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## **More severe intellectual disability was found in teenagers than younger children with Down syndrome**

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## Short running title

Intellectual disability in Down syndrome

## ABSTRACT

**Aim:** We investigated the severities and profiles of intellectual disability (ID) in a population-based group of children with Down syndrome and related the findings to coexisting autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD).

**Methods:** There were about 100 children with Down syndrome living in Uppsala county, Sweden, at the time of the study who all received medical services from the same specialist outpatient clinic. The 60 children (68% male) were aged 5-17 years at inclusion: 41 were assessed within the study and 19 had test results from previous assessments, performed within three years before inclusion. We compared two age groups: 5-12 and 13-18 years old.

**Results:** Of the 60 children, 49 were assessed with a cognitive test and the 11 children who could not participate in formal tests had clinical assessments. Mild ID was found in 9% of the older children and in 35% of the younger children. Severe ID was found in 91% of the older children and 65% of the younger children. Verbal and non-verbal domains did not differ.

**Conclusion:** Intellectual level was lower in the older children and patients with Down syndrome need to be followed during childhood with regard to their ID levels.

**Keywords:** Attention deficit hyperactivity disorder, autism spectrum disorder, cognitive profile, Down syndrome, intellectual disability.

### Key Notes

- This population-based study investigated the severities and profiles of intellectual disability in 60 children with Down syndrome who received medical services from the same specialist outpatient clinic. .
- When we compared children aged 5-12 and 13-18 years we found that teenagers with Down syndrome were more likely to have severe and profound intellectual disabilities than younger children.
- Intellectual disability levels should be followed in children with Down syndrome.

### INTRODUCTION

Impaired intellectual function is a central feature of Down syndrome and intellectual disability (ID) is mainly a consequence of functional and developmental brain disturbances (1,2).

In addition to ID, many children with Down syndrome display other neurodevelopmental disorders, particularly autism spectrum disorder (ASD) (3,4), attention deficit hyperactivity disorder (ADHD) (5) and other externalising and, or, internalising behavioural problems that affect their daily life (6). A study from Israel reported that the prevalence of ADHD was 43.9% among children with Down syndrome (7) and a systematic review and meta-analysis,

estimated that ASD affected 16% of children with Down syndrome (8). Children with Down syndrome have delays across different developmental domains including language, gross motor, fine motor, cognitive, personal-social and self-help skills (7).

Chapman (8) compared the cognitive, behavioural phenotype in adolescents with Down syndrome and 16 individuals with corresponding cognitive impairment of unknown origin.

The author reported that those with Down syndrome had poorer skills in auditory-verbal working memory and comprehension than the other group, as well as more limited narrative language skill.

Patterson et al carried out a systematic review of 13 studies of cognitive development at various stages of childhood in Down syndrome, in order to study the implications for interventions. These included six studies that assessed overall cognitive performance based on intellectual quotient (IQ) and seven that explored specific cognitive domains. The studies that assessed IQ reported a decline across time. However, studies assessing change in cognitive domains were, for the most part, not interpretable because of large age ranges. The authors concluded that cognitive trajectories in children and adolescents with Down syndrome cannot be clearly defined based on published data (1).

Channell et al (9) studied adolescents aged 10-15 with Down syndrome and reported no significant decline in IQ with age, suggesting IQ stability during adolescence for individuals with Down syndrome. However, several participants in their study only managed to reach the floor level for the test they used, limiting the interpretation of the results.

In order to identify key public health research areas with regard to Down syndrome, the American National Center on Birth Defects and Developmental Disabilities at the Centers for Disease Control and Prevention and the National Down Syndrome Society sponsored a meeting to address important research questions. The meeting identified several research priorities, such as the causes of co-morbid mental health conditions, the natural history of

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cognition and behaviour and effective interventions to improve cognitive outcomes. The summary of the findings strongly recommended the use of population-based resources longitudinal follow ups to identify patients (10).

To our knowledge, there have been no population-based studies that have included the systematic testing of intellectual levels with verbal and non-verbal domains, related to co-occurring developmental disorders, in children and adolescents with Down syndrome.

Hence, the aim of this study was to apply a cross-sectional explorative approach to assessing the severities and profiles of ID in a population-based cohort of children and adolescents with Down syndrome, according to cognitive test data. Our second aim was to relate the results to co-occurring ASD and ADHD.

## **METHODS**

### **Study cohort**

The study was performed in the county of Uppsala, Sweden, which has around 350,000 inhabitants (Figure 1). About 100 children with Down syndrome live in the county and they are all provided with medical services by a specialist outpatient clinic at Uppsala University Children's Hospital, who work in close collaboration with the habilitation teams in Uppsala County. All individuals with Down syndrome are followed according to the national Swedish guidelines (11), which are in general agreement with those from the United States (12).

Parents of the 60 children (68% male) with Down syndrome, who were born from 1994-2006 and met the age criterion of 5-17 years at 1 January 2012, were invited to participate in the study to identify the prevalence of ASD and ADHD (13). In addition, a cognitive assessment to determine the severity and profile of their child's ID was carried out. In the present study, IQ data were analysed in the 60 children with a mean age of 11 years at inclusion. At the

time of the cognitive assessment, three individuals had turned 18 years. At inclusion, 37 children were between five and 12 years and 23 were teenagers, between 13-17 years. Just over two-thirds (41) of the 60 children had taken part in the ASD and ADHD study (13). The IQ test data and ID levels for the remaining 19 children were obtained from health records.

All subjects attended special classes for children with ID located in mainstream schools and their education was in accordance with the special national educational curriculum for pupils with ID.

## **Neurodevelopmental assessments**

### ***IQ assessments***

Intellectual disability was defined according to Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> Edition (DSM-IV) (16), which was being used at the time when the study started, including criteria for both intellectual and adaptive functioning deficits. ID severities were classified according to IQ, as: mild (50-70), moderate (35-50), severe (20-35) and profound ID with an IQ of less than 20 (16).

A cognitive test had been performed on 49 of the 60 children: 20 were tested by the same neuropsychologist, 25 children were tested by one of the psychologists in the habilitation team less than three years before the study started and the remaining four children had a cognitive test that was performed earlier than that, before they started school at the age of six.

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Of the total group of 60 children, 41 were tested with the Wechsler Preschool and Primary Scale of Intelligence, 3<sup>rd</sup> Edition (WPPSI-III) (14,15), seven with the Wechsler intelligence scale 4<sup>th</sup> edition (16) and one with Leiter International Performance Scale - Revised (17). Of the 49 children that could be tested, 26 had been tested at the ages of five or six years, due to the need for a cognitive evaluation before they started school. The ages when the remaining 23 children were tested were equally distributed between 7-18 years. Eight children had been tested twice, before and during the study.

An uneven profile was considered to be present when there was a difference of at least 20 IQ points between verbal and non-verbal domains, corresponding to a significance at the 1% level (18).

It was not possible to perform formal cognitive tests in 11 children due to very severe ID. Instead, they were clinically assessed by a special educator in the habilitation team in collaboration with an experienced neuropaediatrician. The assessments were based on medical and habilitation records since birth as well as professional knowledge of the children.

All cognitive tests took place at the study subjects' schools or at the local habilitation centre. Each child or adolescent was accompanied by a parent or an assistant from the school during the test situation. When they depended on sign language, the parent or assistant interpreted when necessary.

The assessments made by the special educator were also performed in the habilitation centre.

In order to compare the IQs in the younger and older subjects, the level of ID was categorised into mild (IQ 50-70) and severe (IQ <50) in line with Hagberg et al (19) Thus, severe ID comprised three levels: moderate (IQ 35-50), severe (IQ 20-35) and profound (IQ less than 20), as defined by DSM-IV (16) and DSM-5 (20). A definitive IQ was established in 40 subjects, but only the level of ID - mild, moderate, severe or profound - could be determined in the remaining 20 subjects.

#### **Adaptive function assessments**

The Adaptive Behavior Assessment System 2<sup>nd</sup> Edition (ABAS-II) (21) was filled out by the parents and teachers. The Vineland Adaptive Behavior Scales, 2<sup>nd</sup> Edition (Vineland test) (22) complemented ABAS-II when possible, since many subjects reached the floor level in the ABAS-II.

#### **Autism and ADHD assessments**

The ASD and ADHD assessments of 41 of the 60 subjects, which were reported in detail in our previous study (13), revealed that, in addition to ID, 17 (41%) met the criteria for ASD and 14 (34%) met the criteria for ADHD. Nine of these 31 subjects had a combination of ASD and ADHD. The autism measurements used in the previous study were the Social Communication Questionnaire (SCQ), the Autism Diagnostic Interview – Revised and the Autism Diagnostic Observation Schedule. ADHD was assessed with the Strength and Difficulties Questionnaire and the Swanson, Nolan and Pelham version IV Scale. In all cases, the measures were combined with a clinical assessment (13).



## Ethics

The Regional Ethical Review Board of Uppsala approved the study.

## RESULTS

### Intellectual disability

The total group of 60 children (68% male) had an age range of five to 18 years at the time of testing with a mean age of 11. Based on the data for all the tests that were performed, all the children had ID. In the group of 37 children aged 5-12, 13 (35%) had mild ID and 24 (65%) had severe ID. The corresponding figures in the older age group of 23 teenagers aged 13-18 were two (9%) and 21 (91%), respectively (Table 1). The odds ratio (OR) for severe ID in relation to age was 5.69 (95% CI 1.15-28.16,  $p=0.031$ ). More boys than girls had severe ID, although the difference was not significant (OR 2.83, 95% CI 0.82-9.76,  $p=0.111$ ) (Table 2).

The most marked difference in mild and severe ID levels was between children younger and older than eight years of age (OR 16.0, 95% CI 3.2-81.0,  $p < 0.001$ ).

In the eight children who had two cognitive tests, the interval between the tests varied between four and 11 years. The severity of ID increased in seven of these children. The child with similar ID levels at the two tests had the first test at 11 years of age and all the other children had their first test at 5-7 years of age (Table 3). Two of the children, tested before the study, had borderline intellectual functioning with IQs between 70 and 84.

It was possible to assess the intellectual profiles with regard to verbal and non-verbal domains in 20 of the 49 children who had a cognitive test: 11 of these had a higher IQ score in the verbal domain, six had higher scores in the non-verbal domains and three had identical scores. The mean and standard deviation IQ in the verbal domains ( $65.2 \pm 12.7$ ) was slightly higher than the results for the non-verbal domains ( $63.0 \pm 12.3$ ). However, the

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difference was not significant according to a paired samples t-test ( $t_{19} = 1.9, p = 0.07$ , Cohen's  $d = 0.01$ ). No information on the profiles could be obtained for the remaining 29 subjects. It was not possible to evaluate the processing speed in any child due to a generally low level of cognitive function in this cohort of children.

### ***Adaptive function***

The General Adaptive Composite (ABAS-II) score from the parents and, or, teachers was obtained for 35 children: 24 children of these children, all with severe or profound ID, had a general adaptive composite score corresponding to floor level.

A complete Vineland test was obtained from the parents of 13 children. Nine children had both ABAS-II and Vineland test data. In the five children with ABAS-II results at the floor level, the Vineland test gave a more detailed result. Thus, the Vineland test particularly supported the classification of ID levels by differentiating between severe and profound ID.

### ***ASD, ADHD and levels of cognitive function***

Of the 41 subjects tested, 17 had ASD, 14 had ADHD and nine of those had both ASD and ADHD (13). The subjects with ASD generally had more severe ID: two children had mild ID and 15 had severe ID (OR 7.50, 95% CI 1.40-40.18) (Table 4). The children with ADHD had varying levels of ID: three had mild ID and 11 had severe ID (OR 2.52, 95% CI 0.57-11.18) (Table 5).

## DISCUSSION

This study, which aimed to identify the levels and profiles of ID, was based on the total population of children and adolescents with Down syndrome in the county of Uppsala, who were 5-17 years of age. To our knowledge, this was the first population-based study to analyse the levels of ID, adaptive functioning, verbal and non-verbal profiles in children with Down syndrome with and without coexisting ASD and ADHD.

The WPPSI-III provides a full-scale IQ with a verbal and non-verbal IQ (14). The test is designed for children in the age span 2.5-7.25 years but is commonly used in older children with a low level of cognitive function (21). Hessler et al (23) demonstrated the floor level effects and lack of sensitivity of IQ measurements in their group of children with ID who were tested using the WISC-III, standardised for children from the age of six. The authors discussed the need to develop tools to measure cognitive abilities in lower functioning individuals.

Both the ABAS-II (21) and the Vineland test (22) were used as tests of adaptive function as the ABAS-II is less accurate in children with severe and profound ID. All subjects with severe or profound ID had results at the floor level, namely a score of 40, on the ABAS-II. With the Vineland test, it was possible to obtain a more differentiated adaptive score to guide the classification of the lowest ID levels.

In the total group of 60 subjects, significantly more children in the older age group, who were 13-18 years at the time of testing, had severe ID compared to the younger age group of 5-12 years. Mild ID was significantly more common in the younger age group than the older age group. There was a clear statistical difference in the distribution of mild and severe ID from the age of eight years.

In addition, the IQ levels had fallen in all but one of the eight children who were individually assessed at two time points, in line with the age-related findings for the total study cohort.

These findings also agreed with the results from a systematic review that reported a decline of IQ across time in children with Down syndrome (1). Thus, longitudinally population-based studies of young children with Down syndrome are important.

In contrast to earlier reports, our results did not confirm higher scores in non-verbal versus verbal tests. This was also true for those with ASD and ADHD. However, it should be pointed out that the tests could only be performed on a limited number of subjects, who had a cognitive level that enabled them to take part in the test procedure.

A limitation of the study was that the cognitive assessment of some of the older children with severe ID had to be based on results from a test adapted for young children aged 2.5-7.25 years. However, the WPPSI-III includes both the verbal and non-verbal domains and the test has been found to be acceptable and useful for older children with severe ID in clinical contexts.

One strength of the study was the population-based design and the fact that the subjects were all recruited from a specialist clinic targeting all children with Down syndrome in the county and were followed by the same neuropaediatrician. Another strength was the fact that all the children who could be tested formally had been assessed by an experienced psychologist in the habilitation team. However, it should be emphasised that the results need to be corroborated and that there is a need for further studies and expansion of the sample.

## **CONCLUSION**

In this population-based cohort of 60 children with Down syndrome, we found a significantly lower level of ID in the teenage group compared to the younger group. We observed a decline of IQ in the majority of those who had two cognitive tests, performed at a younger and older age. All the children tested had even cognitive profiles with regard to verbal and non-verbal domains.

We suggest that most children with Down syndrome would benefit from a re-evaluation of their cognitive function, in order to adapt their educational curriculum before entering secondary school.

## **Abbreviations**

ABAS-II, Adaptive Behavior Assessment System, 2<sup>nd</sup> Edition; ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> Edition; ID, Intellectual disability; IQ, Intelligent quotient; WPPSI-III, Wechsler Preschool and Primary Scale of Intelligence, 3<sup>rd</sup> Edition; Vineland test, Vineland Adaptive Behavior Scales, 2<sup>nd</sup> Edition.

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## CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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**Table 1** Level of intellectual disability (ID) in relation to age

Age (years)	Mild ID	Severe ID	Total
5-12	13 (35%)	24 (65%)	37
13-18	2 (9%)	21 (91%)	23
<b>Total</b>	15 (25%)	45 (75%)	60

IQ 50-70 mild intellectual disability, IQ <50 severe intellectual disability.

**Table 2** Level of intellectual disability (ID) in relation to gender

Gender	Mild ID	Severe ID	Total
Male	7 (17%)	34 (83%)	41
Female	7 (37%)	12 (63%)	19
<b>Total</b>	14	46	60

IQ 50-70 mild intellectual disability, IQ<50 severe intellectual disability.

**Table 3** Level of intellectual disability in the eight children with two cognitive tests

Subject	Test 1			Test 2		
	age (years)	method	ID-level	age (years)	method	ID-level
1	6	WPPSI-III	Moderate	13	WPPSI-III	Severe
2	7	WPPSI-III	Borderline	11	WISC-IV	Moderate
3	6	WPPSI-III	Mild	11	WPPSI-III	Moderate
4	5	Griffiths*	Mild	11	WISC-IV	Moderate
5	10	WPPSI-III	Severe	17	WPPSI-III	Severe
6	5	Griffiths*	Borderline	16	WISC-IV	Moderate
7	6	Griffiths*	Moderate	16	WPPSI-III	Severe
8	5	Griffiths*	Mild	14	WPPSI-III	Moderate

IQ 70-84 borderline intellectual functioning, IQ 50-70 mild intellectual disability, IQ 35-50 moderate intellectual disability, IQ 20-35 severe intellectual disability, IQ <20 profound intellectual disability according to ICD-10 and DSM-IV.

\* Griffiths' test had been used as the primary test in children at ages 5-6 years.

**Table 4** Levels of intellectual disability (ID) in relation to ASD

<b>ID</b>	<b>No ASD</b> <b>n = 24</b>	<b>ASD</b> <b>n = 17</b>	<b>Total</b> <b>n=41</b>
Mild ID	12 (86%)	2 (14%)	14
Severe ID	12 (44%)	15 (56%)	27
<b>Total</b>	<b>24</b>	<b>17</b>	<b>41</b>

IQ 50-70 mild intellectual disability, IQ <50 severe intellectual disability.

**Table 5** Levels of intellectual disability (ID) in relation to ADHD

<b>ID</b>	<b>No ADHD</b> <b>n=27</b>	<b>ADHD</b> <b>n=14</b>	<b>Total</b> <b>n=41</b>
Mild ID	11 (41%)	3 (21%)	14
Severe ID	16 (59%)	11 (79%)	27
<b>Total</b>	<b>27</b>	<b>14</b>	<b>41</b>

IQ 50-70 mild intellectual disability, IQ <50 severe intellectual disability.

Figure 1 Flow chart for the IQ test procedure

