Article original

Clinical characteristics of children with autism spectrum disorders: a cross-sectional study of cases attended at three centers specializing in neurodevelopmental disorders in Kinshasa, Democratic Republic of Congo (DRC)

Caractéristiques cliniques des enfants avec troubles du spectre de l'autisme : une analyse transversale des cas soignés dans trois centres spécialisés dans les troubles neurodeveloppementaux à Kinshasa, en République Démocratique du Congo (RDC)

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Summary

Context and objective. Autism spectrum disorders (ASD) in sub-Saharan African (SSA) countries are poorly studied. The aim of the present study was to describe the socio-demographic and clinical characteristics of children with autism and to identify associated factors. *Methods.* This was a cross-sectional study of children with ASD attended at three specialized centers in Kinshasa. We confirmed a ASD diagnosis through clinical observation using Diagnostic and Statistical Manuel of Mental Disorders four Text Revision (DSM-VI-TR) criteria and standardized autism diagnostic tools. We analyzed socio-demographic and clinical characteristics and main comorbidities of ASD. The comparison of proportions was done using Pearson's chi-square test. One-way ANOVAs were calculated to test differences in averages. *Results.* A total of 120 children (72.5 % male) were examined. Their mean age at diagnosis was 7.83 ± 3.4 years, while parents were alerted at 1.8 ±0.78 years. Language delays were the main alert sign (54%) and the main symptom (62%). Social interaction disorders (11.7 %) were under-reported by parents. The core signs of ASD were disorders of social interaction (90.5%), behavior (80%) and language (62.5%). The main ASD symptoms were associated with epilepsy

Résumé

Contexte et objectif. Les troubles de spectre de l'autisme (TSA) en Afrique subsaharienne (ASS) sont très peu étudiés. L'objectif de la présente étude était d'examiner les caractéristiques socio-démographiques et clinique des enfants avec autisme et d'identifier les facteurs associés. *Méthodes.* Il s'agissait d'une étude transversale des enfants avec TSA des trois centres spécialisés à Kinshasa. Le diagnostic de l'autisme était confirmé par l'observation cliniques selon les critères diagnostic and Statistical Manuel of Mental Disorders four Text Revision (DSM-VI-TR) et les outils diagnostiques standardisés de childhood autism rating scale (CARS) and Autism Diagnostic Interview, Revised (ADI-R). Les paramètres d'intérêt englobaient les données sociodémographiques et cliniques ainsi que les principales comorbidités. La comparaison des proportions a été faite à l'aide test du chi-carré de Pearson. Des ANOVA à sens unique ont été calculées pour tester les différences de moyennes. *Résultats.* Au total, 120 enfants (sexe masculin 72,5 %) ont été examinés. Leur âge moyen au moment du diagnostic était de 7,83 ± 3,4 ans alors que les parents étaient alertés à 1,8 ±0,78 ans. Les retards de langage étaient le principal signe d'alerte (54 %) et le principal symptôme (62 %). Les troubles des interactions sociales (11,7 %) étaient sous rapportés par les parents. Les principaux signes étaient les troubles de l'interaction sociale (90,5 %), du comportement (80 %) et du langage (62,5 %). Les principaux symptômes des TSA étaient

(p=0.027), cerebral palsy (p=0.026) and hearing impairment (p=0.045). *Conclusion.* The diagnostic and language delay co-occurring with epilepsy and hearing impairment are the main clinical features of autism in the DRC. This study suggests that screening children for autism and its main comorbidities using a multidisciplinary approach should be a priority in Kinshasa.

Keywords: Autism, Spectrum disorders, comorbidity, language delays

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associés à l'épilepsie (p=0,027), à la paralysie cérébrale (p=0,026) et à une déficience auditive (p=0,045). *Conclusion.* Le profil clinique de l'autisme en RDC se caractérise par le retard de diagnostic et de langage en cooccurrence avec l'épilepsie et la déficience auditive. Le dépistage de l'autisme et ses principales comorbidités chez les enfants dans une approche multidisciplinaire sont prioritaires à Kinshasa.

Mots-clés : Autisme, Caractéristiques cliniques, Comorbidité, Retard de diagnostic, Kinshasa.

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Introduction

Autism Spectrum Disorder (ASD) is characterized by social interaction impairments, communication disorders, and restricted and repetitive behavior in early childhood (1-2). Worldwide, the prevalence of ASD varies between 0.6-1.5 % in developed countries (1-3) while the prevalence of ASD is largely unknown in low-income countries, including throughout sub-Saharan Africa (SSA) (3-4). However, hospital-level data taken from SSA indicates that ASD prevalence varies between 0.07-33.5% of children (4-5). The clinical characteristics of ASD in children are heterogeneous and complex, which makes early diagnosis challenging (1, 5-6). Further, this clinical variability in how specialists diagnose autism has a subsequent influence on the management of the condition around the world (3-5). According to Elsabbagh et al. (3), the heterogeneity of clinical characteristics stems from continuous changes in diagnostic criteria, clinical description, and disparity in global prevalence rates (3). Across SSA, the knowledge and awareness of ASD among healthcare professional that is needed to recognize early signs and symptoms and, thereafter, make an accurate and timely diagnosis are limited (4-5,8-12). Therefore, an accurate diagnosis and the management of associated clinical characteristics remain neglected and poorly understood throughout the continent (4). Further, health professionals in SSA often misdiagnose the clinical characteristics of ASD in children as deafness, mutism, psychosis, epileptic encephalopathy, attention deficit hyperactivity disorder (ADHD), or as an intellectual disability (ID) (5). The parents, extended families, and communities throughout SSA often consider the signs and symptoms of ASD in children to be manifestations of bewitchment or witchcraft (5,10,13).

Consequently, these children with ASD receive late diagnosis and treatment which has a significant effect on their prognosis (5,10,13). According to Franz, *et al.* (14), SSA had the lowest number of empirical studies and publications on ASD (14). Of the limited studies conducted, they indicate that African children are more likely than Caucasian children to receive a late diagnosis (13). Studies that show high frequencies of ASD in African immigrants in Europe confirm this comparative view. For immigrant families there can be language barriers, which make it difficult for them to easily access appropriate medical care for their children. Furthermore, the clinical characteristics displayed by African children with ASD are more severe and complex. Studies show these children frequently have severe speech and language delays as well as an ID (4,8,10-11,15).

Recent studies speak to this point, noting ASD in children in SSA is mainly characterized by language delay and the presence of comorbidities, including an ID and epilepsy (5,7,11-13). Although these studies describe the clinical characteristics of ASD at the time of diagnosis (5,10-11), they provide little information on the clinical characteristics in early childhood, comorbidities, or prevalence rates throughout the region (5,8,10). Therefore, the present study aimed to examine the socio-demographic and clinical characteristics of children with and, thereafter, identify the factors associated with the disorder.

Methods

Study design, period, and scope

We conducted a cross-sectional study that consecutively enrolled household the children of ASD according to the criteria of axis I of the Diagnostic and Statistical Manuel of Mental Disorders four Text Revision (DSM-VI-TR) (2) in specialized neurodevelopmental disorders' units of three medical centers located in Kinshasa city, the capital of the DRC. Three centers, namely, the Centre Neuro-Psycho-Pathologique (CNPP) , Centre d'Évaluation et d'Intervention des Enfants avec Handicap Mental et Autisme (CEIEHMA) , The Village Bondeko de Kabambare (VBK) were selected because they are the main reference centers for children with neurodevelopmental disorders in the city of Kinshasa and its surroundings.

The CNPP is the only Public University Hospital in the DRC which offers specialized care and oversees the training, research, and management of psychiatric and neurological disorders psychiatric.

The Village Bondeko de Kabambare (VBK) is the first and the most important among 18 schools dedicated to the education of children with developmental delays, intellectual deficiency, deafness, muteness, and other neuro-pediatric disorders.

The Centre d'Évaluation et d'Intervention des Enfants avec Handicap Mental et Autisme (CEIEHMA) is a private health facility, specialized for diagnostic assessments, specialized education, and psycho-educational interventions for children with autism or related disorders.

Study population and sample

By convenience sampling, we consecutively recruited children under 18 years old with neurodevelopmental disorders presenting at least one core symptom of autism according to DSM-IV-TR Axis I criteria, defined as being at risk of autism.

Inclusion criteria

To have the diagnosis of autism confirmed by the principal investigator (PI), a qualified psychiatrist in charge of children with neurodevelopmental disorders at the Neuro- Psycho- Pathological Center (CNPP) and/or the co-investigator, a clinical psychologist and autism specialist from the CEIEHMA. To have socio-demographic information and developmental history provided by the child's parents or carers. To have parent consent to clinical and psychological evaluation of the child using standard autism diagnostic tools, the results of electrophysiological (electroencephalogram (EEG), audiometry) and psychological (IQ) evaluations.

Non-inclusion criteria

All children having other severe medical and sequel conditions that might have interfered with the clinical picture were excluded. The absence of a parent or caregiver with knowledge of these children's development from birth, which was necessary for the additional interview stage of the selection process described above.

The children were under 3 years of age, meaning that they did not meet Diagnostic and Statistical Manuel of Mental Disorders four Text Revision (DSM-VI-TR criteria (2).

Diagnosis confirmation and tools

The final diagnosis was confirmed by the Principal Investigator (PI) based on clinical observation of DSM-IV-TR criteria and using the standardized autism diagnostic tools: the childhood autism rating scale (CARS) (16) and Autism Diagnostic Interview, Revised (ADI-R) (17) administered by Principal Investigator (PI) and/or co-Principal Investigator (CO-PI).

Variables of interest

The main outcome included the clinical characteristics of children under 18 years old with confirmed ASD and their socio-demographic characteristics.

Socio-demographic characteristics. For each child, the following socio-demographic information was included: the current age and sex of the child, parental level of education, parental age at child's birth.

Clinical characteristics: For each child, the following variables related to the clinical features of autism were included: the child's birth weight, the age at diagnosis of autism, the main symptoms at the time of diagnosis, the age of the child at the time of parental/caregiver concern, main symptoms at the time of concern, and the autism severity as identified by the childhood autism rating scale (CARS) (16).

Comorbidities: For each child, the following comorbidities were assessed: the presence or absence of epilepsy, the presence or absence of cerebral palsy, the presence or absence of ADHD, and the presence or absence of a hearing impairment.

Sampling procedure

The core investigators team comprised five investigators. The Principal Investigator (PI), a trained psychiatrist in charge of children with neurodevelopment disorders at the CNPP; the Co-PI, a Clinical psychologist and autism specialist from the CEIEHMA; and one additional investigator from each recruitment site (a neurologist at CNPP, a psychiatrist at the Village Bondeko of Kabambare (VBK), and a pediatrician at CEIEHMA). The additional investigators were responsible for the initial identification of children at risk of autism in their respective centers and, thereafter, referring these children to the PI who visited all three recruitment sites.

The Co-PI was involved in the selection process only when a child presented with more complicated symptoms. In these cases, the PI and Co-PI conducted a dual evaluation process to minimize selection errors. Given the clinical heterogeneity of autism and the difficulty health professionals have in diagnosing the disorder, the PI implemented three strategies to increase the probability of recruiting the maximum number of children at risk of autism and to minimize pre-selection errors. First, all investigators were invited to attend a one-week capacity building training on autism Diagnostic and Statistical Manuel of Mental Disorders four Text Revision (DSM-VI-TR) criteria (2) and standardized diagnostic tools including Modified Checklist for Autism in Toddlers (M-CHAT), the childhood autism rating scale (CARS) (16) and Autism Diagnostic Interview, Revised (ADI-R) (17) held by an international autism expert from Ghent University in Belgium. Second, all investigators, including the PI and Co-PI, and under the supervision of this expert, carried out a pre-test by screening children with the main symptoms of autism as described by the axis I criteria of Diagnostic and Statistical Manuel of Mental Disorders four Text Revision (DSM-VI-TR) (2). Thirty-three (n=33) children with a confirmed autism diagnosis from CIEHMA (unknown to the training participants) were involved in this pre-test screening exercise. Finally, a checklist containing the main symptoms of autism according to axis I of DSM-IV-TR (2) was given to each of the co-investigators for the pre-selection process (see annex 1).

During the initial screening, children having at least one symptom of autism according to axis I criteria of the DSM-IV-TR were defined as being at risk of autism. They were categorized as screened-positive or negative for autism. All these children screened positive were then referred to the PI who confirmed or not the diagnosis using the Diagnostic and Statistical Manuel of Mental Disorders four Text Revision (DSM-VI-TR) criteria, and standardized tools including the childhood autism rating scale (CARS) (16) and Autism Diagnostic Interview, Revised (ADI-R) (17).

The PI then conducted structured interviews with parents of autism positive screened children and collected data from the children's medical dossier. Complete medical history from pregnancy to birth included information on developmental milestones, date of the onset and progression of autism symptoms, the behavior in their environment (at home, at school, and other social gathering such as at church).

For the children's identified by the PI as having complex and/or atypical symptoms or in case of doubtful diagnosis, an additional clinical observation was conducted conjointly by the PI and the co-PI using the ADI-R for the confirmation (included) or not (excluded) of the autism diagnosis.

All these children diagnosed with ASD were assessed clinically, and the PI gathered socio-demographic information along with a complete medical history for each child. Each child also underwent an audiometry test along with an electroencephalogram (EEG). Finally, an intelligence quotient (IQ) was administered.

Ethic Consideration

The study was observational, and prior to embarking on the above data collection process, the principal investigator sought and obtained the approval and informed consent of the parents of the children with autism and the authorities of the three centers, with the guarantee of anonymous data processing, before presenting the study to the Department of Psychiatry and the Faculty of Medicine of the University of Kinshasa.

Statistical analysis

In this study, the data were analyzed using SPSS software. Any relationships between the aforementioned categorical variables were evaluated using the Pearson's chi-square test and the adjusted standardized residuals were analyzed as "post hoc" after Bonferroni corrections [αcor = 0.05/(number of rows × number of columns)]. Subsequently, the normality of the quantitative data was assessed by applying the Shapiro-Wilk Test, and the equality of variances between the groups was assessed by the Levene's Test. One-way ANOVAs were calculated to test differences in averages. In addition to one-way ANOVAs, the means were compared according to the Welch Test, when the equality of variances was not assumed. To detect the significant differences, the student-Newman-Keuls post hoc test for differences in means was applied.

Results

A total of 405 children (243 boys and 162 girls) with developmental disorders and an average age of 6.91 (SD=4.3) years were screened. Of the 405 children with developmental disorders, 120 children were diagnosed with autism based on clinical observations following DSM-IV-TR (2) criteria and using CARS (16) and ADI-R (17) were included in this study. Of the 120 children diagnosed with ASD, 61 (50.8 %) were from Village Bondeko de Kabambare (VBK), 31 (25.8 %) children were from CEIEHMA, and, finally, 28 (23.3 %) children were from CNPP. The other 248 children were excluded from the study due to other medical conditions that could have interfered with the clinical picture. Of them, 211 were diagnosed with other disorders including epilepsy, cerebral palsy, ADHD, sequelae of a post-anoxic encephalopathy, or meningitis. The parents or primary caregivers of 27 children refused or did not accompany their children to the healthcare centers included in this study. Rather, a domestic worker familiar with the child accompanied them. The lack of a parent or caregiver familiar with these children's development since birth, which was necessary for the additional interview stage of the selection process described previously, these children were excluded from the study. Finally, 10 children were under 3 years old which meant they did not meet the DSM-IV-TR criteria (2).

Socio-demographic characteristics

The mean age (SD) of children when they received a diagnosis was 7.9 ± 3.4 years old. The number of boys involved in the study 83 (72.50 %) outnumbered the number of girls 37 (27.5%). At the time of diagnosis, girls involved in this study were the same age (Mean 7.7 ± 3.6 years) as boys (Mean =8.0 ± 3.3 years; p =.74).

The parental mean age at their child's birth was 42.1 ± 6.2 for fathers and 33.7 ± 6.6 years for mothers. Most fathers involved in this study had a high level of education with 50% having achieved a university level education. Conversely, 48.3 % of mothers had obtained a high school education. Table 1 presents the varied socio-demographic characteristics of children involved in this study.

Table 1. Sociodemographic characteristics of the 120 children diagnosed with ASD in Kinshasa, DRC

Variables	n	%
Children Mean Age (years)	7.9 ± 3.4	
Boys' age	8.0 ± 3.3	
Girls' age	7.7 ± 3.6	
Parents' age at birth (years)		
Father's age	42.1 ± 6.2	
Mother's age	33.7 ± 6.6	
Sex		
Girls	33	27.5
Boys	87	72.5
Parents' level of education		
Father		
Elementary	19	15.8
High School	41	34.2
University	60	50.0
Mother		
Elementary	28	23.3
High School	58	48.4
University	34	28.3

Clinical features

Age when early alert signs presented and age at diagnosis of Children with ASD

The mean age early alert sign reported was 1.8 ± 0.8 years and at the time of diagnosis, the mean age (SD) of children with ASD was 7.9 ± 3.0. The child's age when the presenting alert signs were observed varied with the type of presenting core alert signs (p = .002; Fig. 1A). Social interaction disorders were observed at an earlier age (17 months or 1.4 years; p = .002) than communication/language disorders, which were observed at 26 months (2.2 years).

Early alert signs and main symptoms parents reported to the PI at the time of diagnosis

The presence and proportion of these three core development abnormalities that alerted parents and justified referral to the PI for an evaluation for autism did not change over time. Table 2 presents the different clinical characteristics of children with ASD (Table 2).

Table 2. Clinical characteristics and core symptom domains of ASD among 120 children in Kinshasa, DRC

Variables	Mean ± SD	
Birth weight (Kg)	3.2 ± 0.6	
Mean Age (years) at ASD diagnosis	7.9 ± 3.4	
Mean Age at first alert sign (months)	22.0 ± 9.3	
Early alert sign (Indicated by parents)	**N**	**%**
Communication disorder	65	54.2
Behavioral disorder	31	25.8
Social Interaction disorder	24	20.0
Main symptoms at ASD diagnosis (indicated by parents)		
Communication disorder	75	62.5
Behavioral disorder	31	25.8
Social interaction disorder	14	11.7

The early alert signs parent reported having noticed the following symptoms: communication difficulties in 54.2 % of the children, behavioral problems in 25.8 % of the children, and finally social interaction difficulties in 20.0 % of the children. The main symptoms parents reported to the PI were communication difficulties in 62.5 % of children, behavioral problems in 25.8%, and social interaction difficulties in 11.7% of the children.

There was a relationship between the presenting core symptom of children with ASD and the recruitment center (p = 0.027). Behavioral disorders were more frequent (p = 0.0092) among children recruited from the second site, VB, and less frequent among children from the third site, CIEHMA (p =0 .017). But p-values of these relationships were greater than the α corrected (.05/9 or .0055).

At the time of diagnosis by the PI, there were no relationships between the main symptoms observed by parents and age (p = 0.302), sex (p = 0.391), birth weight (p = 0.570), age of the father (p = 0.74), age of the mother (p = 0.88), father's education level (p = 0.23), mother's education level (p = 0.560) and child's age at the time parents noticed alerts signs (F (p = 0.29).
ASD core symptom domains, Age at diagnosis and the healthcare center

The mean age at the time of diagnosis for the children varied according to the recruitment site (p =0.04). The average age of the children at diagnosis (9.4 years) selected in the private health center (CIEHMA) was significantly higher than those recruited from VB (7.4 years), (p = 0.01; Fig. 1B).

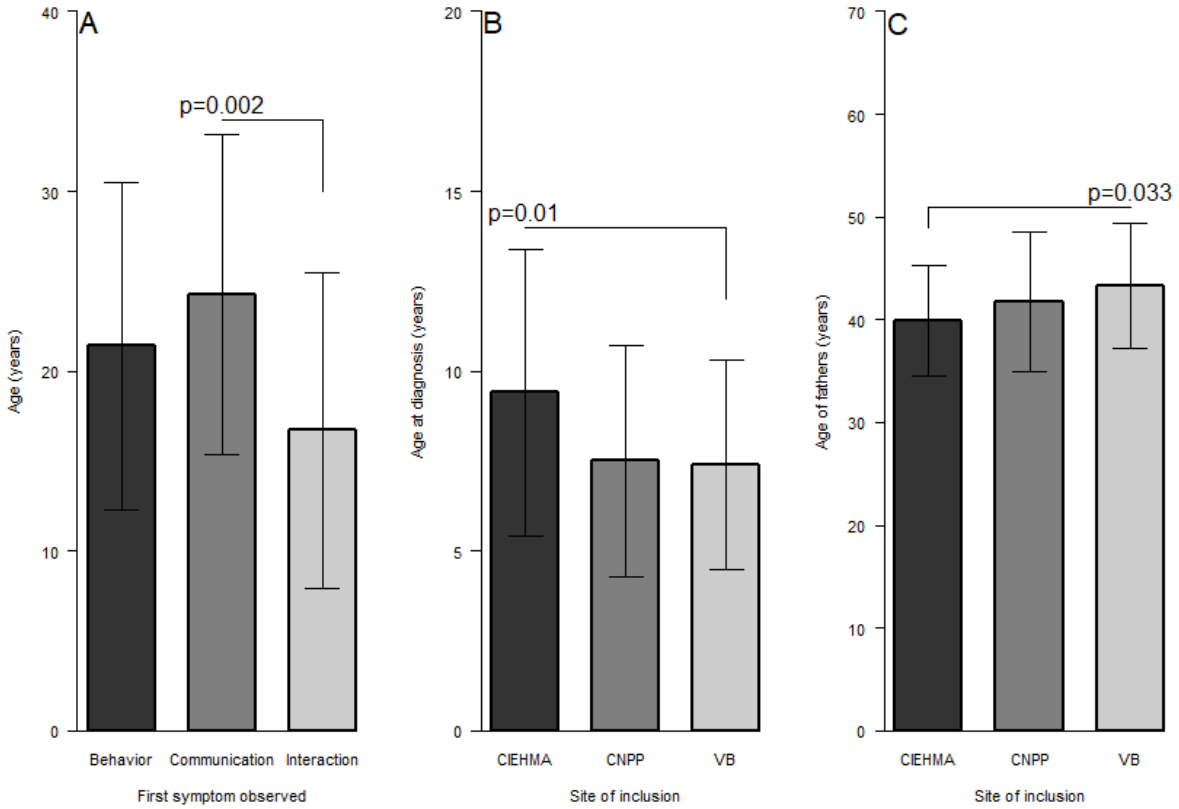

Figure 1. Differences of means of A) children's age (in months) by core alert symptoms (First symptom) observed; B) children's age and C) their father's age by sites of inclusion.

Figure Legends:
CEIEHMA : Centre d'Évaluation et d'Intervention des Enfants avec Handicap Mental et Autisme. CNPP: Centre Neuro-Psycho-Pathologique. VB*K*: Village Bondeko (de Kabambare)

The core alert signs, age of fathers and the center of recruitment.

There was also a significant relationship between the core alert signs and the recruitment center (p = 0.027). Behavioral disorders were more common in children at the second site (p = 0.01) than in children at the third site (p = 0.02). But the p values of these relationships were greater than the α corrected values (.05 / 9 or .0055). Table 3 captures the underlying factors relating to the children's different clinical characteristics and their respective healthcare centers.

Table 3. Pearson's chi square test results between core alert symptoms of ASD among 120 and the treatment center in Kinshasa, DRC

Site of inclusion	CEIEHMA	CNPP	VB
	n (ASR)	n (ASR)	n (ASR)
Core alert symptom of ASD			:7
- Communication	(1.8)	(- .9)	(-.7)
- Behaviors	-2 .4)	- .6)	(2.6)
- Interaction	.4)	1.8)	(1.9)

ASR: Adjusted Standardized Residuals

The age of fathers varied with the center of recruitment (p = 0.038). The average age of the fathers of children selected in the private health center (CIEHMA) (39. 9 ± 5.4 years) was significantly lower (p = 0.033, Fig. 1C) than that of fathers with children from VB (43.3 ± 6.1 years).

The other variables did not vary accordingly with the child's recruitment site (all p-value > 0.05). These include age at diagnosis (p = 0.91), gender (p = 0.25), birth weight (p = 0.39), father's age (p =0.84), mother's age (p = 0.62), and the father's level of education (p = 0.96), and the mother's education level (p = 0.8).

Clinical characteristics and comorbidities

The main symptoms children with ASD exhibited were social interaction difficulties which were present in 90.5 % of the children, unfamiliar or strange behavior which 80% of the children exhibited, and language difficulties which occurred in 60.5% of the children, as outlines in Table 4.

Table 4. Frequency of main symptoms by domain among 120 children diagnosed with ASD in Kinshasa, DRC

Abnormalities	Symptoms and signs of ASD	N	%
Social Interaction			
	Lack of eye contact	114	95.00
	Avoids physical contact	108	90.00
	Lack of interest in peers	102	86 .67
	Absence of imitation	98	81.67
	Solitary activities	92	76 .67
	Fear or afraid of strangers	82	68. 33
	Exhibiting deafness/indifference	78	65.00
Language and communication			
	Impairments in joint attention	107	89.17
	Lack of language /non-verbal	75	62.50
	Monologues	72	60.00
	Lack of pointing out objects	65	54.17
	Does not initiate conversation	63	52.50
	Reduced sharing of interests	55	45.83
Stereotyped behavior, interests, or activities			
	Turbulent	102	85.00
	Howl	94	78.33
	Inattention	84	70.00
	Echolalia	74	61.67
	Repetitive clapping	73	60.83
	disobeys verbal commands	60	50.00
	Sniffing everything	58	48.33
	Attachment to unusual objects	56	46.67

	Self-harm/Injury	54	45.00
	Excessive touching of objects	52	43.33
	Putting hands over ears	48	40.00
	Unmotivated laugh	45	37.50
	Hand flapping	44	36.67
Other symptoms/signs			
	Insomnia	65	54.17
	Adverse reaction to sounds	63	52.50
	Selective eating	58	48.33
	Looking out corner of eye	55	45.83
	Others	45	37.50

Of the 120 children, epilepsy was visible in 87 (72.5 %) of the children while cerebral palsy was visible in 8 (14.2%) children. ADHD was visible in 17 (6.7%) and a hearing impairment was visible in 30 (27.8 %, n=108). As noted in Table 5, the mean score of CARS at diagnosis was 40.39 ± 6.35.

Table 5. Mean scores on CARS and frequency of comorbidities and severity of ASD among 120 children in Kinshasa, DRC.

Variables	**Mean**	**SD**
Mean score of CARS	40.4	6.3
Comorbidities at time of diagnosis (%)	**N**	**%**
Epilepsy	87	72.5
ADHD	17	14.2
Hearing impairment (N=108)	30	27.8
Cerebral Palsy (CP)	8	6.7

There was no significant relationship between the alert signs observed by parents and the presence of comorbidities such as cerebral palsy (p = 0.42), epilepsy (p = 0.784), ADHD (p =0 .92), and a hearing impairment (p = 0.6).

There was a relationship between the main symptom at diagnosis and the presence of epilepsy (p = 0.027). Epilepsy was more common in children whose main symptom was a behavioral disorder (p = 0.007; α corrected .05/6 = 0.008). On the other hand, the children whose main symptom at diagnosis was a communication disorder also had less epilepsy (p = 0.007; α corrected .05/6 = 0.008).

Furthermore, there was a noticeable relationship between the main symptom at diagnosis of autism and the presence of cerebral palsy (p = 0.026). Cerebral palsy was more dominant in children whose main symptom was a social interaction disorder (p = 0.018), while it was less common in children whose main symptom was a communication disorder (p = 0.023). Of interest, the main symptom was associated with a hearing impairment (p = 0.045). Hearing impairments were less common among children with a communication disorder (p = 0.023). However, all these two p-values were higher than α corrected (0.05/6 =0.008, table 6).

Table 6. Pearson's chi square test results between core symptoms of ASD and comorbidities among 120 children in Kinshasa, DRC.

Site of inclusion	CEIEHMA	CNPP	VB

	n (ASR)	n (ASR)	n (ASR)	
Core alert symptom of ASD				:7
- Communication	⁅1.8)	(- .9)	(-.7)	
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- Interaction	.4)	1.8)	⁅1.9)	

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The age of fathers varied with the center of recruitment (p = 0.038). The average age of the fathers of children selected in the private health center (CIEHMA) (39. 9 ± 5.4 years) was significantly lower (p = 0.033, Fig. 1C) than that of fathers with children from VB (43.3 ± 6.1 years).

The other variables did not vary accordingly with the child's recruitment site (all p-value > 0.05). These include age at diagnosis (p = 0.91), gender (p = 0.25), birth weight (p = 0.39), father's age (p =0.84), mother's age (p = 0.62), and the father's level of education (p = 0.96), and the mother's education level (p = 0.8).

Clinical characteristics and comorbidities

The main symptoms children with ASD exhibited were social interaction difficulties which were present in 90.5 % of the children, unfamiliar or strange behavior which 80% of the children exhibited, and language difficulties which occurred in 60.5% of the children, as outlines in Table 4.

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	disobeys verbal commands	60	50.00
	Sniffing everything	58	48.33
	Attachment to unusual objects	56	46.67
	Self-harm/Injury	54	45.00
	Excessive touching of objects	52	43.33

	Putting hands over ears	48	40.00
	Unmotivated laugh	45	37.50
	Hand flapping	44	36.67
Other symptoms/signs			
	Insomnia	65	54.17
	Adverse reaction to sounds	63	52.50
	Selective eating	58	48.33
	Looking out corner of eye	55	45.83
	Others	45	37.50

Of the 120 children, epilepsy was visible in 87 (72.5 %) of the children while cerebral palsy was visible in 8 (14.2%) children. ADHD was visible in 17 (6.7%) and a hearing impairment was visible in 30 (27.8 %, n=108). As noted in Table 5, the mean score of CARS at diagnosis was 40.39 ± 6.35.

Table 5. Mean scores on CARS and frequency of comorbidities and severity of ASD among 120 children in Kinshasa, DRC.

Variables	**Mean ± SD**	
Mean score of CARS	40.4 ± 6.3	
Comorbidities at time of diagnosis (%)	**N**	**%**
Epilepsy	87	72.5
ADHD	17	14.2
Hearing impairment (N=108)	30	27.8
Cerebral Palsy (CP)	8	6.7
Cerebral Palsy (CP)	8	6.7

There was no significant relationship between the alert signs observed by parents and the presence of comorbidities such as cerebral palsy (p = 0.42), epilepsy (p = 0.784), ADHD (p =0 .92), and a hearing impairment (p = 0.6).

There was a relationship between the main symptom at diagnosis and the presence of epilepsy (p = 0.027). Epilepsy was more common in children whose main symptom was a behavioral disorder (p = 0.007; α corrected .05/6 = 0.008). On the other hand, the children whose main symptom at diagnosis was a communication disorder also had less epilepsy (p = 0.007; α corrected .05/6 = 0.008).

Furthermore, there was a noticeable relationship between the main symptom at diagnosis of autism and the presence of cerebral palsy (p = 0.026). Cerebral palsy was more dominant in children whose main symptom was a social interaction disorder (p = 0.018), while it was less common in children whose main symptom was a communication disorder (p = 0.023). Of interest, the main symptom was associated with a hearing impairment (p = 0.045). Hearing impairments were less common among children with a communication disorder (p = 0.023). However, all these two p-values were higher than α corrected (0.05/6 =0.008, table 6).

Table 6. Pearson's chi square test results between core symptoms of ASD and comorbidities among 120 children in Kinshasa, DRC.

	Core symptoms at ASD diagnosis			P value
Comorbidities	Communication	Behavior	Interaction	
Epilepsy				.027
Yes, n (ASR)	48 (-2.7)	27 (2.1)	12 (1.2)	
No, n (ASR)	27 (2.7)	4 (-2.1)	2 (1.2)	

Cerebral Palsy				.026
Yes, n (ASR)	2 (-2.3)	3 (.8)	3 (2.4)	
No, n (ASR)	73 (2.3)	28 (-.8)	11(-2.4)	
Hearing impairment (n=108)				.045
Yes, n (ASR)	13 (-2.5)	11 (1.7)	6 (1.4)	
No, n (ASR)	54 (2.5)	16 (-1.7)	8 (-1.4)	

ASR: Adjusted standardized residuals

At the time of diagnosis by the PI, there were no relationships between the main symptoms observed by parents and autism severity (p = 0.54), and the existence of ADHD (p =0.57).

Discussion

This study aimed to determine the socio-demographic characteristics and early clinical characteristics of 120 children with ASD and the presence of comorbidities from epilepsy, behavioral disorders, to language and hearing impairments.

Socio-demographic characteristics of 120 children with ASD in Kinshasa, DRC

Sex

The overrepresentation of males with autism in this study and across all three centers confirms previous data on the gender ratio of autism throughout SSA (4,5,10). It is well known that the risk of having neurodevelopmental disorders, including autism among males is 2-4 times higher than females. As May and Adesina (19) argue, the factors contributing to this increased rate among males are complex and involve the interaction between genetic factors such as the female protective effect, hormones, and environmental factors, including stress, and sociocultural factors. As in other country cases (20-21), parents or primary caregivers and doctors in healthcare centers in Kinshasa often prioritize the symptoms and education of boys with ASD over those of girls, which - when all else is considered - may explain the additional delays girls experience to receive an autism diagnosis in comparison to boys.

Age at Diagnosis of 120 children with ASD in Kinshasa, DRC

The age at diagnosis of the children in this study was high (7.9 years) in comparison to the age at diagnosis of children in European countries (3.1 years) (15, 22) and in South Africa (11) where the average age at diagnosis is 3.4 years. This indicates a 4.5-year delay in receiving an autism diagnosis in SSA when compared to high resource countries. These results mirror the delays in diagnosis found in Nigeria in 2017 (13) and in an earlier study conducted in Kinshasa, DRC in 2016 (10). In these studies, the mean age at diagnosis was 9.45 ± 4.33 years and 8.20 years old respectively.

This delay in diagnosis in several SSA countries and, particularly DRC can be explained by a poorly organized health care and screening system combined with a lack of knowledge of the clinical characteristics of autism (11). This supports the hypothesis of previous studies that argue a poorly organized healthcare system and a child's poor socio-cultural environment explain the delay in receiving an autism diagnosis (24-25). As such, the delayed diagnosis observed in this study is associated with the lack of adequate information among parents and health professionals on the clinical manifestations of autism in the DRC (5,10).

Health Facility and the Age at Diagnosis

A lack of knowledge of autism among both parents and healthcare professionals is one of the central reasons for the long trajectory children endure before receiving an autism diagnosis. Parents and children can see more than two or three doctors or other health professionals before receiving a clear and accurate diagnosis (26). As other studies suggest, the comorbidities of epilepsy or hearing impairment with behavioral problems can mask the signs and symptoms of autism, which reduce the likelihood of an expedited diagnosis (5,26-27). However, this study finds that Congolese children who present with seizures or behavioral and hearing impairments among their first alert signs, experience a shorter therapeutic trajectory to receive a correct autism diagnosis than Congolese children who do not present with these conditions. This observation highlights not only the importance of the medical services available to parents and children, but also the collaboration between a variety of healthcare specialists who are able to consult with each other and refer children for further diagnostic evaluation.

In comparison with VB (one of the public healthcare centers involved in this study) an autism diagnosis was delayed at the private healthcare center (CEIEHMA). Importantly, the autism clinic

within the private health center also has a school, which children with neurodevelopment disorders, including autism, attend. Further, the children recruited from the private healthcare center had fewer behavioral problems and less somatic comorbidities than those from the other sites, which may indicate an autism that is less severe or atypical (15) Indeed, the prevalence of behavioral difficulties and epilepsy in children that were recruited from the private healthcare center was low. Taken together, the presence of less severe or potentially atypical cases of autism may make early diagnosis more challenging because parents do not pay specific attention to their child's symptoms and healthcare professionals are not trained sufficiently to diagnose less severe or atypical cases of autism (15).

Conversely, children recruited at the school center (VBK) and University center (CNPP) were diagnosed at a younger age by almost three years (see Figure 1). Among these children there was also a high prevalence of behavioral difficulties and comorbidities such as ADHD, epilepsy, and a hearing impairment, which implies a link between more severe signs and an earlier diagnosis. This is noteworthy given that the presence of epilepsy (and associated stereotypies and behavioral disorders) may generally mask the clinical features of autism and lead to a misdiagnosis and/or a delayed diagnosis (5,27). Nevertheless, in contrast to the private healthcare center (CEIEHMA), there is a participatory collaboration between the child psychiatrist and the ENT specialist at the two public healthcare centers (CNPP and VB). This collaboration facilitates earlier detection of symptom or signs of ASD and referral for diagnostic testing. The mean time lag from parental concern of autism signs or symptoms to diagnosis in these cases was 64 months (5.4 years), which although earlier remains a significant delay.

Parental Education Levels and Age at Diagnosis

Importantly, fathers' high level of education was not correlated with their child receiving an early autism diagnosis, which suggests further nuance is needed when interpreting previous observations that suggest a link between parents who have attained a high level of education and an early age autism diagnosis. Other studies have argued a high level of education among parents suggests those parents are more knowledgeable about autism and may have sufficient financial resources to seek specialist treatment for their children (28-29). Yet, although 50% of fathers involved in this study had achieved a university degree, their high level of education did not translate to increased knowledge of autism. More specifically, this research suggests that although parents who are younger and educated may have a general awareness of neurodevelopmental disorders, including autism and its early signs, which motivates them to seek medical assistance, there still exists a lack of knowledge among Congolese parents about the heavy toll autism can have on their child and (at times) a disbelief that their child could ever develop autism. Taken together, these may compound the problem of receiving an early autism diagnosis in DRC.

Clinical characteristics of 120 children with ASD in Kinshasa, DRC

Age at autism alert sign

Parents observed the first alert signs of autism in their children at a relatively young age (1.8 years). Studies conducted elsewhere on the continent reveal a somewhat similar pattern. In a recent study in Nigeria, parents observed the first clinical signs at age 1.5 years (13). Generally, parents noticing autism onset symptoms and signs before 2 years was observed across studies dealing with African and Caucasian children. As this study highlights, however, early observation by parents in DRC did not lead to an early diagnosis, which is similar in other countries in SSA. On average, children in SSA are diagnosed with autism 4.5 years after their parents observe the first clinical signs.

Conversely, in many of the studies conducted in Western countries, observing the first alert signs of autism at an early age (before 2 years old) lead to a diagnosis at an early age (10,13,30-31).

This difference between Western and African countries may be explained by poor diagnostic assessment for autism and follow up for African children with developmental problems (31). More specifically, this study suggests that a delayed autism diagnosis, particularly in DRC, cannot be linked to a complete lack of awareness or misunderstanding of the early signs of autism among parents and doctors when these signs present early. Rather, the results of this research imply that healthcare specialists are only currently treating isolated signs and symptoms directly associated with autism without considering associated conditions, including ADHD, epilepsy, behavioral and language disorders, and a hearing impairment. It is essential healthcare practitioners, parents, and teachers consider referring children who exhibit these associated conditions for an autism evaluation to narrow the mean time lag between concern and diagnosis.

Alert signs and symptoms reported by parents when autism is diagnosed.

In this study, social interaction disorders were observed earlier (1.4 year) than communication disorders (2.2 years; p< .01; see figure 1). In contrast and according to Zwaigenbaum *et al.* (31), the first signs of a social interaction disorder in children in Canada were observed between the ages of 6-12 months. Further, Zwaigenbaum *et al.* (31) describe the behavioral and social abnormalities, as they are manifest between 1 and 2 years. Another study in the United States established that both behavioral disorders and social interaction disorders appeared around the first year for autism monitoring (32). According to Landa *et al.* (32), poor social interaction and behavioral disorders are the main clinical signs of autism in American children. Conversely, studies reveal that parents are often alerted because of their children exhibiting a speech delay (5,13,33). Crucially, how these patterns of communication and social interaction are interpretation, however, are culturally determined. Throughout SSA, a child's lack of interaction with adults or child not observing adults is a sign that a child has good social etiquette, a good education, and respect for adults (13). This distance between adults and children who may be exhibiting early alert signs of autism only serve to compound an already challenging diagnostic trajectory.

Main signs observed by PI during diagnosis

Language and speech impairment

Communication disorders were the primary reason for both an early diagnosis and subsequent behavioral concerns.

A language delay was the most prevalent early symptom (62.5%) parents noticed across all three recruitment sites. This can be explained by the societal importance Congolese parents place on speech and language skills for their child's integration into the family unit and externally, particularly at school. This confirms previous findings where a language delay was the most common early symptom (53.5 to 77.0% cases) of ASD noticed by the parents of Caucasian children (34) as well as African children (8,10-11). Language impairment is characterized by the absence of language or speech (4,7,10-11) Caucasian children (34).

In South Africa, Springer et al. (10) found 94 % non-verbal language among black African children in comparison to Caucasian children (42 %). Franz et al. (9) noted that the characteristics of clinical autism in African children are still poorly understood and that studies have methodological limitations, including use of small samples and a lack of adapted tools (4). Indeed, a delay or absence of language has also been found in minorities groups. This may be associated with the disparity that exists in access to children with ASD in these communities.

The delay or absence of language may be also explained by the under-diagnosis of mild or atypical forms of ASD (15), which both require a well-trained team including speech therapists and adapted tools. In the case of DRC and, particularly in Kinshasa, there is a scarcity of qualified speech and language disorders specialists who are essential for the diagnosis and treatment of autism comorbidities such as a language or hearing impairment.

Social interaction disorders

The PI's assessment revealed that social interaction disorders were more frequent, followed by behavioral and speech disorders, which confirms the presence of impairments in these three areas in the SSA context. The prevalence of social interaction disorders (95 %) was like the results of most African and Western studies (13,33), which confirm that a social interaction impairment is a core sign of autism. In a hospital-based study in Nigeria, all children with ASD showed poor eye contact and had difficulties with socialization (13). The social interaction disorder, a core symptom of the autism triad, was underreported and of greater alarm to parents than speech and behavior disorders. This suggests that the challenge for healthcare professionals and, particularly specialists is to recognize and then interpret the signs and symptoms of autism in order to make an early diagnosis in the SSA setting.

Behavioral disorders

Behavioral disorders were seen in three out of four children in this study. The high prevalence of behavioral difficulties (75 %) in this study may be related to the presence of comorbidities such as epilepsy and an intellectual disability (5,8,34). According to Bello-Mojeed et al. (13) 83.3% of study participants in Nigeria showed aggression, 83% were resistant to changes, and 78 % had crying tantrums. Regarding tantrums/crying, Young et al. (34) observed a frequency of 28.4%. Children with Intellectual Disability (ID) and those with ASD often exhibit similar symptoms, such as self-harm behavior and stereotypies (27). Self-injury is frequently seen in children with a dual diagnosis of ASD and ID (8).

Epilepsy (72.5 %) and a hearing impairment (27.8 %) were the most important comorbidities in this study. This stands in contrast to previous empirical research where the prevalence of these comorbidities did not exceed 45% in the case of epilepsy (26) and 9.5 % in the case of hearing impairments (36). By contrast, the proportion of ADHD among the children involved in this study was comparable to other empirical results (37-38). Epilepsy and a hearing impairment were associated with the main symptoms of autism and the recruitment sites. Regarding the presence of epilepsy, this study suggests epilepsy is more readily recognized as an alert sign among parents and doctors in DRC. More specifically, parents are more at ease about pursing treatment for suspected epilepsy than for autism. As a neurodevelopmental disorder, epilepsy is also better understood by healthcare specialists. Consequently, the presence or suspected presence of epilepsy can motivate parents to seek a consultation at one of the healthcare facilitates involved in this study.

Crucially, there is good collaboration across medical services as well as between these services and the center's specialist teachers which likely facilitated an earlier autism diagnosis. This is also relevant regarding the number of children with a hearing impairment (27.8 %), which is also linked to the close collaboration between Ear, Nose and Throat (ENT) and neurodevelopment specialists at the public healthcare centers.

Further, unlike the other public healthcare center (e.g.: CNPP) which treats both children and adults for a variety of psychiatric and behavioral disorders or epilepsy, parents face little to no stigma for taking their child to Village Bondeko de Kabambare (VBK) for consultation and treatment. In comparison, CNPP is widely referred to in a derogatory way by people in DRC and, particularly in Kinshasa, as the hospital for those who are insane or crazy which may explain why there are double the number of cases of children with epilepsy and those with a hearing impairment at VB (45 and 18 cases respectively) in comparison to CNPP.

Nevertheless, despite derogatory labels ascribed to children who are taken to and treated at CNPP, it is noteworthy that the prevalence of hearing impairment and epilepsy cases at CNPP is still higher that the case numbers for the same comorbidities at CIEHMA, the private health care center. As alluded to previously, this private center for research, evaluation, and the care of children with mental disabilities is embedded within a specialized school facility for the management of autism and other neurodevelopmental disorder. This likely explains why the prevalence of epilepsy and hearing impairments was low. Parents are less likely to take their children and, thereafter, enroll them in this school when their child has severe neurodevelopmental disorders.

Consequently, although a high frequency of epilepsy (72.5 %) and hearing impairments (27.8 %) can be linked to research populations at the various participating healthcare centers, which comprise centers specializing in the diagnosis, management, and treatment of neurodevelopmental disorders centers (5), the observed high frequency of epilepsy must also be put into perspective given the possible selection bias of active and non-active epilepsies, the inclusion of febrile seizures and infantile spasms, and heterogeneities of the study population.

In sum, this research suggests that the presence of comorbidities can influence the parents and caregivers' choice of healthcare center for children with ASD (5,27). These health care facilities host children suffering from the effects of sequelae related to pre- and post-natal complications, chronic otitis, and infections of the nervous system which are prevalent and known factors in early cerebral morbidity in SSA (39).

Weakness of the study

This study is based on information obtained partially from parents. Parents may interpret their children's characteristics differently and may forget important details concerning early developmental phases, including early alert signs and symptoms of ASD as well as their child's age at the onset of these signs. Further, although many children with neurodevelopmental disorders in Kinshasa are referred to one of the three healthcare centers included in this research, this study is unable to determine the proportion of children in Kinshasa, and in DRC more generally, with ASD signs who have never been examined by a qualified health professional. Lastly, this study employed clinical observation according to the Diagnostic and Statistical Manuel of Mental Disorders four TR (DSM-IV-TR) criteria to confirm an autism diagnosis among children included in this study. The primary motivation behind the use of the DSM-IV-TR criteria rather than the more recent DSM 5 criteria relates to when the research team conducted the clinical observations and collected

the data. The DSM 5 criteria was not yet available when the research team collected the data between 2008-2010. That said, the term ASD was already used in literature on autism. As such, in this article, the term ASD is generic and represents autism, Asperger's syndrome, and pervasive developmental disorder not otherwise specified. In doing so, the significance of this research is two-fold. First, this study begins to fill a critical gap in how we understand and diagnose autism in an African country with limited resources by drawing on a large sample of children (boys and girls) diagnosed with autism after a rigorous clinical evaluation process using standardized tools, Childhood Autism Rating Scale (CARS) and Autism Diagnostic Interview-Revised (ADI-R). Relatedly, this study also seeks to detail the early clinical features of ASD and the range of comorbidities.

Conclusion

Many children in the present study were boys diagnosed with autism at school age.

The clinical characteristics of children with ASD were delayed diagnosis and language, co-occurrence with epilepsy and hearing impairment. Thus, the present study suggests screening for autism and its main comorbidities in children followed up in neurodevelopmental disorder care centers as part of a multidisciplinary team to reduce the delay in diagnosis and management of autism in Kinshasa, DRC. Finally, this study encourages further research to refine the relationships between complaints at diagnosis and comorbidities.

Conflict of interest

The authors declared that they have no conflict of interest regarding this manuscript.

Author's contributions

Davin Mbeya Mpaka: designed and executed the study, diagnostic evaluation, interpretation and confirmation with the standard autism tools (CARS and ADIR) , assisted with the data analyses, and wrote the final manuscript .

Adelin Makubu N'situ: collaborated towards the design, executed the study;

Thierry Ma-Nzuzi Matonda**:** organized, analyzed the data and wrote part of the results;

Ally Omba Ndjukendi**:** collaborated towards the design, executed, and wrote the study.

Joachim Ebwel Mukau: collaborated towards the design, diagnostic evaluation, interpretation and confirmation with the standard autism tools (CARS and ADIR) and wrote approve the manuscript;

Gilbert Lelo Mananga**:** collaborated towards, both the writing and editing of the final full manuscript;

Daniel E-Andjafono Luwa Okitundu: collaborated towards the design, executed the study, and wrote and approve the manuscript;

Guy Makila Bumoko: collaborated towards, both the writing and editing of the final manuscript;

Luck Lukusa: designed and executed the study.

Valentin Malanda Ngoma**:** collaborated towards the writing and approve final manuscript;

Annick Vogel: collaborated towards the writing and approve final manuscript;

Espérance Kashala-Abotnes**:** collaborated towards the writing and approve final manuscript;

Samuel Ma-miezi Mampunza: designed this study and collaborated towards the writing and approve the final manuscript.

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