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SPHN – The Swiss Aging Citizen Reference (SACR)

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Abstract. In Switzerland by 2045, we expect 2.7 Mio citizens aged 65+ of whom 1.0 Mio. aged 80+. A priority and focus of personalized health research is therefore aging biology to extend healthy life expectancy. Novel molecular and imaging features will emerge as candidate targets for risk prediction and screening of chronic diseases. It is of utmost importance to test the clinical and public health utility of candidate biomarkers evolving from this research in citizen reference cohorts. We will build a Swiss Aging Citizen Reference (SACR), a testable and scalable reference cohort offering interoperable, searchable, and accessible data. 1000 participants from existing Swiss citizen cohorts will be combined and analyzed for DNA methylation and MRI brain imaging. SACR will serve as a testbed for clinical and public health utility of candidate biomarkers. As for a proof-of-concept study, we will conduct an agnostic search for structural and functional brain features associated with epigenetic aging acceleration to examine the potential of epigenetic age acceleration as the intermediate aging biomarker and to better understand the aging mechanism in brain.

Keywords. SPHN, personalized health, citizen reference, aging, DNA methylation, brain imaging

1. Introduction

The number of older citizens in Switzerland is growing. In 2045 pensioners aged 65+ are expected to account for over 2.7 million inhabitants, with over 1 million aged 80+. It is of strategic importance for the country from both, economic and public health perspectives, to maximize the healthy life expectancy of future elderly people.

Molecular and imaging biomarkers evolving from personalized health research depend on a healthy reference for utility testing. Citizen cohorts with prospectively sampled biomaterial are essential for investigating the reference distribution of exposome, risk prediction and screening biomarkers and their independent value in predicting morbidities. Among many indices and markers of biological aging, DNA methylation in blood has been demonstrated as a robust aging biomarker, with potential to interrogate molecular mechanism behind aging. DNA methylation-derived epigenetic

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age acceleration was cross-sectionally associated with poorer cognitive performance (fluid intelligence), lower grip strength, poorer lung function, and with frailty.

Cognitive decline and neurological disorders are becoming one of the most significant socio-economic burdens of our aging society. One of the fundamental questions in human neuroscience is how molecular and cellular processes in the living brain drive cognitive changes over the lifespan. In recent decades the study of brain structure and function in health and disease has been greatly aided by the advent of magnetic resonance imaging (MRI) and started revealing how acute focal lesions and chronic neurodegeneration can lead to impaired cognition and disease states.

In this SPHN driver project we will build a Swiss Aging Citizen Reference (SACR) as a public health pillar for personalized health in Switzerland, where we implement brain imaging biobank into existing Swiss citizen cohorts to test the clinical and public health utility of candidate biomarkers including epigenetic age acceleration.

2. Methods

We build a scalable SACR infrastructure to integrate existing Swiss citizen cohorts, SAPALDIA, SKIPOGH, and CoLaus|PsyCoLaus, offering interoperable, searchable, and accessible data for researchers. The SACR population will continue to grow by integrating additional citizen cohorts in the future.

DNA methylome and MRI brain imaging data will be obtained for 1000 SACR citizens from the three cohorts. DNA methylome is already available in SAPALDIA and will be obtained for SKIPOGH and CoLaus|PsyCoLaus. MRI brain imaging has been conducted in CoLaus|PsyCoLaus and will be complemented for SAPALDIA and SKIPOGH. As for a proof-of-concept study, structural and functional features derived from quantitative MRI indicative for brain's myelin, iron and free tissue water content will be agnostically searched for association with epigenetic age acceleration.

3. Expected results

From the proof-of-concept study, we will identify brain microstructure features associated with epigenetic age acceleration, which is considered as an early biological aging marker, therefore we will provide evidence towards the validity of epigenetic age acceleration as intermediate aging biomarker. Further analyses on the brain imaging features towards aging phenotypes, e.g. cognitive function, will contribute to better understanding of brain aging, and potentially to its prediction at an early stage.

4. Public health impacts

As a result of this SPHN driver project, we will have a testable and scalable reference "SACR". This will constitute the public health pillar for personalized health in Switzerland, offering interoperable, searchable, and accessible data for personalized health researchers. Archived biomaterial and data from SACR participants will be accessible for testing the clinical and public health utility of candidate biomarkers and exposome features in predicting biological age and age-related (multi-)morbidities.