Associations of cognitive performance with cardiovascular magnetic resonance phenotypes in the UK Biobank

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Aims

Existing evidence suggests links between brain and cardiovascular health. We investigated associations between cognitive performance and cardiovascular magnetic resonance (CMR) phenotypes in the UK Biobank, considering a range of potential confounders.

Methods and results

We studied 29,763 participants with CMR and cognitive testing, specifically, fluid intelligence (FI, 13 verbal-numeric reasoning questions), and reaction time (RT, a timed pairs matching exercise); both were considered continuous variables for modelling. We included the following CMR metrics: left and right ventricular (LV and RV) volumes in end-diastole and end-systole, LV/RV ejection fractions, LV/RV stroke volumes, LV mass, and aortic distensibility. Multivariable linear regression models were used to estimate the association of each CMR measure with FI and RT, adjusting for age, sex, smoking, education, deprivation, diabetes, hypertension, high cholesterol, prior myocardial infarction, alcohol intake, and exercise level. We report standardized beta-coefficients, 95% confidence intervals, and P-values adjusted for multiple testing. In this predominantly healthy cohort (average age 63.0 ± 7.5 years), better cognitive performance (higher FI, lower RT) was associated with larger LV/RV volumes, higher LV/RV stroke volumes, greater LV mass, and greater aortic distensibility in fully adjusted models. There was some evidence of non-linearity in the relationship between FI and LV end-systolic volume, with reversal of the direction of association at very high volumes. Associations were consistent for men and women and in different ages.

Conclusion

Better cognitive performance is associated with CMR measures likely representing a healthier cardiovascular phenotype. These relationships remained significant after adjustment for a range of cardio-metabolic, lifestyle, and demographic factors, suggesting possible involvement of alternative disease mechanisms.

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Introduction
Cardiovascular disease and cognitive impairment are growing public health problems, particularly in ageing global populations. Existing work suggests interactions across heart–brain organ systems. The brain has been proposed as a target for end-organ damage from cardiovascular disease and risk factors. Indeed, cardiometabolic morbidities have been linked to accelerated cognitive decline and their treatment with slowed progression of dementia. Cardiovascular risk factors have been associated with both vascular and Alzheimer’s dementia. In individuals without dementia, vascular risk factors correlate with worse cognitive performance, with an additive effect from increasing number of risk factors. Furthermore, cardiovascular risk factors are associated with poorer brain health across grey and white matter macrostructure and microstructure assessed on brain magnetic resonance imaging.

There is support for common heart–brain disease pathways mediated by atherosclerosis and arteriosclerosis. However, the precise mechanisms by which cardiovascular diseases and risk factors may cause cognitive impairment are incompletely understood, and it is not known if alternative mechanisms may play a role in the observed associations. Exploring the relationship between cognitive performance and indices of cardiovascular structure and function may provide novel insights into these relationships and their underlying mechanisms; however, to date, this has not been studied in large cohorts.

We studied, in the UK Biobank, associations of cardiovascular magnetic resonance (CMR) indices of cardiovascular structure and function with cognitive performance measures. We considered potential confounding from a wide range of cardiometabolic, lifestyle, and demographic exposures.

Methods
Study population and setting
The UK Biobank is a large prospective cohort study incorporating data from over half a million participants from across the UK. Individuals aged 40–69 years old were identified through National Health Service (NHS) registers and recruited over a 4-year period between 2006 and 2010 from a range of urban and rural settings. The protocol is publicly available. Baseline assessment comprised detailed characterization of socio-demographics, lifestyle, environmental factors, medical history, tests of cognitive function, and a series of physical measures. Individuals who were unable to consent or complete baseline assessment due to illness or discomfort were not recruited. The UK Biobank Imaging Study, which aims to scan 100,000 of the original participants (48,000 completed, February 2021) includes, among a wide range of other assessments, detailed CMR imaging.

Ethics
This study was covered by the ethical approval for UK Biobank studies from the NHS National Research Ethics Service on 17 June 2011 (Ref 11/NW/0382) and extended on 10 May 2016 (Ref 16/NW/0274). All participants provided written informed consent.

Measures of cognitive function
We assessed cognitive measures available in terms of biological relevance and repeatability. We selected two components from the UK Biobank cognitive function assessment for inclusion in our analysis: fluid intelligence (FI) and reaction time (RT). The FI test is intended to measure the capacity to solve problems that require logic and reasoning independent of acquired knowledge. The RT exercise is designed to provide a crude measure of raw processing speed, reaction speed, and attention. Overall, these two tests provide broad assessment of several different aspects of cognitive performance. Additionally, these are robust measures, with demonstrated reliability (internal consistency) and longitudinal stability in previous work. Furthermore, their availability for a large subset of the UK Biobank imaging cohort permits adequately powered analyses of associations with CMR imaging phenotypes.

Fluid intelligence
Assessment of FI consisted of a series of 13 verbal-numeric reasoning questions completed within 2 minutes. A point was awarded for each correct answer; incorrect, or unanswered questions received a score of zero. The final score was the sum of correct answers with a maximum score of 13. Thus, higher FI scores correspond to higher cognitive performance. The Cronbach alpha reliability for this test is 0.62. The full protocol for FI assessment in UK Biobank is published elsewhere; we provide a summary of the questions in Supplementary data online, Table S1. As the FI variable in our sample was normally distributed, it was treated as a continuous numerical variable for purposes of modelling, as per established methods.

Reaction time
The RT test consisted of four rounds of a pairs matching exercise. In each round, participants were shown 12 pairs of cards on a screen and asked to press a button as soon as a matched pair of cards appeared. The final RT score is calculated as the mean time in milliseconds to correctly identify matches over four rounds. Hence lower RT scores represent faster processing speed and better cognition. The Cronbach alpha reliability for this test is 0.85. The full protocol for the RT test is available in a dedicated document.

CMR image acquisition and analysis
UK Biobank CMR scans are performed using 1.5 T scanners (MAGNETOM Aera, Syngo Platform VD13A, Siemens Healthcare, Erlangen, Germany) according to a standardized protocol. Assessment of the left and right ventricles (LV and RV) includes a complete short-axis stack acquired using balanced steady-state free precession sequences. Conventional LV and RV volumetric measures were extracted using a fully automated quality controlled pipeline previously developed and validated in a large subset of the UK Biobank, as detailed elsewhere. Aortic distensibility represents the relative change in area of the aorta (aortic strain) per unit pressure. Aortic strain was measured using transverse cine images of the aorta and divided by central pulse pressure from Vicorcorereadings at the time of imaging. Aortic distensibility results were obtained from a previous analysis of UK Biobank scans using a
Cognitive performance and CMR phenotypes

Statistical analysis

Statistical analysis was performed using R version 3.6.222 and RStudio Version 1.3.1093.23 We included all participants with CMR and at least one of FI or RT. Participants with dementia, ascertained from UK Biobank algorithmically defined health outcomes, were excluded (n = 13). We tested, in individual multivariable linear regression models, the association of CMR metrics with measures of cognitive performance (FI and RT). Based on existing literature and biological plausibility, we considered the following covariates, determined a priori: age, sex, smoking, alcohol intake, exercise level, education, deprivation, diabetes, hypertension, high cholesterol, and prior myocardial infarction. There was no evidence of multicollinearity based on a conservative variance inflation factor threshold of <2. For ease of interpretation and to allow comparison of magnitude of effects across CMR measures, we report standardized beta-coefficients with corresponding 95% confidence intervals and P-values. Thus, results are standard deviation change in FI/RT per 1 SD increase in CMR measure. P-values are adjusted by Benjamin Hochberg method, where all CMR-related P-values across the set of models are adjusted together, setting a conservative false discovery rate of <5%.24 We performed sex-stratified analyses and tested for interaction effects by age and sex. All models were assessed for potential non-linearity using squared and cubic polynomial terms.

Ascertainment of covariates

We used age at the imaging visit. Sex was taken as recorded at baseline. Educational level, smoking status (current vs. never/previous), and alcohol intake (intake frequency) were based on self-report. Material deprivation is reported as the Townsend index, a measure of material deprivation relative to national averages.25 A continuous value for the amount of physical activity measured in metabolic equivalent (MET) minutes/week was calculated by weighting different types of activity (walking, moderate, or vigorous) by its energy requirements using values derived from the International Physical Activity Questionnaire study.26 Diabetes was coded based on self-report of the diagnosis, self-reported use of ‘medication for diabetes’, or serum glycated haemoglobin >48 mmol/mol. Hypertension was coded based on self-report of the diagnosis or self-reported use of ‘medication for high blood pressure’. High cholesterol was coded based on self-report of the diagnosis, self-reported use of ‘medication for high cholesterol’, or serum total cholesterol >7 mmol/L. Prior myocardial infarction was ascertained from UK Biobank algorithmically defined outcome data.27

Results

Baseline population characteristics

There were 32 107 participants with CMR measures and without dementia, of these, FI and RT were available for 29 243 and 29 683 participants, respectively. Overall, there were 29 763 participants with CMR data and at least one cognitive function measure (Figure 1). The analysis sample comprised 14 379 men and 15 384 women. Mean age was 63.0 (±7.5) years. Rates of diabetes, hypertension, high cholesterol, and smoking were 3.0%, 13.5%, 22.3%, and 6.2%, respectively, with greater burden in men (Table 1). Overall, the analysis sample was healthier and more affluent than UK national averages. Average FI and RT were 6.7 (±2.1) items and 573 (518, 644) ms, respectively, as measured at the imaging visit.

Association of CMR indices with FI

In fully adjusted models, higher FI (better cognition) was associated with larger LV volumes in end-diastole and end-systole, higher LV stroke volume, and greater LV mass (Table 2 and Figure 2). The association with LV ejection fraction was not statistically significant. Higher FI was associated with greater aortic distensibility (Table 2 and Figure 2). Higher FI was also associated with larger RV volumes in end-diastole and end-systole, and with larger RV stroke volumes (Supplementary data online, Table S2). All associations were consistent for both men and women (Table 2 and Supplementary data online, Table S2). There was no evidence of interaction effect with sex or age in relationships with the LV or RV measures (Supplementary data online, Table S3). There was a significant interaction effect with age for the association between FI and aortic distensibility (Supplementary data online, Table S3), with participants with higher aortic distensibility showing less rapid age-related decline in FI (Supplementary data online, Figure S1).

Association of CMR indices with RT

In fully adjusted models, lower RT (better cognition) was associated with larger LV volumes in end-diastole, higher LV stroke volume, and greater LV mass (Table 2 and Figure 3). Lower RT was also associated with greater aortic distensibility, but this relationship was not
statistically significant. Overall, associations were consistent for both men and women (Table 2). There was no evidence of interaction effect with sex or age in relationships with the LV or RV measures (Supplementary data online, Table S3).

Non-linearity of relationships

All models were screened for non-linearity with cubic and squared polynomials. For both FI and RT, in fully adjusted models, there was a trend towards attenuation of associations at the high extremes of the distribution for LV volumes and mass (very high volumes and mass). This appeared most convincing for the relationship between FI and LV end-systolic volume, where there was suggestion of attenuation and possible reversal of the direction of association at the very high extremes of the distribution (Supplementary data online, Figure S2). However, nested model testing indicated that none of the non-linear models showed a statistically significant improvement over linear model fits (Supplementary data online, Table S4).

Discussion

Summary of findings

In this predominantly healthy cohort of 15 384 women and 14 379 men from the UK Biobank, we demonstrated association of better
cognitive performance with CMR measures likely representing a healthier cardiovascular phenotype, independent of a range of lifestyle, demographic, and vascular risk factors. Specifically, better cognitive performance (higher FI and lower RT) was associated with larger LV and RV volumes, greater LV and RV stroke volumes, higher LV mass, and greater aortic distensibility. There was some evidence of non-linearity for the relationship between FI and LV end-systolic volume, with a trend towards reversal of the direction of association at the high extremes of the distribution (very high volumes), suggesting that LV volumes larger than the normal range are linked to greater aortic distensibility (statistically non-significant but suggesting a trend). Interpretation of single CMR metrics in isolation, outside the context of the other metrics, may be misleading.

**Interpretation of cardiovascular phenotypes**

Although there was no prerequisite for healthy status for recruitment into UK Biobank, there is a significant healthy participant effect, as such, our results reflect trends within a spectrum of normality. This means that in this analysis, for the most part, we do not report transitions from health to ‘disease’, but rather trends within a predominantly healthy sample. It is also essential that interpretation of the nature of cardiac phenotypes considers the overall pattern of associations as interpretation of single CMR metrics in isolation, outside the context of the other metrics, may be misleading.

Our findings demonstrate association of better cognitive performance with larger ventricular cavity volumes, larger LV and RV stroke volumes, and higher LV mass. This pattern of associations is indicative of better right and left ventricular contractile function (higher stroke volumes) and a pattern of ventricular remodelling, interpreted within the spectrum of normality, akin to decelerated heart ageing (reverse of alterations seen in healthy ageing). There was some evidence of reversal of the direction of associations between FI and LV end-systolic volume at the high extremes of the distribution (very high volumes), suggesting that LV volumes larger than the normal range are linked with poorer cognition. However, within our analysis sample, the non-linear models did not show a statistically significant improvement over linear model fits. This may be because there were few participants with extreme values in our sample. Better cognitive performance was also linked to greater aortic distensibility (statistically significant using a false discovery rate of 5%).

### Table 2  Multivariable linear regression models representing standard deviation change in fluid intelligence and reaction time per one standard deviation increase in CMR measures

|                          | Whole cohort | Men | Women |
|--------------------------|--------------|-----|-------|
| **LVEDVi (mL/m²)**       |              |     |       |
| FI                       | 0.043 a     | 0.046 a | 0.040 a |
|                         | (0.031, 0.056) | (0.030, 0.062) | (0.020, 0.060) |
|                         | 1.45 × 10⁻⁵ | 3.06 × 10⁻⁵ | 9.31 × 10⁻⁵ |
| RT                      | -0.028 a    | -0.031 a | -0.024 a |
|                         | (-0.040, -0.015) | (-0.047, -0.015) | (-0.044, -0.004) |
|                         | 1.24 × 10⁻⁵ | 1.64 × 10⁻⁴ | 0.018 |
| **LVESVi (mL/m²)**       |              |     |       |
| FI                       | 0.040 a     | 0.044 a | 0.035 a |
|                         | (0.028, 0.053) | (0.028, 0.059) | (0.014, 0.055) |
|                         | 2.76 × 10⁻¹⁰ | 6.28 × 10⁻⁸ | 0.001 |
| RT                      | -0.019 a    | -0.020 a | -0.017 a |
|                         | (-0.031, -0.006) | (-0.036, -0.005) | (-0.038, 0.004) |
|                         | 0.003       | 0.011  | 0.104 |
| **LVEF (%)**             |              |     |       |
| FI                       | -0.018 a    | -0.026 a | -0.009 a |
|                         | (-0.030, -0.006) | (-0.043, -0.010) | (-0.026, 0.008) |
|                         | 0.003       | 0.002  | 0.303 |
| RT                      | 0.002       | 0.002  | 0.002 |
|                         | (-0.010, 0.014) | (-0.014, 0.018) | (-0.015, 0.019) |
|                         | 0.725       | 0.831  | 0.792 |
| **LVSVi (mL/m²)**        |              |     |       |
| FI                       | 0.026 a     | 0.027 a | 0.026 a |
|                         | (0.015, 0.038) | (0.011, 0.043) | (0.008, 0.044) |
|                         | 1.17 × 10⁻⁵ | 7.70 × 10⁻⁴ | 0.004 |
| RT                      | -0.024 a    | -0.028 a | -0.019 a |
|                         | (-0.035, -0.012) | (-0.043, -0.012) | (-0.037, -0.001) |
|                         | 7.81 × 10⁻⁵ | 5.03 × 10⁻⁴ | 0.039 |
| **LVMi (g/m²)**          |              |     |       |
| FI                       | 0.048 a     | 0.042 a | 0.058 a |
|                         | (0.034, 0.063) | (0.023, 0.060) | (0.035, 0.081) |
|                         | 3.50 × 10⁻¹¹ | 1.09 × 10⁻⁸ | 6.87 × 10⁻⁷ |
| RT                      | -0.039 a    | -0.045 a | -0.032 a |
|                         | (-0.053, -0.025) | (-0.063, -0.027) | (-0.055, -0.010) |
|                         | 8.25 × 10⁻⁸ | 1.26 × 10⁻⁴ | 0.005 |
| **PDA AoD (× 10⁻⁶/mmHg)** |         |     |       |
| FI                       | 0.030 a     | 0.033 a | 0.032 a |
|                         | (0.014, 0.045) | (0.010, 0.057) | (0.010, 0.053) |
|                         | 2.02 × 10⁻⁴ | 0.006  | 0.003 |
| RT                      | -0.017 a    | -0.016 a | -0.015 a |
|                         | (-0.032, -0.001) | (-0.039, 0.006) | (-0.036, 0.006) |
|                         | 0.036       | 0.159  | 0.171 |

*Results are standardized beta coefficients followed by 95% confidence interval in brackets and corresponding *P*-value displayed below. Each cell represents results from an individual linear regression model. Models are adjusted for: age, sex (whole cohort only), education, deprivation, diabetes, hypertension, high cholesterol, prior myocardial infarction, smoking, alcohol, and exercise. PDA AoD has been scaled to remove skew.*
Figure 2  Univariate linear regression models of the association between fluid intelligence and CMR measures. Each graph displays a kernel density plot of one CMR variable against one cognition variable. The nine coloured rings each represent a decile of the data, while the remaining 10% lies in the uncoloured area. Univariate linear regression is shown by black line. All plot areas are trimmed at the 1st and 99th percentile in both x and y directions. Fluid intelligence has had uniform random jitter/noise (-0.5, 0.5) added for visual smoothing. CMR, cardiovascular magnetic resonance; i, indexation to body surface area; LVEDVi, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume; LVSVi, left ventricular stroke volume; PDA AoD, Aortic distensibility at the proximal descending aorta.

Figure 3  Univariate linear regression models of the association between reaction time and CMR measures. Each graph displays a kernel density plot of one CMR variable against one cognition variable. The nine coloured rings each represent a decile of the data, while the remaining 10% lies in the uncoloured area. Univariate linear regression is shown by black line. All plot areas are trimmed at the 1st and 99th percentile in both x and y directions. CMR, cardiovascular magnetic resonance; i, indexation to body surface area; LVEDVi, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume; LVSVi, left ventricular stroke volume; PDA AoD, Aortic distensibility at the proximal descending aorta.
significant for FI). Aortic distensibility is a measure of local aortic compliance and a maker of aortic bioelastic function, with higher distensibility values indicating better vascular health. Conversely, poorer cognitive function was associated with smaller ventricular volumes and lower LV mass, together with smaller LV and RV stroke volumes, and lower aortic compliance. Overall, this presents a picture of a cardiac phenotype with poorer myocardial function, small, perhaps stiff, ventricles, and higher aortic stiffness. This suggests that poorer cognition is associated with adverse cardiovascular phenotypes, perhaps resembling a heart failure preserved ejection fraction (HFpEF) phenotype.

**Comparison with existing literature**

Existing evidence is limited to small cohorts of select populations with highly variable study designs. Several studies report poorer cognitive function indices in small heart failure cohorts. Zuccalà et al. report an independent association between poorer LV function on echocardiography and worse performance in a number of cognitive tests (mini mental state examination, Raven score) in 57 patients with heart failure. In a study of structural brain abnormalities in heart failure patients, Vogels et al. report greater peryventricular and white matter hyperintensities, lacunar and cortical infarcts, and global and medial temporal lobe atrophy in 58 patients with heart failure compared with controls. Similarly, studies in dementia cohorts demonstrate links with adverse cardiovascular phenotypes. Oh et al. describe a correlation between greater left atrial enlargement on echocardiography (an early indicator of raised filling pressures and diastolic dysfunction) and adverse white matter changes on brain magnetic resonance imaging in 93 patients with dementia. Two other cohort studies demonstrate greater prevalence of diastolic dysfunction (assessed by echocardiography) in individuals with Alzheimer’s disease compared with controls. Limited studies have examined associations with other cardiovascular phenotypes. In a cohort of 303 participants, Manolio et al. report association of greater cerebral atrophy on brain MRI with greater internal carotid artery thickness on ultrasound (a marker of atherosclerosis risk).

Whilst direct comparisons with our study are not possible, in general, existing work supports associations between adverse cardiovascular phenotypes and poorer cognitive function metrics. In particular, there is evidence to support association of poorer cognitive function indices with heart failure, which is perhaps more pronounced in those with diastolic heart failure. This is consistent with our findings demonstrating association of poorer cognitive function with smaller LV/RV cavities and lower LV/RV stroke volumes. Overall, this pattern of associations is suggestive of an adverse remodelling phenotype most in keeping with an HFpEF pattern of dysfunction, in which diastolic impairment is a prominent feature.

**Potential underlying mechanisms**

Numerous studies highlight links between individual cardiovascular risk factors (diabetes, high cholesterol, smoking, hypertension, and obesity) and worse cognitive performance. Furthermore, association of cardiovascular risk factors and subclinical cardiovascular disease with worse cognition and dementia has been demonstrated in multiple large epidemiological studies. More specific associations between cardiac risk factors and both vascular and Alzheimer’s disease have also been demonstrated in large cohorts. The systemic atherosclerotic arterial disease that occurs as a consequence of these vascular risk factors may have direct adverse impact on both cardiovascular and brain health through local hypoperfusion and systemic embolic phenomena (Figure 4).

Associations between cognitive function and cardiovascular phenotypes in the present study were not attenuated by adjustment for a wide range of vascular risk factors. This raises the possibility of alternative disease mechanisms contributing to heart–brain associations. For instance, limited studies propose that Aβ deposition, which is hallmark of Alzheimer’s disease, may also be pathologica deposited in the myocardium producing electrographic and echocardiographic manifestations typical of cardiac amyloid. Cardiac amyloid is characteristically associated with an HFpEF pattern of dysfunction. This is consistent with the cardiac phenotype most consistently linked with cognitive impairment and in keeping also with observations in the present study. However, these phenotypes are not specific to cardiac amyloid and may be seen with a wide range of other exposures.

Another possibility is that poorer brain and cardiovascular health may both be a consequence of accelerated multisystem ageing. For instance, persistently elevated inflammatory cytokines, which is a proposed driver of accelerated ageing, has been linked to both cardiovascular disease and Alzheimer’s disease. Regardless of the underlying cause, it seems likely that these pathways initiate a positive feedback cycle of adverse heart–brain interactions with cardiac dysfunction resulting in chronic systemic hypoperfusion, disruptions to cerebral perfusion, and further exacerbation of brain injuries (Figure 4).

Whatever the underlying mechanisms, our findings suggest links between cardiovascular and cognitive health which might, with further investigation and validation, underpin novel clinical approaches to risk assessment for associated outcomes such as myocardial infarction and dementia.

**Strengths and limitations**

In this study, we made use of the large and standardized UK Biobank dataset to describe novel associations between cognitive function and CMR phenotypes. The extensive algorithm-coded morbidity, demographic, and lifestyle data available permitted adjustment for a wide range of covariates. However, inherent to the observational cross-sectional study design, the possibility of residual confounding cannot be excluded, and it is not possible to establish a strict causal relationship from the results. Further, the large sample size in this study may reveal statistically but not clinically relevant associations. With this in mind, we have taken a strict hypothesis-based approach to the analysis, applied conservative correction of P-value thresholds, and consider biological (rather than clinical) interpretation of the findings. Common to all research in the field of cognitive performance and dementia, the questionnaires and scoring systems used to quantify cognitive performance may not accurately reflect global cognitive ability and may be subject to bias depending on underlying educational status and other factors. In addition, there is, as is expected with such cohorts, evidence of healthy selection in UK Biobank, thus the associations observed in this study describe, predominantly, relationships within the limits of healthy populations. Therefore, the pattern of associations observed may not be directly applicable to disease cohorts. Another limitation of our work is that despite considering the potential confounding effect of an extensive range of...
exposure variables, we do not identify the underlying mechanism for the observed associations. In a separate analysis, addition of body mass index as covariate to fully adjusted models also did not alter observed associations. Future work dedicated to exploring underlying mechanisms is needed to better understand the links between brain and heart health.

Conclusions

In this cohort of 29,763 UK Biobank participants, better cognitive performance was associated with CMR and aortic distensibility measures likely representing a healthier cardiovascular phenotype. The associations were in general consistent between men and women and remained robust after adjustment for a range of lifestyle, demographic, and vascular risk factors, implying potential importance of alternative underlying mechanism. These findings thus support links between cardiovascular and cognitive health, inform understanding of associated mechanisms, and suggest a rationale for a cross-system approach to risk assessment for associated disease outcomes.

Supplementary data

Supplementary data are available at European Heart Journal - Cardiovascular Imaging online.

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Figure 4 Potential underlying mechanism of heart–brain associations. Figure created with BioRender.com.
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Conflict of interest: none declared.

Data availability statement

This research was conducted using the UKB resource under access application 2964. UK Biobank will make the data available to all bona fide researchers for all types of health-related research that is in the public interest, without preferential or exclusive access for any persons. All researchers will be subject to the same application process and approval criteria as specified by UK Biobank. For more details on the access procedure, see the UK Biobank website: http://www.ukbiobank.ac.uk/register-apply/.

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