Title page

Voice acoustics as a potential biomarker for autism spectrum disorder

Authors

Frédéric Briend, PhD[1,2]* ; Céline David, PhD[2] ; Silvia Silleresi, PhD[3] ; Joëlle Malvy, MD, PhD[1,2] ; Sandrine Ferré, PhD[1,2] ; Marianne Latinus, PhD[1,2,4]*

Affiliations

[1] EXAC·T, Centre Universitaire de Pédopsychiatrie, CHRU de Tours, Tours, France

[2] UMR 1253, iBrain, Université de Tours, INSERM, 37000 Tours, France

[3] University of Milano-Bicocca, Department of Psychology, Milan, Italy

[4] Centro de Estudios en Neurociencia Humana y Neuropsicología. Facultad de Psicología. Universidad Diego Portales, Santiago, Chile

* These authors contributed equally to this work

Corresponding Author: Marianne Latinus: marianne.latinus@univ-tours.fr

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Running title

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Abstract

Early identification of children on the autism spectrum is crucial for early intervention with long-term positive effects on symptoms and skills. The need for improved objective autism detection tools is emphasized by the poor diagnostic power in current tools. Here, we aim to evaluate the diagnostic power of genuine acoustic features of the voice in children with autism spectrum disorder (ASD) with respect to a heterogeneous control group (composed of neurotypical children and children with Developmental Language Disorder [DLD] and children with sensorineural hearing loss with Cochlear Implant [CI]). This retrospective diagnostic study was conducted at the University Child Psychiatry Center of Tours (France). A total of 108 children, including 38 diagnosed with ASD (8.5 ± 0.25 years), 24 typically developing (TD; 8.2 ± 0.32 years) children and 46 children with atypical development (DLD and CI; 7.9 ± 0.36 years) were enrolled in our studies. We applied a ROC (Receiving Operator Characteristic) supervised clustering algorithm combined with cross-validation to develop a diagnostic model that can differentially diagnose a child with unknown disorder. The acoustic properties of speech samples produced by children in the context of a nonword repetition task were examined. We showed that voice acoustics predicted the diagnosis of autism with an overall accuracy of 91% [CI95%, 90.40%-91.65%] against TD children, and of 85% [CI95%, 84.5%-86.6%] against an heterogenous group of non-autistic children. Accuracy reported here with multivariate analysis is higher than in previous studies. Our findings demonstrate that easy-to-measure voice acoustic parameters could be used as a diagnostic aid tool, specific of ASD.

Introduction

The human voice carries a wealth of information regarding a speaker, its physical characteristics, state of mind and health. From birth, the voice is used to signal information on well-being to surrounding adults, and infant cries are part of the preliminary assessment of neonates' health. Atypical acoustic cry features are associated with central nervous system dysfunction in human neonates (LaGasse et al., 2005) and rodent pups (Scattoni et al., 2009). Autism spectrum disorder (ASD) is a class of prenatal neurodevelopmental disorders (Bonnet-Brilhault et al., 2018) defined by the co-occurrence of two main diagnostic criteria: a socio-emotional impairment and a behavioral deficit manifested by repetitive behaviors and interests (Lord et al., 2018). Socio-emotional impairments affect both the production and perception of social signal. To this day, there is no reliable biomarker of ASD, and diagnostic is essentially based on a pluridisciplinary clinical assessment of the child (Bonnet-Brilhault et al., 2018). Atypical voice prosody is one of the earliest markers of ASD (Fusaroli et al., 2017; Guo et al., 2022; Kanner, 1943; Paul et al., 2005), evaluated in diagnostic tools such as ADOS (Lord et al., 2000); here, we asked whether genuine voice features could be used as a diagnostic biomarker, specific of ASD.

Machine learning techniques are increasingly used for medical diagnosis, especially clustering which is a powerful tool for detecting patterns in datasets. Several studies have used clustering methods in order to develop diagnostic biomarker of various pathologies in animal models (Cohen et al., 2005; Nikas and Low, 2011) and in human trials (Alashwal et al., 2019; Tokuda et al., 2021; Trevithick et al., 2015). A classical and robust clustering algorithm, the k-Means clustering algorithm (Forgy, 1965) yields high discriminating power to diagnose a single unknown subject in a given disorder state (Alashwal et al., 2019; Nikas and Low, 2011). Here, we used voice acoustics (Fig. 1) as the selected features included in this common clustering

method to evaluate their diagnostic power of ASD relative to typical development and other pathologies. We evaluated the diagnostic power of voice acoustics in comparison not only to TD children (study 1) but also to children with other disorders sharing common deficits with ASD: sensorineural hearing loss and Developmental Language Disorder (DLD, study 2). These two pathologies were chosen due to observed commonalities in the language domain between children with DLD and autism (Georgiou and Spanoudis, 2021) and between children with sensorineural hearing loss and with cochlear implants (CI) and autism (Robertson, 2013). The acoustic properties of speech samples produced by autistic children in the context of a nonword repetition task (NRT) (Dos Santos and Ferré, 2018) were examined. Data were analyzed with unsupervised and ROC (Receiving Operator Characteristic) supervised clustering algorithm.

Results

Classification of autistic children with respect to TD children

To investigate the discriminative power of voice acoustics between autistic children and TD children, we performed K-means clustering analysis (KCA). Data were randomly split into a train group (N = 33; 20 ASD, 13 TD) and a test group (unknown data; N = 16; 9 ASD; 7 TD); this was done 500 times. Unsupervised KCA with the 19 acoustics variables was conducted on the train group, and the model was cross-validated using unknown data from the test group. We observed a percent of variation (PV, the dispersion between the two clusters; see Methods) of 83.20% $\pm$ 1.33, a sensitivity of 0.74 $\pm$ 0.11 and a specificity of 0.92 $\pm$ 0.12 in the training group. The unsupervised KCA correctly classified 73.1% [71.8%-74.4%] of ASD and 92.3% [91.4%-93.1%] of TD children (Fig. 2b).

Our goal was to find optimum KCA settings, which best separate the ASD and the TD group to develop diagnostic model. Therefore, we performed ROC curve analysis, to conduct ROC-supervised KCA (Bonnet-Brilhault, 2020; Nikas and Low, 2011) on training and test data with

500 bootstrap replications. The four most discriminant (Area Under the Curve [AUC] > 80%) acoustics parameters according to ROC analysis on the training group were mean F1, mean HNR, mean shimmer and jitter skewness. The ROC-supervised KCA setting yielded a considerable improvement over unsupervised KCA: as shown in Fig. 2, the ROC-supervised KCA had a PV of 63.85% ± 3.00, a sensitivity of 0.89 ± 0.06 and a specificity of 0.94 ± 0.10; it classified correctly 89% [88.1%-90.0%] of ASD and 93% [92.7%-94.3%] of the TD group. ROC supervision allows decreasing false negatives.

Classification of autistic children with respect to a control population

Next, we evaluated the diagnostic power of voice acoustics in comparison not only to TD children but also to children with other disorders sharing common deficits with ASD: sensorineural hearing loss and Developmental Language Delay. As previously described, we conducted a ROC-supervised KCA on the data of all participants, considering children with DLD, children with CI and TD children in the same group of heterogeneous control group (CTRL). See Supplementary table 1 for details about the unsupervised KCA.

Two acoustic parameters discriminated ASD from CTRL children according to ROC analysis: mean shimmer and F1, with an AUC, respectively of 85.23% and 82.36% (the separation is depicted in the Fig. 3c). The ROC-supervised KCA had a PV of 57.42% ± 3.04, a sensitivity of 0.86 ± 0.05 and a specificity of 0.84 ± 0.08; it classified correctly 85.56% [84.5%-86.6%] of ASD and 84.2% [83.5%-85.0%] of the CTRL group. More specifically, in this latter heterogeneous population, 68.3% [66.8%-70.5%] of DLD, 85.6% [84.4%-86.8%] of CI and 93.9% [93.1%-94.7%] of TD were correctly classified (Fig. 3b).

Discussion

Voice as clustering diagnostic approach?

The ROC-supervised KCA analysis, with classification accuracy around 90%, had an extremely high diagnostic power when separating ASD from TD children above previously reported classification value (between 80 and 85% (Bonneh et al., 2011; Guo et al., 2022). Moreover, our method proves robust and reliable in discriminating autistic children from children without ASD, including other disorders (84%).

Importantly, acoustic factors predictive of autism diagnosis are mainly ones related to imperfect control of the vocal folds' vibrations (e.g., jitter, shimmer) rather than the f0 *per se* (Fusaroli et al., 2017), consistent with clinical description of a peculiar voice quality in autism and previous observations (Bone et al., 2014). The pattern characteristics of autism, with respect to TD children, was lower average F1, higher HNR, higher shimmer and lower jitter skewness. A lower jitter skewness reflected a more normal distribution of jitter across nonwords; TD children presented positively skewed and less tailed distribution, highlighting that most vocal sounds had similar shimmer and jitter. A higher HNR suggested that vocal sounds of children on the autism spectrum are overall less noisy than those produced by TD children. The lower F1 in the ASD group did not reflect gender balance differences across groups as in the TD group male and female children had similar F1 values (938 Hz and 937 Hz). Note that when including the other pathologies, only mean F1 and mean shimmer remained diagnostic features. Average F1 values were at the minimum 100 Hz lower in autistic children than in the other children; this is unlikely explained by gender imbalance as the second lowest F1 was observed for female (815 Hz) of the CI group, and F1 was the largest in male of the same group. F1 frequency is related to the length of the vocal tract (Vorperian and Kent, 2007) and tend to decrease with age; a lower F1 could reflect either an accelerated maturation of the vocal tract or differences in cranio-facial anatomy (Tripi et al., 2019) and the presence of increased minor physical anomalies in autistic children (Tripi et al., 2018). Shimmer, which is a measure of cycle-to-cycle variation in amplitude of the *f0*, presented an increased value of almost 16% in autism;

although discriminant as in Guo et al., (2022), the opposite result was found in children speaking mandarin. Shimmer differences could reflect morphological differences or differences in control of the vocal cords of autistic children and other children (Teston, 2014). Therefore, these voice features could be an external marker of atypical neurodevelopment occurring before birth (Bonnet-Brilhault et al., 2018). Note that in the current study we aimed to test whether voice could be used as a diagnostic tool, and therefore we tested older children with stable diagnostic. Future studies should aim at studying the diagnostic power of infant's cries at birth or within the first year of life to test the validity of voice acoustics as a true biomarker of autism.

Previous studies that compared ASD to other populations are sparse and rely on different grouping strategies: Oller et al., (Oller et al., 2010) reported 62% accuracy in the classification of ASD children with DLD in a non-TD group, Bone et al., (2013) reported a 78% of correct classification between ASD and DLD. Here, classifying children with DLD in the typically developing group, we obtained high classification rates of ASD not only with respects to TD, but also to other pathologies. The approach developed here combining feature selection, through ROC-supervision, a clustering analysis and cross-validation demonstrates that voice features have a strong, specific, diagnosis power for ASD: accuracy was well-above chance for children with DLD and children with CI. This provides new information on the diagnostic importance of voice features in ASD, in particular in relation to other neurodevelopmental disorders (e.g., DLD).

Central nervous system dysfunction affects vocal folds and by domino individual's voice. This is why automated voice analysis using recordings of patient speech is increasingly being used in psychiatry (Fagherazzi et al., 2021) and neurology as digital biomarkers of disease (i.e., in Major depressive disorder (Zhang et al., 2020), schizophrenia (Parola et al., 2020), Parkinson's disease (Tracy et al., 2020), Alzheimer's Disease (König et al., 2015), …). However, this computational method should not be delegated solely to a machine (Gross, 2020), even if it is

based on formal reasoning, this method should be used in complementarity to clinical diagnosis of experts.

This clustering method is a first step towards the development of an early diagnostic biomarker specific to ASD. Indeed, in this study, all children had minimal verbal capabilities and data were selected to have the most optimum dataset; future studies should assess the diagnostic power of vocal acoustic based on non-linguistic vocal samples acquired in less controlled environment. In addition, data presented here comes from children between 6 and 12 while, in high-income countries the average age of ASD diagnosis is around age 4 (Sheldrick et al., 2017), and around 5 worldwide (van 't Hof et al., 2021). To be truly a biomarker of autism and understand its potential diagnostic value, these results should be replicated in younger children and possibly using cry features of babies. Moreover, in order to develop a sensitive diagnosis test, future works should include typical cases met in clinical practice, with disorders more often seen as comorbidities of ASD such as attention deficit hyperactivity disorder (ADHD), motor problems without social impairment, severe anxiety, and other behavior disorders (Sheldrick et al., 2017).

Overall, our work suggests that easy-to-measure voice features, potentially linked to abnormal early neurodevelopment, can help in the diagnosis of autism spectrum disorder. Voice features in clustering methods can be used as a potential biomarker for autism and paves the way to a new objective tool to aid clinical and differential diagnosis of ASD. The method developed here is in part automated, and in the future, a hand-in tool should be developed to automatically output diagnostic information. Early detection of ASD is crucial because it is likely to lead to an improved outcome. Thus, based on our simple clustering algorithm method, future work should investigate the acoustic cry features of baby as a potential biomarker for autism.

Author contributions

Methods and Materials

Participants

One hundred and eight children were enrolled in our retrospective studies. Study 1 (Fig. 2a) is composed of 38 children on the autism spectrum (1 girl; 8.5 ± 0.25 years) and 24 TD children (12 girls; 8.2 ± 0.32 years), and in Study 2 (Fig. 3a), 21 children with DLD (9 girls; 7.9 ± 0.51 years) and 25 children displaying severe-to-profound sensorineural hearing loss fitted with CIs (8 girls; 8 ± 0.22 years) were added. Data of 24 children were excluded from the analysis (see Experimental protocol and data acquisition). Therefore, the final sample comprised 84 children distributed as follows: 29 ASD (0 girl; 8.4 ± 0.29 years; age range [6.3 12]; ADOS severity score: 6.19 ± 0.45; CARS: 27.7 ± 0.7), 20 TD (10 girls; 7.99 ± 0.33 years; age range [6 10.5]), 20 CI (6 girls; 8.2 ± 0.19 years; age range [6.5 9.9]; 12 with bilateral CI; 6 with right CI; 2 with left CI; age at first implantation 1.86 ± 0.15) and 15 DLD (7 girls; 8.2 ± 0.37 years; age range [6.5 10.8]). Demographic and clinical information regarding the final sample is presented in Table 1. Youth with ASD received an expert clinical diagnosis based on Diagnostic and Statistical Manual of Mental Disorders – fifth Edition – (DSM-V) (American Psychiatric Association, 2013); the Autism Diagnostic Interview-Revised (Lord et al., 1993), and/or the Autism Diagnostic Observation Schedule (Lord et al., 1989) were used by experienced clinicians of the Excellence Center of Autism (Exac·t), Tours, France to inform diagnostic decisions. Children with DLD also received an expert clinical diagnosis based on the DSM-V

(American Psychiatric Association, 2013) Nonverbal cognitive abilities were assessed either by Raven Progressive Matrices or Block Design and Matrix Reasoning of the WISC-IV (data of 5 TD children are missing).

This study was carried out in accordance with the recommendations of the local ethics committee (Comité de Protection des Personnes [CPP] Tours Ouest 1, n°2006-RS), with written informed consent from all parents of the children and assent from the children, in accordance with the Declaration of Helsinki.

Experimental protocol and data acquisition

Acoustic data were extracted from 20 speech samples recorded in the context of a nonword repetition task (Dos Santos and Ferré, 2018), therefore reducing the influence of social interaction in voice production. Briefly, children had to repeat 50 or 70 nonwords of varying phonological complexity, presented with a computer either with only auditory or with both audio and visual information. Nonwords were created using 1, 2 or 3 of the three most common vowels among the languages of the world, namely [a], [i], [u], and from a concise list of consonants which included two stops ([k], [p]), two fricatives ([f], [s]), one liquid [l]. Nonwords had either a CV, CVC# or CCV structures (Dos Santos and Ferré, 2018). Phonological analysis of the data presented in the current manuscript are published elsewhere (David et al., 2021; Silleresi et al., 2020). Among the 50 or 70 nonwords, the 20 ones with less phonological errors were chosen for acoustical analysis. Acoustic parameters were analyzed using the open-source software Praat (Boersma, 2002). For each nonword, we extracted 9 acoustics parameters (Fig. 1): mean fundamental frequency (f0), mean formant frequencies (F1 to F4), mean formant dispersion (FD), mean harmonic-to-noise ratio (HNR), mean jitter (cycle-to-cycle variation in frequency of f0) and mean shimmer (cycle-to-cycle variation in intensity of f0); they were then averaged across the 20 nonwords. In addition, because ASD is characterized with increased

intra-individual variability (Bonneh et al., 2011; Latinus et al., 2019; Milne, 2011), shape parameters (e.g., skewness and kurtosis) of f0, FD, HNR, jitter and shimmer were computed using Matlab2018b functions, leading to 19 variables (Fig. 1). Note that in the Matlab kurtosis function, the normal distribution has a kurtosis value of 3 (Fig. 1e).

Acoustic data are excluded according to two categories of rejection criteria: the nonword repetition task performance and acoustic rejection. For the first criteria, children whose performance in the repetition of vowels was considered outlier ([Q1-1.5xIQR] with Q1: lower quartile and IQR: interquartile range) were removed from the analysis (N = 9: 2 ASD, 2 DLD, 5 CI), to avoid bias due to the mispronunciation of certain vowels which can influence acoustics. For the second criteria, based on acoustical analysis (recording quality or outlier value of acoutsic parameters with respect to the population), another 15 children (7 ASD; 4 DLD; 4 TD) were excluded from the analysis (ROC-supervised k-means classification results including all participants but those with poor recordings quality are shown in Supplementary table 2).

Development of clustering diagnostic model

Our goal was to determine if acoustic features of the voice could be used as a diagnostic biomarker specific for autism by k-means classifying ASD against typical and other atypical development, thus we randomly dichotomized data in diagnostic model group and unknown data group. In order to validate our model performance, we used bootstrapping and resampling methods.

To develop the diagnostic model, we randomly selected n ASD and n control as train data (70% of data), and then we applied k-means (50 iterations, Hartigan & Wong algorithm); this was repeated 500 times through bootstrap with replacement of data from the entire population.

Because there is no general rule regarding the number of bootstrap resampling to use, we choose the value at which our main criteria (selectivity and sensitivity) appear stable beyond reasonable doubt, through multiple testing with different numbers of resampling (Supplementary Fig. 1). The number of clusters was set to two, since we aimed to determine ASD diagnostic against a control population (TD children only, or control children). We performed k-means clustering analysis (KCA) in an unsupervised way with the nine acoustic and derived acoustic variables (N = 19) and assessed its performance. Then, in order to enhance our KCA, we performed receiver operating characteristic (ROC) as proposed by Nikas and colleagues (2011) and used an AUC (Area Under the Curve) ROC curve, as measure of separability to evaluate the most discriminative acoustic parameters. This latter probability is an assessment of the discriminative power of a given variable with respect to two measures, here the two groups involved. For example, with a given variable, an AUC of 1 is synonym of a separation between groups with 100% accuracy, and the given variable is considered as an excellent classifier. *A contrario*, the worst discrimination between the two groups has an AUC = 0.50 (i.e. no discrimination capacity). In this way, the ROC curve allows us to optimize our KCA by supervising it using acoustic variables with best discriminative power. We used a threshold of AUC > 0.80 (80%) corresponding to a good discrimination (Hosmer et al., 2013).

This model was then tested to identify the diagnostic group of the test data (30% of the entire data, corresponding to the data not used in model building) according to their KCA classification, always for each of the 500 bootstrap replications. To realize this, test data were added one-by-one for each participant and classified by supervised and unsupervised KCA. Hence, diagnostic of the participant was predicted/classified based on its data; accuracy was measured as the number of times a test participant was classified with the correct diagnostic, referred to as classification performance.

To assess the performance of our KCA, we measured selectivity, sensitivity and the classification performance of our model. Moreover, by the goodness of fit as quality criteria of KCA, we assess clustering effectiveness by a percent of variation (PV) corresponding to the total within-cluster sum of squares by the total of within and between-cluster sum of squares.

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Competing interests

The authors declare no competing interests.

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Figure and their legends
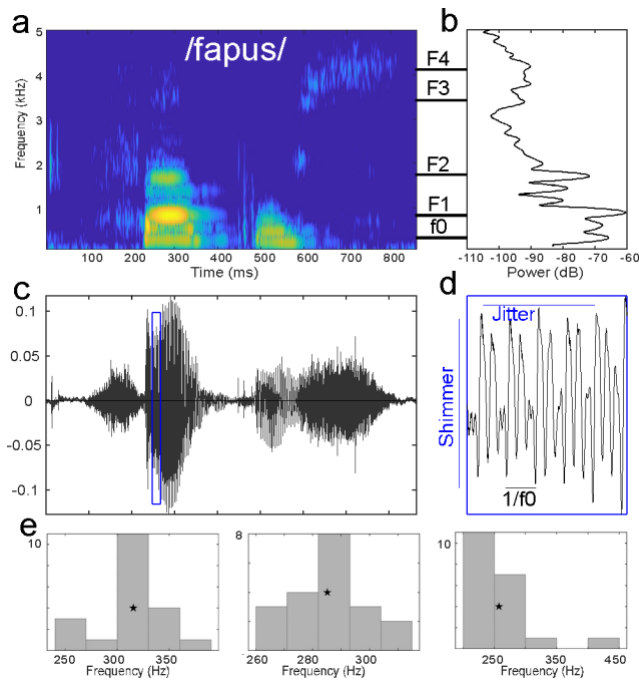
Fig. 1. Experimental design. a, Spectrogram of one of the nonwords produced in the nonword repetition task. **b,** Average power spectrum. **c,** Amplitude waveform. **d,** Zoom on the amplitude waveform to illustrate shimmer and jitter. **e,** Distribution of mean f0 measured in the 20 selected nonwords for a skewness (left panel; skewness = 0), and kurtosis (middle panel; kurtosis normalize = 0) corresponding to a normal distribution and for altered (right panel) skewness (3.1) and kurtosis (9.5).
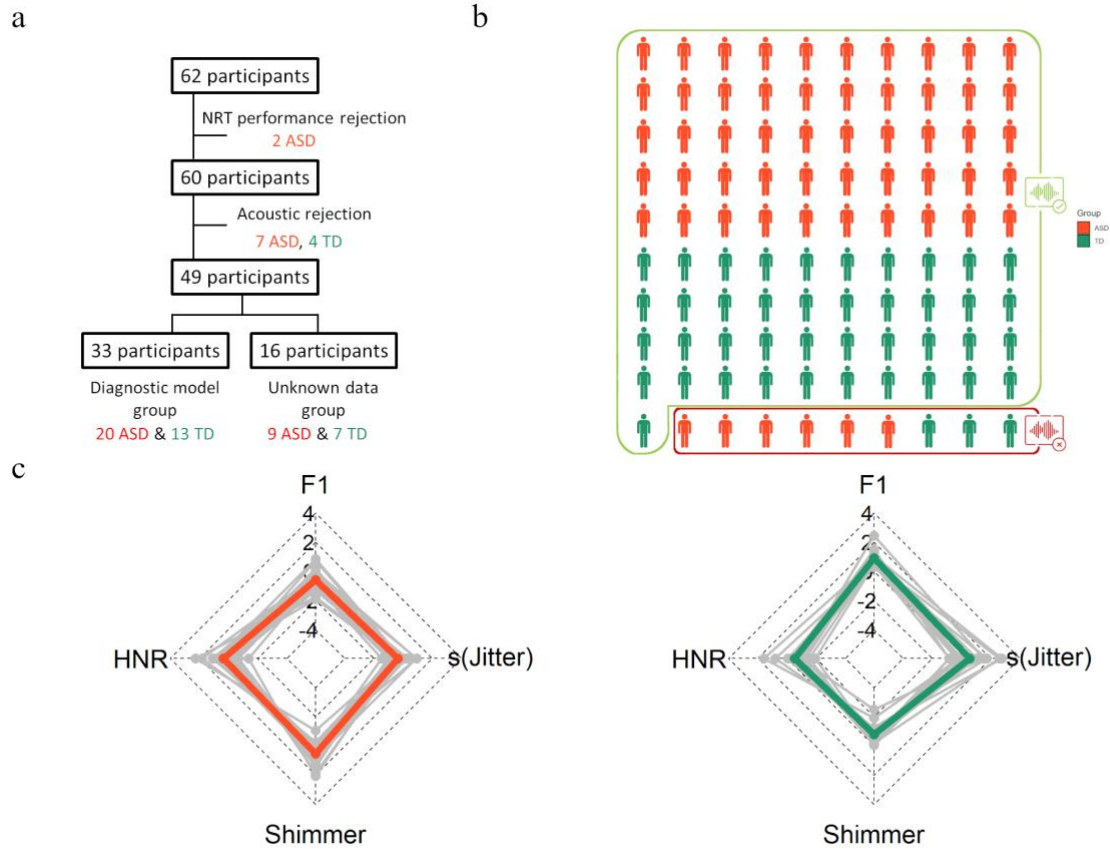
Fig. 2. Classification of autistic children with respect to TD children (study 1). a, Procedure of inclusion of the participants and random dichotomization of the data in diagnostic model group and unknown data group. NRT: Nonword Repetition Task; ASD: Autism Spectrum Disorder; TD: typically developing children. **b,** Extrapolation of the classification on 100 subjects. Participants with good diagnosis are surrounded by a green rectangle (93%), the misclassified by a red one. **c,** Illustration of the acoustic profile by radar chart according to the four most significant voice features, namely, harmonic-to-noise ratio (HNR), formant frequencies 1 (F1), skewness of Jitter [s(Jitter)] and Shimmer generated the best ROC-supervised KCA setting.
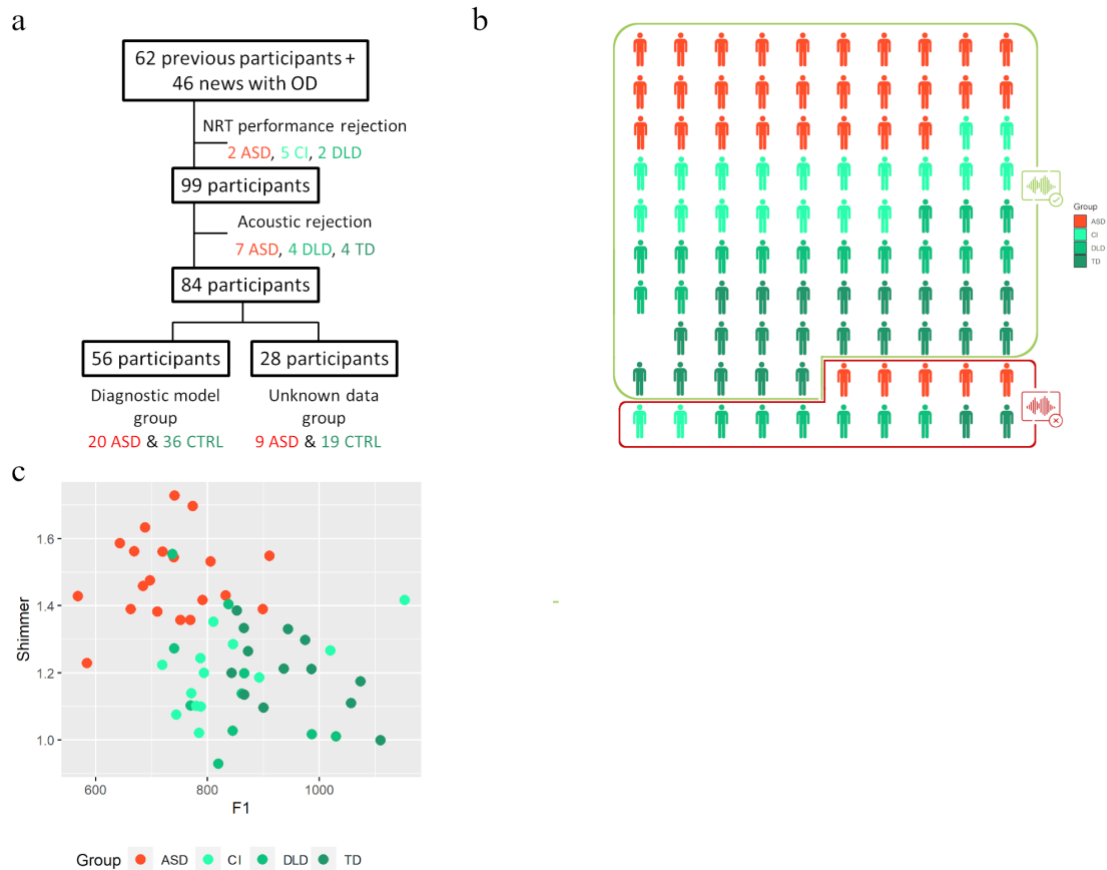
Fig. 3. Classification of autistic children with respect to a diverse control population (study 2). a, Procedure of inclusion of the participants and random dichotomization of the data in diagnostic model group and unknown data group. OD: Other Disorders; NRT: Nonword Repetition Task; ASD: Autism Spectrum Disorder; CTRL: heterogeneous control group (composed of children with developmental language disorder [DLD] and cochlear implant [CI]). **b,** Extrapolation of the classification on 100 subjects. Participants with good diagnosis are surrounded by a green rectangle (84%), the misclassified by a red one. **c,** The top two most significant voice features, namely, formant frequencies 1 (F1) and Shimmer generated the best ROC-supervised KCA setting. Those three parameters are plotted against each other.

Data availability

All data generated and/or analyzed during this study are available from the corresponding author (ML) on reasonable request. For all clustering runs, we used R (http://cran.r-project.org). Code used in this manuscript is available at GitHub (https://github.com/FredericBr/VoiceMarker).

Table

	N	Male / Female	Age *(years)*	FRI ± sem *(Percentile)*	RPM ± sem *(Percentile)*	NRT Score ± sem *(%)*
ASD	29	29 / 0	8.42 ± 0.29	88.6 ± 5.56 (22)	50.7 ± 13.8 (7)	80 ± 3.1
TD	20	10 / 10	7.99 ± 0.33	121.7 ± 4.43 (15)		96 ± 0.92
DLD	15	8 / 7	8.15 ± 0.27	93 ± 3.14 (11)	36.9 ± 10.7 (4)	49 ± 6.3
CI	20	14 / 6	8.16 ± 0.16	96.6 ± 4.26 (20)		42 ± 4.6

Table 1: Demographic and clinical information of the sample. Number in brackets represent the number of participants contributing data to the measure. FRI: Fluid Reasoning Index calculated with the prorate sum of Block Design and Matrix Reasoning scores in WISC-IV; RPM: Raven's Progressive Matrices; NRT: Nonword Repetition Task; ASD: Autism Spectrum Disorder; TD: Typically developing children; DLD: children with Developmental language disorder and CI: children with Cochlear Implant.

Supplemental information

	KCA	
	Unsupervised (19 variables)	ROC-supervised (2 variables)
Diagnostic model group (20 ASD vs 36 CTRL)		
Sensitivity	0.78 (0.08)	0.86 (0.05)
Specificity	0.72 (0.11)	0.84 (0.08)
(+)Likelihood Ratio	0.63 (0.10)	0.77 (0.09)
(-)Likelihood Ratio	0.86 (0.05)	0.91 (0.02)
Percent of variation	86.79 (0.81)	57.42 (3.04)
Unknown data group (9 ASD vs 19 CTRL)		
Sensitivity (mean)	0.78 (0.07)	0.86 (0.04)
Specificity (mean)	0.72 (0.09)	0.84 (0.08)
(+)Likelihood Ratio (mean)	0.62 (0.09)	0.76 (0.09)
(-)Likelihood Ratio (mean)	0.86 (0.04)	0.92 (0.02)
9 ASD % Correct [CI95%]	77.82 [76.57-79.02]	85.56 [84.49-86.57]
19 CTRL % Correct [CI95%]	72.03 [71.11-72.93]	84.24 [83.49-84.96]
Total % Correct [CI95%]	73.89 [73.15-74.61]	84.66 [84.05-85.26]
Percent of variation	86.84 (0.77)	57.48 (2.88)

Table S1: Summary of the results of N = 500 KCA after rejecting participants who were outliers in either nonword repetition task performance, or acoustic measurements and those who had poor quality recordings. Each clustering method was tested both in an unsupervised and ROC-supervised way. The percent of variation of a clustering method assesses the clustering fitting of that method in a given setting. ASD: Autism Spectrum Disorder participants; CTRL: heterogeneous control group (composed of children with developmental

language disorder [DLD] and cochlear implant [CI]); CI95%: Confidence interval of 95%. Data

are presented as mean (Standard Deviation).

	KCA	
	Unsupervised (19 variables)	ROC-supervised (2 variables)
Diagnostic model group (22 ASD vs 44 CTRL)		
Sensitivity	0.81 (0.07)	0.83 (0.05)
Specificity	0.57 (0.10)	0.79 (0.10)
(+)Likelihood Ratio	0.49 (0.07)	0.69 (0.11)
(-)Likelihood Ratio	0.86 (0.05)	0.91 (0.03)
Percent of variation	86.51 (0.77)	60.42 (2.51)
Unknown data group (11 ASD vs 22 CTRL)		
Sensitivity (mean)	0.81 (0.06)	0.83 (0.05)
Specificity (mean)	0.57 (0.09)	0.79 (0.09)
(+)Likelihood Ratio (mean)	0.49 (0.06)	0.69 (0.10)
(-)Likelihood Ratio (mean)	0.86 (0.04)	0.90 (0.03)
11 ASD % Correct [IC95%]	81.53 [80.47-82.54]	83.36 [82.35-84.34]
22 CTRL % Correct [IC95%]	57.98 [57.05-58.90]	78.19 [77.40-78.95]
Total % Correct [IC95%]	65.83 [65.10-66.65]	79.92 [79.29-80.52]
Percent of variation	86.51 (0.73)	60.45 (2.39)

Table S2: Summary of the results of N = 500 KCA with all data except those with poor recording quality. Each clustering method was tested both in an unsupervised and ROC-supervised way. The percent of variation of a clustering method assesses the clustering fitting of that method in a given setting. ASD: Autism Spectrum Disorder participants; CTRL: heterogeneous control group (composed of children with developmental language disorder

[DLD] and cochlear implant [CI]); CI95%: Confidence interval of 95%. Data are presented as mean (Standard Deviation).
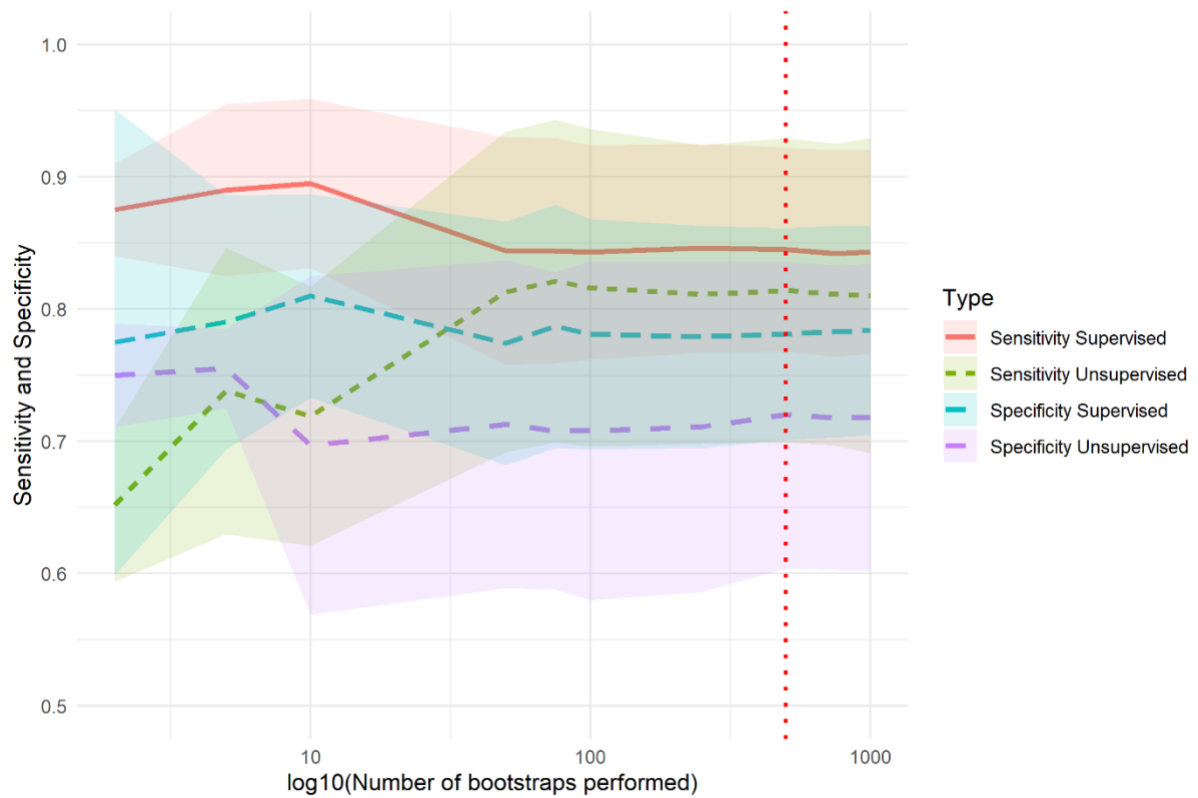
Supplementary Fig. 1. Number of bootstraps for K-means clustering Analysis decided by convergence criteria. The number of bootstrap samples that it takes to get a stable histogram is the optimal, increasing bootstraps will not change the sensitivity and specificity. Here for the study 2, 500 bootstrap iterations were used and materialized by red vertical dotted line.