# Brain volumes alterations in relapsing-remitting multiple sclerosis patients versus healthy controls in comparison to **QyScore®** normative database

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# INTRODUCTION
## BACKGROUND

**Brain atrophies** have been suggested as **surrogate markers** of neuroaxonal loss and disease progression of Multiple Sclerosis (MS).[1,2]

**Automatic brain volumes measurements** on a large-scale healthy controls (HC) database provides comparison data and enables the assessment of the presence of atrophy in clinical routine patients.

The use of a **normative reference database** of HC is essential to detect the neurodegeneration and axonal loss associated with a pathological state.

## Objectives

To assess MRI differences in brain structures volumes between **relapsing-remitting MS (RRMS) and HC individuals,** in comparison to a large-scale normative database of HC.

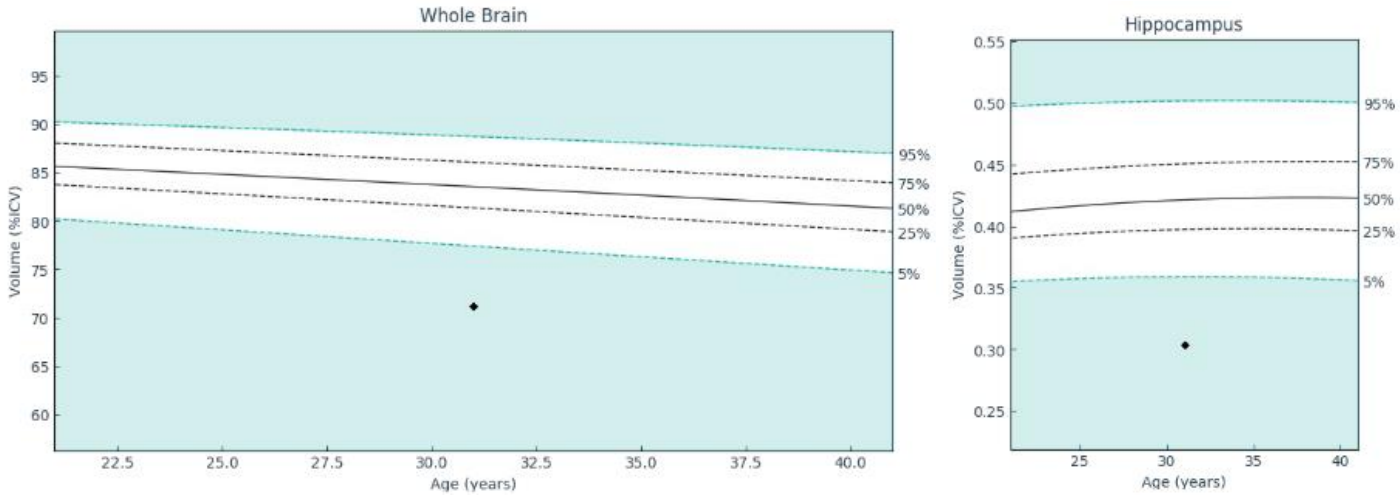
[1]Vollmer et al. 2015, [2]De Stefano et al. 2016

# INTRODUCTION
## NORMATIVE REFERENCE DATABASE

Comparison of **individual data against healthy norms** has been used in clinical practice for years.[1]

A normative reference database supports the precise indication of an individual's brain structure volume using an **age-based reference chart**.

**The comparison with thousands of age- matched HC** within a database will significantly increase the clinical value of volumetric information.




Total brain and hippocampus volume normalized to the intracranial volume (ICV) ratio from a MS patient represented as a black dot.

[1]Department of Health and Human Services, CDC 2010 "2000 CDC Growth Charts for the UnitedStates: Methods and Development" (http://www.cdc.gov/nchs/data/series/sr_11/sr11_246.pdf)

# MATERIALS & METHODS

## Data description

| Database | QyScore® normative database | Independent test datasets | |
|---|---|---|---|
| | | HC | RRMS |
| **N** | 1292 | 29 | 27 |
| **Age**<br>mean ± sd<br>[min - max] | 55.6 ± 20.7<br>[20 - 90] | 41.6 ± 11.4<br>[22 - 54] | 40.3 ± 7.3<br>[29 - 50] |
| **Sex**<br>M/F | 595/697 | 10/19 | 8/19 |

The normative database is composed of MRI data acquired using **Siemens, GE and Philips at 1.5T and 3.0T scanners.**

## Segmentation methods

- Automated quantification by QyScore®
- Whole-brain, grey matter, white matter and hippocampus volumes
- Volumes normalized by intracranial volume (%ICV)

## Metrics

Comparison of **HC** and **RRMS** against age-matched volumes in the normative database

- Standard **z-scores**
- **Volume** (%ICV)

## Statistical analysis

- Group differences were evaluated with a **two tailed t-test**

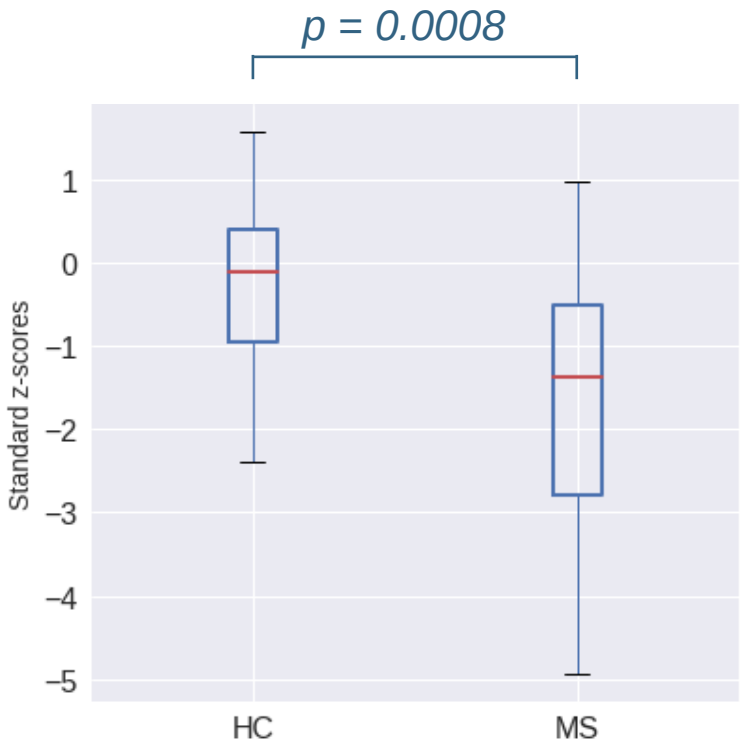
# RESULTS
## WHOLE BRAIN

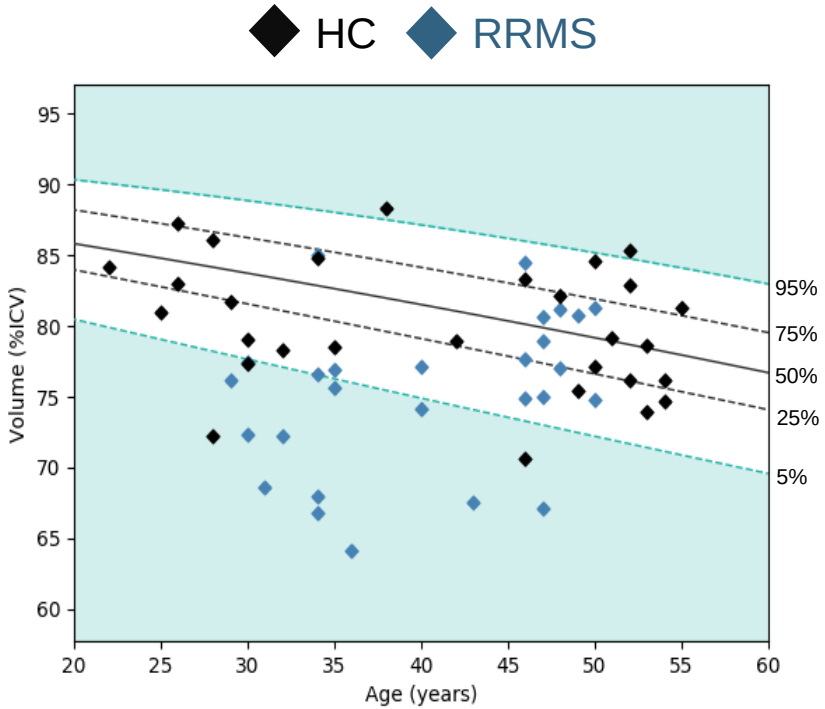
### Group effect

Standard z-scores in the RRMS group were **significantly smaller** than HC group

### Age effect

- RRMS patients under age 45 tend to have **smaller whole brain volume** (< 5th percentile) than HC individuals of a similar age (p = 0.025).
- **No significant differences** were present between HC and RRMS patients older than 46 years old.



# RESULTS
## GREY MATTER, WHITE MATTER & HIPPOCAMPUS

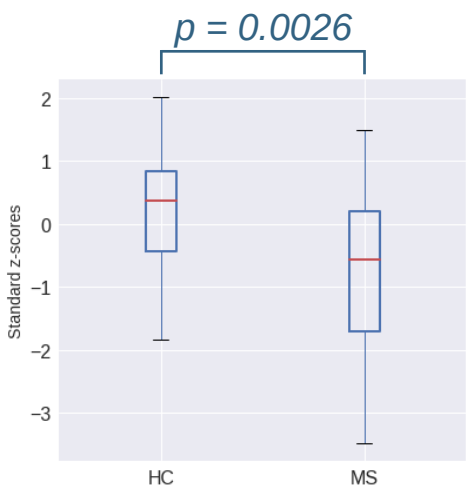
### Group effect

Grey and White matter standard z-scores in the RRMS group were **significantly smaller** than the HC group and **did not differ** for the hippocampus structure.

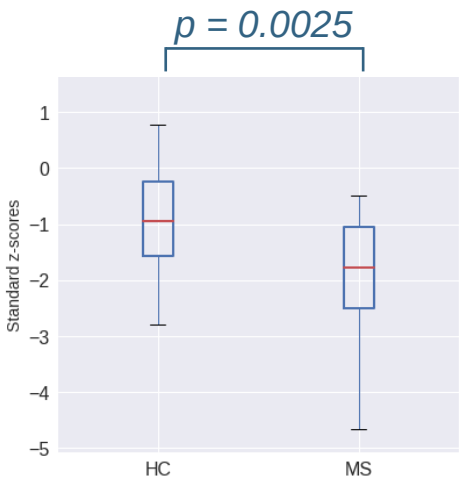
### Age effect

- RRMS patients under age 45 tend to have **smaller white matter volume** (< 5th percentile) than HC individuals of a similar age (p = 0.003).
- **No significant differences** were present between HC and RRMS patients older than 46 years old.

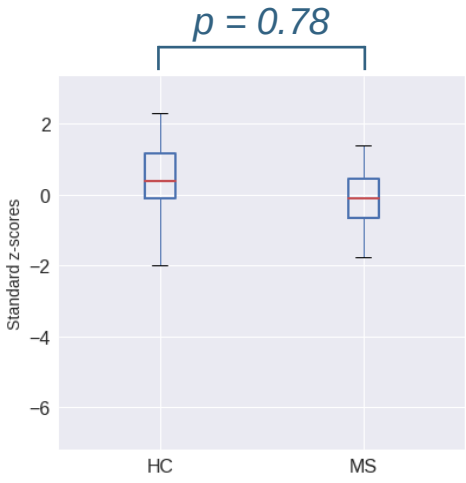
**Grey matter**

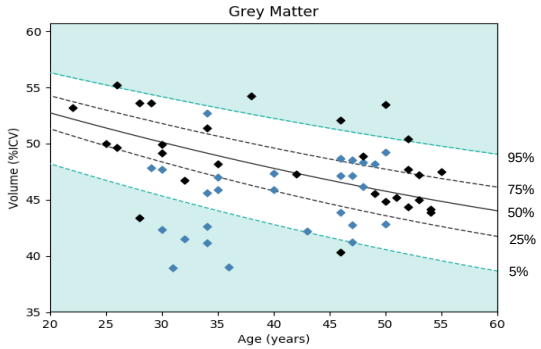


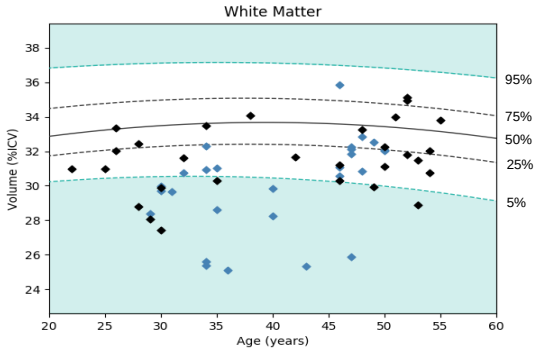

**White matter**

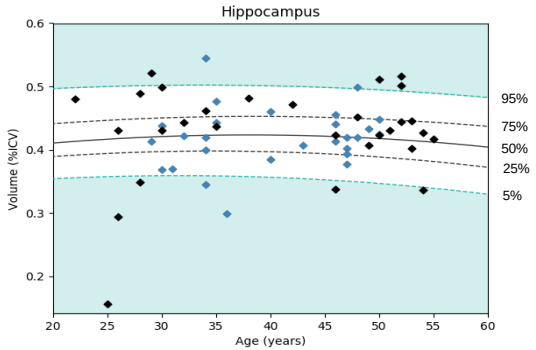



**Hippocampus**



# CONCLUSIONS

In our study, RRMS patients:

- showed **reduced** whole brain, grey and white matter volumes in comparison with HC
- under 45 y.o tend to have **smaller** whole brain and white matter volumes (< 5th percentile, $p < 0.05$) in comparison with HC of a similar age.

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The comparisons to normative reference data provided through QyScore® **are in line** with previously reported results[1,2,3,4] on RRMS patients tissue atrophies.

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The age-related findings are in line with a recent study[1] indicating that the whole brain atrophy in MS patients up to **30-40 years old** is **MS specific,** while the atrophies observed in older patients are more due to normal brain aging.

**The use of a normative database for the interpretation of brain volumetric analysis, such as the QyScore® normative database, can improve the individual assessment of brain neurodegeneration in RRMS patients in the clinical routine setting**

[1]Azevedo et al., 2019 [2]Vollmer et al. 2015, [3]De Stefano et al. 2016 [4]Bergsland et al. 2017