

Accelerated Ageing in Depression: A Study of Two Cohorts

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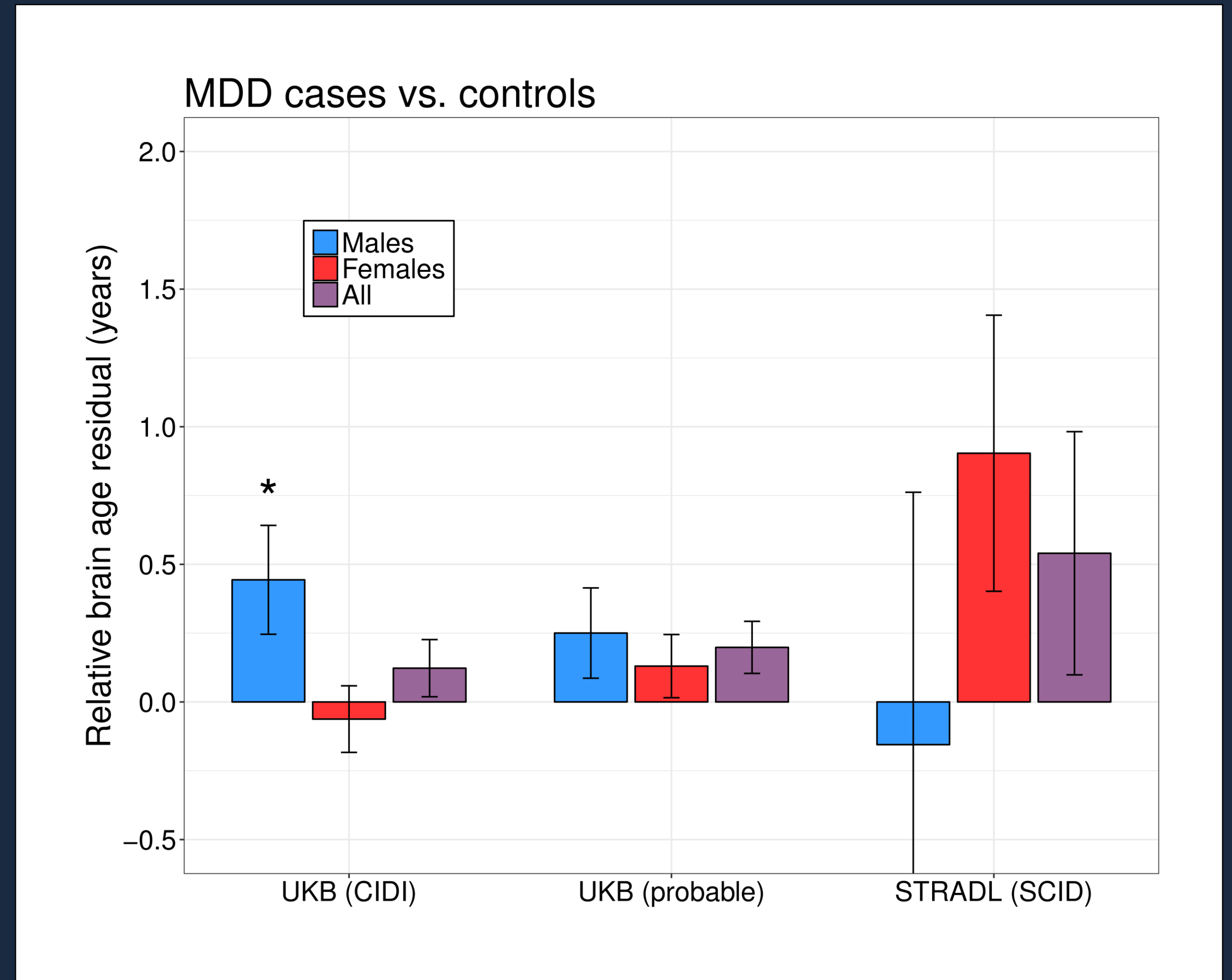
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Depressed individuals had slightly older-appearing brains than controls

Medication was associated with greater brain ageing acceleration



INTRODUCTION

- Major depressive disorder (MDD) is a severe psychiatric disorder associated with shortened lifespan and comorbidities of advancing age
- Accelerated biological ageing may underlie these associations
- Machine learning (ML) can be used to predict age from brain structure
- Greater brain-predicted age than chronological age represents accelerated brain ageing and poorer brain health

METHODS

1. UKB (CIDI-assessed): 3,837 cases, 8,807 controls (53.5% F; age M=63.2)
2. UKB (probable MDD): 4,957 cases, 6,073 controls (52.5% F; age M=62.7)
3. STRADL (SCID-assessed): 249 cases, 582 controls (57.2% F; age M=59.8)
4. brainageR (www.github.com/james-cole/brainager) to predict brain age
5. Assessed males & females both separately and together
6. GLM to test effects of MDD on brain age residual (predicted brain age corrected for chronological age, sex & imaging covariates)
7. Further analyses to stratify history of MDD by current symptoms and use of psychotropic medications

RESULTS

- **MDD history** Slightly higher brain age among MDD cases:
 - Largest difference of 0.90 yrs for STRADL females (n.s.)
 - Nominal difference of 0.44 yrs for UKB (CIDI) males (p=.046)
- **Current MDD** Some effects slightly stronger:
 - Difference of 0.72 yrs for UKB (probable) males (p=.029)
- **Medication** Stronger effects for MDD cases on psychotropic medications:
 - Difference of 2.74 yrs for STRADL females (p=.017)
 - Significant differences of 0.69-1.34 yrs for five UKB groups (q<.05)

DISCUSSION

- MDD has a small acceleration effect on brain ageing
- Greater brain age acceleration effects among medicated MDD cases
- Does medication accelerate brain ageing or just identify those with more severe MDD? Longitudinal follow-up required

UKB

Subset of UK Biobank imaging participants

STRADL

Stratifying Resilience and Depression Longitudinally sample

CIDI

Comprehensive International Diagnostic Interview (short form)

Probable

MDD status derived from multiple questionnaire items

SCID

Structured Clinical Interview for DSM-IV

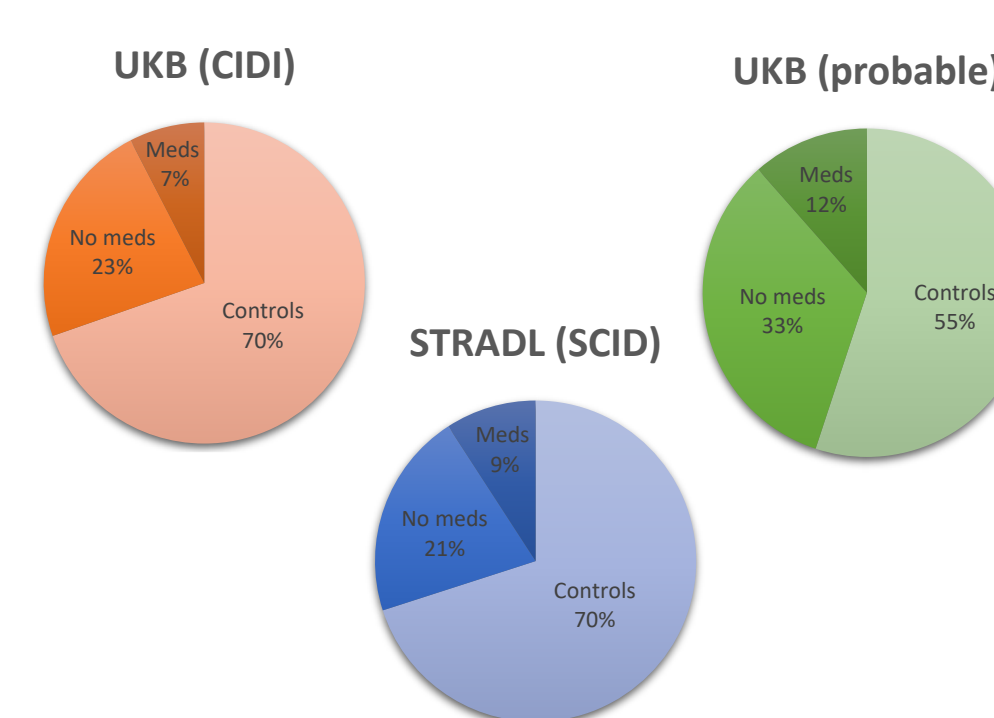
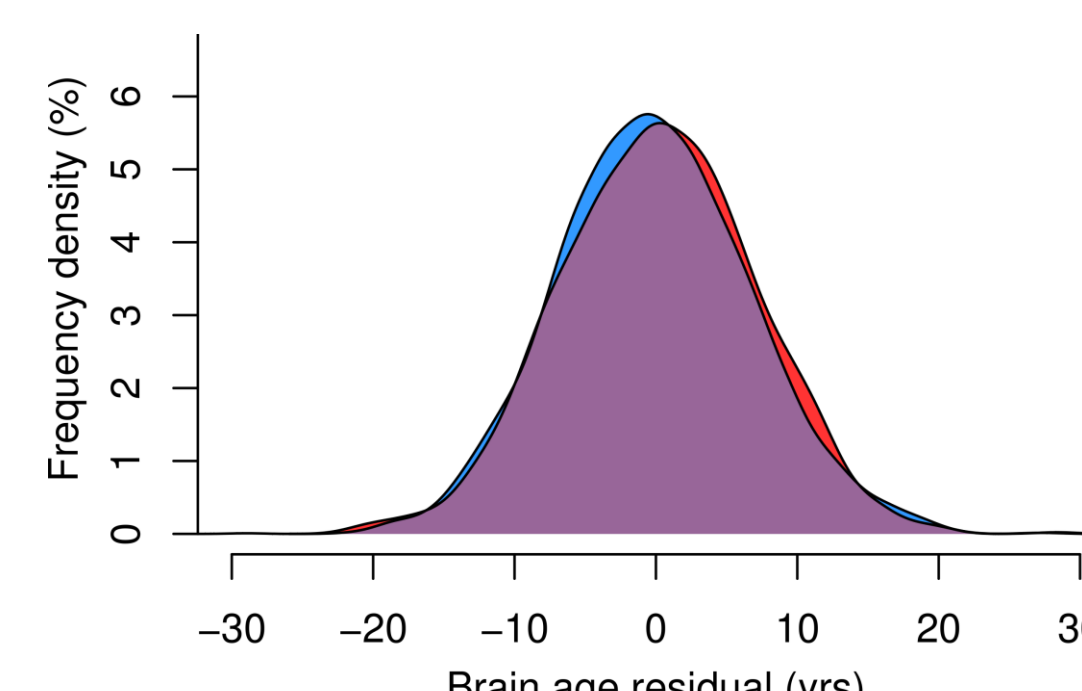


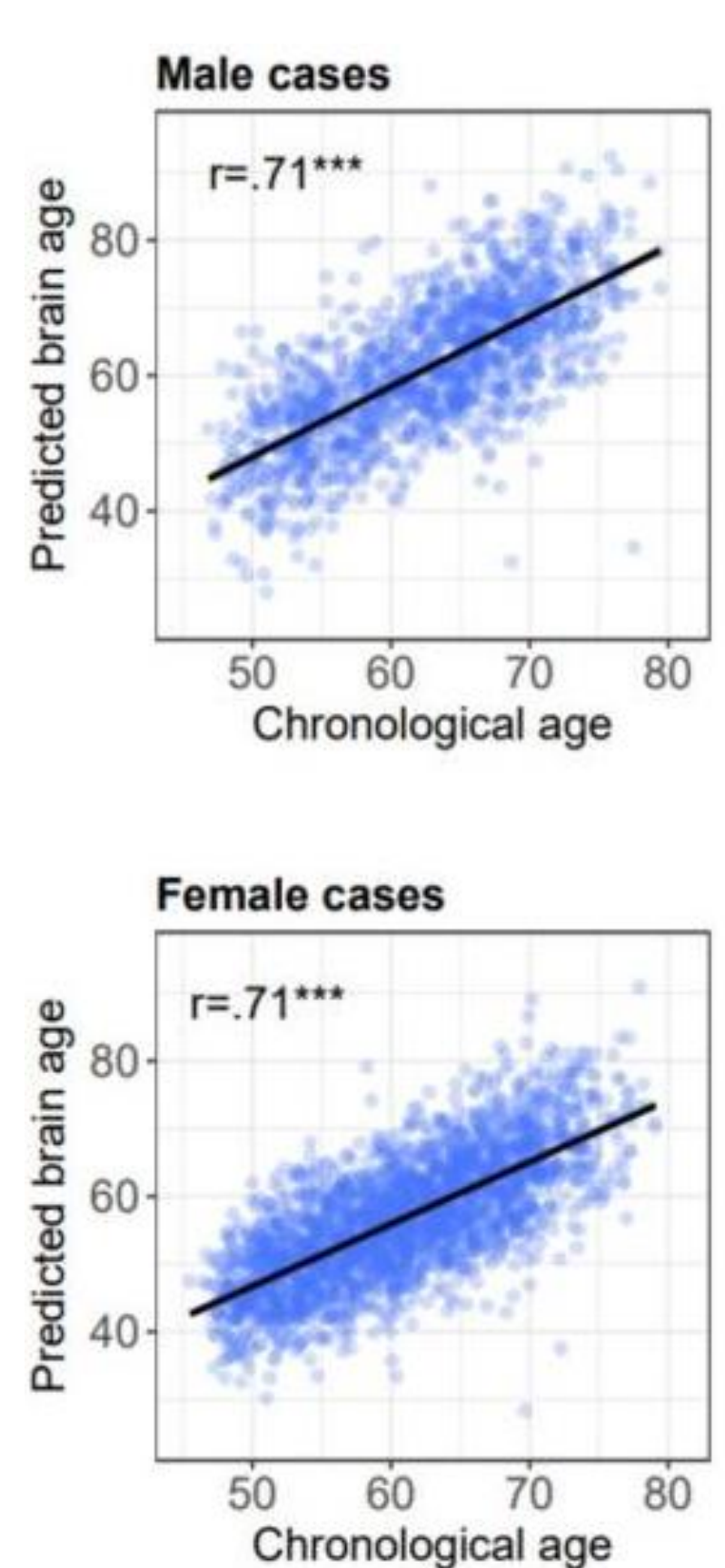
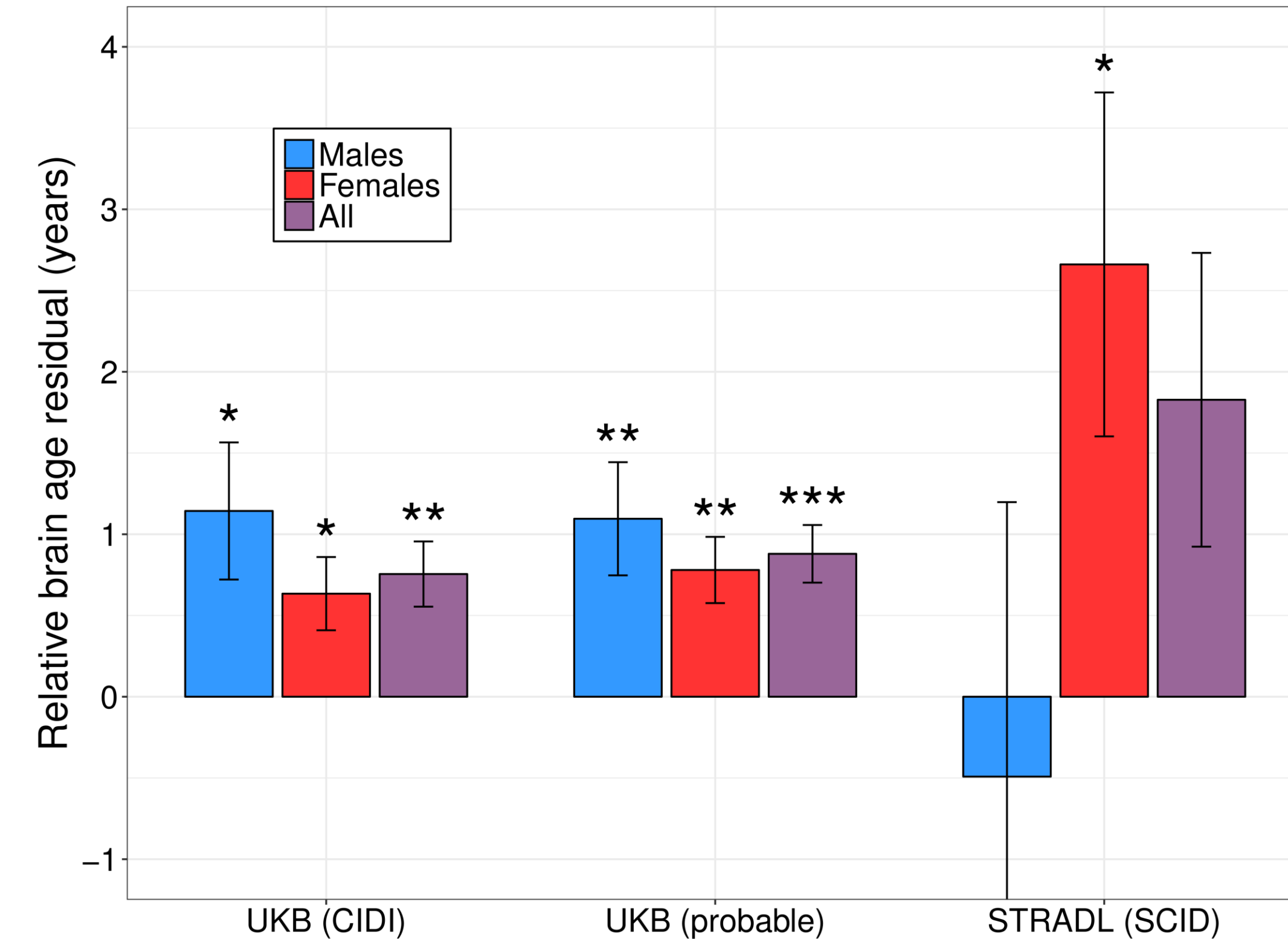
Table: MDD case-control residualised brain age differences by group

Data set	Group	Control mean	Case mean	Difference	Effect (β)
UKB (CIDI)	Males	-0.174	0.270	0.444	.025*
	Females	-0.067	-0.130	-0.062	-.005
	All	-0.124	-0.000	0.123	.008
UKB (probable)	Males	-0.177	0.073	0.250	.016
	Females	-0.046	0.084	0.130	.013
	All	-0.118	0.080	0.198	.014
STRADL (SCID)	Males	-0.001	-0.157	-0.155	-.009
	Females	-0.336	0.567	0.904	.088
	All	-0.171	0.370	0.540	.056

Table: MDD case-control differences stratified by medication use

Data set	Group	Diff (meds)	β (meds)	Diff (no meds)	β (no meds)
UKB (CIDI)	Males	1.342	.043**	0.199	.009
	Females	0.403	.024	-0.232	-.018
	All	0.689	.030**	-0.066	-.005
UKB (probable)	Males	1.117	.049**	0.022	.000
	Females	0.688	.047**	-0.092	-.006
	All	0.853	.047***	-0.027	-.003
STRADL (SCID)	Males	-0.502	-.008	-0.011	.016
	Females	2.741	.164**	0.081	.020
	All	1.810	.100*	-0.018	.017

Medicated vs. unmedicated



ACKNOWLEDGEMENTS

UK Biobank and STRADL participants
Wellcome Trust Strategic Award
UK Medical Research Council and BBSRC
Dr Mortimer and Theresa Sackler Foundation
Royal College of Physicians of Edinburgh

