera et al., 2019)
fMRI	HC=37 ASD=42	n.s.	n.s.	Connectivity of pairs of ROIs in DMN	SVM	AUC=62.6%	(Tang et al., 2019)
fMRI	HC=553 ASD=501	Site specific	Site specific	ROI-based FC	SAE	93.59%	(Wang et al., 2019a)
fMRI	HC=276 ASD=255	Site specific	Site specific	ROI-based FC	SVM	90.6%	(Wang et al., 2019b)
fMRI	HC=159 ASD=120	Site specific	78.1%	Low-order and high-order FC	Ensemble	72.6%	(J. Wang et al., 2019)

Modality	Subjects	Age(years)	Sex-male	Feature	Classifier	Accuracy	Reference
fMRI	HC=81 ASD=117	9.32±5.62	75.6%	Time-series of independent components	NN	96.3%	(Xiao et al., 2019)
fMRI	HC=45 ASD=15	28.3±6.1	100%	ROI-based FC	SLR	75%	(Yamagata et al., 2019)
fMRI	HC=47 ASD=45	11.1±2.3	80.4%	Subnetworks learned by hypergraph inference	STM	87.7%	(Zu et al., 2019)
fMRI	HC=573 ASD=529	Site specific	Site specific	Feature extracted by CNN	Ensemble	82.7%	(Ahmed et al., 2020)
T1w	HC=75 ASD=76	11.5±2.0	100%	Multiscale descriptor of brain regions	SVM	AUC=75%	(Alvarez-Jimenez et al., 2020)
fMRI DWI	HC=468 ASD=403	Site specific	Site specific	Features constructed by graph signal processin	SVM	60.9%	(Brahim and Farrugia, 2020)
fMRI	HC=556 ASD=432	Site specific	Site specific	ROI-based FC and corresponding network metrics	SVM	70.1%	(Chaitra et al., 2020)
T1w	HC=131 ASD=119	Site specific	Site specific	3D HOG	SVM	AUC>75%	(Chen et al., 2020)
fMRI T1w	HC=521 ASD=561	Site specific	Site specific	FC, anatomical and geometric measures	RF	sMRI:0.78-1 fMRI:0.79-1	(Dekhil et al., 2020)
DTI	HC=139 ASD=124	8-17.9	50.2%	FA, MD, AD, skewness RD	SVM	73%	(Elnakieb et al., 2020)
fMRI	HC=157 ASD=145	16.4±6.5	100%	Likelihood maps derived from HMM	SVM	74.9%	(Fan et al., 2020)
T1w	HC=1166 ASD=1060	Site specific	Site specific	Brain morphometric features	LR	AUC=0.79	(Ferrari et al., 2020)
T1w	HC=186 ASD=155	n.s.	n.s.	Morphological brain networks (feature selection)	SVM	52%	(Georges et al., 2020)
fMRI	HC=88 ASD=73	n.s.	13.9±6.3	Nodal hub measures and connectivity features	NN	81.2%	(Gupta et al., 2020)
fMRI	HC=468 ASD=403	Site specific	Site specific	ROI-based FC	NN	69.8%	(Hu et al., 2020)
fMRI	HC=197 ASD=159	Site specific	Site specific	FC based on multi-atlas	Ensemble	77.6%	(F. Huang et al., 2020)
fMRI	HC=530 ASD=505	Site specific	Site specific	ROI-based average time series and graph-based feature selection	DBN	76.4%	(Z.-A. Huang et al., 2020)
fMRI	HC=464 ASD=402	Site specific	Site specific	Network embedding	GCN	73.1%	(H. Jiang et al., 2020)
fMRI	HC=540 ASD=483	Site specific	93.8%	ROI-based FC and graphic measures	NN	60%	(Kazeminejad and Sotero, 2020)
T1w	HC=1046 ASD=946	Site specific	site specific	Normalized image	NN	64%	(Ke et al., 2020)

J Neurosci Methods. Author manuscript; available in PMC 2022 April 13.

Modality	Subjects	Age(years)	Sex-male	Feature	Classifier	Accuracy	Reference
fMRI	HC=530 ASD=505	Site specific	Site specific	ROI-based FC (NN-based feature selection)	LR	73%	(Khan et al., 2020)
fMRI	HC=556 ASD=442	7-58	Site specific	ROI-based FC	SVM	69.2%	(Lanka et al., 2020)
fMRI	HC=15903 ASD=1711	n.s.	n.s.	ROI-based FC	NN	67.0%	(Leming et al., 2020)
fMRI	HC=184 ASD=186	Site specific	Site specific	ROI-based FC	NN	63%-85%	(Li et al., 2020)
fMRI	HC=468 ASD=403	17.1±8.0	83.5%	ROI-based DFC	SVM	76.8%	(J. Liu et al., 2020)
fMRI	HC=548 ASD=506	16.6±8.1	85.3%	ROI-based FC	SVM	72.2%	(Y. Liu et al., 2020)
fMRI	HC=245 ASD=272	n.s.	n.s.	ROI-based FC	SVM	65.0%	(Mhiri and Rekik, 2020)
fMRI	HC=401 ASD=408	16.5±6.7	84.3%	FC and personal characteristic	NN	73.2	(Niu et al., 2020)
fMRI	HC=468 ASD=403	16.94	83.5%	Graph constructed based on FC	Ensemble NN	73.1%	(Rakhimberdina et al., 2020)
fMRI T1w	HC=449 ASD=368	Site specific	Site specific	ROI-based FC and structural connectivity	Ensemble NN	85.1%	(Rakic et al., 2020)
fMRI	HC=350 ASD=306	6-18	n.s.	The effect of gender and severity FC	RF	62.5%-73.75%	(Reiter et al., 2020)
fMRI	HC=300 ASD=300	11.87±2.8	81%	ROI-based FC	NN	70.3%	(Ronicko et al., 2020)
fMRI	Total 1035	n.s.	n.s.	FC	NN	84.1%	(Sewani and Kashef, 2020)
T1w	HC=500 ASD=500	14.7	n.s.	Normalized raw image	3D-CNN	70%	(Shahamat and Abadeh, 2020)
fMRI	HC=530 ASD=505	Sie specific	Site specific	ROI-based FC	CNN	70.2%	(Sherkatghanad et al., 2020)
fMRI	HC=532 ASD=620	Site specific	Site specific	fALFF ReHo ALFF Centrality	3D-CNN	64%	(Thomas et al., 2020)
fMRI DTI	HC=234 AT=95 AS=53	6.5-64	Site specific	FC and derived FA map	MVSRC	57.8%	(J. Wang et al., 2020)
fMRI	HC=530 ASD=419	16.9±7.8	84.6%	ROI-based FC	NN	74.5%	(Y. Wang et al., 2020)
fMRI	HC=530 ASD=505	6-64	84.8%	ROI-based FC	NN	75.3%	(Yang et al., 2020)
fMRI	HC=468 ASD=403	6-64	n.s.	ROI-based FC	NN	79.2%	(Yin et al., 2020)

Modality	Subjects	Age(years)	Sex-male	Feature	Classifier	Accuracy	Reference
fMRI	HC=203 ASD=133	n.s.	n.s.	Monkey derived FC	SLR	82.14%	(Zhan et al., 2020)
fMRI	HC=47 ASD=45	7-15	78.2%	Low-order and high-order FC	SVM	83%	(F. Zhao et al., 2020)

Note: HC = healthy controls. ASD = Autism spectrum disorder. HR = high ASD risk infants. Age(years): the age in years and its standard deviation, some studies only give an age range. Sex(male): the percentage of males in entire datasets. N.S: not specified in study.