

# Delays in the progress of developmental skills among adolescent schizophrenia patients with and without a co-morbid pervasive developmental disorder

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## Abstract

**Background:** Delays in the progress of developmental skills have been associated with both schizophrenia and pervasive developmental disorders. This study aimed to evaluate developmental delays among adolescents suffering from schizophrenia. Further, as both neuroimaging and genetic studies have reported an overlap of symptoms between schizophrenia and pervasive developmental disorders, we aimed to compare the nature and number of these delays among patients with and without a co-morbid pervasive developmental disorder.

**Methods:** The study comprised a consecutive sample of 18 adolescents with schizophrenia and their families. The diagnosis of schizophrenia was assessed with the Kiddie Schedule for Affective Disorders and Schizophrenia for the DSM-IV. The Diagnostic Interview for Social and Communication Disorders version 11, which includes 43 items focusing on developmental skills, served in assessing delays in the progress of developmental skills.

**Results:** All adolescents suffering from schizophrenia exhibited some developmental delays. The most frequent delays were in reading their first book, independent sitting, riding a tricycle, cooperative play, and role play with their age peers, followed by riding a bicycle, tying their shoelaces, expressing meaningful words, spontaneously joining in with their age peers, parallel play and drawing recognizable objects or persons. The median number of delays among adolescents with schizophrenia was 3. The number of delays in developmental skills was significantly higher ( $p=0.001$ ) among adolescents with co-morbidity than among those without it. Developmental delays in three specific skills - cooperative play ( $p=0.002$ ), role play with their age peers ( $p=0.002$ ) and reading their first book ( $p=0.025$ ) - occurred significantly more often among schizophrenia patients with a co-morbid pervasive developmental disorder than among those with no co-morbidity.

**Conclusions:** Developmental delays are frequent among adolescents suffering from schizophrenia. Schizophrenia patients with a co-morbid pervasive developmental disorder exhibit significantly more developmental delays than do patients suffering from schizophrenia alone.

## Background

Schizophrenia is a severe, pervasive mental disorder characterized by positive symptoms such as hallucinations, delusions and disorganized speech, in addition to negative symptoms such as marked apathy, a paucity of speech, and blunt or incongruent emotional responses. The onset of schizophrenia before the age of 18 is commonly categorized as early-onset schizophrenia. This form of schizophrenia can have either an acute or gradual onset. The onset of schizophrenia before the age of 13 years is considered childhood-onset schizophrenia, which in most cases shows an insidious onset (1). The prevalence of childhood-onset schizophrenia is less than one in 10 000 children, but the prevalence of schizophrenia-related disorders among adolescents is about 1-2% (2, 3).

Differences between children destined to develop schizophrenia and the general population have been reported across a range of developmental domains. According to a study by Walker and Lewine (4), which used childhood home movies, children who later developed schizophrenia exhibited less responsiveness, eye contact and positive affect as well as more problems in fine and gross motor coordination than did their healthy siblings. Jones and Rodgers (5) reported in their birth-cohort study that children who later developed schizophrenia showed speech problems and delays in milestones of motor development, especially in walking, more often than other children did. Also, a preference for solitary play at ages four to six was associated with later schizophrenia. According to another birth-cohort study by Isohanni et al. (6), children who later developed schizophrenia showed delays in learning to stand, walk and become potty trained when compared to their healthy peers. Cannon et al. (7) reported that patients suffering from schizophrenia learned to walk later and managed worse in standard motor skills at ages three, five and nine than did healthy controls. Also, receptive language development impairments were related to schizophrenia. Internalizing problems as well as peer rejection occurred more often among those who later developed schizophrenia than among healthy individuals.

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Pervasive developmental disorders (PDDs), affecting 0.6-1% of the general population (8), share a core triad of abnormalities: 1. qualitative impairments in reciprocal social interactions, 2. qualitative impairments in verbal and non-verbal communication, and 3. restricted social imagination with repetitive and stereotyped patterns of interests and behaviour (9). In the ICD-10 classification (10), PDDs comprise two major categories: Childhood autism and Asperger's syndrome, as well as some rare or residual subgroups (e.g. Atypical autism and Rett's syndrome).

Many parents with an infant later diagnosed with autistic spectrum disorders (a broad variant of PDDs) recall noticing atypical behaviours already during the child's first year of life (11, 12). According to De Giacomo and Fombonne (13), however, the majority of parents report concerns about their child's development when s/he reaches the age of 18 to 24 months. Teitelbaum et al. (14) used home video recordings and analysed the movements of 17 children with autistic spectrum disorders aged four to six months. Infants who later developed autistic spectrum disorders exhibited delays in rolling over, sitting, crawling and walking skills. Both gross and fine motor skills have proved to be more impaired in young children with autistic spectrum disorders than in those with other kinds of developmental problems (15); they also learned their first word later than did other children (16). Further, Paul et al. (17) reported that such children showed more deficits in receptive communication and daily living skills, as well as in self-help skills such as bathing, feeding and dressing than did children with other developmental delays. In their review, Mitchell et al. (18) listed atypical patterns of social orienting and attention, atypical patterns of social affect, a lower likelihood to respond to their name, or use of gazing to modulate social interaction, unusual visual exploration, repetitive movements, and atypical sensory responses as behavioural markers useful in differentiating children with autistic spectrum disorders from those with normal development.

The present study aimed to evaluate delays in the progress of developmental skills among a consecutive sample of adolescents suffering from schizophrenia. As both neuroimaging and genetic studies have reported that there is an overlap of symptoms between schizophrenia and PDDs (19, 20), our second aim was to compare the nature and number of these delays between adolescent schizophrenia patients with or without a co-morbid PDD. We hypothesized that developmental delays among adolescents suffering from schizophrenia would be frequent, and that the nature and number of these developmental delays would be much the same among adolescents with and without a co-morbid PDD.

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## Materials and methods

### Participants and procedure

The data were collected between 2009 and 2011 in the Hospital District of Helsinki and Uusimaa, which is located in Southern Finland and comprises approximately 1.4 million inhabitants of whom ca. 82 500 were 13- to 17-year-old adolescents. During the study period, the hospital district had three rehabilitation units for adolescents with schizophrenia. The study comprised a consecutive sample of patients ( $n=18$ , 7 males, 11 females, mean age 15.6 years, SD 1.4 years, range 13-17 years) and their families from all three of these rehabilitation units. The diagnosis of schizophrenia was based on an assessment with the Schedule for Affective Disorders and Schizophrenia for School-Aged Children - Present and Lifetime (K-SADS-PL) for the DSM-IV (21), performed by a clinical psychiatrist. Four persons suffered from childhood-onset schizophrenia, whereas among the others, onset of the disorder occurred at age 13 or later in life. Altogether 17 participants scored an IQ > 70 (mean 93, SD 16) in a standard psychological assessment (WISC-III/WAIS-III) performed during or before the study period. Based on life chart information, all participants showed a primary IQ in normal range. One adolescent had suffered from epilepsy in early childhood, but was seizure-free and without anti-epileptic medication during the study period. A non-contrast brain MRI was performed in all participants and evaluated by a clinical radiologist. The result was normal in all cases. Ten adolescents who were suffering from schizophrenia had no co-morbid PDDs. Of the eight participants with PDDs, two suffered from childhood autism (F84.0), three from atypical autism (F84.1), and three from Asperger syndrome (F84.5). For further details, see Waris et al. (22).

### Methods

#### Background information

Of the 18 participants, birth records were available for 16, records from well-baby clinics (maternity and child care clinics which operate as a part of the Finnish national health care clinics, and are regulated by nationwide guidelines) for 15, and school health care reports for 17.

## DISCO

The Diagnostic Interview for Social and Communication Disorders (DISCO) version 11, developed by Wing and Gould (23), is a semi-structured interview administered to parents or other primary caregivers. The interview takes two to three hours and contains 387 questions about current skills, the development of these skills, and atypical behaviour (e.g. repetitive stereotyped activities, emotions, maladaptive behaviour and psychiatric disorders and forensic problems) during the lifespan of the adolescents. The DISCO is designed for both clinical and research use to assess autism spectrum disorders in individuals of all ages and ability levels; a computerized algorithm was developed for this latter purpose. The DISCO has good inter-rater agreement (24) and high agreement between the DISCO and the Autism Diagnostic Interview-Revised (ADI-R) classification has also been reported (25). In the present study, one of the authors (P.W.), trained in the use of the DISCO assessment, interviewed all participants' parents.

The DISCO includes 43 items that focus on developmental skills. The items are classified into 17 subgroups: gross motor skills, toilet training, feeding, dressing, hygiene, domestic skills, independence, receptive communication, expressive communication, non-verbal communication, social interaction with adults, social interaction with age peers, social play, imagination, cognitive skills and achievements, pictures-reading-writing, and visuo-manual and spatial skills (see Table 1).

In the DISCO, the average ages when a normal child is expected to achieve these above-mentioned developmental steps, have been adopted from the Vineland Adaptive Behavior Scales (26).

The DISCO includes a question about the child's age when the parents/caregivers for the first time became worried about their child's development.

## Ethics

After receiving verbal and written information about the study, all participants and their parents provided their written informed consent. The study plan was scrutinized by The Ethics Committee of the Helsinki and Uusimaa Hospital Districts. The permission to conduct the study was granted by the pertinent institutional authorities of the Helsinki University Central Hospital and Hyvinkää Hospital Area.

**Table 1. Delays in developmental skills among 18 adolescent schizophrenia patients with (PDD+, n=8) and without (PDD-, n=10) a co-morbid pervasive developmental disorder. Fisher's Exact Test served to compare the groups. Effect sizes (Phi) are reported.**

Development skill	All	PDD+	PDD-	p	Phi
<b>Gross motor skills</b>					
Independent sitting	9/18 (50.0%)	4/8 (50%)	5/10 (50.0%)	NS	0.000
Walking	2/18 (11.1%)	1/8 (12.5%)	1/10 (10.0%)	NS	0.040
Riding a tricycle	6/18 (33.3%)	3/8 (37.5%)	3/10 (30.0%)	NS	0.079
Riding a bicycle	5/18 (27.8%)	2/8 (25.0%)	3/10 (30.0%)	NS	0.055
<b>Toilet training</b>					
Clean and dry during the day	3/18 (16.7%)	2/8 (25.0%)	1/10 (10.0%)	NS	0.200
Clean and dry at night	1/18 (5.6%)	1/8 (12.5%)	0/10 (0.0%)	NS	0.271
<b>Feeding</b>					
Eating solid food	2/18 (11.1%)	1/8 (12.5%)	1/10 (10%)	NS	0.040
Giving up the bottle or breast	2/18 (11.1%)	2/8 (25%)	0/10 (0.0%)	NS	0.395
Feeding self with a spoon and fork	0/18 (0.0%)	0/8 (0.0%)	0/10 (0.0%)		
Using a knife and fork	2/18 (11.1%)	2/8 (25.0%)	0/10 (0.0%)	NS	0.395
<b>Dressing</b>					
Pulling pants down and up	2/18 (11.1%)	2/8 (25.0%)	0/10 (0.0%)	NS	0.395
Independent dressing (no buttons)	2/18 (11.1%)	2/8 (25.0%)	0/10 (0.0%)	NS	0.395
Tying shoelaces	5/18 (27.8%)	4/8 (50.0%)	1/10 (10.0%)	NS	0.444
<b>Hygiene</b>					
Drying hands without help	2/18 (11.1%)	2/8 (25%)	0/10 (0.0%)	NS	0.395
Bathing and drying without physical help	3/18 (16.7%)	3/8 (37.5%)	0/10 (0.0%)	NS	0.500
<b>Domestic skills</b>					
Fetching and carrying or taking a simple message	3/18 (16.7%)	3/8 (37.5%)	0/10 (0.0%)	NS	0.500
Completing a small task without help	2/18 (11.1%)	2/8 (25.0%)	0/10 (0.0%)	NS	0.395

Development skill	All	PDD+	PDD-	p	Phi
<b>Independence</b>					
Going into the garden alone	1/18 (5.6%)	1/8 (12.5%)	0/10 (0.0%)	NS	0.271
Going to a local shop on own	1/18 (5.6%)	1/8 (12.5%)	0/10 (0.0%)	NS	0.271
Could be left alone at home for half a day	2/18 (11.1%)	2/8 (25.0%)	0/10 (0.0%)	NS	0.395
<b>Receptive communication</b>					
Obedying instructions independent of context	3/18 (16.7%)	3/8 (37.5%)	0/10 (0.0%)	NS	0.500
<b>Expressive communication</b>					
Meaningful words	5/18 (27.8%)	3/8 (37.5%)	2/10 (20.0%)	NS	0.194
Combining 2-3 words	2/18 (11.1%)	2/8 (25.0%)	0/10 (0%)	NS	0.395
Age when speech could be understood easily by strangers	1/18 (5.6%)	1/8 (12.5%)	0/10 (0.0%)	NS	0.271
Asking questions	1/18 (5.6%)	1/8 (12.5%)	0/10 (0.0%)	NS	0.271
<b>Non-verbal communication</b>					
Indicating an object or person to share interest	3/18 (16.7%)	3/8 (37.5%)	0/10 (0.0%)	NS	0.500
<b>Social interaction with adults</b>					
Selective social attachments in pre-school years	1/18 (5.6%)	1/8 (12.5%)	0/10 (0.0%)	NS	0.271
<b>Social interaction with age peers</b>					
Watches age peers with interest	1/18 (5.6%)	1/8 (12.5%)	0/10 (10.0%)	NS	0.271
Spontaneously joins in with age peers	5/18 (27.8%)	4/8 (50.0%)	1/10 (10.0%)	NS	0.444
<b>Social play</b>					
Parallel play	3/18 (27.8%)	3/8 (37.5%)	0/10 (80.0%)	NS	0.500
Cooperative play	6/18 (33.3%)	6/8 (75.0%)	0/10 (10.0%)	0.002	0.791
<b>Imagination</b>					
Waving goodbye	1/18 (5.6%)	1/8 (12.5%)	0/10 (0.0%)	NS	0.271
Simple pretend play alone	2/18 (11.1%)	2/8 (25.0%)	0/10 (0.0%)	NS	0.395
Role play with age peers	6/18 (33.3%)	6/8 (75.0%)	0/10 (0.0%)	0.002	0.791

Development skill	All	PDD+	PDD-	p	Phi
<b>Visuo-manual and spatial skills</b>					
Jigsaw of 10 or more pieces	2/18 (11.1%)	2/8 (25.0%)	0/10 (0.0%)	NS	0.395
Drawing recognizable objects or persons	5/18 (27.8%)	4/8 (50.0%)	1/10 (10.0%)	NS	0.444
<b>Pictures, reading and writing</b>					
Identifying objects in pictures	1/18 (5.6%)	1/8 (12.5%)	0/10 (0%)	NS	0.271
Reading first book	10/18 (55.6%)	7/8 (87.5%)	3/10 (30.0%)	0.025	0.575
Writing some words without copying	2/18 (11.1%)	1/8 (12.5%)	1/10 (10.0%)	NS	0.040
<b>Cognitive skills and achievements</b>					
Simple addition	1/18 (5.6%)	1/8 (12.5%)	0/10 (0.0%)	NS	0.271
Identifying coins	2/18 (11.1%)	2/8 (25.0%)	0/10 (0.0%)	NS	0.395
Knowing the names of the days	1/18 (5.6%)	1/8 (12.5%)	0/10 (0.0%)	NS	0.271
Hours and half hours on the clock	2/18 (11.1%)	2/8 (25.0%)	0/10 (0.0%)	NS	0.395

## Statistics

Fisher's exact test, the Likelihood Chi Square test, Independent t-test and Mann Whitney U-test served to compare the groups. The findings were considered significant when  $p < 0.05$ . Bonferroni correction was not used to control for type I errors due to the multiple comparisons, as it has been criticized for dramatically increasing the risk of type II errors (27-29). Instead, effect sizes are reported. The magnitude of the effect size was interpreted as follows: 0.00 to under 0.10, negligible association; 0.10 to under 0.20, weak association; 0.20 to under 0.40, moderate association; 0.40 to under 0.60, relatively strong association; 0.60 to under 0.80, strong association; and 0.80 to 1.00, very strong association (30). The data were analysed with SPSS version 21.0 (Macintosh) (31).

## Results

### The whole study group

All 18 adolescents with schizophrenia exhibited some developmental delays. The delays in developmental skills are presented in Table 1. The most frequent delays occurred in reading their first book, independent sitting, riding a tricycle, cooperative play, and role play with their age peers, followed by riding a bicycle, tying their shoelaces, producing meaningful words, spontaneously joining in with their age peers, parallel play and drawing recognizable objects or persons. Of the 43 developmental skills studied, the median number of skills with a delay was 3. The mean age of the adolescents when, for the first time, their parents became worried that something might be wrong with their child's development was 99.7 months (8.3 years) (SD 65.12, range 12-204).

### Comparisons between the two groups

Of the 43 developmental skills studied, schizophrenia patients with a co-morbid PDD exhibited a delay in a total of 42 (97.7%) specific skills. Those with no co-morbid PDD experienced delays in only 12 (27.9%) specific developmental skills. The difference between the groups was significant ( $\chi^2=22.395$ ,  $p<0.001$ ).

The number of skills with a delay was significantly higher among adolescents with a co-morbid PDD than among those without one (adolescents with co-morbidity: mean=12.3, SD 10.3, median 7.5, range 3-35, vs. adolescents with no co-morbidity: mean=2.3, SD 1.5, median 2, range 1-6;  $U=2$ ,  $p=0.001$ ).

Three specific developmental skills - cooperative play, role play with their age peers, and reading their first book - showed delays in development significantly more often among schizophrenia patients with a co-morbid PDD than among those with no co-morbidity. The effect sizes showed relatively strong or strong associations (see Table 1).

The mean age of the adolescents when, for the first time, their parents became worried that something might be wrong with their child's development was significantly lower among adolescents with a co-morbidity than among those without one (adolescents with a PDD: mean=62.25 months (5.2 years), SD=50.70, range 12-168, vs. adolescents without a PDD: mean=129.6 months (10.8 years), SD=61.34, range 36-204;  $t=2.49$ ,  $p=0.012$ ).

## Discussion

Our first hypothesis was that adolescents suffering from schizophrenia would exhibit delays in their developmental skills. Indeed, all 18 adolescents exhibited some developmental delays. The most prevalent developmental delays were in the areas of gross and fine motor development, speech development, social interaction and play. These findings are in agreement with those of earlier studies (4-7).

Our second hypothesis predicted that the nature and number of developmental delays would be much the same among adolescents with and without a co-morbid PDD. Contrary to our hypothesis, the median number of delays in developmental skills was significantly higher among adolescents with schizophrenia and a co-morbid PDD than among those with no such co-morbidity. Also, those with both disorders exhibited a significantly larger variety of developmental delays than did those suffering from schizophrenia alone. However, only three developmental skills showed delays significantly more often among schizophrenia patients with a co-morbidity than among those without one. These three skills were cooperative play, role play with their age peers and reading their first book. Cooperative play and role play with their age peers are known to be typical problem areas among children with PDDs, due to their serious deficits in the

development of imagination and social interaction, which are considered as core abnormalities of the disorder group (9). Reading is one of the most important skills learned at school (32). Previous studies have revealed that many individuals with autism spectrum disorders exhibit deficits in reading comprehension that do not match their intelligence (33, 34). Further, in their recent meta-analysis, Brown et al. (35) found that having autism spectrum disorder predicts that an individual will more likely experience problems with reading.

The mean age of the adolescents when, for the first time, their parents became worried that something might be wrong with their child's development was significantly lower among adolescents with a co-morbidity than among those without one. This finding is in line with that of a recent study by Veness et al. (36) reporting that parents whose children suffered from autistic spectrum disorders worried about their child's development significantly earlier than did parents whose children suffered from other kinds of developmental problems. However, unlike the results of De Giacomo and Fombonne (13), the parents of only two adolescents reported worries before their children were at the age of two. The difference observed between our two groups may stem from the fact that the number of developmental delays was significantly higher among those with both disorders than among those with schizophrenia alone.

Despite the overlap in genetic and neuroimaging studies as well as in symptoms between PDDs and schizophrenia, the developmental profiles of adolescents with schizophrenia and PDDs appear to differ substantially from those with schizophrenia alone. From a developmental perspective, the impact of PDDs manifests as more frequent and more early-onset developmental delays. However, shedding more light on these differences will require additional studies that compare our patients to PDD patients without schizophrenia. The strengths of our study include recruiting patients on a consecutive basis from inpatient units in a geographically defined area. In addition, structured instruments with good psychometric properties were used in combination with primary documents from early childhood, which are readily available in Finland. One must bear in mind, however, that the parents were asked to recall the childhood behaviour of their already adolescent offspring. Consequently, such data do not necessarily reflect actual behaviours, but subjective memories. The small sample size reduces the generalizability of our findings, so the results must be regarded as preliminary.

## Conclusions

Developmental delays are frequent in adolescents suffering from schizophrenia. Patients with schizophrenia and a co-morbid PDD show significantly more developmental delays than do patients with schizophrenia alone.

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