

Worse neurocognitive decline in sexual minority older adults driven by greater vulnerability to physical and mental health risk factors: a UK Biobank study

Riccardo Manca¹, Annalena Venneri¹

¹ Department of Medicine and Surgery, University of Parma, Parma, Italy

Introduction

Epidemiological and observational studies have identified neurocognitive health disparities for people from sexual and gender minorities [1-3]. While sexual minority older adults (SMOAs) are more likely to report cognitively problems subjectively, **objective investigations** into greater risk of dementia and neurodegeneration have yielded **inconsistent findings**.

Currently, there is also limited evidence that specific risks may induce vulnerability to neurocognitive decline in SMOAs [4,5].

AIM

Therefore, the aim of this study was to quantify the impact of several **psycho-social and health-related risk factors** on **cognitive decline and brain alterations** in SMOAs.

Methods

A total of 14,784 50+ participants from the UK Biobank with data on sexual history, clinical, cognitive and brain MRI were included:

- **605 SMOAs identified based on self-reports on same-sex behaviours**
- **14,179 heterosexual older adults (HOAs)**

RISK FACTORS

Mental health

- **Depression**
- **Anxiety**
- **Any psychiatric diagnosis**
- **Childhood trauma**
- **Traumatic experiences in life**

Physical health

- **Diabetes**
- **Obesity**
- **Disability**
- **Cardiovascular**
- **Cancer**
- **Other serious illnesses**

OUTCOMES

- **Cognitive performance**
- **Regional grey matter volumes**
- **White matter microstructural integrity indices**

Table 1 | Characteristics of the participant samples.

Characteristic	SMOA (n = 605)	HOA (n = 14,179)	t	p
Age	56.8 ± 4.9	58.1 ± 5.1	5.87	<0.001
Education ^a	71.4/28.6	57.4/42.6	47.0 ^b	<0.001
Sex (F/M, %)	43.3/56.7	50.7/49.3	12.8 ^b	<0.001

^a University education/below university (%)

^b Chi-square test

The impact of risk factors on cognitive performance, regional grey matter volumes (GMV) and white matter (WM) microstructural integrity was investigated using MANCOVAs. Interactions between each factor and sexual behaviour group was assessed.

Repeated-measures models were used to assess the impact of risk factors on cognitive performance decline over 2 years. Age, education and sex were used as covariates.

Results

At baseline, SMOA performed better on several tests (*Table 2*) but had higher risk of **diabetes, serious illnesses, anxiety, depression, psychiatric diagnosis, childhood and life trauma** than HOAs.

Table 2 | Cognitive profiles of the participant samples.

Characteristic	SMOA (n = 605)	HOA (n = 14,179)	t	p
Matrix pattern	0.55 ± 0.13	0.54 ± 0.13	2.77	0.006
Fluid intelligence	6.37 ± 1.88	6.20 ± 1.79	2.31	0.021
Picture vocabulary - SA	0.44 ± 0.08	0.42 ± 0.07	7.25	<0.001
Picture vocabulary - PS	3112.83 ± 1005.10	3221.45 ± 1052.38	2.49	0.013
Tail Making Test - A	226.07 ± 65.75	231.06 ± 79.63	1.52	0.129
Tail Making Test - B	568.14 ± 247.45	580.77 ± 240.67	1.26	0.207
Choice reaction time	598.12 ± 95.57	608.41 ± 107.43	2.32	0.021
Paired associates	7.48 ± 2.03	7.30 ± 2.11	2.06	0.039
SDMT	18.63 ± 4.29	18.38 ± 4.83	1.29	0.196

SA: Specific ability, PS: Processing speed, SDMT: Symbol Digit Modalities Test
In bold: significant between-group differences after false discovery rate correction for multiple comparisons

Childhood trauma had a worse impact on baseline complex processing speed (i.e., SDMT) performance of SMOAs than HOAs (*Figure 1*).

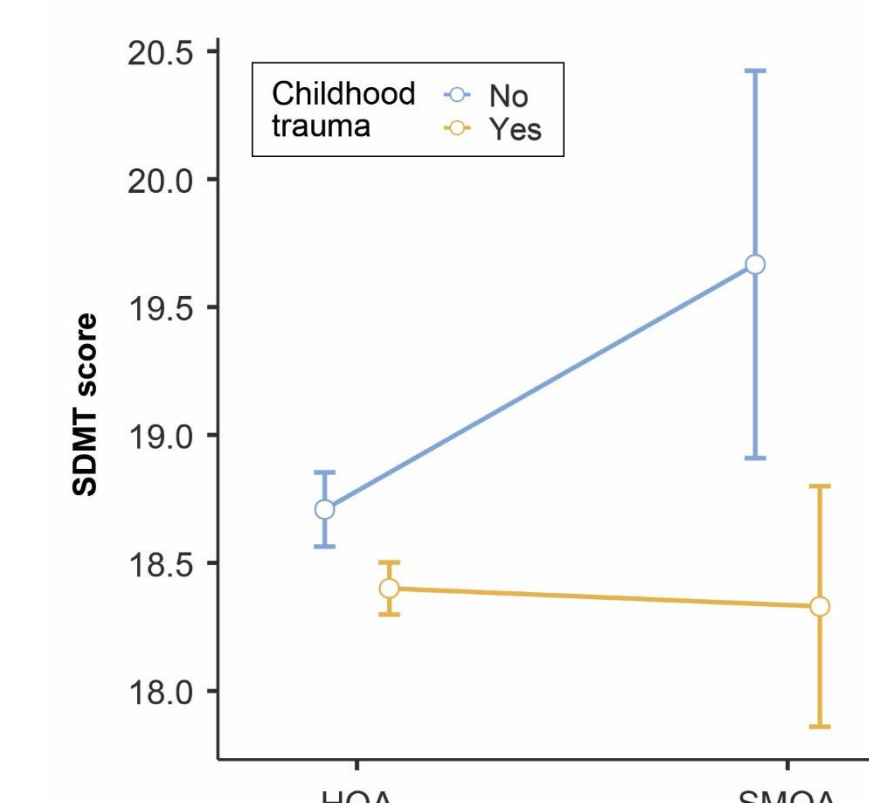


Figure 1 | Differential impact of childhood trauma on SDMT performance at baseline.

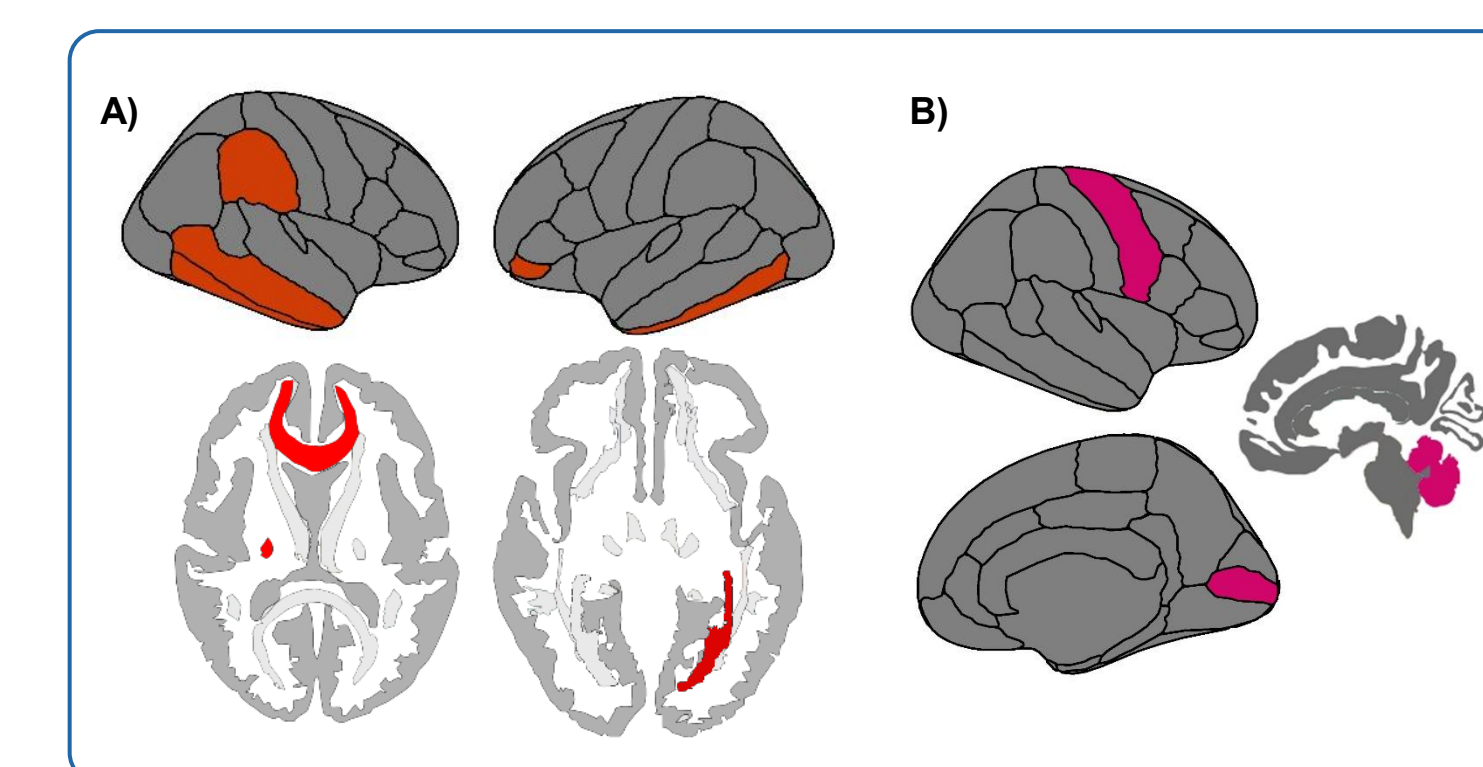


Figure 2 | Differential impact of risk factors on GMV and WM microstructural integrity at baseline in **A) SMOAs** and **B) HOAs**.

In SMOAs: Depression, psychiatric diagnosis, diabetes and other serious illnesses were associated with smaller GMV of **temporal, inferior parietal and cerebellar regions** (*Figure 2a*).

In HOAs: Anxiety and childhood trauma were associated with smaller GMV of **cerebellar and primary motor and visual cortices** (*Figure 2b*).

Moreover, in repeated-measures analyses, **diabetes** had also a greater impact on longitudinal **decline in episodic memory** (i.e., paired associates learning) in the SMOA than in the HOA group (*Figure 3*).

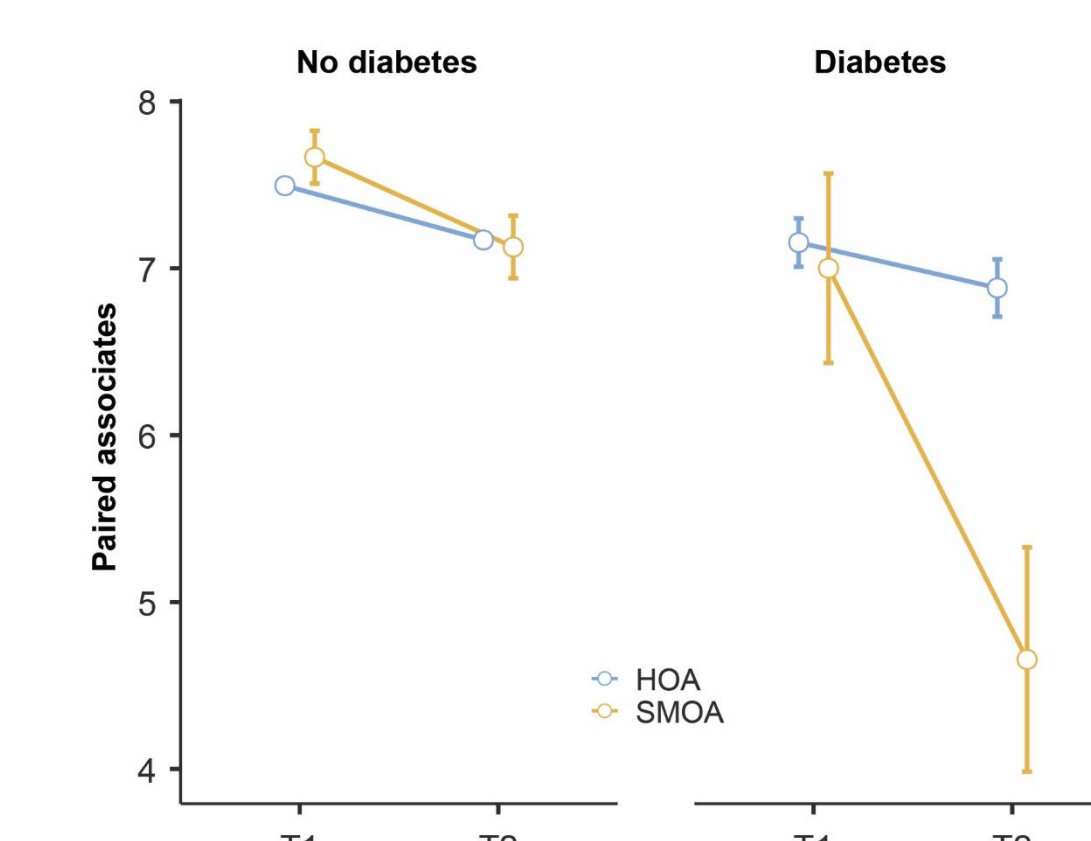


Figure 3 | Differential impact of diabetes on longitudinal episodic memory decline.

Conclusions

Despite better cognitive performance at baseline, SMOAs show **greater cognitive health vulnerability** than HOAs to diabetes and mental health issues.

Such vulnerability appears to be driven by underlying **brain alterations in associative cortices** and in **WM tracts** associated with similar risk factors.

This is the first evidence that physical and mental health issues have greater impact on the brain of SMOAs fostering greater cognitive deterioration.

REFERENCES

- [1] Romanelli RJ et al. (2023). DOI: 10.1089/lgbt.2023.0095
- [2] Manca R & Venneri A (2020). DOI: 10.2174/1567205018666210114111556
- [3] Manca R et al. (2022). DOI: 10.3389/fnhum.2022.909868
- [4] Manca R & Venneri A (2020). DOI: 10.1093/geronl/ggad110
- [5] Manca R et al. (2025). DOI: 10.3390/brainsci15010090