

MIDLIFE EXPOSURES TO CIVILIAN CONFLICT ASSOCIATED WITH ACCELERATED BIOLOGICAL AGEING BUT BETTER COGNITIVE PERFORMANCE IN OLDER AGE

An examination of the impact of the Northern Ireland (NI) Troubles within the Northern Ireland cohort for the longitudinal study of ageing (NICOLA)



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30 SECOND LAY SUMMARY

We all know that stress is bad for our health, and it can increase our chances of developing memory problems in later life. NI experienced a long period of civil conflict from the 1960s known as “the Troubles” and we wanted to know what impact it had on people and their memory in later life. Using data collected in the NICOLA study we found that most people reported that the Troubles had significant impact on their life. The potential impact of this stress can be seen in that those most affected by the Troubles are biologically older than their actual age would suggest. However, despite this the most traumatised individuals have better memory performance than those less traumatised. Our next steps are to look to see if this is due to unique individual or societal factors.

AIMS

To examine the impact of the NI Troubles on biological age as determined by DNAm based epigenetic clocks and cognitive performance in participants over 60 within the NICOLA study.



Figure 1: Geographical recruitment in the NICOLA study

BACKGROUND

Epigenetic modifications, such as DNA methylation (DNAm) are potential mechanisms whereby social or environmental exposures experienced over the life course may influence health outcomes. From the late 1960s the civilian population of NI lived through a conflict known as the Troubles with lasting effects on the physical and mental health of the NI population

METHODS

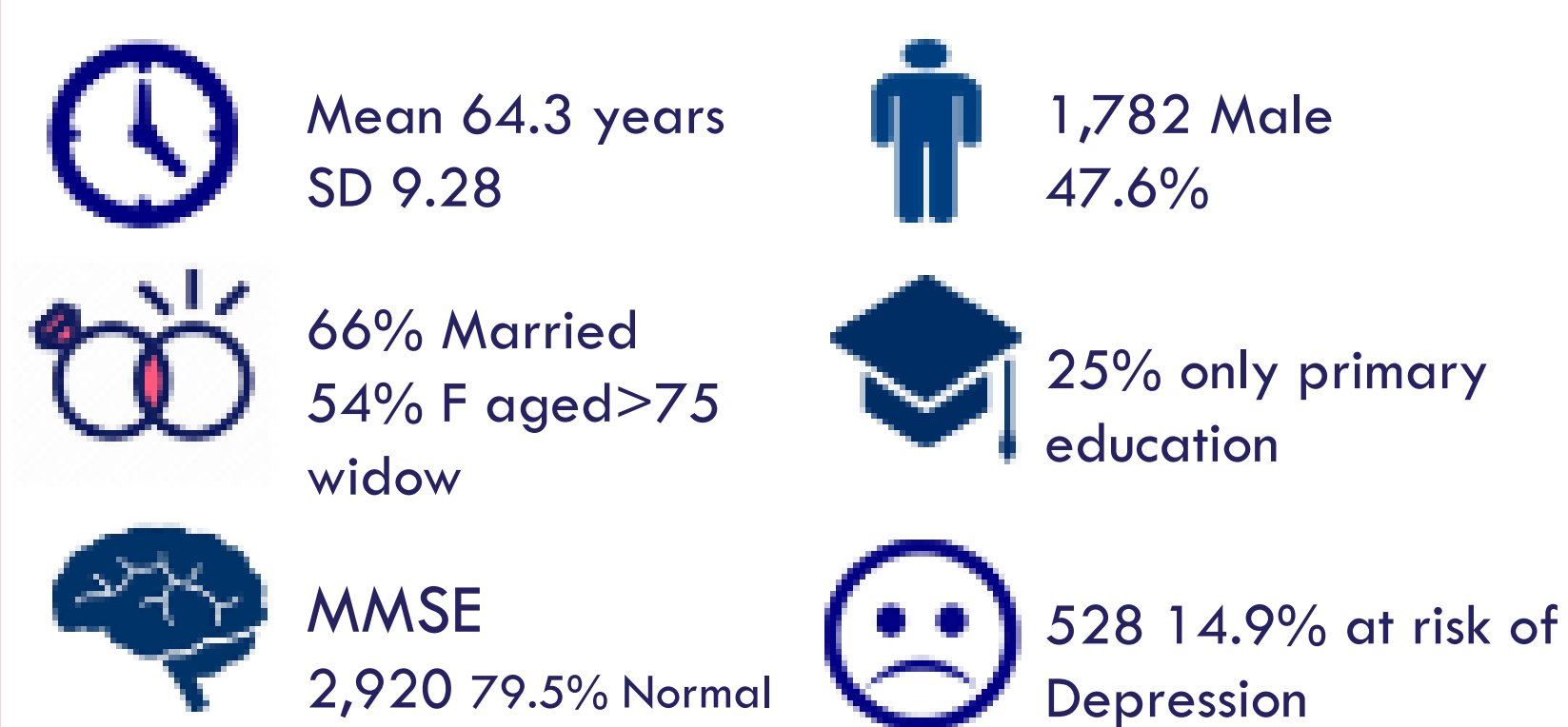


The NICOLA study¹ is a longitudinal study of **8,283 community dwelling adults, aged 50 or older** (see Figure 1) that have been deeply phenotyped using a range of social, economic and health assessments. DNAm was derived for 2,000 participants with high quality DNA extracted from whole blood using the Infinium Methylation EPIC BeadChip. Epigenetic clock data was generated for 1,953 individuals.

RESULTS

6,571 NICOLA participants aged 60+ who completed assessment of key variables were examined.

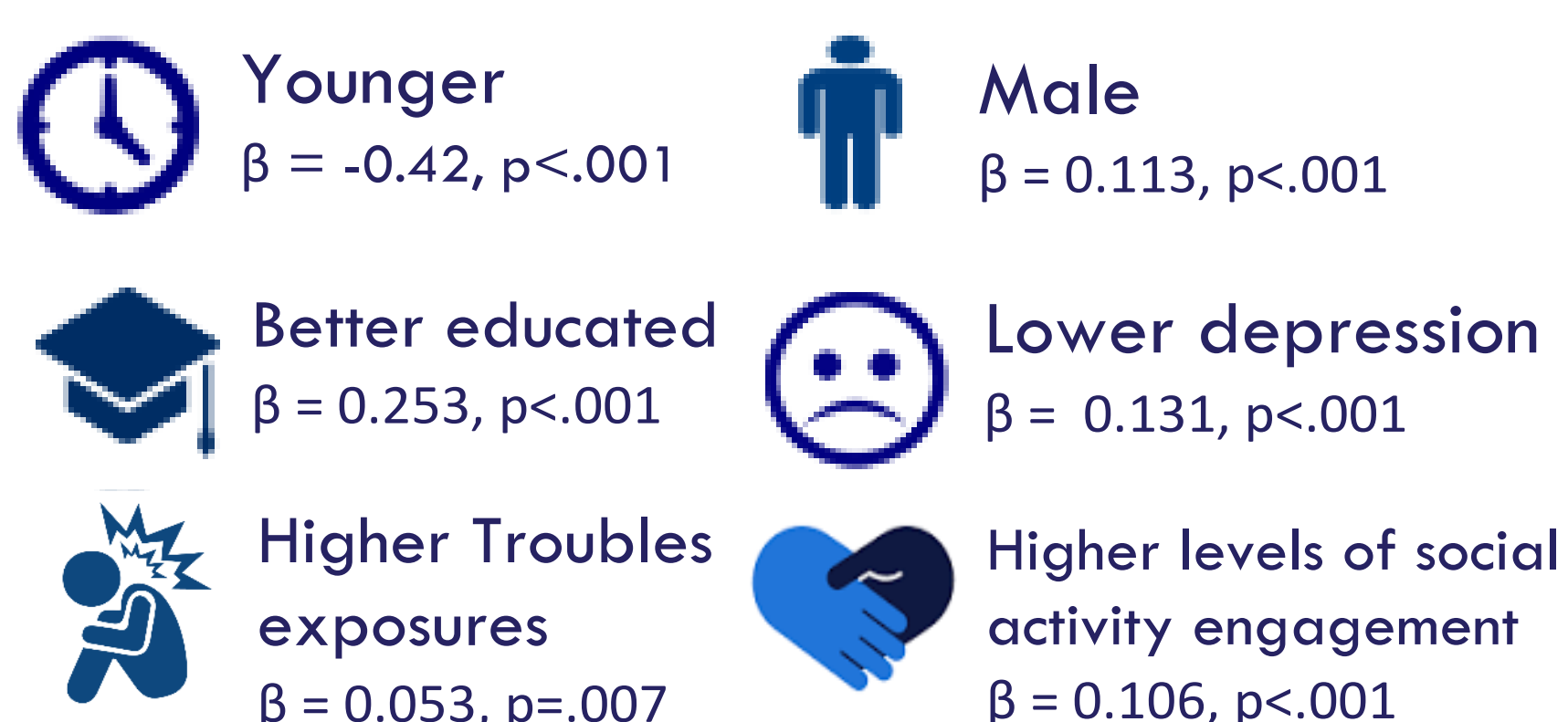
Descriptive analysis is shown below.



45.9% (2,183) participants reported the NI Troubles had a moderate to an extreme impact on their lives and **11.6%** (961) reported >15 Troubles related events including knowing someone that was murdered, witnessing bombs, or themselves experiencing violence. **6.4%** (269) would meet DSM criteria for post-traumatic stress disorder (PTSD).

Cognitive performance was assessed using the Mini Mental State Examination (MMSE) mean 28.44 (SD 1.84), Montreal Cognitive Assessment (MOCA) mean 25.33 (SD 3.27) and animal naming.

BETTER cognitive performance was associated with being



Using standardised measures of age acceleration (termed IEAA as adjusted for age and white cell composition) for the DNAm based epigenetic clocks Horvath, PhenoAge and PACE we tested linear regression models for troubles exposure.

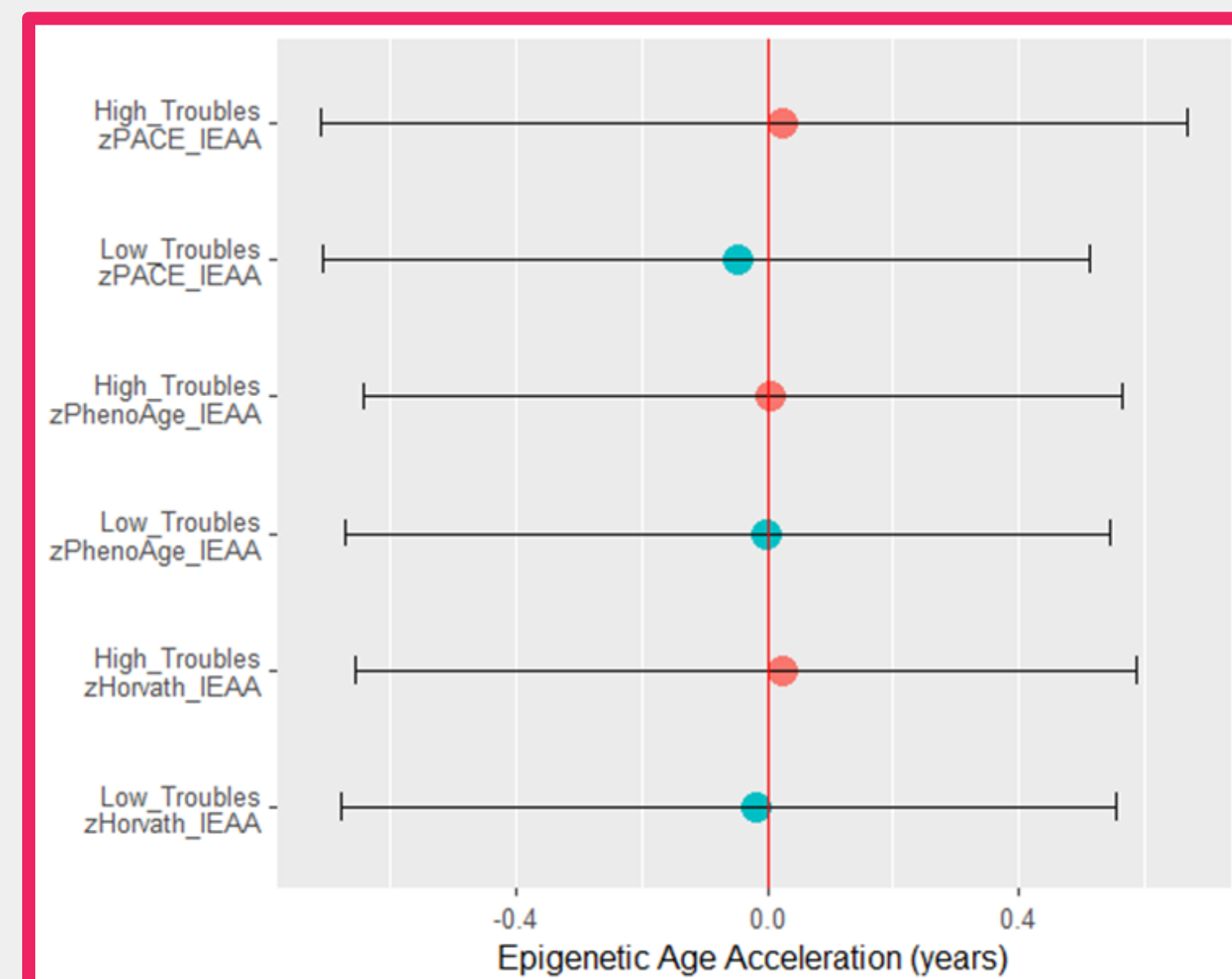


Figure 2: IEAA for three epigenetic clocks with anything to the right of the y axis indicating biological age acceleration in years. High Troubles group are red and Low Troubles are blue

The interaction term between Troubles Exposure and Social Activity Engagement was significant at $\beta = -0.054, p = 0.01$

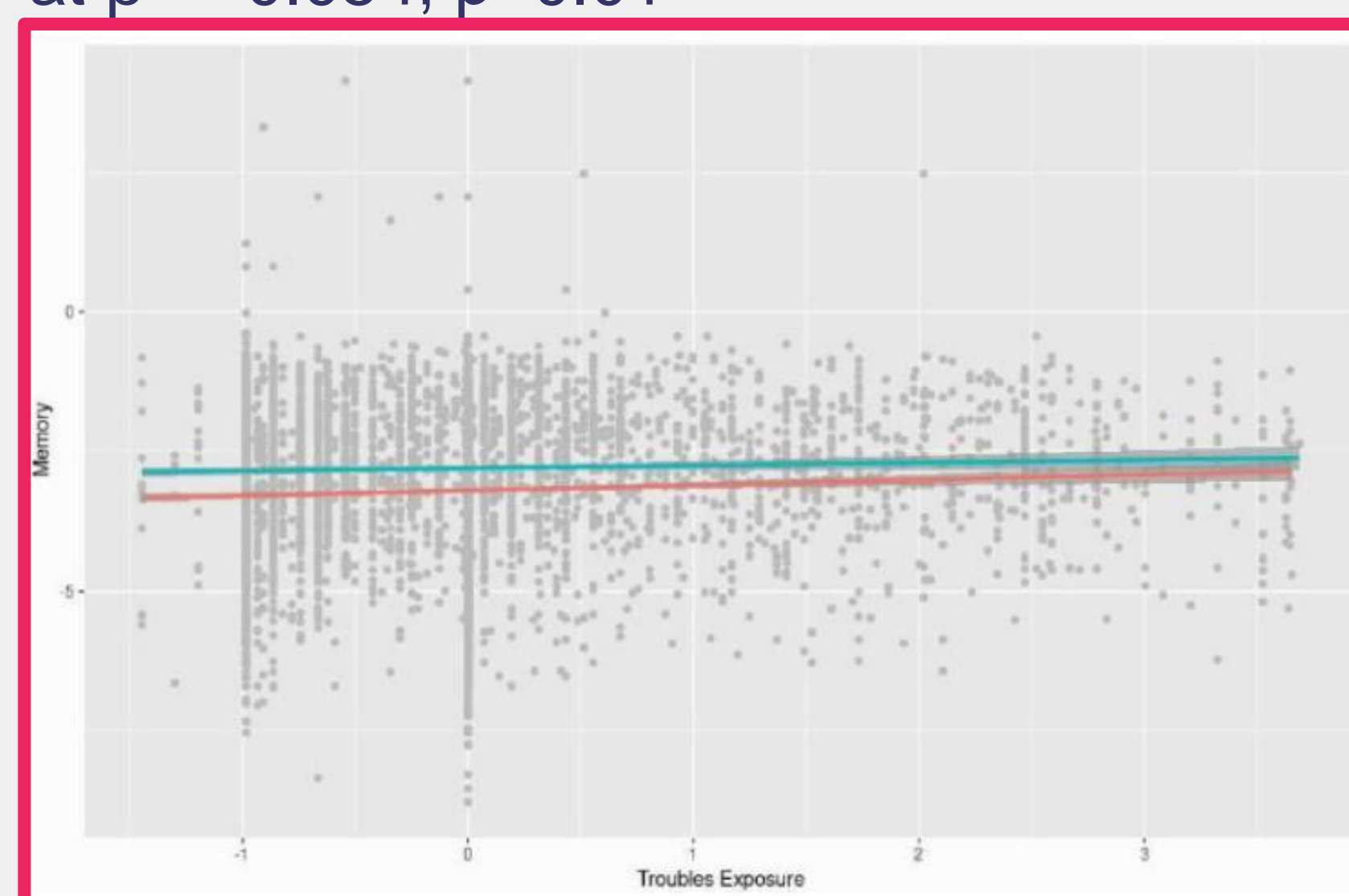


Figure 3: Moderation effect of social activity

Figure 3 (above) shows the moderation effect of Social Activity Engagement on effect of Troubles Exposure on Episodic Memory. Green line indicates higher levels of social activity compared to lower (red line).

DISCUSSION

Those reporting experiencing a traumatic event had **better** cognitive performance that those that did not with on average a **0.49 higher score on MMSE** ($p < 0.001$), **0.91 higher MOCA score** ($p < 0.001$) and recalled on average **1.82 more animals** ($p < 0.001$).

Those with greater Troubles exposure had **accelerated biological ageing** (see Figure 2) but sensitivity analysis identified depression, smoking and social activity engagement as contributors. At higher levels of social activity engagement (green line), there is less of an effect of Troubles Exposure on Memory (see Figure 3).

FUTURE PLANS

Further exploratory analysis within the NICOLA dataset is ongoing to investigate results shown. Cognitive resilience and other supportive social factors may explain additional variability between Troubles exposure and cognitive performance.

Additional stress exposures throughout the life course including Adverse Childhood Experiences (ACE) will be examined in international harmonised longitudinal studies of ageing.

1. Neville C, Burns F, Cruise S, Scott A, O'Reilly D, Kee F, et al. Cohort profile: the Northern Ireland Cohort for the Longitudinal Study of Ageing (NICOLA). International Journal of Epidemiology. 2023 PMID: 37011634 DOI: 10.1093/ije/dyad026

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CONTRIBUTIONS CP, CH, LS, FK, BMCg, AMcK were responsible for study concept and design. CP prepared initial drafts of the manuscript and revisions. CP, CH, LS completed statistical analysis. All authors contributed to the critical revision of the manuscript, proof reading and approval of the final version.



<https://www.qub.ac.uk/sites/NICOLA/>

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