# Predicted brain age as a cognitive biomarker in Multiple Sclerosis

Denissen S[1,2], De Cock A[1], Costers L[1], Baijot J[1], Laton J[1,3], D'hooghe MB[4], D'Haeseleer M[4], Dive D[5], De Mey J[6], Van Schependom J[1,7], Sima D[2], Nagels G[1,2,8]

[1] AIMS lab, Center for Neurosciences, UZ Brussel, Vrije Universiteit Brussel, Brussels, Belgium
[2] icometrix, Leuven, Belgium
[3] Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, United Kingdom
[4] National Multiple Sclerosis Center Melsbroek, Melsbroek, Belgium
[5] Department of Neurology, University Hospital of Liege, Esneux, Belgium
[6] Department of Radiology, UZ Brussel, Brussels, Belgium
[7] Department of Electronics and Informatics (ETRO), Vrije Universiteit Brussel, Brussels, Belgium
[8] St Edmund Hall, University of Oxford, Oxford, UK

## INTRODUCTION

Ageing is a complex process that can be regarded from multiple perspectives, among which:

- **Chronological age:** Traditional way of quantifying ageing, being the number of years from birth
- **Brain age**: The age of the brain predicted from a healthy reference curve

Brain-Predicted Age Difference (BPAD) recently evoked as an elegant summarizing marker, providing immediate intuition in the extent of brain damage.

**BPAD = brain age - chronological age**

Findings by Cole et al. 2019:

- The brain age of persons with MS is overestimated compared to their chronological age
  ➔ Mean [CI] BPAD: 10.3 [8.5-12.05] years)
- Every 0.64 years BPAD increase accompanies a 1-point increase in EDSS

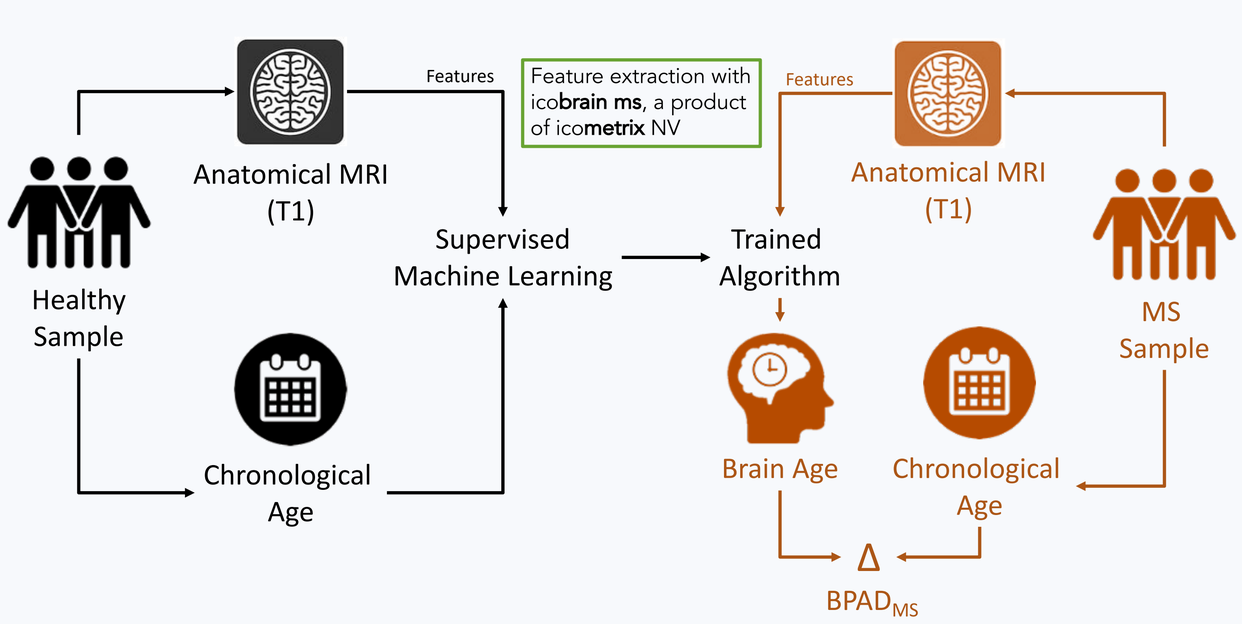
Findings by Boyle et al. 2019:

- Correlation BPAD – cognition in healthy population

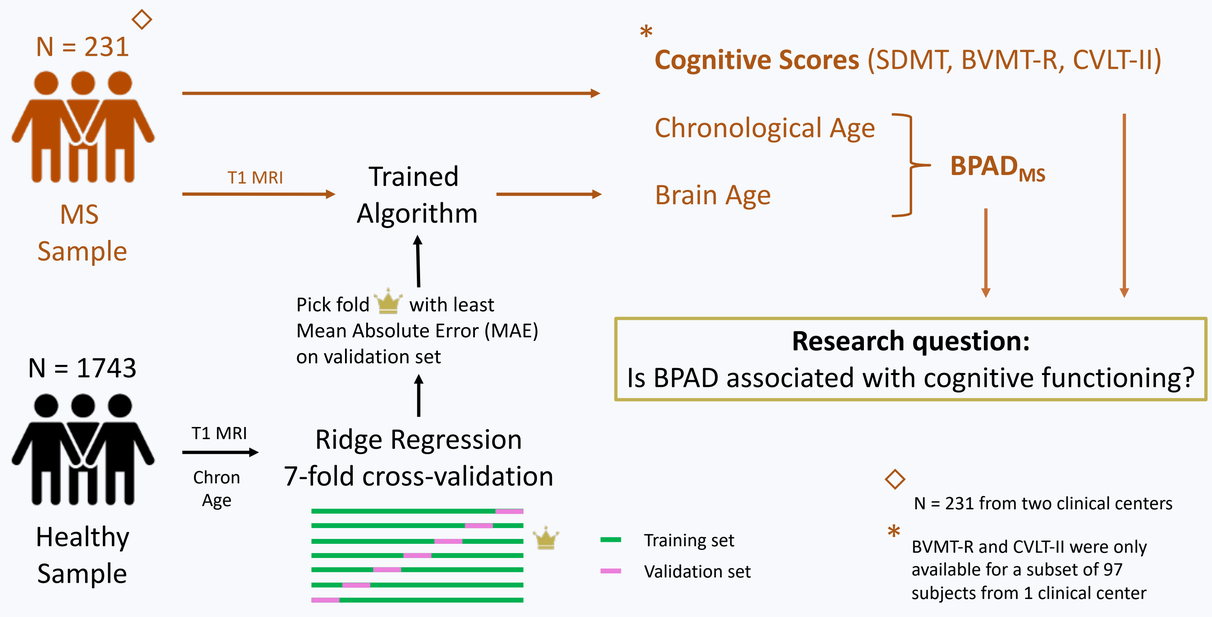
## RESEARCH QUESTION

Is BPAD related to the most affected cognitive domains in MS, i.e. information processing speed and memory?

## METHODOLOGY – BPAD calculation




## METHODOLOGY - General



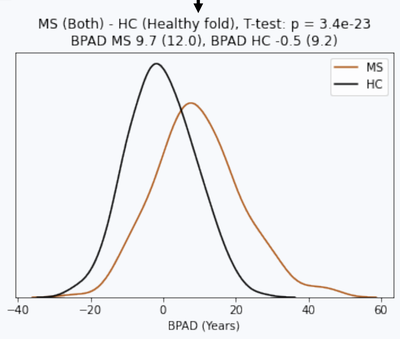

## RESULTS – Comparison Healthy and MS

**Trained Algorithm (Healthy):**
Best fold 👑 : MAE = 7.38 years

**Applied to MS sample:**
MAE = 12.19 years

**BPAD$_{HC}$: -0.5 (9.2) years** **BPAD$_{MS}$: 9.7 (12.0) years** *



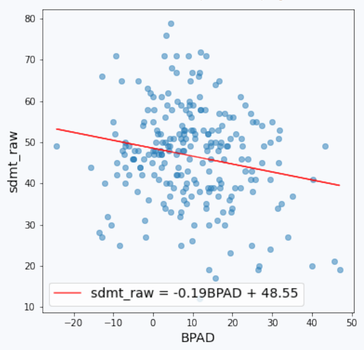



* All values reported as
Mean (Standard Deviation)
BPAD$_{MS}$ of total MS sample (N = 231) shown

## RESULTS - Within MS Sample

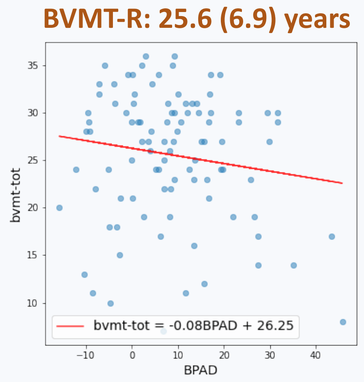
BPAD$_{MS}$

**SDMT: 46.7 (12.0) years**



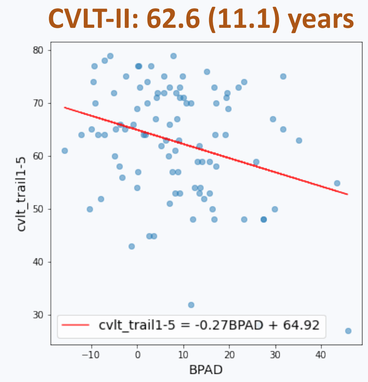

$r_{pearson}$ = -0.19, p = 0.005

**BVMT-R: 25.6 (6.9) years**




$r_{pearson}$ = -0.14, p = 0.157

**CVLT-II: 62.6 (11.1) years**




$r_{pearson}$ = -0.30, p = 0.005

| Abbreviation | Test name | Cognitive domain |
|---|---|---|
| SDMT | Symbol Digit Modalities Test | Information Processing Speed |
| BVMT-R | Brief Visuospatial Memory Test – Revised | Visuospatial Learning and Memory |
| CVLT-II | California Verbal Learning Test – 2nd edition | Verbal Learning and Memory |

Multiple comparison correction: Benjamini-Hochberg method

## CONCLUSION

1. We confirm findings reported by previous studies on increased brain age in persons with Multiple Sclerosis
2. BPAD correlates with the two most affected cognitive domains in MS:
   - Information Processing Speed
   - (Verbal working) Memory

As a summarizing metric of imaging data, Brain-Predicted Brain Age (BPAD) might become an elegant biomarker for cognitive functioning in MS.

## REFERENCES

- Cole PhD, J. H., Raffel MD, J., Friede PhD, T., Eshaghi MD, PhD, A., Brownlee PhD, FRACP, W. J., Chard MD, PhD, D., … Ciccarelli PhD, FRCP, O. (2020). Longitudinal Assessment of Multiple Sclerosis with the Brain-Age Paradigm. *Annals of Neurology*, *88*(1), 93–105. https://doi.org/10.1002/ana.25746
- Boyle, R., Jollans, L., Rueda-Delgado, L. M., Rizzo, R., Yener, G. G., Mcmorrow, J. P., … Whelan, R. (n.d.). *Brain-predicted age difference score is related to specific cognitive functions: a multi-site replication analysis*. https://doi.org/10.1007/s11682-020-00260-3