Epigenomic Age is associated with Leukoaraiosis Volume in stroke patients, Irrespective of Chronological Age.

J. Jimenez-Conde[1], E. Giralt-Steinhauer[1], C. Soriano-Tarraga[1], M. Mola-Caminal[1], C. Avellaneda[1], U. Lazcano[1], R. Vivanco-Hidalgo[1], I. Fernandez-Perez[1], A. Ois[1], A. Rodriguez-Campello[1], E. Cuadrado-Godia[1], J. Roquer[1].

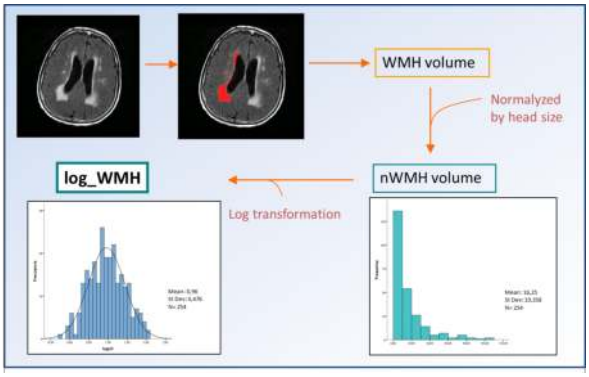
1. Institut Hospital del Mar d'Investigació Mèdica, Neurology, Barcelona, Spain.

Background and Aims:

White matter hyperintensity or leukoaraiosis (LK), is a radiological sign of cerebral small vessel disease and is considered as a good marker of brain aging. However, aging is not only due to chronological age, there are age-related DNA-methylation changes in multiple CpG sites across the genome that can be used to estimate the epigenomic age or biological age (b-Age). We seek to analyze if the possible association between LK and b-Age.

Methods:

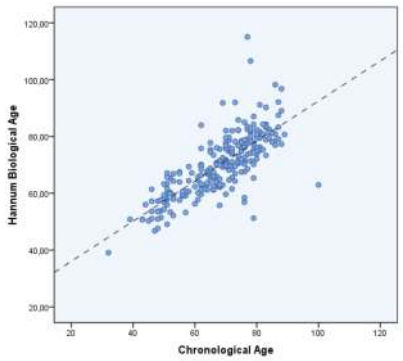
We included 254 individuals with acute ischemic stroke assessed in Hospital del Mar (Barcelona). Demographic and clinical data, chronological age (c-Age), anthropometric data, and vascular risk factors (VRF) were registered. Biological age (b-Age) was estimated with Hannumm algorithm, based on DNA methylation in 65 CpGs. Aging DIfference (AgeDif) was calculated by substracting c-Age from b-Age. LK variable was obtained in a semiautomatic volumetric measurement in FLAIR sequence of MRi. (Graph 1)



Graph 1: Semiautomatic Volumetric Analyseis of WMH (Leukoaraiosis)

	Descriptive	Association with logLK (p-value)
Chronological Age, years. *Mean(SD)*	68,69 (11,71)	<0.001
Hannum Biological Age, years. *Mean(SD)*	70,36 (10,79)	<0.001
DifHannum, years. *Mean(SD)*	1,71 (7,75)	0.012
Sex (Females %)	37,8	0.261
Hypertension (%)	78,3	0.001
Diabetes (%)	41,7	0.010
Hyperlipidemia (%)	60,2	0.494
Ischemic Heart Disease (%)	13,0	0.738
Atrial Fibrillation (%)	26,0	0.648
Previous Stroke (%)	9,8	0.302
Alcohol consumption (%)	27,2	0.025
Smoking status (%)	34,3	0.027
Coffee, Units/day *Mean(SD)*	1,22 (1,35)	0.326
Weight Kg *Mean(SD)*	73,53 (12,45)	0.058
Height , cm *Mean(SD)*	164,58 (9,16)	0.111
Waist, cm *Mean(SD)*	99,01 (16,96)	0.960
Body Mass Index. *Mean(SD)*	27,14 (4,25)	0.264

Table 1: Descriptives and bivariate analysis for association with Leukoaraiosis (logLK)



Graph 2: Scatter plot of Biological Age and its Chronological Age

	Beta	Association with logLK (p-value)
Chronological Age, years. *Mean(SD)*	0,438	0,000
DifHannum, years. *Mean(SD)*	0,138	0,038
Sex (Females %)	0,228	0,003
Hypertension (%)	0,162	0,009
Diabetes (%)	0,150	0,016
Alcohol consumption (%)	-0,188	0,011
Smoking status (%)	0,187	0,022
Weight Kg *Mean(SD)*	-0,098	0,163
Height , cm *Mean(SD)*	-0,104	0,209

Table 2: Multivariate analysis for association with Leukoaraiosis (logLK)

Results:

Bivariate analyses for LK showed significant associations with c-Age and b-Age (both p<0.001) and also with AgeDif (cc:-0.158, p=0.012). When included in a multivariate linear regression model all the variables associated in bivariate analyses, AgeDif remained independently associated (beta:0.138; p=0.038), despite containing c-Age in adjustment. Hypertension (p=0.009), diabetes (p=0.016) and smoking habit (p=0.022) kept significance as well.

Conclusions:

Volume of LK is associated with b-Age measured, by DNA methylation in a cohort of stroke patients.
It was also associated with Age-Acceleration, irrespective of c-Age.
These data supports that healthy aging might modulate LK-burden accumulated throughout life.

IMIM Parc de Salut MAR Barcelona
Institut Hospital del Mar d'Investigacions Mèdiques