

## Dyslipidemia and hypertension as cerebral blood flow predictors in the CRESCENDO cohort of elderly subjects.

Jeremy Deverdun<sup>1,2</sup>, Tasnime Akbaraly<sup>3</sup>, Frederic Ben Naim<sup>4</sup>, Alain Bonafe<sup>5</sup>, Adam Brickman<sup>6</sup>, Celine Charroud<sup>3</sup>, Stephane Chemouny<sup>1</sup>, Jeannette Fareh<sup>7</sup>, Nicolas Menjot de Champfleury<sup>5</sup>, François Molino<sup>8</sup>, Olivier Soulier<sup>4</sup>, Jason Steffener<sup>6</sup>, Florence Portet<sup>3</sup>, Yaakov Stern<sup>6</sup>, Karen Ritchie<sup>3</sup>, and Emmanuelle Le Bars<sup>5</sup>  
<sup>1</sup>Intrasense, Montpellier, Hérault, France, <sup>2</sup>Theoretical Physics, Université Montpellier 2, Montpellier, Hérault, France, <sup>3</sup>Unit 1061 : Neuropsychiatry: Epidemiological and clinical research, Inserm, Hérault, France, <sup>4</sup>Intrasense, Hérault, France, <sup>5</sup>Service de neuroradiologie, CHU Gui de Chauliac, Montpellier, Hérault, France, <sup>6</sup>The Taub Institute for Research on Alzheimer's Disease and the Aging Brain, New York, United States, <sup>7</sup>SysDiag UMR3145, CNRS, Hérault, France, <sup>8</sup>Theoretical Physics, Université Montpellier 2, Montpellier, Hérault, France

**Target audience:** Researcher and clinician involved in the understanding of brain aging and its determinants using cerebral blood flow measurements through Arterial Spin label (ASL) in an epidemiological framework.

**Purpose:** Low Cerebral Blood Flow (CBF) has been shown to be linked to cardiovascular mortality in older people<sup>1</sup> highlighting the importance to understand the impact of factors such as life habits and physiological data on the CBF. The purpose of our study, which is based on a large cohort of elderly healthy subjects issued from French general population, is to assess the correlation between different markers of cardiovascular risks and the ensuing evolution of the CBF twelve years later.

**Methods:** Data comes from the Crescendo (Cognitive REServe and Clinical ENDOfenotype) project in which 394 elderly volunteers from the ESPRIT cohort<sup>2</sup> (initiated in 2000) were invited to undergo a multimodal MRI protocol in 2012. CBF measures were obtained from pulsed ASL sequences (PICORe-QUIPSS II, 52 repetitions, TI2/TE/TR = 2000/20/3000 ms) through a standard processing pipeline<sup>3</sup>. Correction was performed for white matter lesions<sup>5</sup> and partial volume effect<sup>4</sup>. Required tissues segmentations were obtained from the high resolution 3DT1 using the SPM8 software. Regional gray matter CBF were then extracted by overlaying a custom vascular territory atlas consisting of 16 regions, previously normalized to the CBF map. Mean and regional CBF were computed for 245 participants whose ASL analysis could be performed. Amongst them 215 (61.9 % women, m=83.2±3.9 years-old) had complete data on socio-demographic (sex, age and education achievement), health behavior (smoking status and alcohol consumption), health status (body mass index, hypertension, dyslipidemia, diabetes and cognitive performances in the Benton Visual Retention Test) and genetic factors (Apolipoprotein E genotype) assessed at baseline (twelve years before the MRI acquisition).

**Results:** First, global means of CBF in this cohort was 50.4±12.9 ml/100g/min. After performing multivariate linear regression model adjusted for age, sex, gray matter volume and other socio-demographic, health behavior and health status factors, dyslipidemia (p=0.04) and hypertension (p=0.01) were associated with CBF. Participants with dyslipidemia showed lower CBF. Patients with hypertension showed higher CBF. No difference was observed for gender. Second, regional analysis also exhibited significant correlations only for hypertension and dyslipidemia. The correlations were localized in 1) regions of the posterior circulation territories for the hypertension, and 2) regions of the anterior circulation for dyslipidemia with no overlapping (see fig 1).

**Discussion:** Hypertension and dyslipidemia appear as good predictors at 12 years of gray matter CBF variations. Dyslipidemia mainly consists of hypercholesterolemia, is an established risk factor for ischemic heart disease and coronary mortality<sup>6</sup>. Dyslipidemia is associated with a significant decrease of the gray matter CBF which can be an effect of the well-known accumulation of atherosclerotic plaque induced by cholesterol. The average hypertension effect on CBF appears at first sight paradoxical with the literature<sup>7</sup>. Dyslipidemia and hypertension are both cardiovascular risk factors strongly coupled to vascular flow autoregulation. Interestingly enough, the regional analysis shows that the decrease (dyslipidemia) and the increase (hypertension) of the CBF correspond to well-defined non overlapping vascular regions, which are known to exhibit different autoregulation mechanisms of the blood flow<sup>8,9</sup>.

**Conclusion:** By assessing associations between a large range of sociodemographic, life habit and health status variables and CBF means assessed twelve years later in the largest cohort of healthy elderly population, our results suggest that dyslipidemia and hypertension might be important predictors of long term CBF in elderly. Those results raise the question whether change in health status factors might affect CBF and its consequence on cerebral aging.

**References:** [1] B.Sabayan et al, Neurology, 2013; [2] M. Ancelin et al, Encephale, 2006; [3] Z. Wang et al, Magnetic Resonance Imaging, 2008; [4] I. Aslani et al, Magn Reson Med, 2008; [5] P. Schmidt et al, NeuroImage, 2012; [6] J. Stamler et al, JAMA, 1986; [7] L. Beason-Held, Stroke, 2007; [8] M.Beausang-Linder et al, Acta Physiol Scand, 1981; [9] W. Dillon et al, AJNR Am J Neuroradiol, 1998



Figure 1 : Regions of correlation between CBF and hypertension (pink), dyslipidemia (green) overlaid on a vascular atlas