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# Delays in Motor Development in Children with Down Syndrome

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**Background:** Children with Down syndrome (DS) present with delays in motor development. The reduced size of the cerebrum, brain maturation disorders, and pathophysiological processes lead to motor development delay. The aim of this study was to examine the gross motor function and estimate what motor abilities are significantly delayed in children with Down syndrome even if they attend physical therapy sessions. Another purpose of the study was to assess the functional balance.

**Material/Methods:** The study group consisted of 79 children with DS (42 boys, 37 girls), average age 6 years and 3 months  $\pm$  4 years and 6 months. Participants were divided into 3 groups according to (i) age: <3 years old, 3–6 years old, and >6 years old; and (ii) motor impairment scale: mild (SNR 1), moderate (SNR 2), and severe (SNR 3). Children were assessed using the Gross Motor Function Measure-88 (GMFM-88) and Pediatric Balance Scale (PBS).


**Results:** None of the assessed children developed all the functions included in GMFM-88. The standing position was achieved at the specified age by 10% of children in the first age group (<3 years old) and 95% of children aged 3–6 years. Similarly, the walking ability was performed by 10% of children under 3 years old and by 95% of children aged 3–6 years. The median score of PBS was 50 points (min. 34 p. – max. 56 p.). There was a statistically significant correlation between PBS scores and GMFM-88 scores,  $r=0.7$ ;  $p<0.0001$ , and between balance scores and GMFM – 88 E (walking, running, jumping) ( $r=0.64$ ;  $p<0.0001$ ).

**Conclusions:** Motor development, especially standing position and walking ability, is delayed in children with Down syndrome. Balance and motor functions are correlated with each other, so both aspects of development should be consider together in physical therapy of children with Down syndrome.

**MeSH Keywords:** **Down Syndrome • Motor Skills • Neurotransmitter Agents**

**Abbreviations:** **DS** – Down syndrome; **MR** – magnetic resonance; **GMFM-88** – Gross Motor Function Measure-88; **SNR 1** – mild motor impairment; **SNR 2** – moderate motor impairment; **SNR 3** – severe motor impairment; **NAA** – N-acetylaspartate; **Cho** – choline; **mi** – myoinositol; **GABA** – gamma-amino butyric acid; **Glx** – glutamate-glutamine complex; **APP** – beta amyloid precursor protein; **Cu Zn-SOD, SOD-1** – Cu/Zn superoxide dismutase

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## Background

Brain structure and function may influence the development of mental and motor abilities. Structural and functional disorders of the central nervous system may be influenced by genetic conditions. For instance, children with Down syndrome (DS) who have an extra chromosome 21 present with many brain disorders that cause retarded psychomotor development and problems with learning [1].

There are 3 groups of problems affecting the central nervous system that cause psychomotor dysfunctions in DS children:

1. Changes in the shape and number of neurons and changes in cerebrum size;
2. Disorders of the central nervous system maturation;
3. Pathophysiological processes:
  - a. Degenerative processes of the nervous system,
  - b. Disorders in neuronal apoptosis regulation,
  - c. Overexpression of genes that code beta amyloid precursor protein (APP)
  - d. Processes leading to decreased release of neurotransmitters.

Significant changes in cerebrum size appear after the 6<sup>th</sup> month of life [2] and deletions in motor development are also seen from the 6<sup>th</sup> month of life [3]. Volumetric neuroimaging studies have revealed smaller frontal, occipital, and temporal lobes with smaller hippocampal volume, reduced corpus callosum and cerebellum size, decreased superior temporal gyrus, and brainstem volume [3,4]. Such abnormalities in the brain lead to psychomotor dysfunctions among DS subjects. For instance, smaller frontal lobe volumes cause problems with voluntary activities, cognitive deficits, and gait quality, especially in adult life. Increasing age is associated with grey matter reduction in the frontal, parietal, and temporal cortex, similar to alterations in mild Alzheimer's disease [4]. Hypoplasia of the cerebellum in DS children is a symptom caused by overexpression of the GART gene. Changes in the cerebellum involve the reduction of both white and grey matter [4]. A study using MR reported that granule cell density is reduced in DS children to approximately 70% of typically developing children [5,6]. Cerebellum hypoplasia is responsible for muscle hypotonia, problems with movement fluency and axial control (axial truncal muscle), and body balance, coordination, and speech disorders [7–10]. Corpus callosum size is also reduced in children with DS and is associated with mental retardation, problems with coordination, and atypical laterality [6].

Delayed myelination is another cerebral abnormality in DS [11]. Differences are seen from the 22 week of gestation but there are strong manifestations from the 6<sup>th</sup> month of life [11].

Pathophysiological processes caused by overexpression of genes located in chromosome 21 lead to:

- a. Degenerative processes of the nervous system caused by overexpression of genes coding peroxidase enzymes: Cu/Zn superoxide dismutase (Cu Zn-SOD; SOD -1),
- b. Disorders in neuronal apoptosis regulation,
- c. Overexpression of genes that code beta amyloid precursor protein (APP),
- d. Processes leading to decreased ratio of neurotransmitters [12,13].

Upregulation of SOD-1 in fetuses with DS leads to oxidative stress [13]. Increased SOD-1 activity in the mitochondrial intermembrane space is responsible for cognitive impairment and delays motor development by increased free radical generation and chronic oxidative stress [12].

DS subjects, mostly those above 40 years of age, present with progressive cognitive impairment resembling the cognitive profile of Alzheimer's disease [3]. Overexpression of beta amyloid precursor protein (APP) initiates and stimulates neurodegenerative processes resulting in the occurrence of aggregated amyloid fibrils in the brain. It is believed that the overexpression of APP located in chromosome 21 leads to earlier neuronal apoptosis [14–16], which is why the occurrence of dementia symptoms or even Alzheimer's disease is frequent in patients with DS, mostly as they become older [16]. Other neuropathological Alzheimer-type changes in DS patients are the reduced ratio of neurotransmitters such as N-acetylaspartate (NAA), choline (Cho), myoinositol (ml), gamma-amino butyric acid (GABA) in temporal lobes and reduced ratio of NAA, Cho, ml, glutamate – glutamine complex (Glx) in frontal lobes [14,16]. The reduced ratio of neurotransmitters such as Glx and NAA in frontal lobes and NAA, Cho, ml, GABA in temporal lobes and in the hippocampus in DS children may influence delay in developing motor abilities and may lead to problems associated with memorizing and learning [14,16,17].

Nowadays, the prognosis for children with DS is better than in previous years thanks to advanced medical treatment and educational opportunities. Although congenital heart diseases (in 40–50% of children with DS) are still the main cause of death, the survival rate in DS has improved and is reported to be up to 91% at 1 year of age and 85% at age 10 [18]. Similarly, despite increased leukemia susceptibility in children with DS, overall survival rates are approximately 80% [19], which is why life expectancy has increased so much. All of the medical problems that may affect children with DS (e.g., thyroid problems, epilepsy, gastrointestinal defects, orthopedic problems such as atlantoaxial instability, and even leukemia) can be treated by specialists [12]. The purpose of therapy for children with DS is to help them stay healthy and increase their quality of life as early as possible, which is why there are diagnostic methods to determine as early as possible whether the child has DS. Some of these methods are prenatal, for

example amniocentesis, chorionic villus sampling, pregnancy ultrasound, or non-invasive prenatal testing (NIPT), which is a molecular approach for assessing fetal aneuploidy using cell-free fetal deoxyribonucleic acid (cffDNA) from the plasma of pregnant women [12,20]. Others are performed after birth, such as fluorescent *in situ* hybridization followed by chromosomal karyotyping [12].

The sooner the diagnosis is made, the sooner intervention can begin. Knowing that the pathological changes in the number of neurons and changes in the cerebrum size, maturation disorders of the central nervous system, and pathophysiological processes lead to delays in motor development, especially from the 6<sup>th</sup> month of life, we speculated that motor abilities that children develop after the second half of infancy may develop later than other functions of motor development, in part because children with DS require more time and effort than typically developing children to acquire antigravitational skills, such as standing [21].

### Aim

The aim of this study was to examine motor abilities and determine which are significantly delayed in DS children, even if they receive physical therapy. Another purpose of the study was to assess the functional balance as a feature of quality of movement.

## Material and Methods

### Ethics statement

The study was approved by the Bioethics Committee of the Poznan University of Medical Sciences in 2009 (consent ref. no. 23/10, dated 7 January 2010). Written consents were obtained from the parents of the children enrolled in the study and the consents were signed on behalf of the children enrolled.

The study was conducted during 2009–2011. The study group consisted of 79 children with DS (42 boys, 37 girls), mean age: 6 years and 3 months  $\pm$  4 years and 6 months. Participants were divided into 3 groups according to (i) age: <3 years old, 3–6 years old, >6 years old, and (ii) motor impairment rating scale: mild (SNR1), moderate (SNR2) and severe (SNR3). All children attended physical therapy sessions 1 time per week for 2 years. The therapy was conducted by NDT Bobath therapists and sensory integration therapists. The therapy was individually tailored for each child because children with DS have a wide variety of symptoms, although that all of them had laxity, low muscle tone, and psychomotor development deficits. The therapy for each child included developing psychomotor abilities according to individual motor skills assessed in each

child. Therapy also focussed on developing good quality of motor function and normalization of muscle tone. Training balance reaction and postural maintenance and change were also addressed in each child's therapy based on the knowledge of cerebellar hypoplasia, which presents in children with DS. Even children who were younger than 12 months were trained by NDT Bobath therapists, trying to normalize the muscle tone by influencing tone patterns, training protection reaction, and balance reaction appropriate to the age of the child and individual level of motor development. The aim of the therapy of the youngest research group was to facilitate standing position with good postural reactions.

The study took place in the greater Poland region, and involved patients with DS coming from towns and villages of the greater Poland region. Even if a child come from rural areas, she or he had the same therapists, and the same frequency of therapeutic meetings as a child who come from urban areas because each person in research group attended to Poznan Rehabilitation and Orthopedic Center, "YES" Association or to Leszno to Polish Association for Persons with Mental Disability "Kolo". The economic status and education of parents and the influence of these factors on therapy were not considered. The study was approved by the Bioethics Committee of the Poznan University of Medical Sciences.

Children were also assessed using the Gross Motor Function Measure-88 (GMFM-88). The scale was first validated for children with cerebral palsy and is now also validated for children with DS [22–25]. There was no control group because the original validation sample of GMFM-88 included children aged from 5 months to 16 years, so the score of GMFM-88 is the percentage of the score of the original validation group [22–25]. A 5-year-old child without any motor disabilities should present all functions included on the GMFM-88 scale [22–25].

### Gross Motor Function Measure-88 (GMFM-88)

GMFM-88 consists of motor functions grouped into 5 dimensions: 1) GMFM – 88 A: lying and rolling (17 items), 2) GMFM – 88 B: sitting (20 items), 3) GMFM – 88 C: crawling and kneeling (14 items), 4) GMFM – 88 D: standing (13), 5) GMFM – 88 E: walking, running, and jumping (24 items) [22]. According to the GMFM-88 guidelines formulated for the assessment of DS children, the environment should be as familiar for the children as possible to encourage the performance of activities [22]. Sometimes, several meetings were needed to assess a child because of the tendency of DS children to get distracted. Assessment of each child was completed within 1 week to avoid changes in motor functions which otherwise might have appeared due to child development. Each item was measured by observation and scored on a 4-point ordinal scale. The 0 value indicated that a child did not initiate the task, 1 point

**Table 1.** Median GMFM-88 score based on motor impairment scale and age.

	GMFM-88 [%] median (minimum – maximum)			P
	Age <3 years old	Age 3–6 years old	Age >6 years old	
SNR 1	44.57 (5.1–87.73)	91.73 (78–98.46)	98.99 (89.7–100)	<0.0001
SNR 2 – SNR 3	27.68 (12.57–43.37)	89.06 (64.25–98.3)	92.71 (82.73–100)	0.0005

Kruskal-Wallis's Test with Dunn's multiple comparison post-test.

**Table 2.** Median GMFM-88 scores based on motor impairment rating scale.

	Motor impairment rating scale (SNR)			P
	SNR 1	SNR 2	SNR 3	
GMFM-88 [%] median (minimum–maximum)	89.7 (5.1–100)	92.11 (27.68–100)	89.42 (12.57–98.06)	0.56

Kruskal-Wallis Test.

– the child performed less than 10% of a task, 2 points – the child partially completed an item (10% to <100%), 3 points – the child completed an activity (100%) [22–27].

Body balance was estimated by Pediatric Balance Scale (PBS) among children who were able to stand unsupported and who were older than 4 years old [28]. The scale has been created and validated by Franjoine. We assessed all 14 items of PBS on the criterion, based on a 0–4 scale [28]. For instance, retrieving an object from the floor or changing from a standing position to sitting with each test session lasting 10–20 minutes. A child who successfully completed all the tasks could gain a maximum of 56 points. The nearer to maximum the score is, the better the functional balance in the context of everyday life.

### Statistical analysis

Data were analyzed using STATISTICA 8.1 (StatSoft). Nonparametric tests were used to analyze differences between medians in ordinal scales. Mann-Whitney U test was used for comparing two independent samples. A few unrelated samples were tested using Kruskal-Wallis test with Dunn's multiple comparison post-test. The correlation between samples was measured using Spearman's rank correlation. P value 0.05 was considered statistically significant.

## Results

The median GMFM-88 score for girls was 89.66% (5.1%–100%) and for boys: 91.11% (12.43%–100%). There was no significant difference in either group divided by sex (p=0.73).

There was no significant difference between motor functions in DS children in different groups divided according to motor impairment rating scale, p=0.56 (Table 1). However, when both age and motor impairment scale were taken into account, a significant difference between groups was observed (Table 2). Two groups with moderate (SNR 2) and severe (SNR3) motor impairment were combined because of the small number of children with severe motor impairment.

Many functions included in GMFM-88 were considered with respect to the typical age when they should be achieved. The standing position was achieved by 10% of children in the first age group (<3 years old) and 95% of children aged 3 to 6 years. Similarly, the walking ability was performed by 10% of children under 3 years old and by 95% of children aged 3 to 6 years.

Functional balance was assessed in 44 children older than 4 years in the research group (26 girls and 18 boys) by Pediatric Balance Scale (PBS). The median score of PBS was 50 points (min. 34 p. – max. 56 p.). There was not any significant correlation between balance score and gender (p=0.7).

There was a statistically significant correlation between PBS scores and GMFM-88 scores, r=0.7; p<0.0001, especially between balance scores and GMFM – 88 E (walking, running, jumping) (r=0.64; p<0,0001 (Figure 1).

## Discussion

It is common knowledge that DS children develop slowly, but it may not be obvious how slowly their development progresses.



and their parents. Knowing that the cerebellum is responsible for maintaining balance [7], PBS was performed to show cerebellar function. In the measurement of balance, various other methods may be used, including observation of oculovestibular reflexes, vestibulospinal reflexes, and tests using posturography [38]. However, PBS seemed to be the simplest, quickest, and cheapest examination.

Dysfunction in balance may lead to problems in psychomotor abilities [39,40], especially those that are more advanced in childhood motor development, classified as GMFM – 88 E (walking, running, and jumping) [41]. The study showed that there is a correlation between psychomotor ability and GMFM – 88, especially GMFM- 88 E. Balance functions play an important role in development of motor abilities. The cerebellum is important not only for balance but also limb coordination and locomotion [42], and it is well known that the cerebellum is involved in developing motor function at each level of learning motor abilities [10,43]. This is why the therapy for children with DS should consider developing motor skills and improving balance [41,44].

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## Study limitations

The limitations of the study are associated with the expensive MR examination, <sup>1</sup>H-MRS; therefore, information about brain disorders was derived from research literature available in PubMed.

## Conclusions

Psychomotor development, especially standing and walking ability, is delayed in DS children even if they attend physical therapy sessions. Functional balance should be considered in therapy of children with DS because balance may influence development of motor abilities, especially those that are developed in childhood.

## Conflict of interest

None.

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