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The naturalistic follow-up of pervasive developmental disorders–not otherwise specified cases

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ABSTRACT

OBJECTIVES: Pervasive developmental disorders (PDDs) are neurodevelopmental disorders characterized by deficits in social interactions, communication impairments, and the presence of restricted interests and stereotyped behaviours. The issue of diagnostic stability, course, and prognosis of PDDs is an increasing focus of research studies. The aim of this study is to evaluate the individuals who were previously diagnosed with pervasive developmental disorders–not otherwise specified (PDD–NOS) (one of the sub-diagnoses of PDDs) under age six years with respect to their current diagnoses.

METHODS: The participants were selected among the patients who were diagnosed with PDD–NOS under six years of age in our outpatient clinic. We obtained 208 patients' file records. We were able to reach 92 patients' parent by telephone and 58 parents accepted to voluntarily participate. After the excluded cases, finally 51 patients were evaluated in this cross-sectional naturalistic follow-up study. Children Autism Rating Scale (CARS) and Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS) were administered to participants; Autism Behavior Checklist (ABC) was completed by their parents.

RESULTS: There were 44 (86.3%) male and 7 (13.7%) female participants in the study. The current mean age was 8.62 years ($SD = 2.25$). The mean age at the time of first diagnosis was 3.56 years ($SD = 1.22$). The mean duration of the follow-up period was 5.05 years ($SD = 2.27$). Forty-five (88.2%) of 51 patients remained to have one of the PDDs (23 autistic disorder, 22 PDD–NOS) according to DSM-IV-TR. Six patients (11.8%) did not meet the diagnostic criteria of any PDDs. Two of these six patients diagnosed with attention-deficit/hyperactivity disorder and one with mild-level intellectual disability.

CONCLUSIONS: It was observed that 11.8% patients who diagnosed as PDD–NOS less than six years old were found to be off the PDD spectrum. PDD–NOS diagnosis stability was found 43.1% and 45.1% of the patients moved to another PDD diagnosis. These findings should be supported with further studies in Turkey, by increasing sample size, and follow-up duration for understanding the course.

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Pervasive developmental disorder–not otherwise specified; autism spectrum disorder; prognosis

Introduction

Autism spectrum disorder (ASD), which had been defined as pervasive developmental disorders (PDDs) in previous diagnostic and statistical manual of mental disorders (DSM-IV-TR), is characterized by persistent deficits in social communication and social interaction across multiple contexts, including deficits in social reciprocity, nonverbal communicative behaviours used for social interaction, and skills in developing, maintaining, and understanding relationships in DSM-5. In addition to the social communication deficits, the diagnosis of ASD requires the presence of restricted, repetitive patterns of behaviour, interests, or activities [1]. In DSM-IV-TR, there were sub-diagnoses of PDDs: autistic disorder (AD), pervasive developmental disorder–not otherwise specified (PDD–NOS), and Asperger's disorder. PDD–NOS diagnosis is made for people who do not meet criteria for a specific PDD but who have a severe and persistent

impairment in the development of reciprocal social interaction associated with impairment in either verbal or nonverbal communication skills or with the presence of stereotyped behaviour, interests, and activities [2].

Several previous studies have examined the validity of PDD–NOS diagnosis [3–5]. Some of the studies found that there are less restricted, repetitive stereotyped behaviours in PDD–NOS group than AD; however, the literature could not clearly discriminate PDD–NOS from other PDD diagnoses [6,7]. In some epidemiologic studies, PDD–NOS has been found more common than other PDD diagnoses although it is a residual catch-all diagnostic group [8,9].

Diagnostic stability of PDD was also explored in several studies [10–12]; however, there were no studies which examined the diagnostic follow-up of PDD–NOS cases particularly. Only two studies have examined the prognosis of PDD–NOS in long-term

follow-up, but these studies have examined the outcomes and difficulties in the adulthood of patients with PDD–NOS [13,14].

The main objective of our study was to examine the individuals who were previously diagnosed with PDD–NOS under age six years with respect to their current diagnoses.

Methods

Participants

The sample of this study was selected among the patients who were diagnosed with PDD–NOS diagnosis in our outpatient clinic. We obtained 208 patients' data based upon patients' file records. We were able to reach 92 patients' parent by telephone and 58 parents accepted to voluntarily participate in the study. Three of them were excluded as their ages were over 18. Four patients were excluded from the study as their file records showed that their first diagnosis was AD. Finally, 51 patients were evaluated in this study (Figure 1).

There were 44 (86.3%) male and seven (13.7%) female participants in the study. The current mean age of the participants was 8.6 years ($SD = 2.3$). Their mean age at the time of first diagnosis was 3.5 years ($SD = 1.2$). The mean duration of the follow-up period was 5.1 years ($SD = 2.2$) (Table 1). The study was approved by the Clinical Research Ethics Committee of Ege University School of Medicine. The purpose, procedure, and forms to be completed in the study were explained to the parents of the participants. Written informed consents were obtained from all parents included in the study.

Diagnosis and follow-up procedure

This study is a cross-sectional naturalistic follow-up study. At the time of first diagnosis of participants,

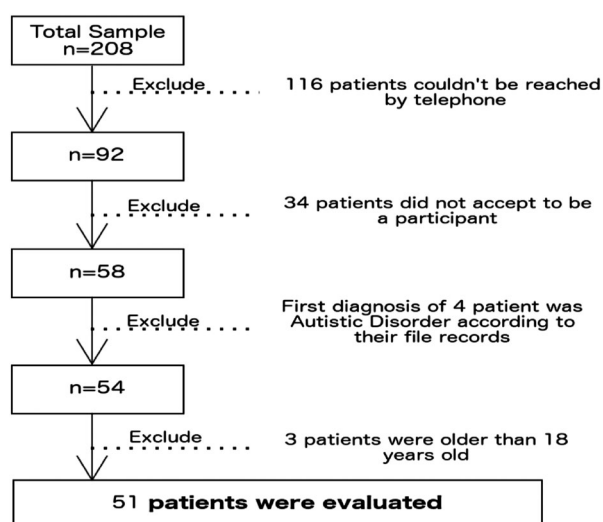


Figure 1. Selection of subjects.

Table 1. Characteristics of participants initially diagnosed as PDD–NOS.

	Mean	Minimum	Maximum	Standard deviation
Age	8.6	4.5	16.0	2.3
Age at diagnosis	3.6	1.5	6.0	1.2
Follow-up duration	5.1	3.0	14.0	2.3

elaborated psychiatric examination was conducted by child psychiatry residents and every child was observed in playroom session by an experienced nurse in our clinic with regard to child's behaviour when interacting with his/her parents and peers. With all these data, final diagnostic decision was made according to DSM-IV-TR (American Psychiatric Association 2000) [2] criteria, during routine procedure. After the diagnosis of PDD–NOS, all participants were referred to special education. During follow-up period, participants have continued their regular psychiatric examinations in our outpatient clinic. In every visit, patients were evaluated with regard to their social communication skills and behaviours based on direct observation of the child, information from parents, and reports of school and special education teachers. Comorbid medical and psychiatric conditions were checked in each session, and psychotropic medication was started if necessary.

In the follow-up assessment for this present study, all participants were re-examined elaborately by the authors using a structured interview using the evaluation form which is developed by the authors and based on the DSM-IV-TR A-B, and C criteria of PDD assessing the social functioning (five items), communication (four items), and stereotypic-ritualistic behaviour/ interests (four items) domains. The children were diagnosed according to DSM-IV-TR criteria of PDD–NOS, by consensus of all authors. In addition to diagnostic process, authors rated the Childhood Autism Rating Scale (CARS) [15,16] based on their observations during the interview. Parents completed the Autism Behavior Checklist (ABC) [17], before the evaluation.

Psychometric measures

Socio-demographic information and evaluation form

This form, developed by the authors, was administered to obtain data about the child's age, gender, developmental history, education, medical history, diagnostic, and therapeutic data. Also, it has questions based on the DSM-IV-TR A-B, and C criteria of PDD, and assesses the social functioning (five items), communication (four items), and stereotypic-ritualistic behaviour/interest (four items) domains.

Childhood Autism Rating Scale (CARS)

CARS is developed by Schopler et al. [15] and it is widely used for diagnosis and rating of autism. Turkish

translation, reliability, and validity studies were conducted by Sucuoglu et al. [16]. The scale consists of 15 individual items. Every item is given points of 1–4 based upon to abnormality degree of observed behaviour. 1 point indicates that behaviour is in normality range and 4 points indicate that behaviour is extremely out of normality range. The score of the scale ranges between 15 and 60. Scores of 30–36 indicate mild to moderate autism and scores above 36 indicate severe autism.

Autism Behavior Checklist (ABC)

ABC is a screening instrument for autism and it consists of 57 items that are observed symptoms in children with autism. The instrument was developed by Krug et al. [17]. The Turkish translation, reliability, and validity study was conducted by Irmak et al. [18]. ABC includes five subscales: sensory (9 symptoms), relating (12 symptoms), body and object use (12 symptoms), language abilities (13 symptoms), and social and self-help abilities (11 symptoms). The score of the checklist ranges between 0 and 159. Total scores of 67 or above are considered to indicate autism with high probability in the original study. However, in the study of Turkish validation, the cut-off score was stated as 39 [18].

Statistical analysis

Statistical analyses of this study were carried out by Ege University School of Medicine's Medical Statistics Department using IBM SPSS Statistics Version 20.0 for Windows. Descriptive statistics were used to present the participant characteristics and follow-up data. CARS and ABC scores were examined using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov test) were performed to determine whether or not the data are normally distributed. Descriptive analyses were presented using means and

standard deviations for normally distributed CARS and ABC variables. Welch analysis of variance (ANOVA) was used to compare these parameters among the diagnostically status (no-diagnosis/PDD–NOS/AD) groups. Levene test was used to assess the homogeneity of variances. According to Levene test, variances of CARS and ABC values of groups were not homogeneous, as well as sample sizes of diagnostic groups were not equal. Therefore, pairwise *post hoc* tests were performed using Games–Howel test. We considered $p < .05$ to be statistically significant.

Results

Socio-demographic and clinical characteristics of participants

The socio-demographic and clinical characteristics of participants were presented in Table 1.

Final DSM-IV-TR diagnoses in the follow-up

As a result of final assessment, 45 (88.2%) of 51 cases met the criteria for one of the PDDs according to DSM-IV-TR. Six cases (11.8%) did not meet the diagnostic criteria of any PDDs. Twenty-three cases were diagnosed with AD, 22 were diagnosed with PDD–NOS in our diagnostic assessment. Two cases had comorbid anxiety disorder, seven cases had attention-deficit/hyperactivity disorder (ADHD), and one case was diagnosed with mild-level intellectual disability (ID) in PDD–NOS group. Two cases were diagnosed with ADHD and one had mild-level ID of the six cases who are out of the PDDs (Table 2).

CARS and ABC scores of participants

The mean CARS scores of no-diagnosis, PDD–NOS, and AD group were found as 17.33 (SD = 2.21),

Table 2. Demographic, clinical, and comorbid psychiatric diagnostic characteristics of participants at follow-up.

	PDD–NOS $n = 22$	AD $n = 23$	No diagnosis $n = 6$	p
Age, years (mean \pm SD)	8.3 \pm 2.6	9.0 \pm 2.2	8.7 \pm 0.7	.54
Age at diagnosis, years (mean \pm SD)	3.3 \pm 1.2	3.7 \pm 1.3	3.6 \pm 0.7	.54
Follow-up duration, years (mean \pm SD)	4.9 \pm 2.6	5.3 \pm 2.1	5.2 \pm 1.3	.81
Use of first words, years (mean \pm SD)	2.2 \pm 0.8	2.8 \pm 1.4	2.0 \pm 1.2	.24
Total IQ	79.15 \pm 10.2	61.87 \pm 16.6	88.67 \pm 26.1	2 < 3; $p = .01$ 1 = 3; $p = .26$ 2 < 1; $p = .03$
Formal education attendance (n)				
Yes	21	13	6	
No	1	10	0	
Special education, years (mean \pm SD)	4.1 \pm 1.8	5.8 \pm 2.1	3.7 \pm 2.4	1 = 3; $p = .72$ 2 > 1; $p = .02$ 2 = 3; $p = .05$
CARS score (mean \pm SD)	23.61 \pm 4.1	31.00 \pm 6.4	17.33 \pm 2.2	2 > 1 > 3 ($p < .001$)
ABC score (mean \pm SD)	21.36 \pm 13.20	49.41 \pm 21.32	2.50 \pm 2.07	2 > 1 > 3 ($p < .001$)
Comorbid diagnosis (n)				
ADHD	7	8	2	
ID	1	15	1	
Anxiety disorder	2	2	0	
Depressive disorder	0	1	0	

Note: PDD–NOS: pervasive developmental disorder–not otherwise specified; AD: autistic disorder; ADHD: attention-deficit/hyperactivity disorder; ID: intellectual disability; 1 = PDD–NOS; 2 = AD; 3 = no diagnosis.

Table 3. Characteristics of the cases who lost the diagnosis of PDDs.

Cases	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age (years)	9.5	8.0	8	8.5	9.5	9
Gender	Male	Male	Female	Male	Male	Male
Age at diagnosis (years)	3	4	4	4.5	3	3
Use of first words (years)	3	4	1	1	1.5	1.5
Total IQ	51	105	101	70	123	82
CARS score	21	16.5	16.5	15.5	15.5	19
ABC score	1	5	4	0	1	4

23.61 (SD = 4.15), and 31.02 (SD = 6.44), respectively (Table 2). The mean CARS scores of these pairwise groups were found significantly different according to welch ANOVA with *post hoc* Games–Howell test ($p < .001$).

The mean ABC scores of no-diagnosis, PDD–NOS, and AD group were found as 2.50 (SD = 2.07), 21.36 (SD = 13.19), and 49.41 (SD = 21.31), respectively (Table 2). The mean ABC scores of these pairwise groups were found significantly different according to welch ANOVA with *post hoc* Games–Howell test ($p < .001$).

Discussion

This study is a cross-sectional naturalistic follow-up of 51 children with PDD–NOS. We found that 45 (88.2%) of these 51 patients remained to have one of the PDD diagnoses and 6 children (11.8%) did not meet the criteria for any PDD diagnoses. Twenty-two children were diagnosed with PDD–NOS (43.1%), 23 children (45.1%) were diagnosed with AD according to DSM–IV–TR criteria in the follow-up.

Our findings were consistent with several other recently published studies. In a recent follow-up study, it has been reported that the diagnosis of ASD (AD and PDD–NOS) was stable over time and 41 (95.3%) out of 43 children retained an ASD diagnosis [11]. In this study, when looking at specific ASD diagnosis, AD diagnosis was stable for 33 out of 37 (89.18%) children, 3 moved to a PDD–NOS diagnosis, and 1 child went off the spectrum. The PDD–NOS diagnosis was stable for only one out of six (16.67%) children, four of the six children who were initially diagnosed with PDD–NOS moved to an AD diagnosis, one to a non-autistic developmental disorder, and only one retained the same diagnosis [11]. With the DSM-5 spectrum approach, 88.2% of our cases remained to have ASD (one of the PDDs; 23 AD, 22 PDD–NOS according to DSM–IV–TR). Although our ASD stability ratio seemed lower than Indian follow-up study, our initial cases only included PDD–NOS.

While 45.1% of our PDD–NOS cases moved to AD, Malhi and Singi [11] reported 66.6% of their cases moved to AD diagnosis from PDD–NOS. Lord et al. [10] indicated that more than half of children initially

diagnosed with PDD–NOS at age two years later met autism criteria at age nine years. They reported that nearly 30% continued to receive diagnoses of PDD–NOS, indicating mild symptoms at age nine years [10]. In another study which was conducted by Turner et al. [12], seven children with PDD–NOS were evaluated seven years after the first diagnosis and three of them moved to autism diagnosis, two children remained to have PDD–NOS diagnosis, one child was diagnosed as Asperger's Syndrome, and one child was out of the autism spectrum in the follow-up [12]. PDD–NOS stability rate is 43.1% in our study, which is higher than Indian study, but the age at first diagnosis of our cases is higher than Malhi and Singi [11] study. Researchers stated that PDD–NOS diagnosis in very young children is the not a stable diagnosis [11,12]. The lack of reliable diagnostic criteria can be one of the explanations for the diagnostic instability [19]. PDD–NOS diagnosis is made for people who do not meet criteria for a specific PDD but who have a severe and persistent impairment [2].

Six patients (11.8%) of our PDD–NOS group did not meet the diagnostic criteria of any PDDs. Lord et al. [10] indicated that more than 10% of children with diagnoses of PDD–NOS at age two years received non-spectrum diagnoses (i.e. not autism or ASD) by age nine years, and Turner et al. [12], of the seven children with PDD–NOS, one child was out of the autism spectrum (14.3%) in the follow-up after seven years from the first diagnosis [12]. Helt et al. [20] reported that 3–25% of children lost their ASD diagnoses in their review. The researchers, investigating the initial characteristics of the children on the outcomes, stated that symptom severity has little predictive power in determining outcome of ASD [21].

The most promising data of our study is the considerable amount of children who are completely out of autism spectrum. In a recent follow-up study from Turkey, which examined the characteristics of children who lost the diagnosis of autism, it was reported that patients from well-educated families with sufficient economic status had more opportunities to gain high quality assessments and intervention programmes [22]. Although we did not enquire the parents' education and family income characteristics in this study, our patients' opportunity to gain high quality

education and intervention programmes were limited. They have been attending to special education that was provided by government, 2–3 hours per week.

Another important implication of this study is PDD–NOS diagnosis was stable in less than half of the sample (43.1%). Although a considerable amount of the children moved to AD diagnosis (45.1%) in the follow-up, with the shift of sub-diagnosis most of the children remained to meet PDD diagnosis (88.2%) in this study. These data imply that, although PDD–NOS diagnosis in early childhood is not stable, most of these children have a PDD diagnosis. This ambiguity might be solved with the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as it removed the separate diagnoses of PDD and defined a new disorder, Social (Pragmatic) Communication Disorder (SCD), which is characterized by a primary difficulty with pragmatics, or the social use of language communication, in the absence of stereotypic behaviour or interests [1]. Furthermore, DSM-5 added disorder's severity term (mild, moderate, and severe) to ASD definition. Children showing milder or subthreshold symptoms of autism might be diagnosed with SCD or mild-level ASD instead of the catch-all diagnosis of PDD–NOS formerly. In a recent study, Kim et al. [23] found that 71% of PDD–NOS diagnosed children have an ASD diagnosis, and 22% of these children had SCD diagnosis when they were evaluated according to DSM-5 criteria.

The results of this study showed that CARS and ABC scores significantly correlated with the diagnosis of PDD as it has been predicted. Significantly lower CARS and ABC scores were observed in patients who lost their diagnoses in the follow-up.

This present study has certain limitations. Firstly, the loss of follow-up cases is high and our sample size is relatively small. This condition can affect the ratio of the cases moved off the spectrum; therefore, studies with larger sample sizes might have different results. Secondly, Turkish adaptations of Autism Diagnostic Interview-Revised (ADI-R) [24] and Autism Diagnostic Observation Schedule (ADOS) [25] are not yet available, so that our diagnostic evaluation is limited to clinical observations and DSM-IV-TR criteria. Although ADI-R and ADOS are accepted as the golden standard diagnostic instruments in PDD diagnosis, some authors have stated that neither ADI-R nor ADOS is required for making a clinical diagnosis of ASD [26]. Thirdly, if we had rated ABC or CARS at the initial assessment procedure in outpatient clinic, we could have speculated about the severity or symptom profile of the patients who moved off the spectrum. This is another limitation of our study. But some researchers examining the initial characteristics of the children on the outcomes stated that symptom severity has little predictive power in determining outcome of ASD, and also intelligence and adaptive

behaviour functioning did not differ the children with optimal outcome and those who remained the spectrum [21,27]. Furthermore, the participants of this study were collected from our clinic, tertiary university hospital, and it might not represent the general population.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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