RELATION BETWEEN QUANTITATIVE MOTION ANALYSIS AND CEREBRAL VOLUMES ANALYSIS IN PERSONS WITH DOWN SYNDROME

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Down Syndrome

DS is often linked to an insufficient development of cerebellum and periferical nervous system

motor deficit, typical features in these subjects, is present at central level and periferical level, as incorrect high rank development expression and as acquired compensatory strategies that could be generator of other orthopaedic anomalies.
The necessity to investigate a possible correlation between NMR images, using VBM, and walking, using motion analysis system, was born.

Aim of this study is to search a relation between cerebral volumes computed by VBM algorithm and walking patterns in people with Down syndrome, in order to investigate the origin of motor problems and to establish appropriate rehabilitation programs.
A voxel-based morphometric study of the brain in children and adolescents with Down Syndrome

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**Materials and Methods**

**MRI acquisition:**

- High-resolution contiguous axial T1-weighted MR images (MRIs) acquisition was performed at the Radiology Department of the San Raffaele Pisana Institute, using a 1.5 Tesla (clinical) Philips Intera scanner (Philips Medical Systems, N.A., Bothell, WA). The MRIs were acquired using the same parameters (3D MR acquisition; repetition time $\text{TR} = 18.0 \text{ ms}$; echo time $\text{TE} = 9.2 \text{ ms}$; flip angle = $30^\circ$; matrix $256 \times 256$; field of view $= 24 \text{ cm}$; voxel size $1.0 \times 1.0 \times 1.0 \text{ mm}^3$).

- The image quality was verified by two examiners (P.O., F.C.), who were unaware of the reciprocal findings. In case of inter observer disagreement, a final consensus was achieved after discussion to ensure image quality, absence of structural abnormalities and motion artefacts. At the same time, the quality of image segmentation and the accuracy of the spatial normalization step were controlled and verified for each subject and each sequence separately.
Materials and Methods

Data analysis:

- Image processing and analysis were performed by SPM2 analysis software package (Department of Cognitive Neurology, University College London, UK; http://www.fil.ion.ac.uk)
- All MRIs were spatially normalized, segmented, and smoothed according to the optimized protocol for VBM (Good, 2001) to automatically compute local absolute differences in the volumes of GM and WM, respectively, by means of customized templates
- To define the normal range, each subject of the control group was compared with the rest of the same group, by means of a Single-case VBM analysis
- On a voxel-by-voxel basis, GM and WM of DS subjects were compared with control group by means of an ANCOVA design, with total intracranial volume, age, sex, weight, height of each subject as nuisance covariates and with a significance threshold of $P < 0.05$ corrected for multiple comparisons
• Young DS brain showed a **GM volume reduction in the cerebellum, frontal and limbic lobes and hippocampi** and a preservation in the temporal, sub-lobar and parietal regions.

• **A WM volume reduction was noted in the cerebellum, frontal and parietal lobes, sublobar and brainstem.** A WM volume preservation was detected in temporal and limbic lobes.

• Finally, the DS group showed lower levels of the CSF surrounding the frontal lobes.
Regional gray matter volume changes

DS decreases:
- anterior
- right

DS increases:
- inferior
- superior

L  R

posterior

left
Regional cerebral spinal fluid volume changes

DS decreases

DS increases

anterior

posterior

right

left

inferior

superior
Conclusions

- To our knowledge, this research provides the first full-brain abnormalities pattern description in youngsters with DS by using high resolution MRI VBM method.
- Our data largely agree with previous neuropathologic and neuroimaging studies in children and supply more information on temporal patterns of neuroanatomical specific regional changes in DS, testing the reliability of VBM to investigate brain abnormalities.
- Our results highlight that gross regional pattern changes in cerebellar, frontal, limbic, hippocampal and temporal regions are quite stable throughout childhood, adolescence and adulthood. On the other hand, frontal and temporal regions seem to be more sensitive to aging, compared to previous VBM studies in adult with DS.
Gait analysis and cerebral volumes in Down's syndrome

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Summary

The aim of this study was to look for a relationship between cerebral volumes computed using a voxel-based morphometry algorithm and walking patterns in individuals with Down's syndrome (DS). In order to investigate the origin of the motor problems in these subjects, a view to developing an appropriate rehabilitation programme.

Nine children with DS underwent a gait analysis (GA) protocol that used a 3D motion analysis system, force plates and a video system, and magnetic resonance imaging (MRI). Analysis of GA graphs allowed a series of parameters to be defined and computed in order to account for the specific characteristics of the gait patterns found. It was possible to obtain a 3D description of gait in terms of distance from normal values. Finally, the results of cerebral volume analyses were compared with the gait pattern found.

A strong relationship emerged between cerebellar volume reduction and quality of gait and also between grey matter volume reduction of some cerebral areas and asymmetrical gait.

An evaluation of high-level motor deficits, reflected in a lack or partial lack of proximal function, is important in order to define a correct rehabilitation programme.

INTRODUCTION

It has been pointed out that the delayed and pathy development of skills in different domains observed in Down's syndrome (DS) is consistent with neuroscientific evidence of atypical brain structure and organisation in this condition (1). Indeed, recent neuroimaging techniques are able to show a complex pattern of structural changes in DS, while magnetic resonance imaging (MRI) studies show that individuals with DS typically have a smaller overall brain volume, with significant reductions recorded in both cerebrum and cerebellum volume (2-4). There is also neuropathological evidence that these differences in brain structure are not present in utero but emerge during early development in the foetus (5).

In Down's syndrome (DS), the loss of neurons in the central nervous system (CNS) is part of a picture of early neurodevelopmental delay. Myelination corresponding to an age of 3-11 months was observed on MRI scans in an 18-month-old child with DS; the authors remarking that the degree of myelination delay correlated well with the observed cognitive delay (6). The point has also been made (7) that the delay in cortical myelination implies disinhibition pathways and might underlie the atypical pattern of acquisition of motor milestones in DS. Other white matter abnormalities reported in individuals with DS include a narrower corpus callosum, which may affect the transfer of semantic information across hemispheres (7). These alterations in cortical volume and pathways may also underlie the model of atypical cerebellar organization of language and motor skills described in DS (8-11).

As remarked elsewhere (1), this model proposes that white matter abnormalities in DS include a corpus callosum advantage for the perception of speech sounds in DS. This study describes a discrepancy between motor performance in response to verbal instruction as opposed to visual demonstration (12). These findings have important implications for motor skill acquisition and strategies of educational intervention in DS.

KEY WORDS: cerebral volumes, Down's syndrome, gait analysis, voxel-based morphometry.

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In view of the documented "slower" movement of DS
Materials and Methods

DOWN GROUP
9 children with DS
6-11 years

CONTROL GROUP
10 children
7-9 years
Materials and Methods

8 optoelectronic TVC
2 force platforms
2 VideoControllers
Materials and Methods

Gait trials

22 markers (Davis protocol)

Self-selected speed

3 trials for consistency

Resting time: 120 s
Materials and Methods

KINEMATICS

Ankle Dorsi-Plantarflex

KINETIC

Ankle Dorsi-Plantarflex Moment

Ankle Power
SINGLE SUBJECT: COORDINATES \((x_{ap}, y_{ap}, z_{ap})\)

CONTROL GROUP:

MEAN VALUE ➔ Coordinates \((x_c, y_c, z_c)\)

STANDARD DEVIATION ➔

\[
\frac{(x - x_c)^2}{a^2} + \frac{(y - y_c)^2}{b^2} + \frac{(z - z_c)^2}{c^2} = 1
\]
Materials and Methods

ANKLE:

x $\rightarrow$ ROM in stance

y $\rightarrow$ maximum momentum

z $\rightarrow$ generated power

And for all joints…
DIST N-AP\(_3\)D

\[ \sqrt{(x_n - x_{ap})^2 + (y_n - y_{ap})^2 + (z_n - z_{ap})^2} \]
Results

S1
More functional gait

S2
Less functional gait

c.i. pelvis

c.i. hip

c.i. knee
Results

S1
Gray matter reduction in cerebellum: No impairment to cerebellar vermis

S2
Gray matter reduction in cerebellum: Cerebellar vermis impairment

DIFFERENCES IN GRAY MATTER VOLUMES IN CEREBELLAR VERMIS
There is correspondence between gait analysis data and cerebral volumes anomalies.

In particular → it seems to exist a relation between gait quality and gray matter volume reduction of cerebellar vermis.

Thank you…