

Supplementary Information (SI) for

Associations Between Alcohol Consumption and Gray and White Matter Volumes in the UK Biobank

Table of Contents

Supplementary Tables

Supplementary Figures

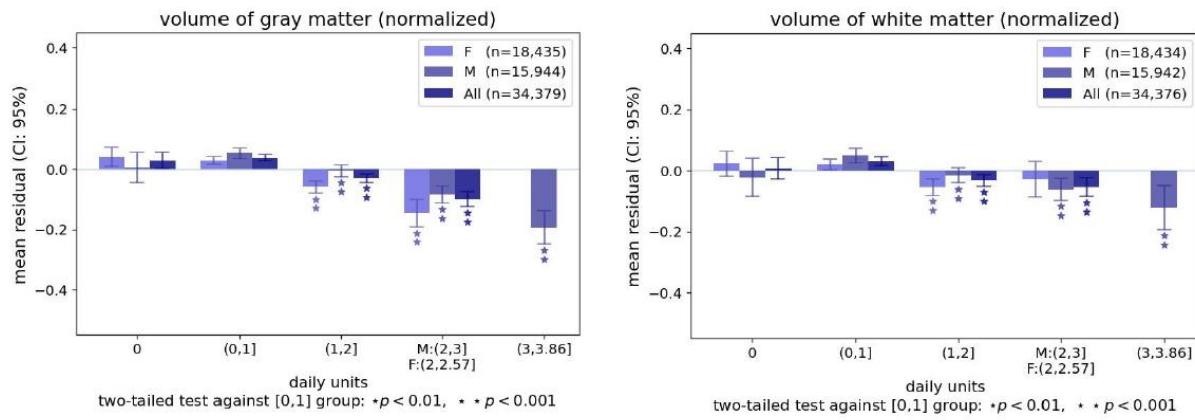
Supplementary Table 1. Regression Results: Volume of Gray Matter (whole brain, normalized)
log intake is measured in standardized log(1 + daily units of alcohol).

Standard Control Variables		Extended Control Variables		
	N: 36,678 (df: 36,585), R ² : 0.514		N: 36,678 (df: 36,578), R ² : 0.520	
Variable	Regression Coefficient (SE), 95% CI	t-stat (p-value)	Regression Coefficient (SE), 95% CI	t-stat (p-value)
log intake	-0.1095 (0.0058), CI: [-0.1209,-0.0982]	-19.0 (p < 1.0e-16)	-0.1125 (0.0057), CI: [-0.1238,-0.1013]	-19.6 (p < 1.0e-16)
log intake ²	-0.0651 (0.0037), CI: [-0.0723,-0.0579]	-17.7 (p < 1.0e-16)	-0.0596 (0.0037), CI: [-0.0668,-0.0524]	-16.2 (p < 1.0e-16)
log intake x male	0.0174 (0.0080), CI: [0.0018,0.0330]	2.2 (p = 2.9e-02)	0.0224 (0.0079), CI: [0.0068,0.0379]	2.8 (p = 4.8e-03)
log intake x std. age	0.0080 (0.0037), CI: [0.0008,0.0152]	2.2 (p = 3.0e-02)	0.0080 (0.0037), CI: [0.0008,0.0151]	2.2 (p = 3.0e-02)
standardized age	-0.5991 (0.0038), CI: [-0.6066,-0.5916]	-157.0 (p < 1.0e-16)	-0.5995 (0.0038), CI: [-0.6069,-0.5921]	-158.0 (p < 1.0e-16)
standardized age ²	-0.0378 (0.0034), CI: [-0.0445,-0.0311]	-11.0 (p < 1.0e-16)	-0.0403 (0.0034), CI: [-0.0469,-0.0336]	-11.8 (p < 1.0e-16)
Against model without log intake and interactions		Against model without log intake and interactions		
Delta R ² : 0.0099		Delta R ² : 0.0099		
F-test: p < 1.0e-16		F-test: p < 1.0e-16		
Excluding Abstainers		Excluding Those that Consume a High Level of Alcohol		
N: 33,773 (df: 33,676), R ² : 0.517		N: 34,383 (df: 34,286), R ² : 0.510		
Variable	Regression Coefficient (SE), 95% CI	t-stat (p-value)	Regression Coefficient (SE), 95% CI	t-stat (p-value)
log intake	-0.1025 (0.0064), CI: [-0.1151,-0.0899]	-15.9 (p < 1.0e-16)	-0.0960 (0.0073), CI: [-0.1104,-0.0817]	-13.1 (p < 1.0e-16)
log intake ²	-0.0701 (0.0045), CI: [-0.0790,-0.0611]	-15.4 (p < 1.0e-16)	-0.0499 (0.0049), CI: [-0.0595,-0.0402]	-10.1 (p < 1.0e-16)
log intake x male	0.0114 (0.0095), CI: [-0.0072,0.0299]	1.2 (p = 2.3e-01)	0.0214 (0.0088), CI: [0.0041,0.0387]	2.4 (p = 1.5e-02)
log intake x std. age	0.0127 (0.0043), CI: [0.0042,0.0212]	2.9 (p = 3.4e-03)	0.0100 (0.0040), CI: [0.0020,0.0179]	2.5 (p = 1.4e-02)
standardized age	-0.6012 (0.0040), CI: [-0.6091,-0.5933]	-149.9 (p < 1.0e-16)	-0.5989 (0.0040), CI: [-0.6066,-0.5911]	-151.2 (p < 1.0e-16)
standardized age ²	-0.0389 (0.0036), CI: [-0.0459,-0.0319]	-11.0 (p < 1.0e-16)	-0.0388 (0.0035), CI: [-0.0457,-0.0319]	-11.0 (p < 1.0e-16)
Against model without log intake and interactions		Against model without log intake and interactions		
Delta R ² : 0.0108		Delta R ² : 0.0038		
F-test: p < 1.0e-16		F-test: p < 1.0e-16		

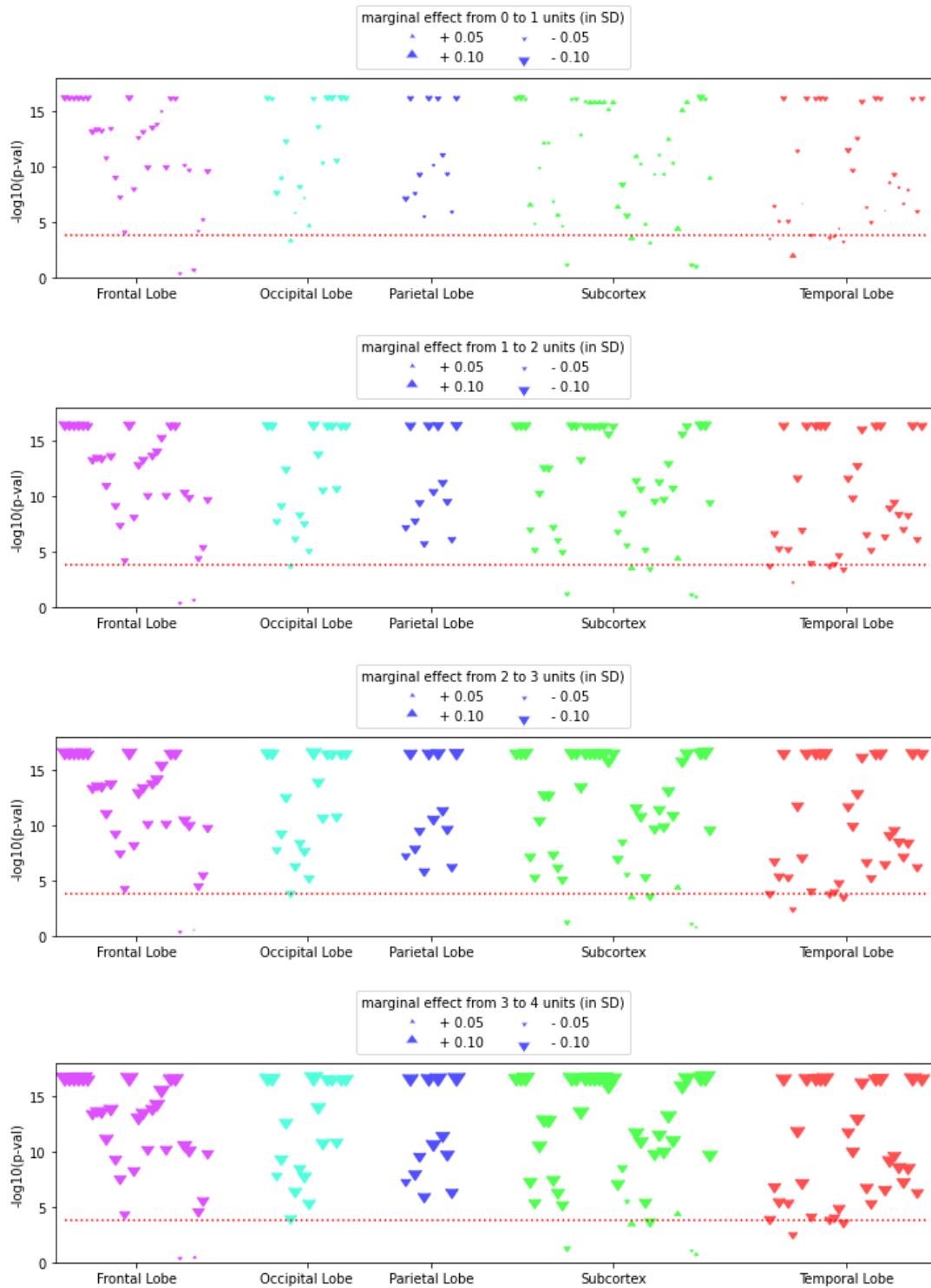
Supplementary Table 2. Regression Results: Volume of White Matter (whole brain, normalized)
log intake is measured in standardized log(1 + daily units of alcohol).

Standard Control Variables		Extended Control Variables	
	N: 36,678 (df: 36,585), R ² : 0.122		N: 36,678 (df: 36,578), R ² : 0.123
Variable	Regression Coefficient (SE), 95% CI	t-stat (p-value)	Regression Coefficient (SE), 95% CI
log intake	-0.0650 (0.0078), CI: [-0.0802,-0.0498]	-8.4 (p < 1.0e-16)	-0.0632 (0.0078), CI: [-0.0784,-0.0479]
log intake ²	-0.0370 (0.0050), CI: [-0.0468,-0.0273]	-7.5 (p = 7.8e-14)	-0.0378 (0.0050), CI: [-0.0475,-0.0280]
log intake x male	0.0164 (0.0107), CI: [-0.0046,0.0374]	1.5 (p = 1.2e-01)	0.0148 (0.0107), CI: [-0.0062,0.0358]
log intake x std. age	0.0111 (0.0050), CI: [0.0014,0.0208]	2.2 (p = 2.5e-02)	0.0110 (0.0050), CI: [0.0013,0.0207]
standardized age	-0.3213 (0.0051), CI: [-0.3313,-0.3112]	-62.6 (p < 1.0e-16)	-0.3218 (0.0051), CI: [-0.3319,-0.3118]
standardized age ²	-0.0127 (0.0046), CI: [-0.0217,-0.0037]	-2.8 (p = 5.7e-03)	-0.0126 (0.0046), CI: [-0.0216,-0.0036]
Against model without log intake and interactions		Against model without log intake and interactions	
Delta R ² : 0.0033		Delta R ² : 0.0032	
F-test: p < 1.0e-16		F-test: p < 1.0e-16	
Excluding Abstainers		Excluding Those that Consume a High Level of Alcohol	
	N: 33,773 (df: 33,676), R ² : 0.124		N: 34,383 (df: 34,286), R ² : 0.124
Variable	Regression Coefficient (SE), 95% CI	t-stat (p-value)	Regression Coefficient (SE), 95% CI
log intake	-0.0599 (0.0087), CI: [-0.0769,-0.0429]	-6.9 (p = 4.6e-12)	-0.0596 (0.0098), CI: [-0.0789,-0.0403]
log intake ²	-0.0369 (0.0061), CI: [-0.0489,-0.0249]	-6.0 (p = 1.7e-09)	-0.0327 (0.0066), CI: [-0.0456,-0.0197]
log intake x male	0.0073 (0.0127), CI: [-0.0176,0.0323]	0.6 (p = 5.7e-01)	0.0148 (0.0119), CI: [-0.0084,0.0381]
log intake x std. age	0.0187 (0.0059), CI: [0.0072,0.0301]	3.2 (p = 1.4e-03)	0.0088 (0.0054), CI: [-0.0019,0.0194]
standardized age	-0.3251 (0.0054), CI: [-0.3357,-0.3146]	-60.2 (p < 1.0e-16)	-0.3223 (0.0053), CI: [-0.3327,-0.3119]
standardized age ²	-0.0133 (0.0048), CI: [-0.0227,-0.0040]	-2.8 (p = 5.3e-03)	-0.0135 (0.0047), CI: [-0.0228,-0.0043]
Against model without log intake and interactions		Against model without log intake and interactions	
Delta R ² : 0.0036		Delta R ² : 0.0014	
F-test: p < 1.0e-16		F-test: p = 5.0e-13	

Supplementary Figure 1. Bar plots representing the average residual volume of whole-brain gray and white matter volume for individuals grouped by the number of daily alcohol units after excluding heavy drinkers and controlling for standard control variables. The mean residuals are in terms of standard deviations of the dependent variable, where zero represents the average residual in the sample. The error bars represent the 95% confidence interval. * $p<0.01$ and ** $p<.0001$ for groups showing a significant difference in pairwise two-tailed t-test (uncorrected) against the group consuming up to one alcohol unit daily. F = females, M = males.

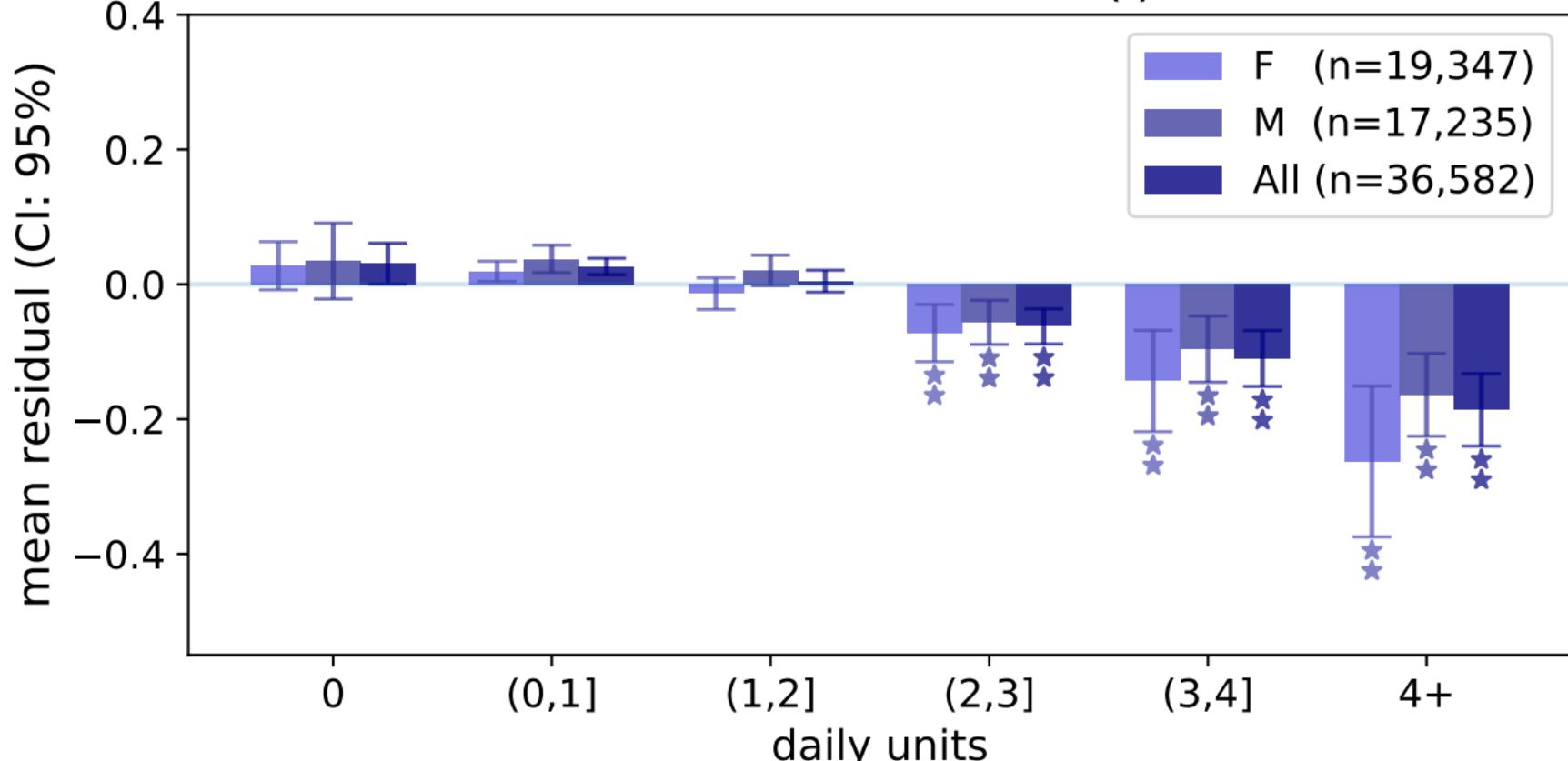


Supplementary Figure 2. Associations between alcohol intake and regional gray matter volume imaging-derived phenotypes predicted from the regression model with standard controls, arranged into brain lobes along the x-axis. For these variables, the significance of the correlation is plotted vertically in units of $-\log_{10}(p\text{-val})$. The dotted horizontal line indicates the threshold corresponding to multiple correction using the Holm method (1.64×10^{-4}).



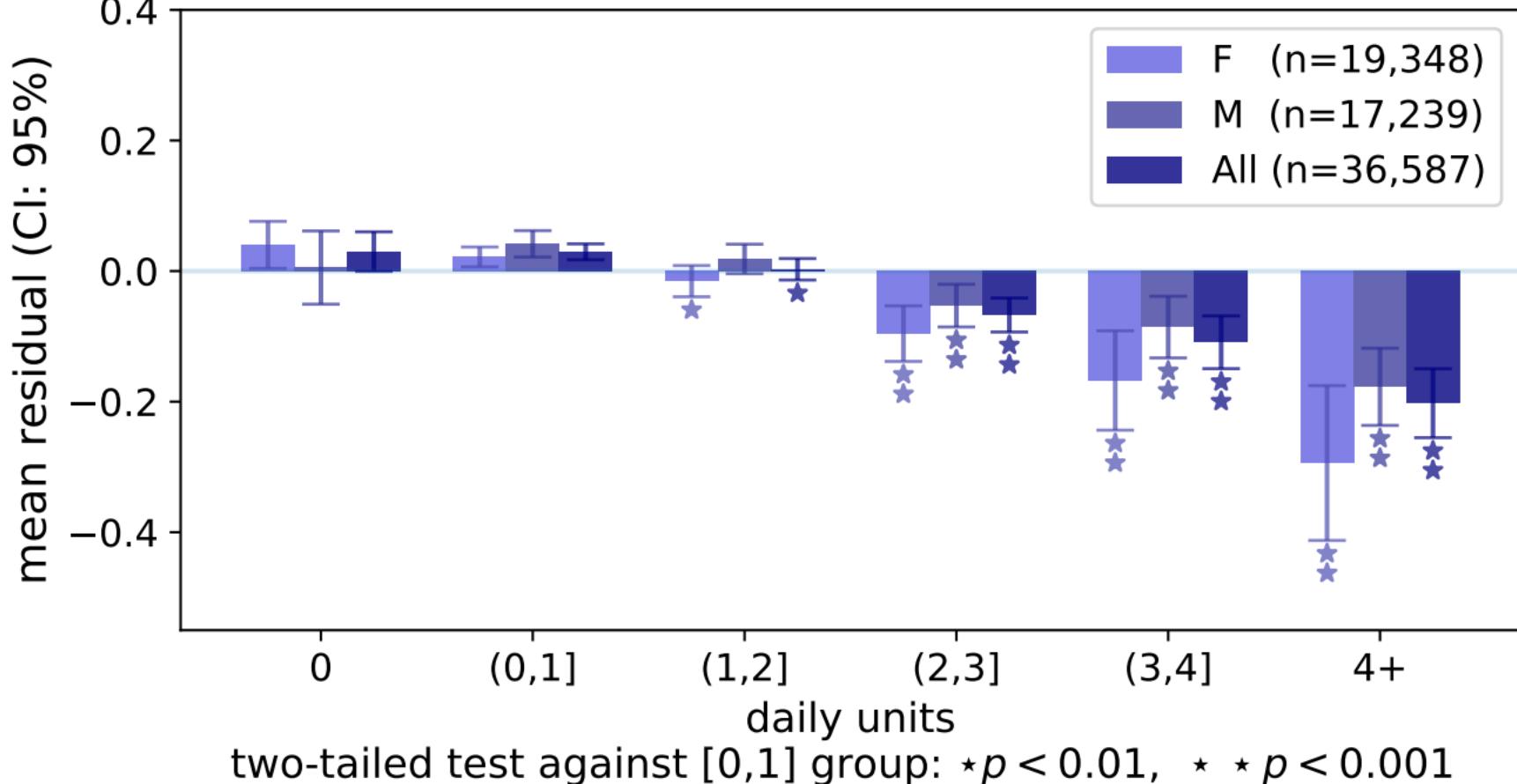
Supplementary Figure 3. Bar plots representing the average residual volume of localized gray matter volume imaging-derived phenotypes for individuals grouped by the number of daily alcohol units after excluding heavy drinkers and controlling for standard control variables. The mean residuals are in terms of standard deviations of the dependent variable, where zero represents the average residual in the sample. The error bars represent the 95% confidence interval. * $p<0.01$ and ** $p<.0001$ for groups showing a significant difference in pairwise two-tailed t-test (uncorrected) against the group consuming up to one alcohol unit daily. F = females, M = males, l = left, r = right.

volume of thalamus (I)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

volume of thalamus (r)



volume of caudate (l)

mean residual (CI: 95%)

0.4

0.2

0.0

-0.2

-0.4

F (n=19,343)
M (n=17,237)
All (n=36,580)

0

(0,1]

(1,2]

(2,3]

(3,4]

4+

daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

volume of caudate (r)

mean residual (CI: 95%)

0.4

0.2

0.0

-0.2

-0.4

F (n=19,342)
M (n=17,243)
All (n=36,585)

0

(0,1]

(1,2]

(2,3]

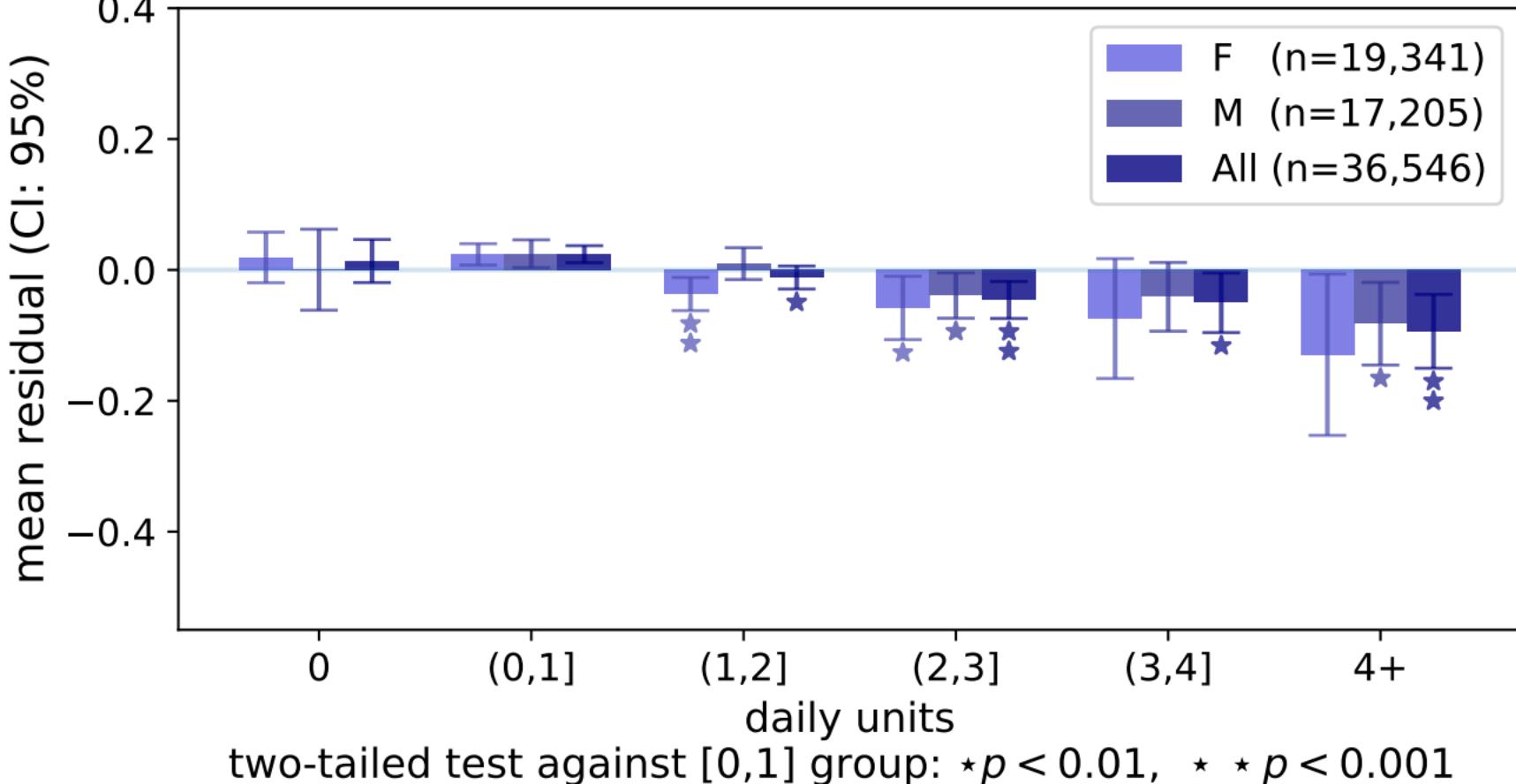
(3,4]

4+

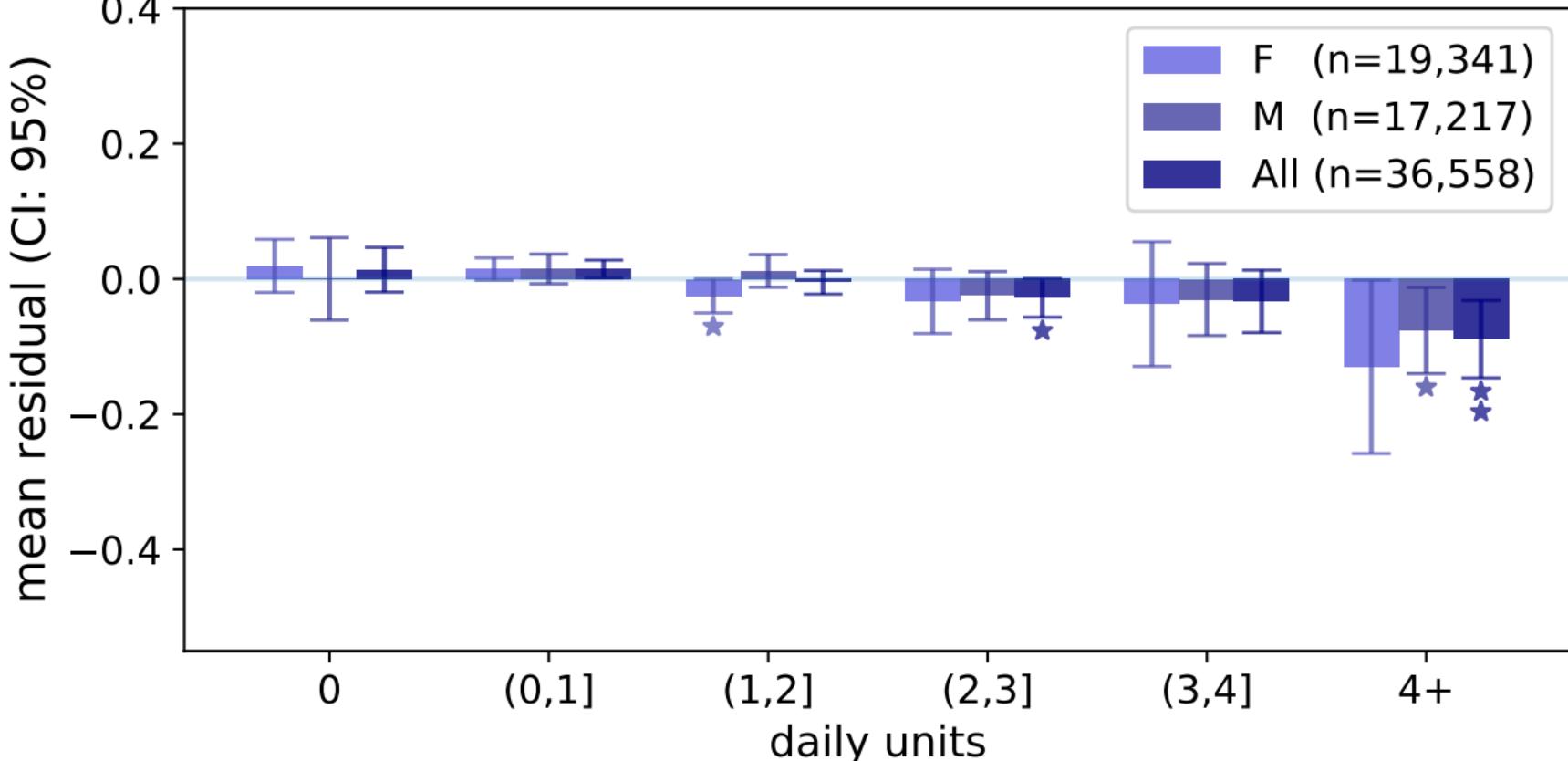
daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

volume of putamen (l)



volume of putamen (r)



volume of pallidum (l)

mean residual (CI: 95%)

0.4

0.2

-0.2

-0.4

0

(0,1]

(1,2]

(2,3]

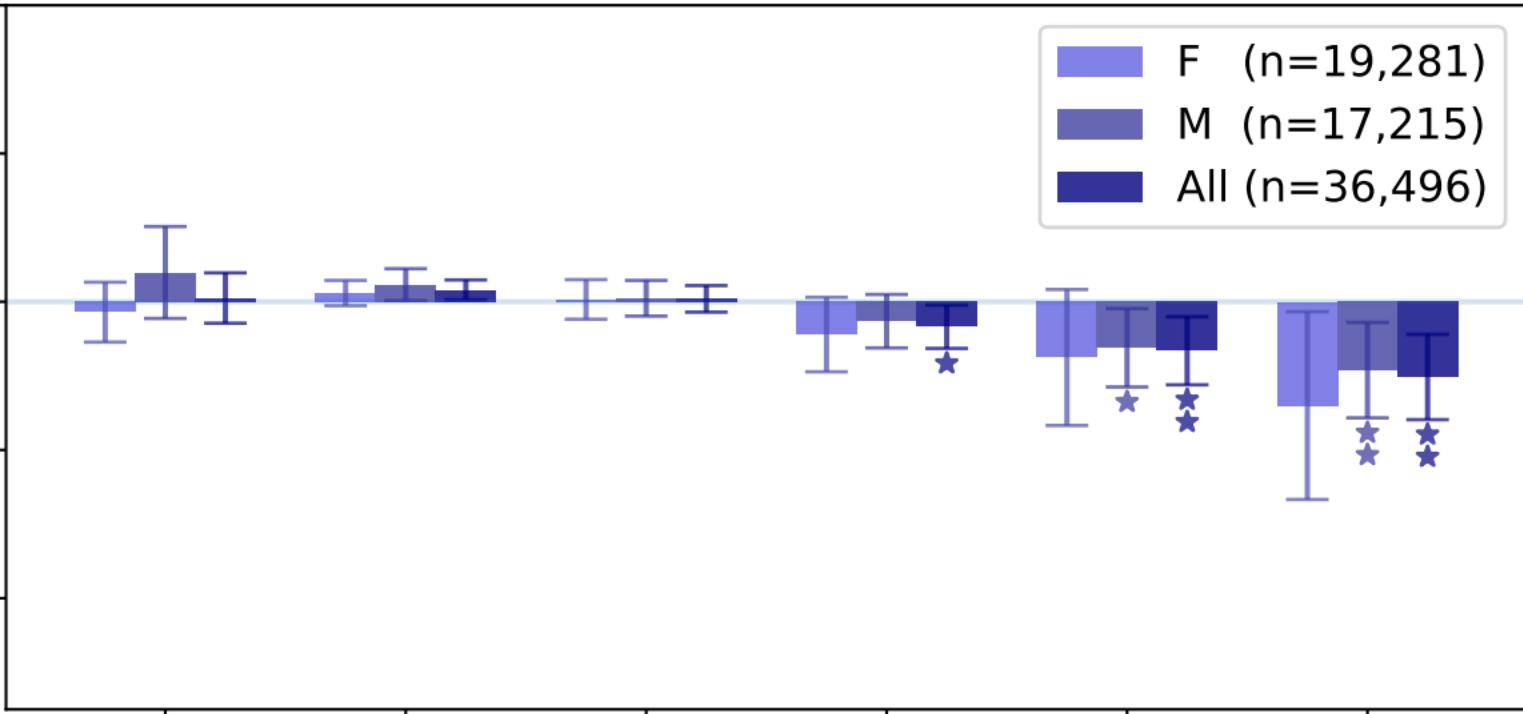
(3,4]

4+

daily units

F (n=19,281)
M (n=17,215)
All (n=36,496)

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$



volume of pallidum (r)

mean residual (CI: 95%)

0.4

0.2

0.0

-0.2

-0.4

F (n=19,288)
M (n=17,221)
All (n=36,509)

0

(0,1]

(1,2]

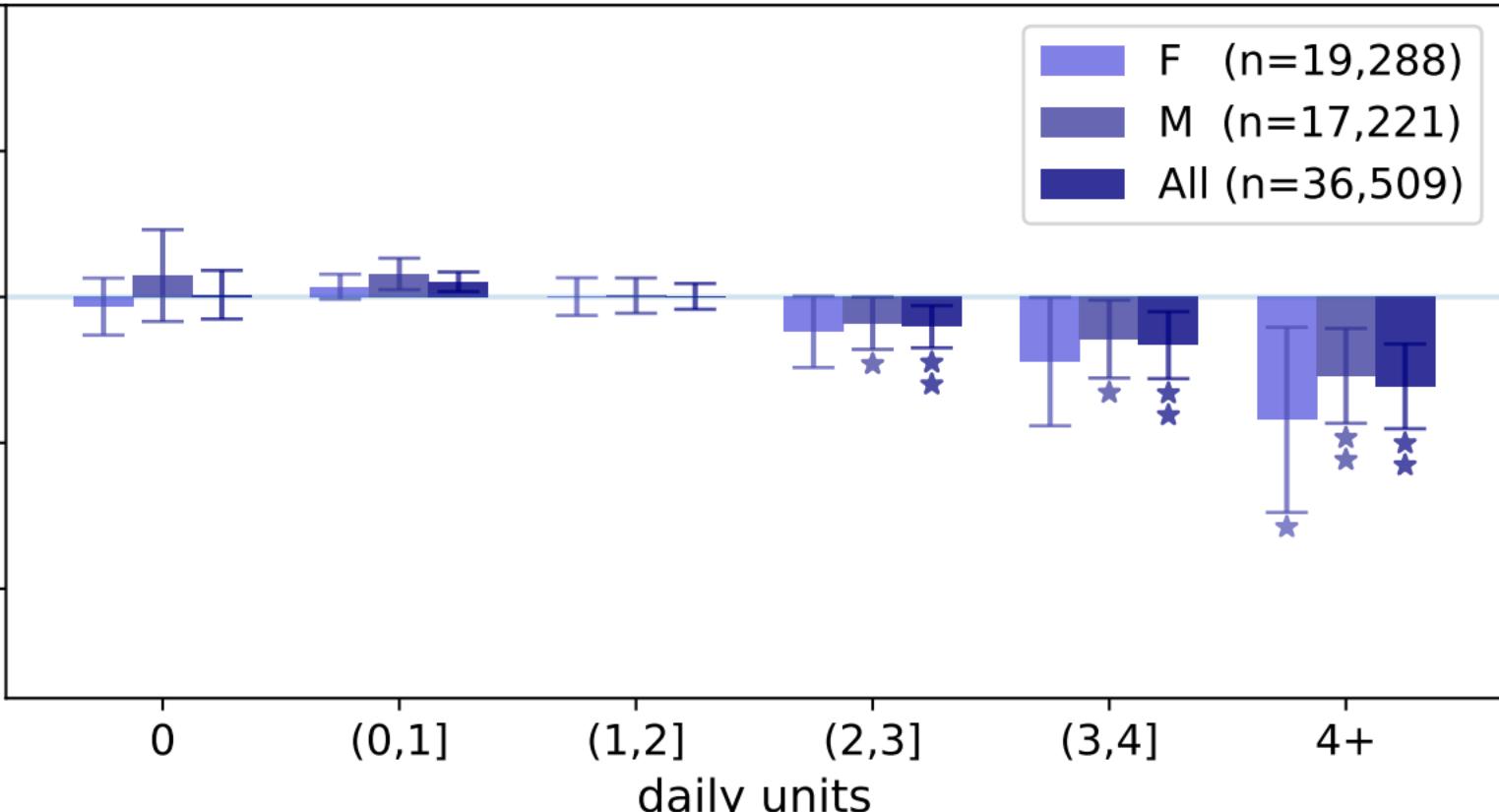
(2,3]

(3,4]

4+

daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$



volume of hippocampus (l)

mean residual (CI: 95%)

0.4

0.2

0.0

-0.2

-0.4

F (n=19,347)
M (n=17,210)
All (n=36,557)

0

(0,1]

(1,2]

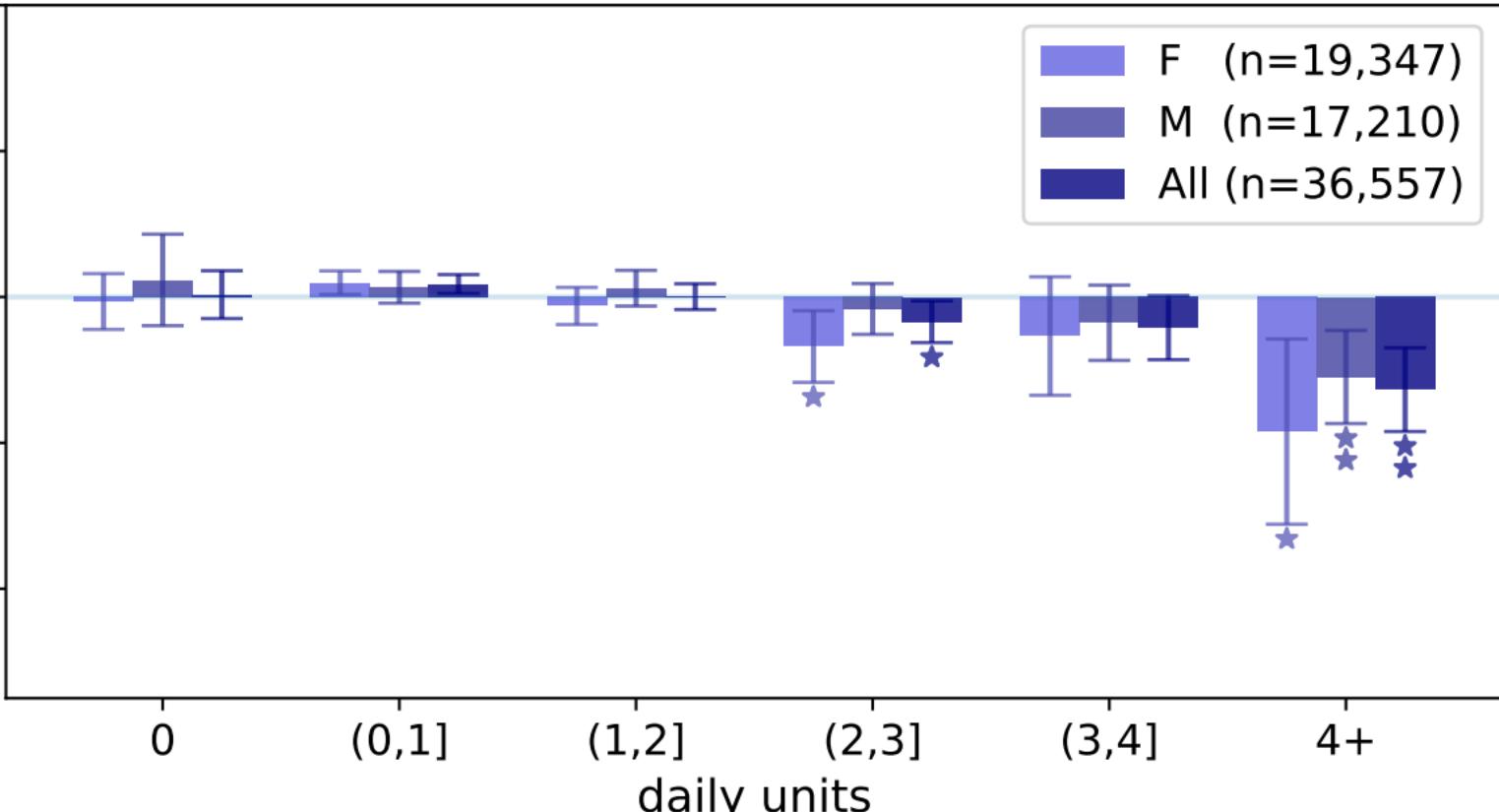
(2,3]

(3,4]

4+

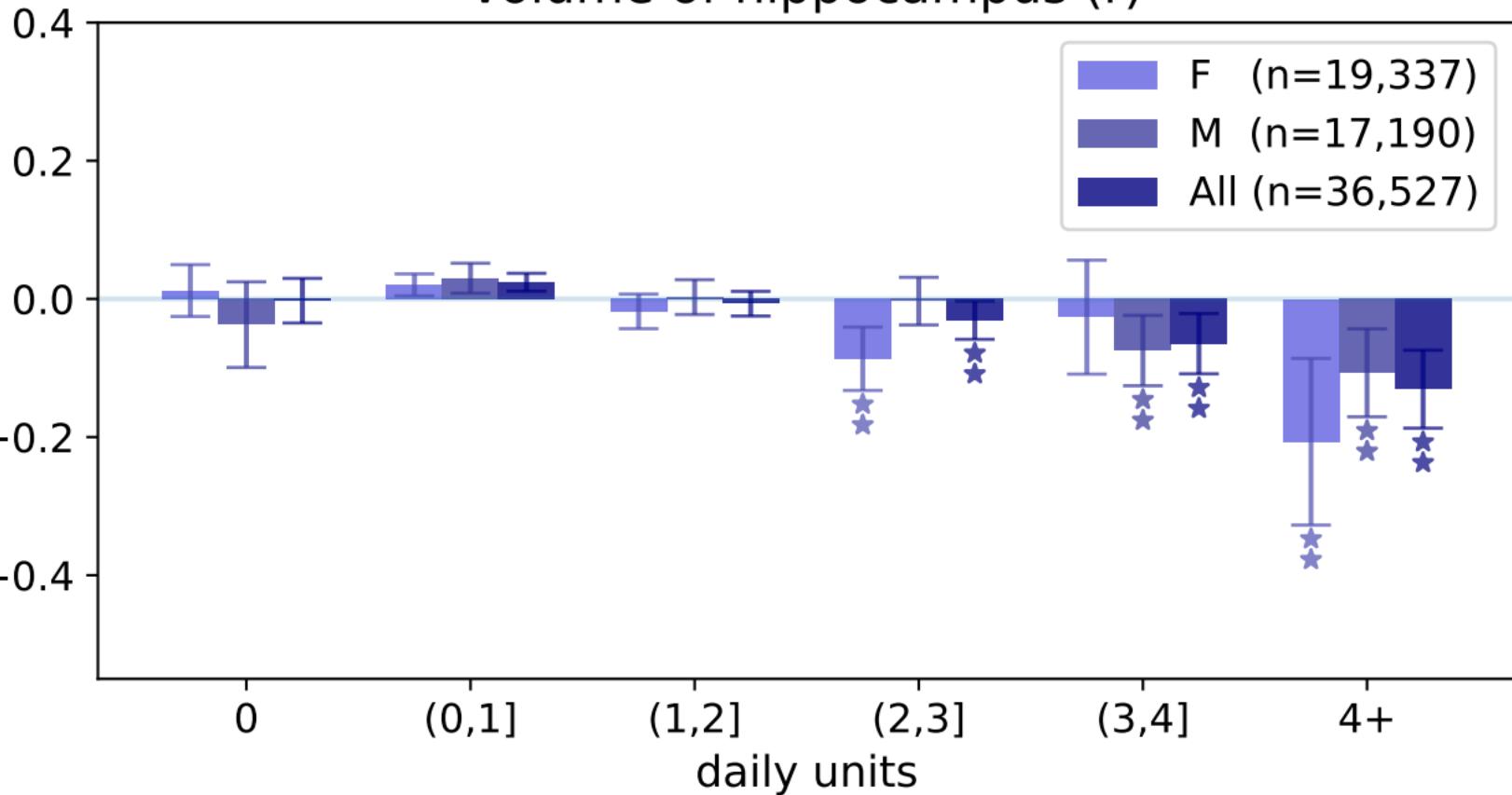
daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$



volume of hippocampus (r)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

volume of amygdala (l)

mean residual (CI: 95%)

0.4

0.2

-0.2

-0.4

0

(0,1]

(1,2]

(2,3]

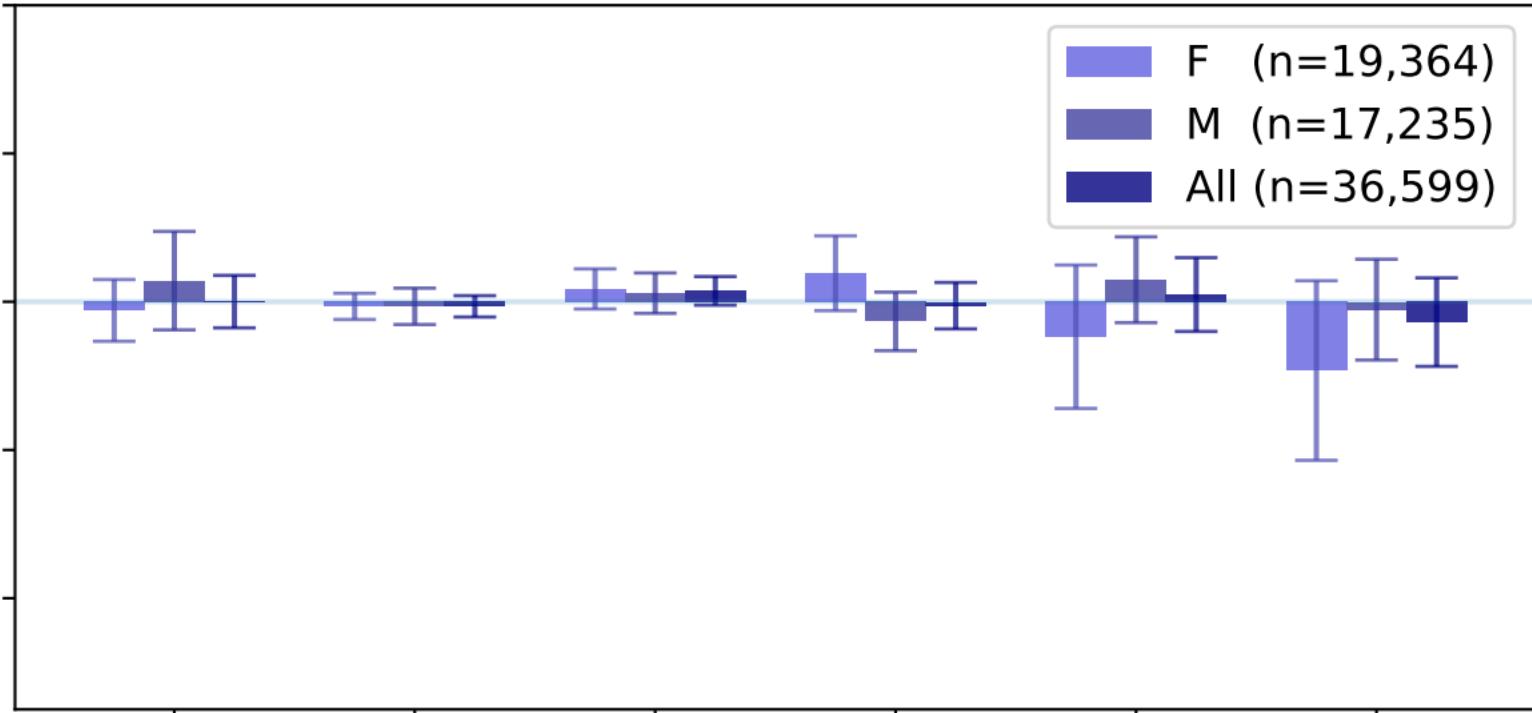
(3,4]

4+

daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

F (n=19,364)
M (n=17,235)
All (n=36,599)



volume of amygdala (r)

mean residual (CI: 95%)

0.4

0.2

-0.2

-0.4

0

(0,1]

(1,2]

(2,3]

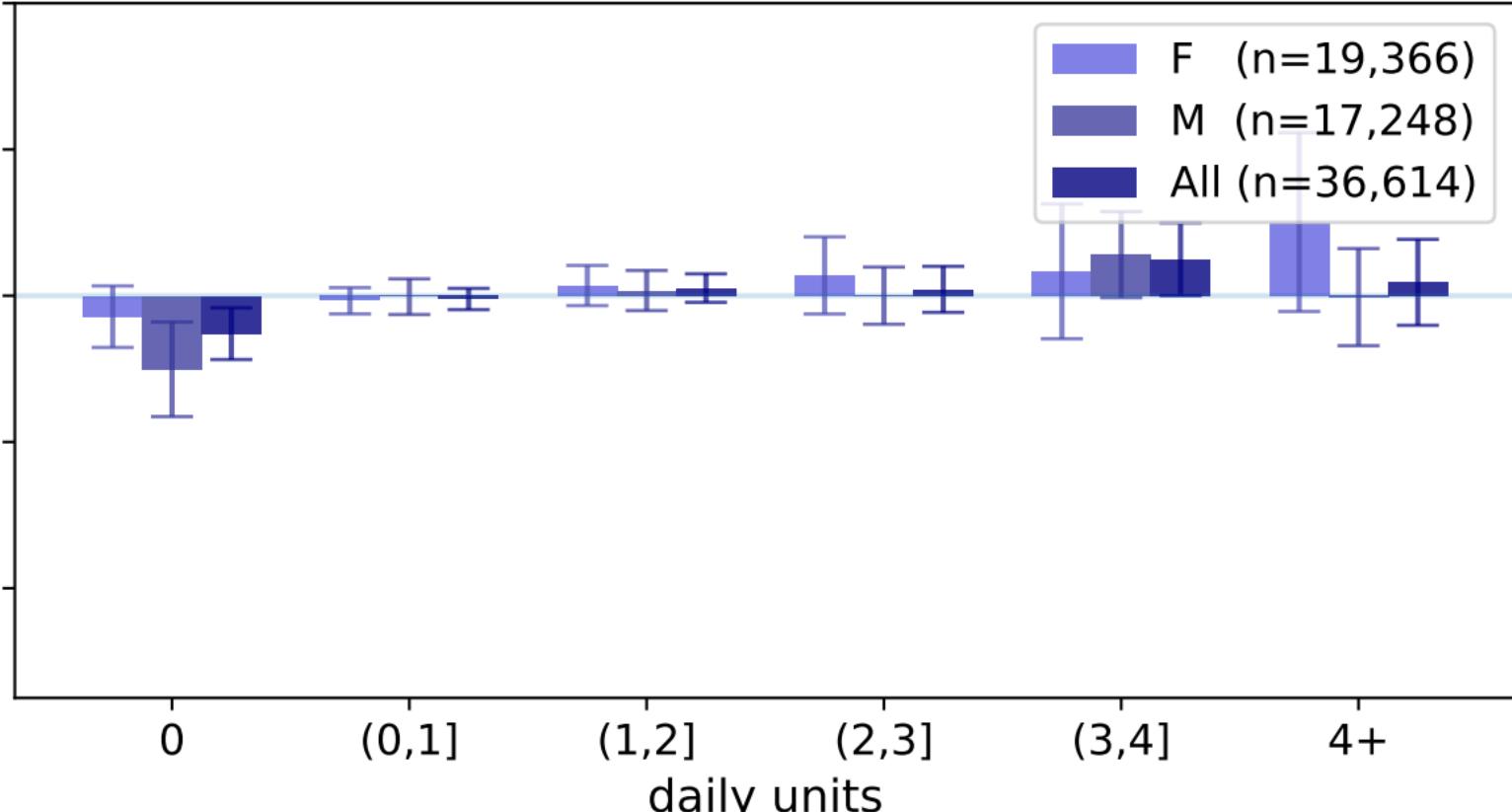
(3,4]

4+

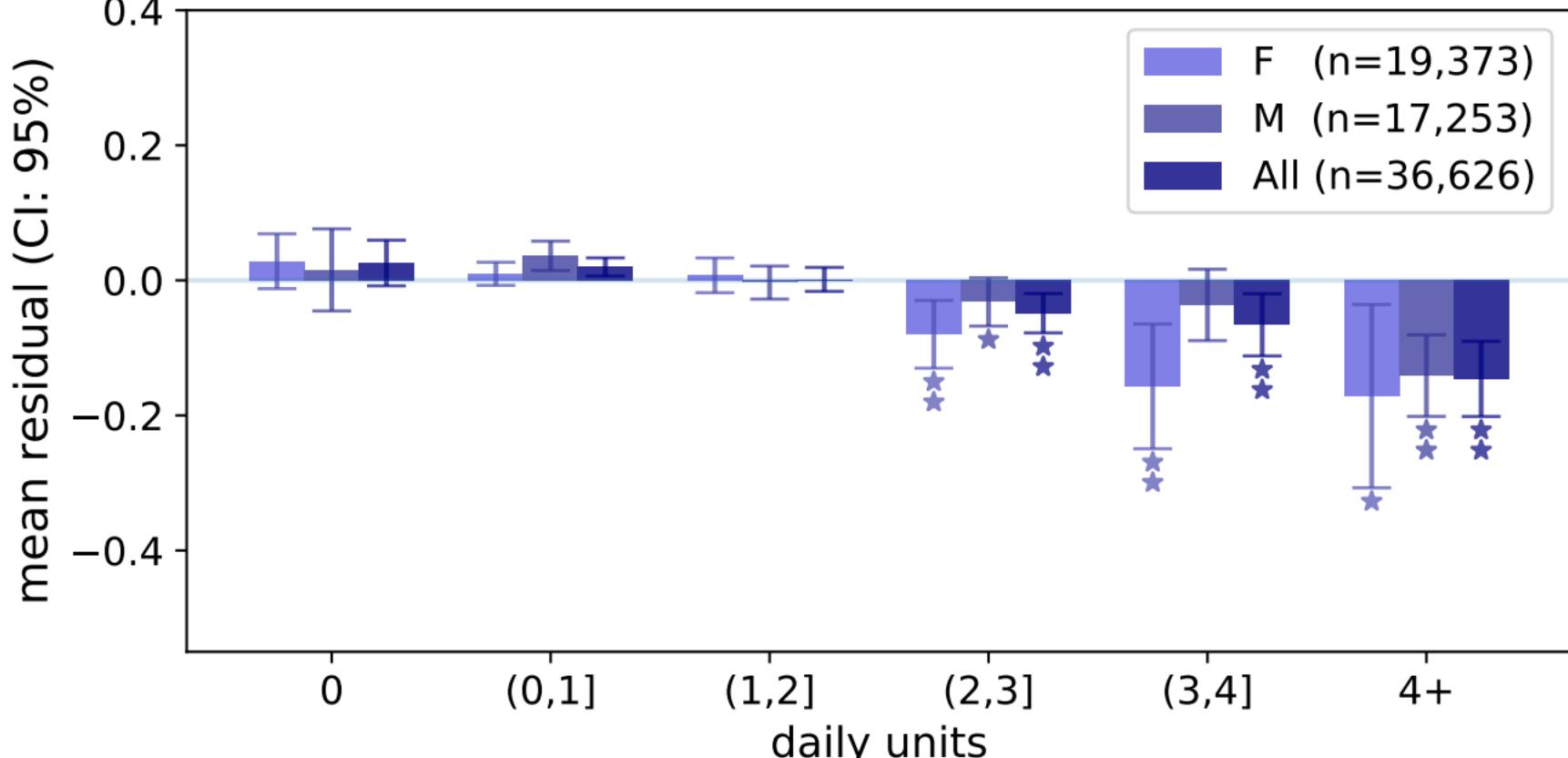
daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

F (n=19,366)
M (n=17,248)
All (n=36,614)



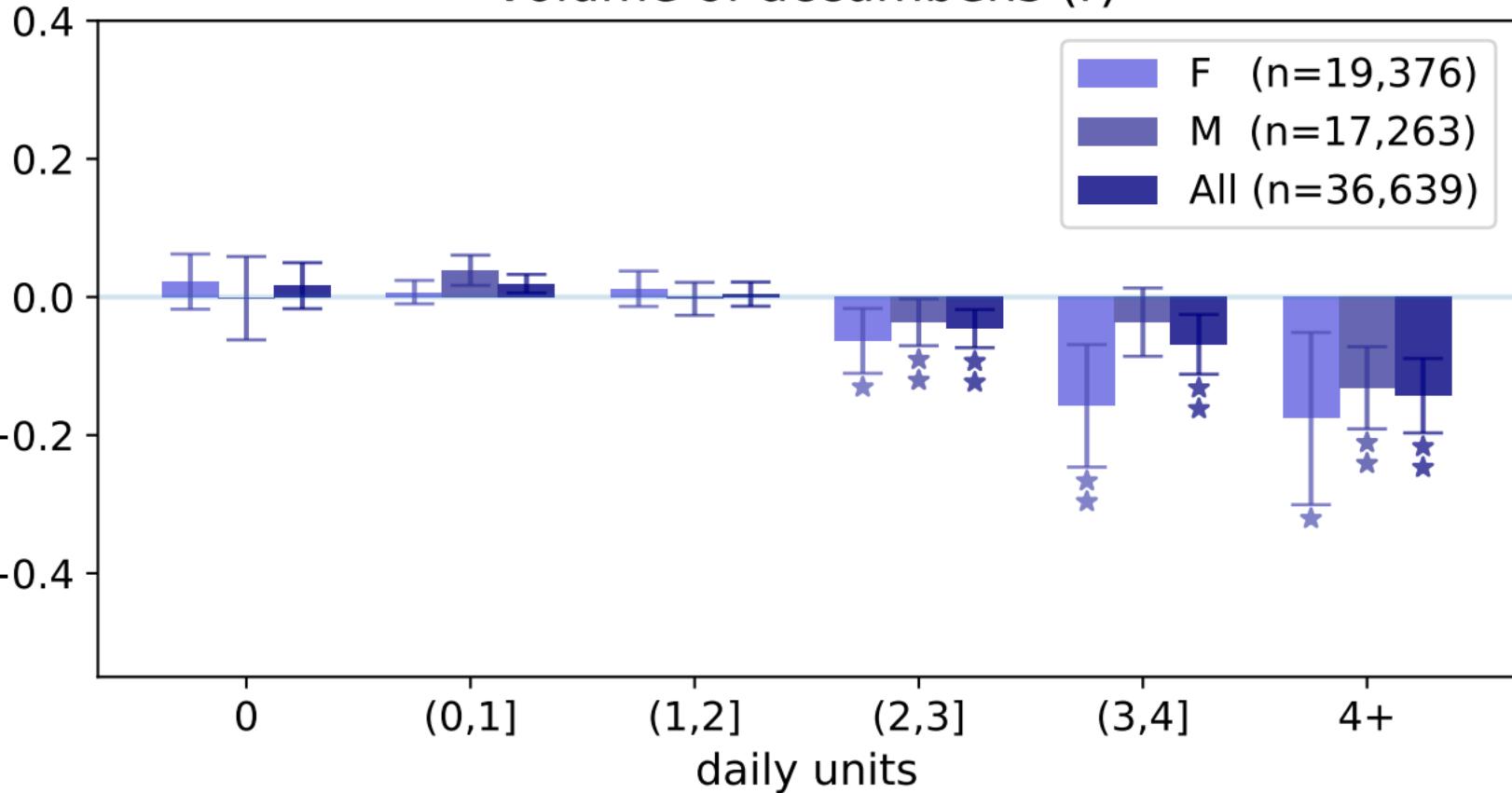
volume of accumbens (l)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

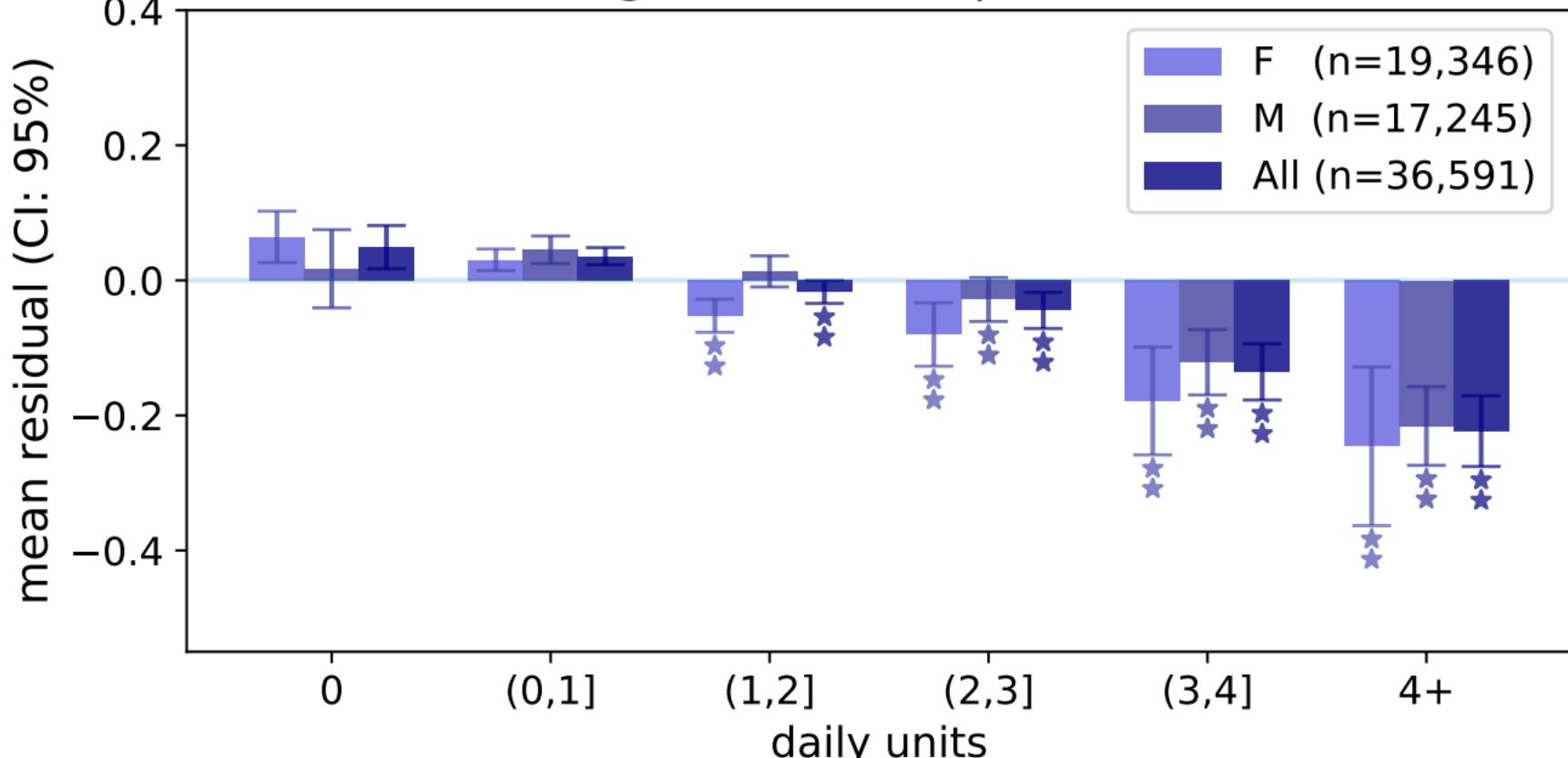
volume of accumbens (r)

mean residual (CI: 95%)

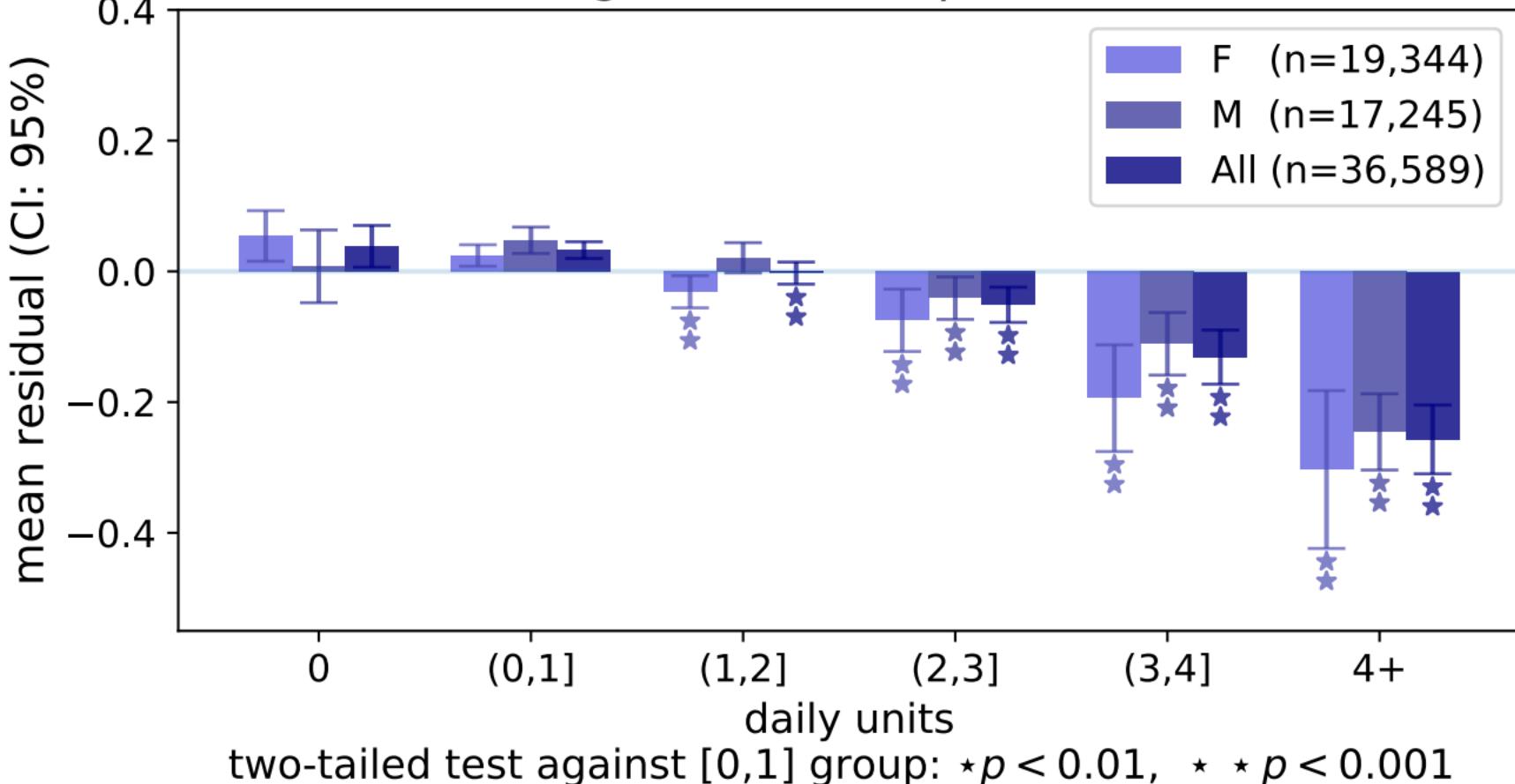


two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in frontal pole (I)

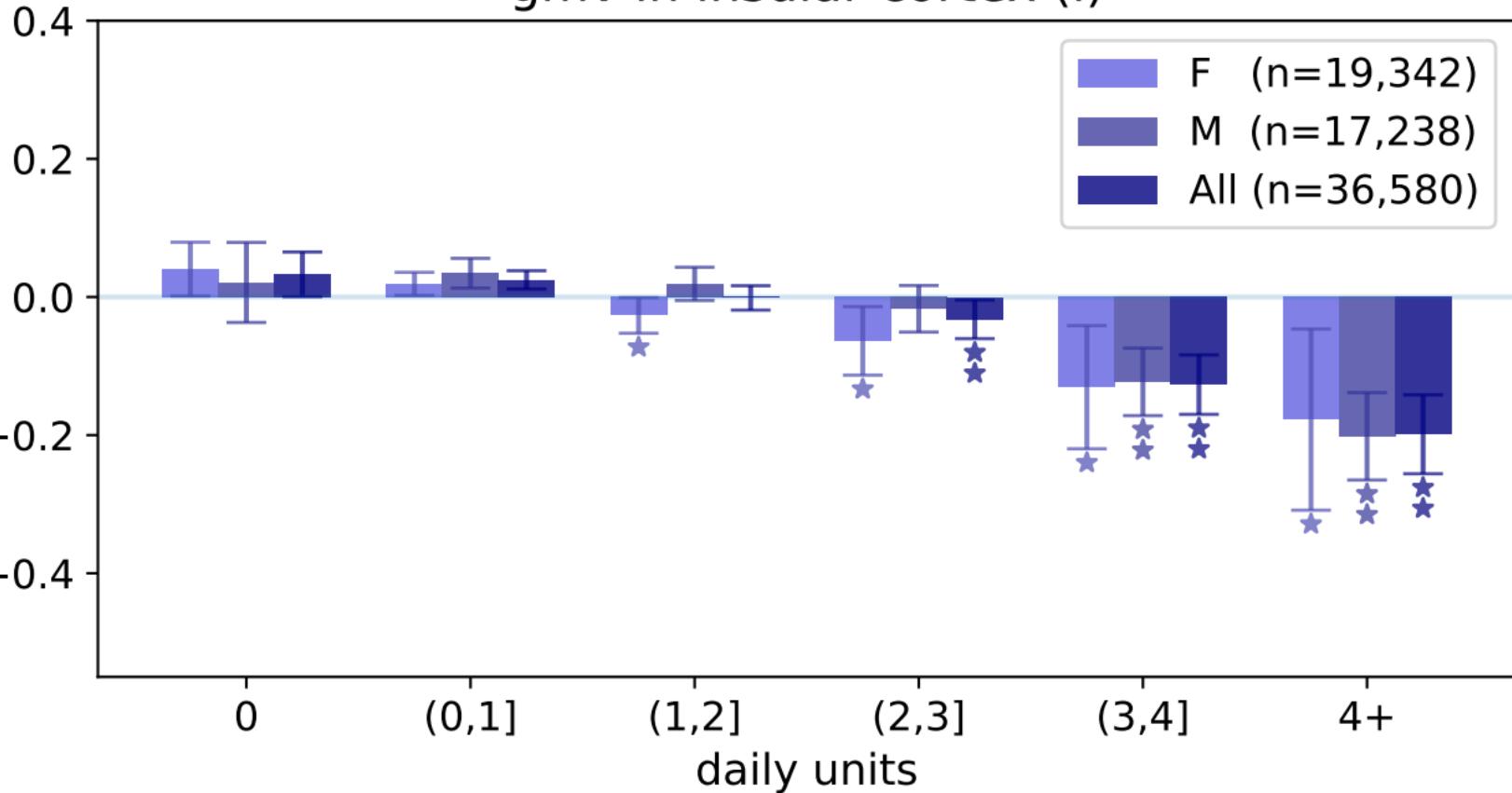


gmv in frontal pole (r)



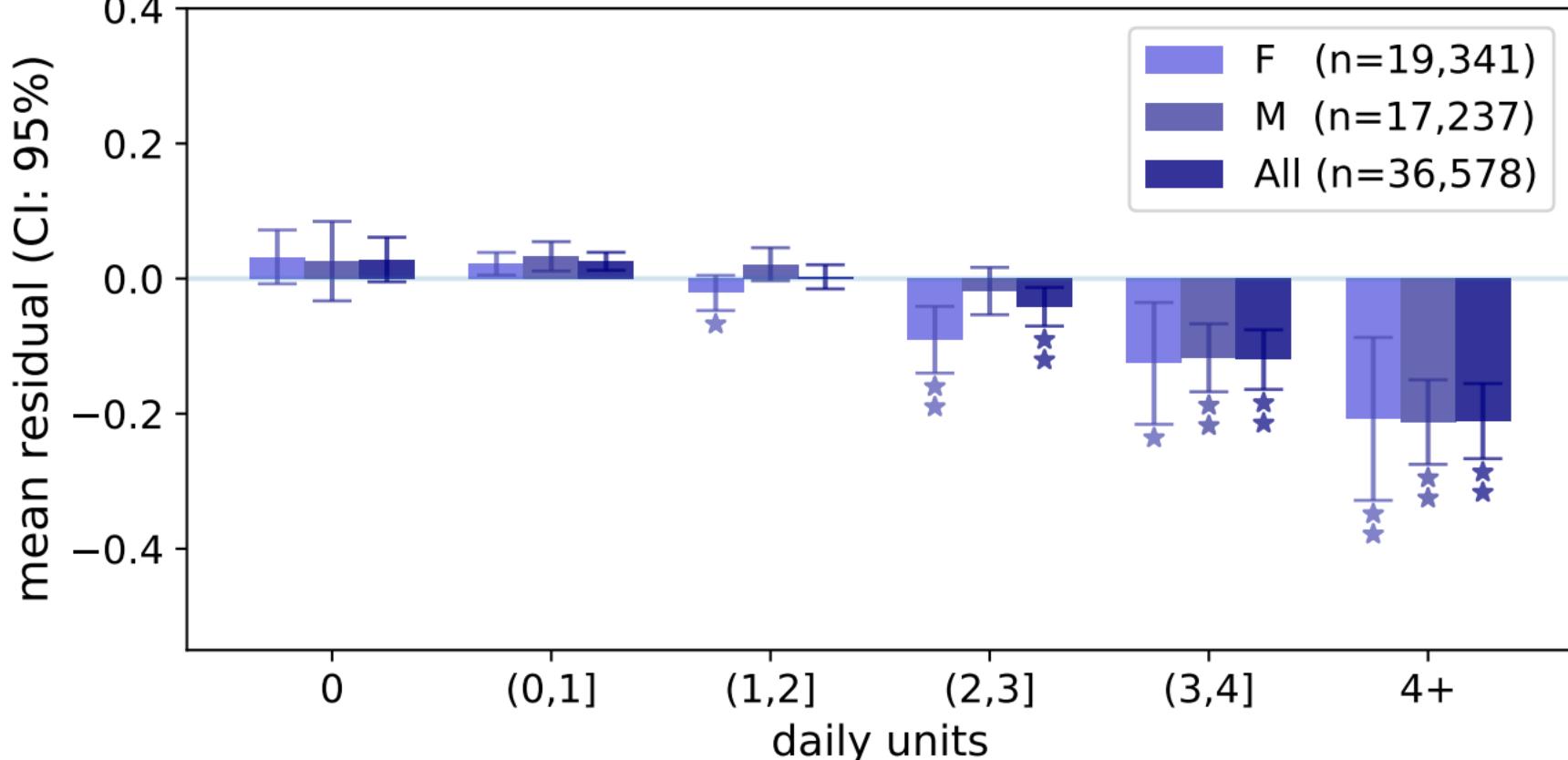
gmv in insular cortex (I)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in insular cortex (r)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in superior frontal gyrus (I)

mean residual (CI: 95%)

0.4

0.2

-0.2

-0.4

0

(0,1]

(1,2]

(2,3]

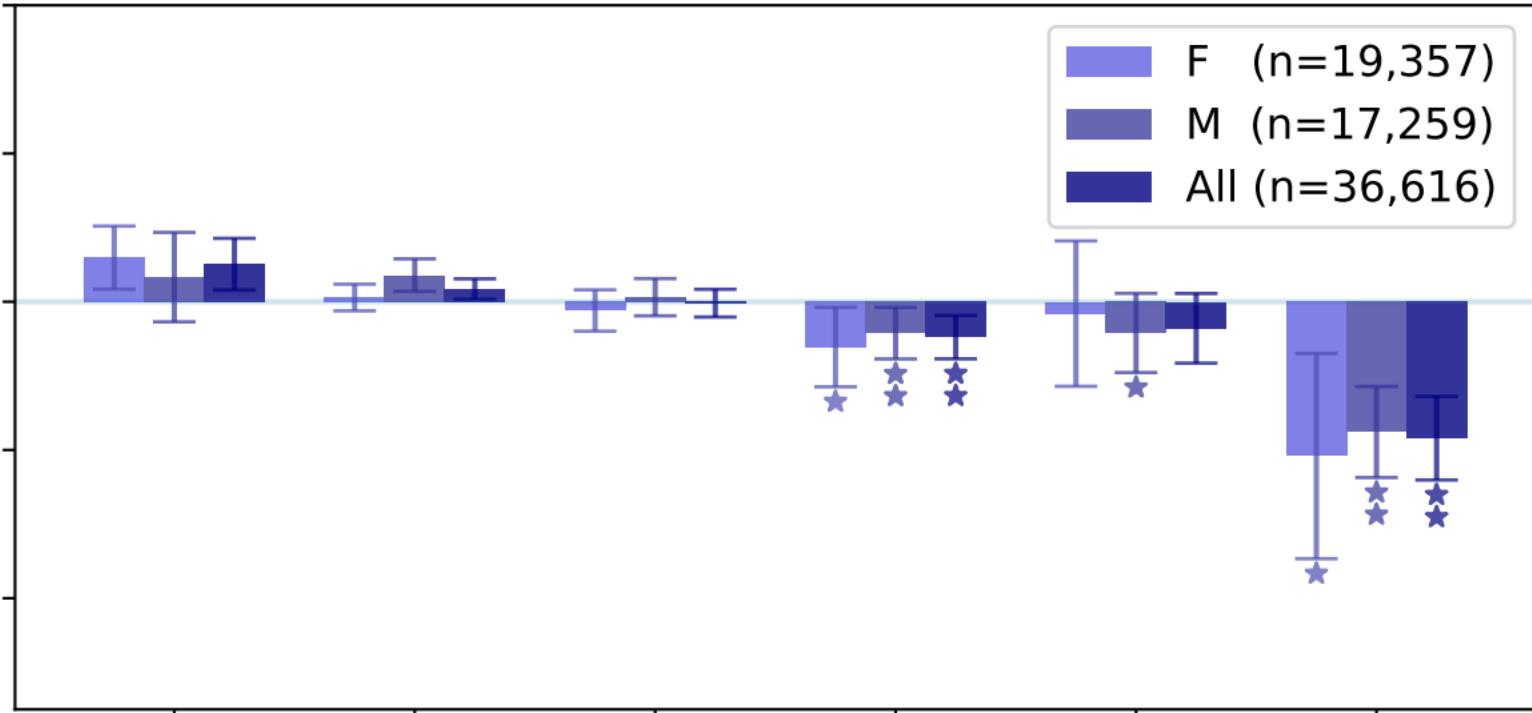
(3,4]

4+

daily units

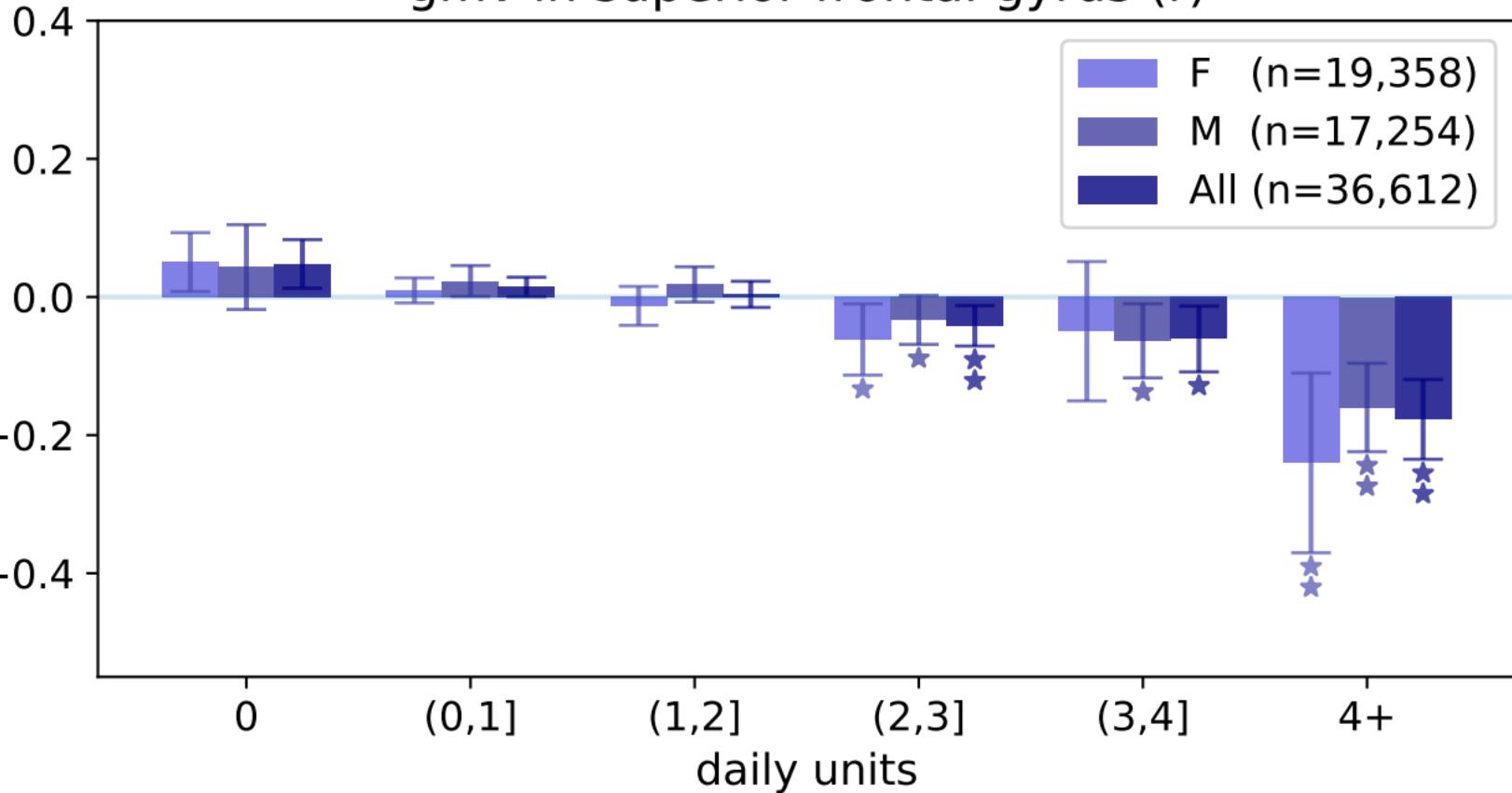
two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

- F (n=19,357)
- M (n=17,259)
- All (n=36,616)



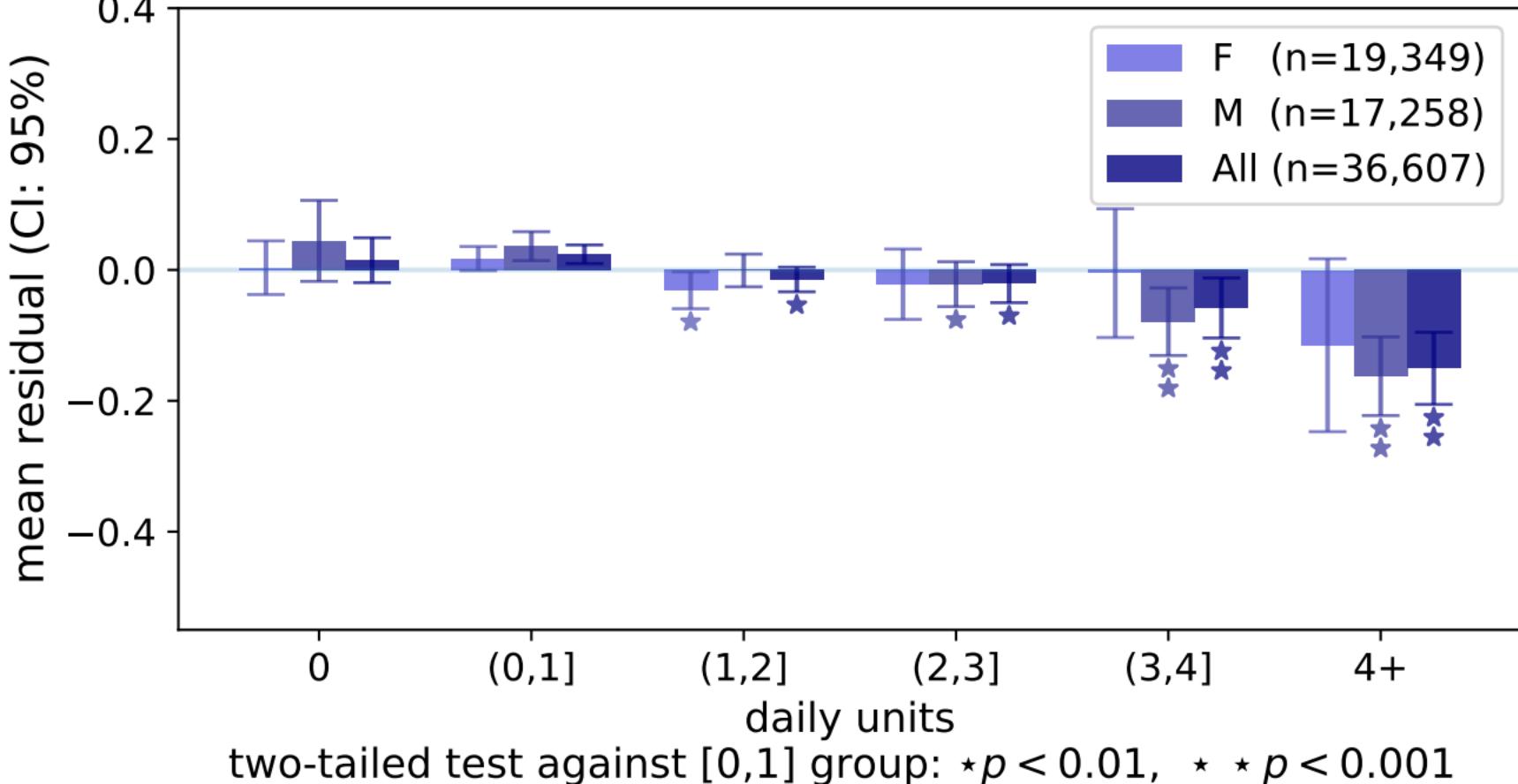
gmv in superior frontal gyrus (r)

mean residual (CI: 95%)



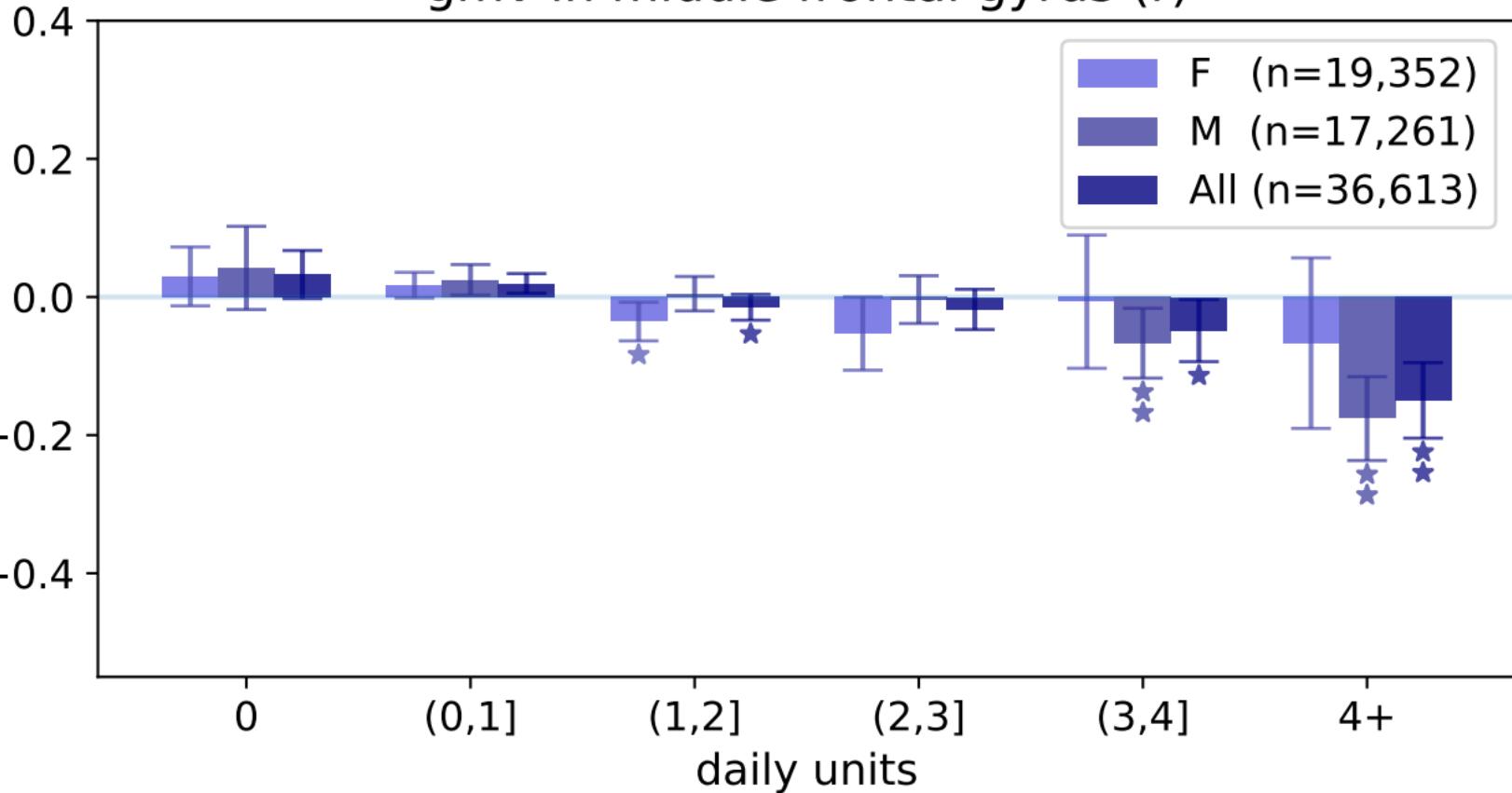
two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in middle frontal gyrus (I)



gmv in middle frontal gyrus (r)

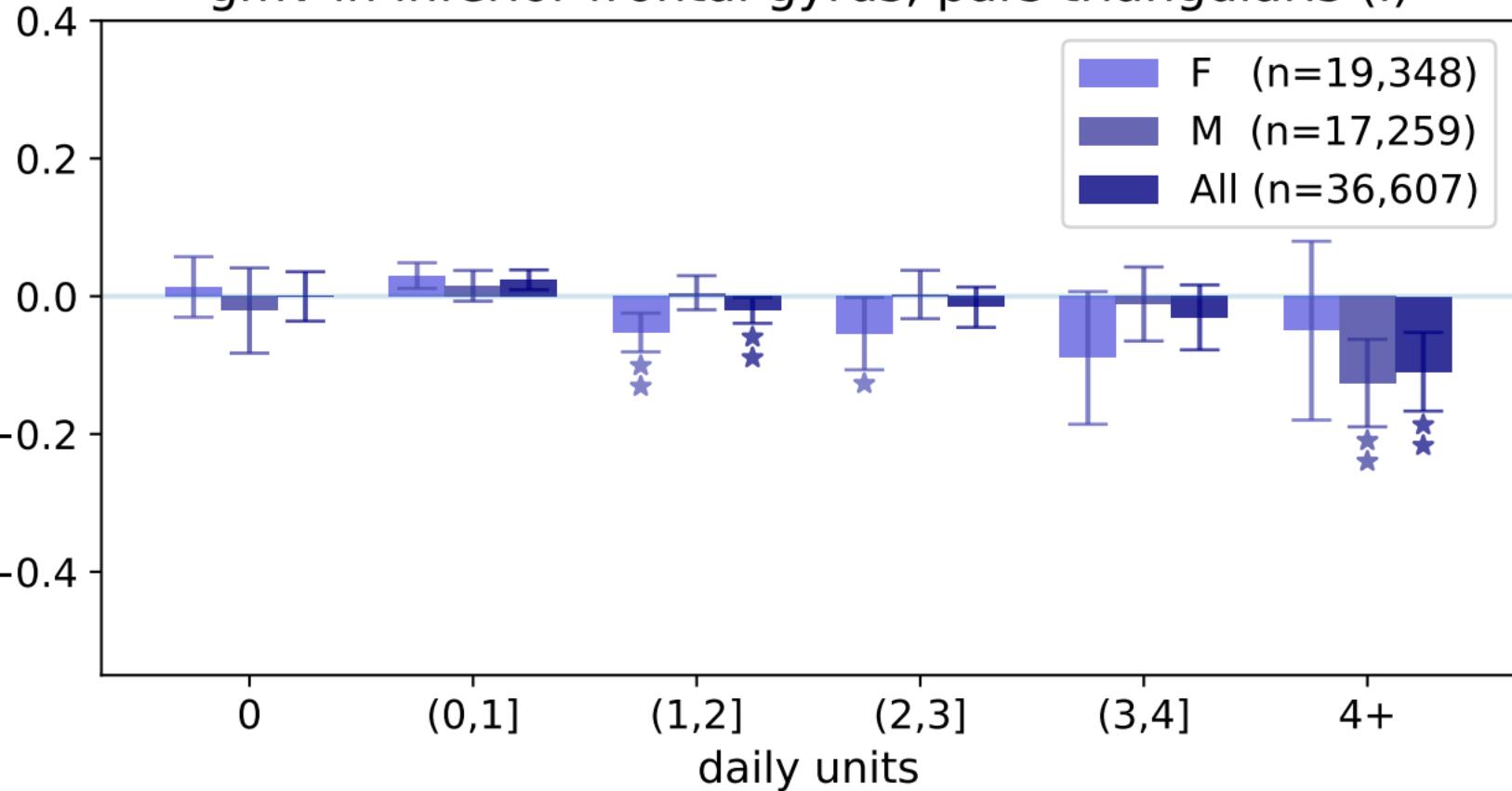
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in inferior frontal gyrus, pars triangularis (I)

mean residual (CI: 95%)

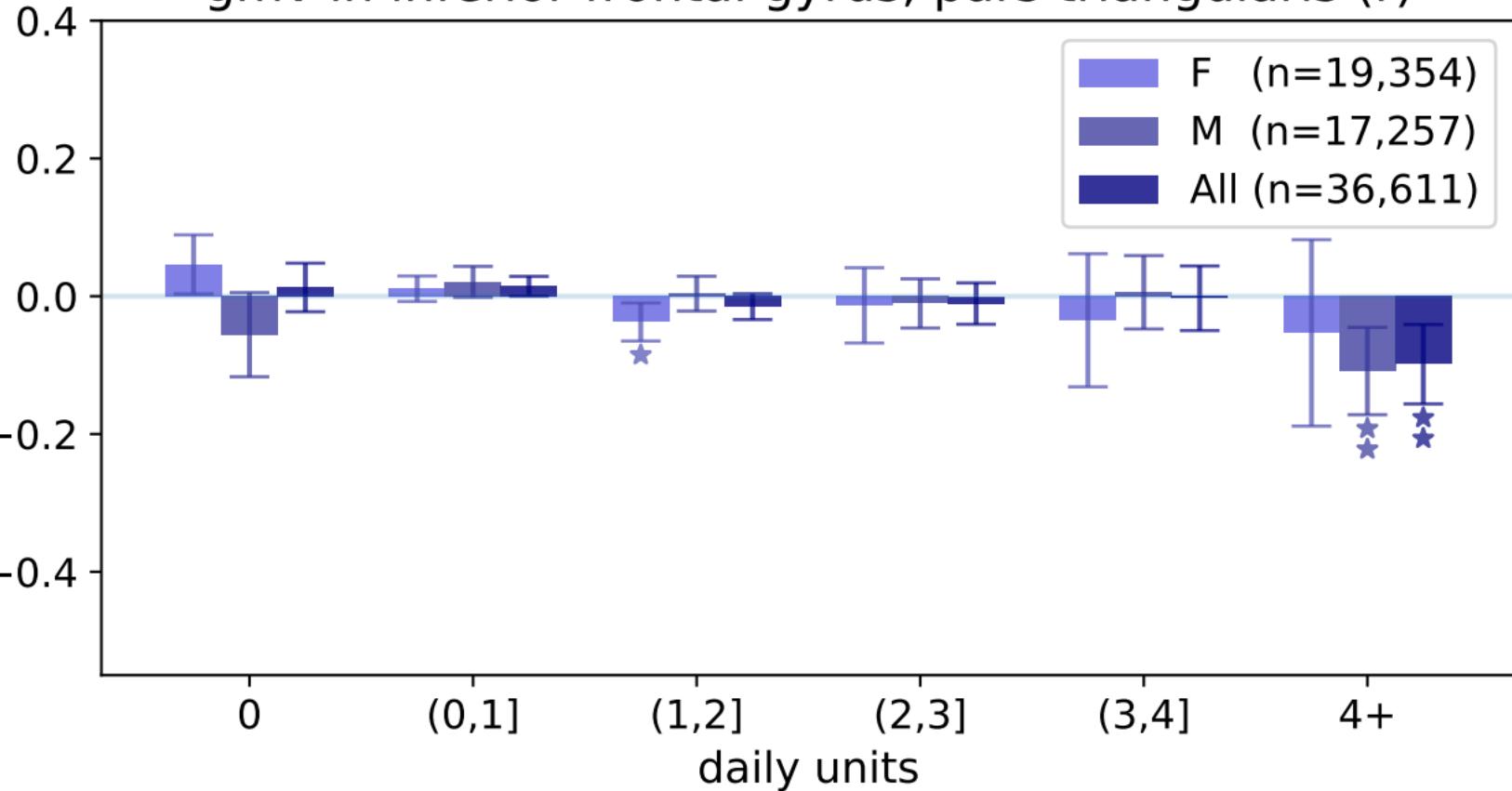


daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in inferior frontal gyrus, pars triangularis (r)

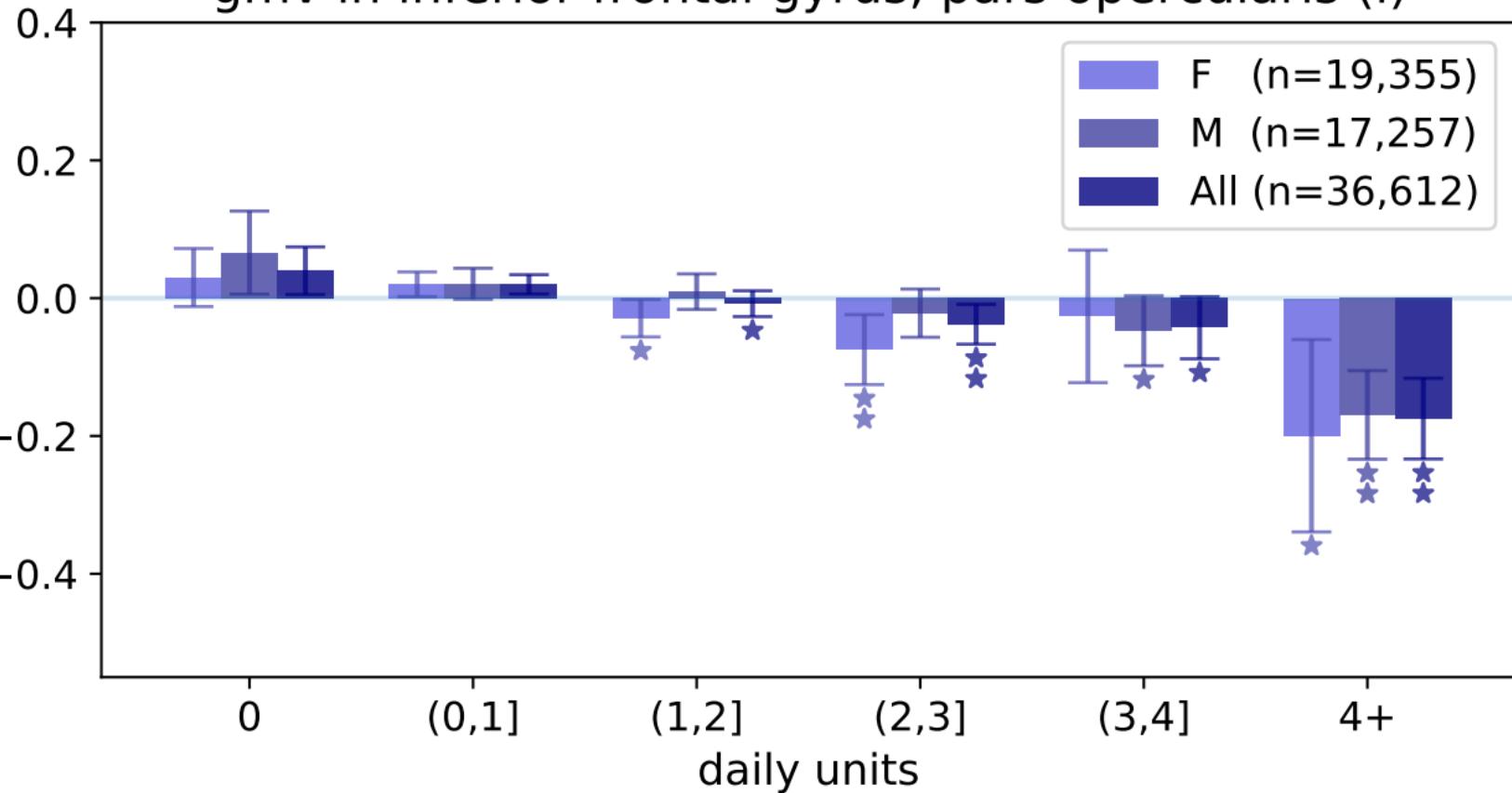
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in inferior frontal gyrus, pars opercularis (I)

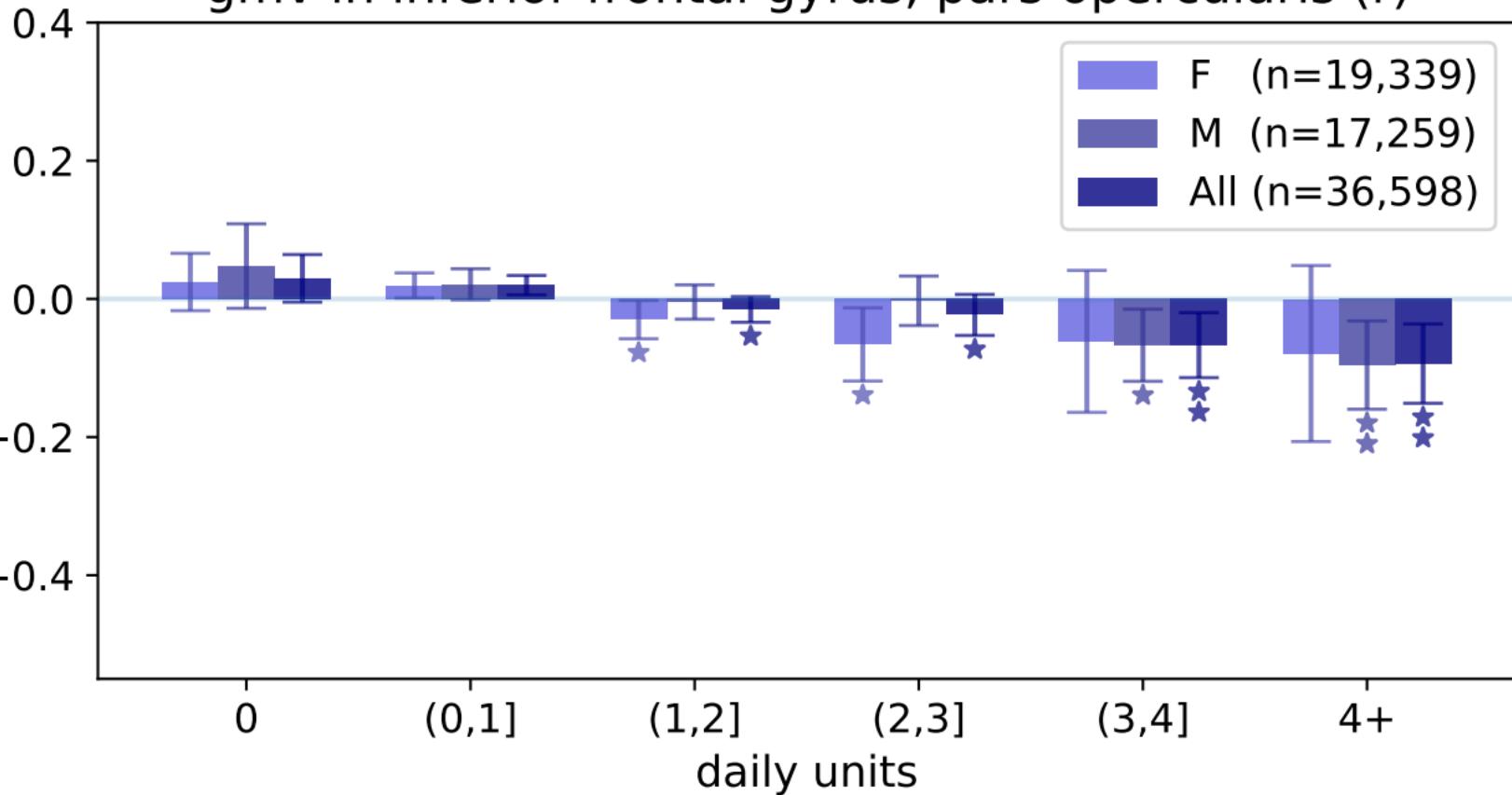
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

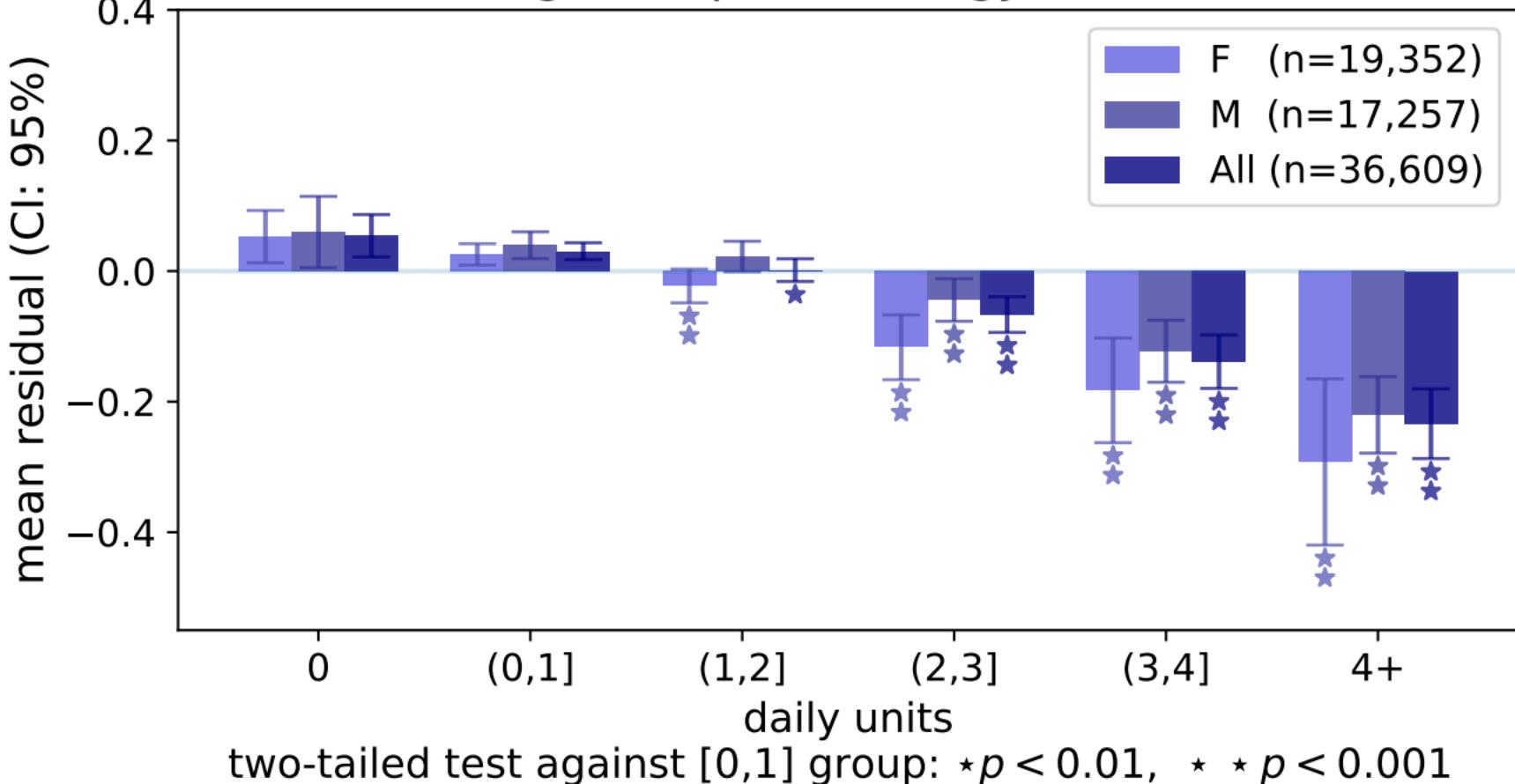
gmv in inferior frontal gyrus, pars opercularis (r)

mean residual (CI: 95%)



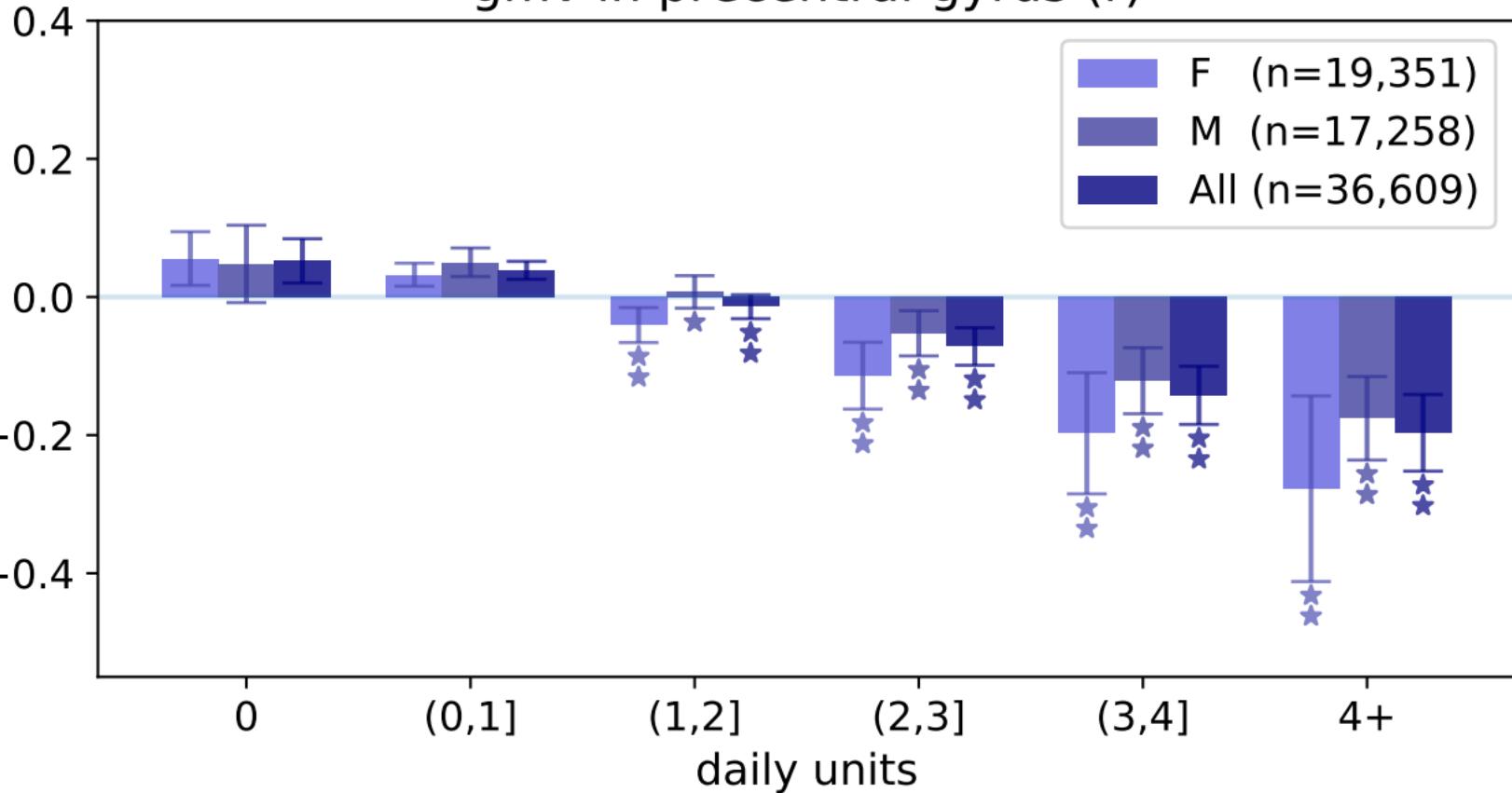
two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in precentral gyrus (l)



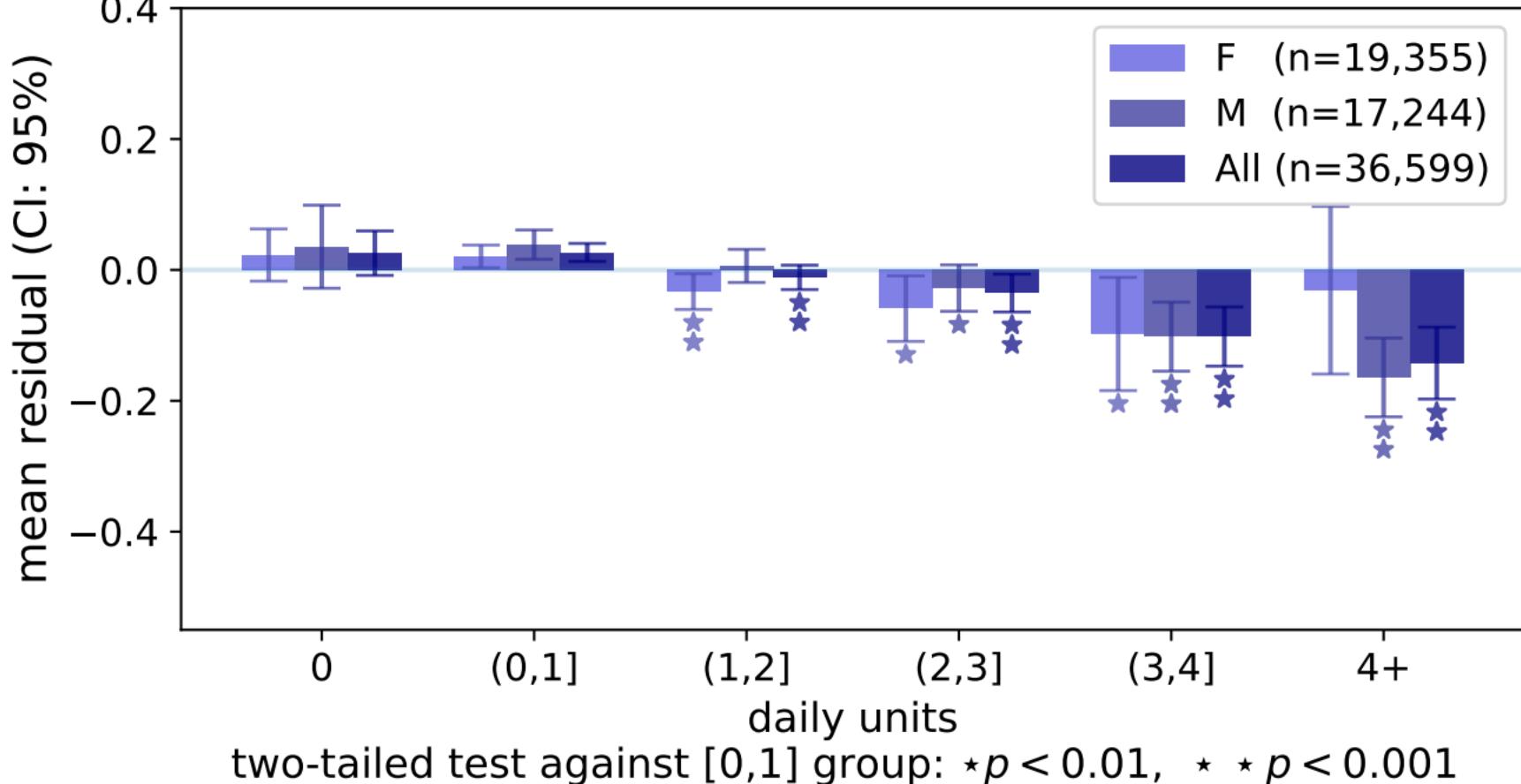
gmv in precentral gyrus (r)

mean residual (CI: 95%)



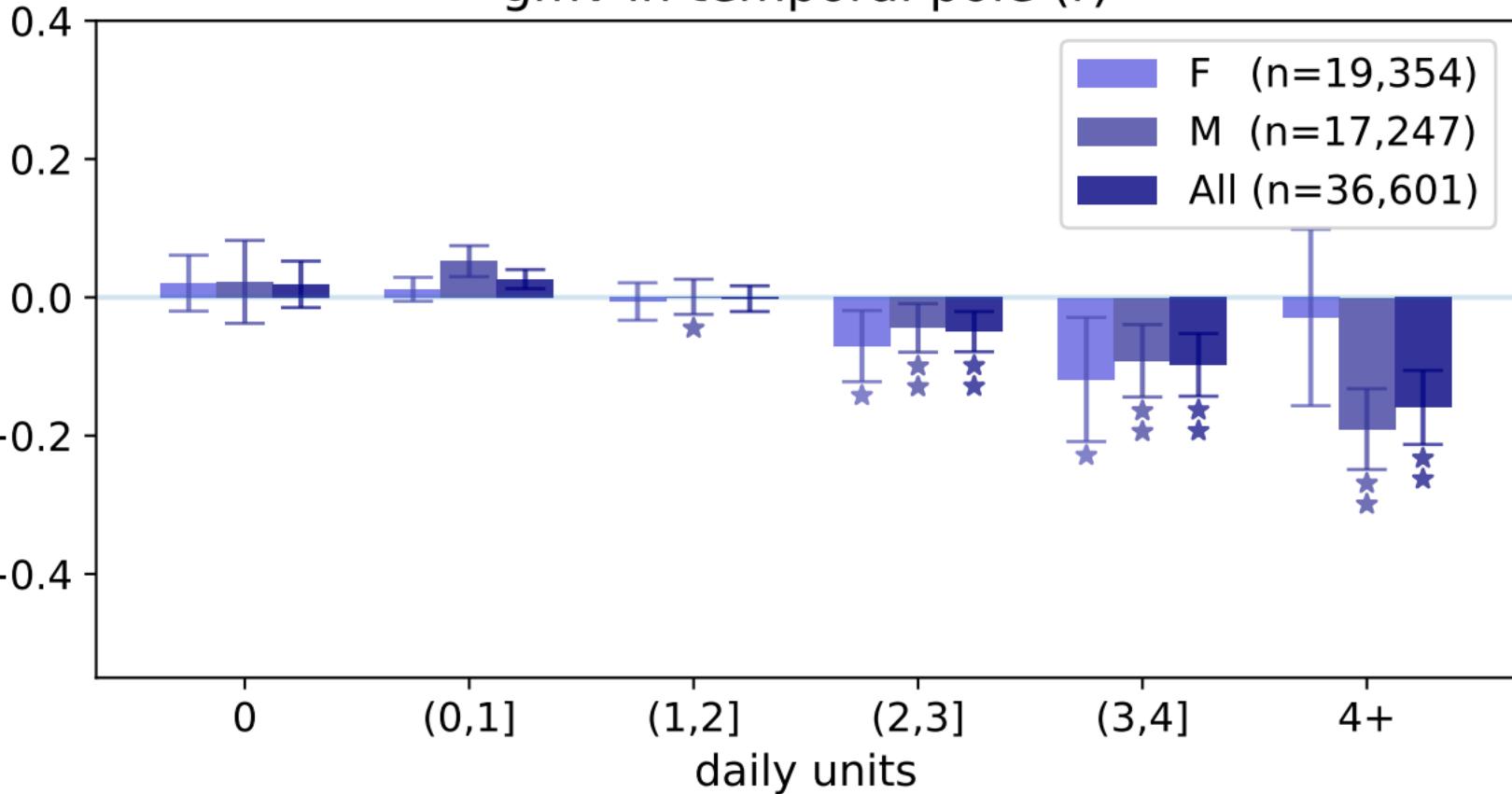
two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in temporal pole (I)



gmv in temporal pole (r)

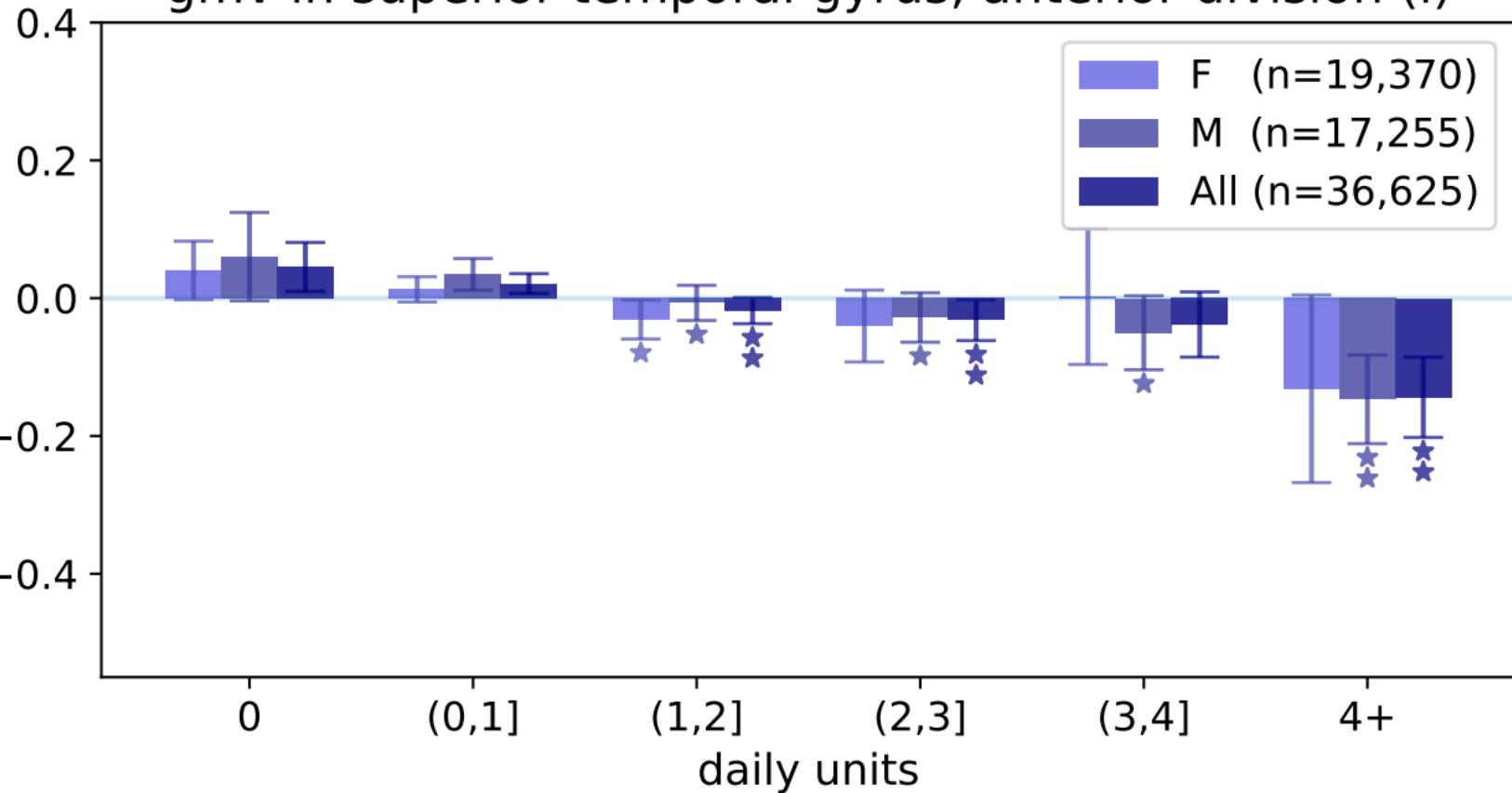
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in superior temporal gyrus, anterior division (I)

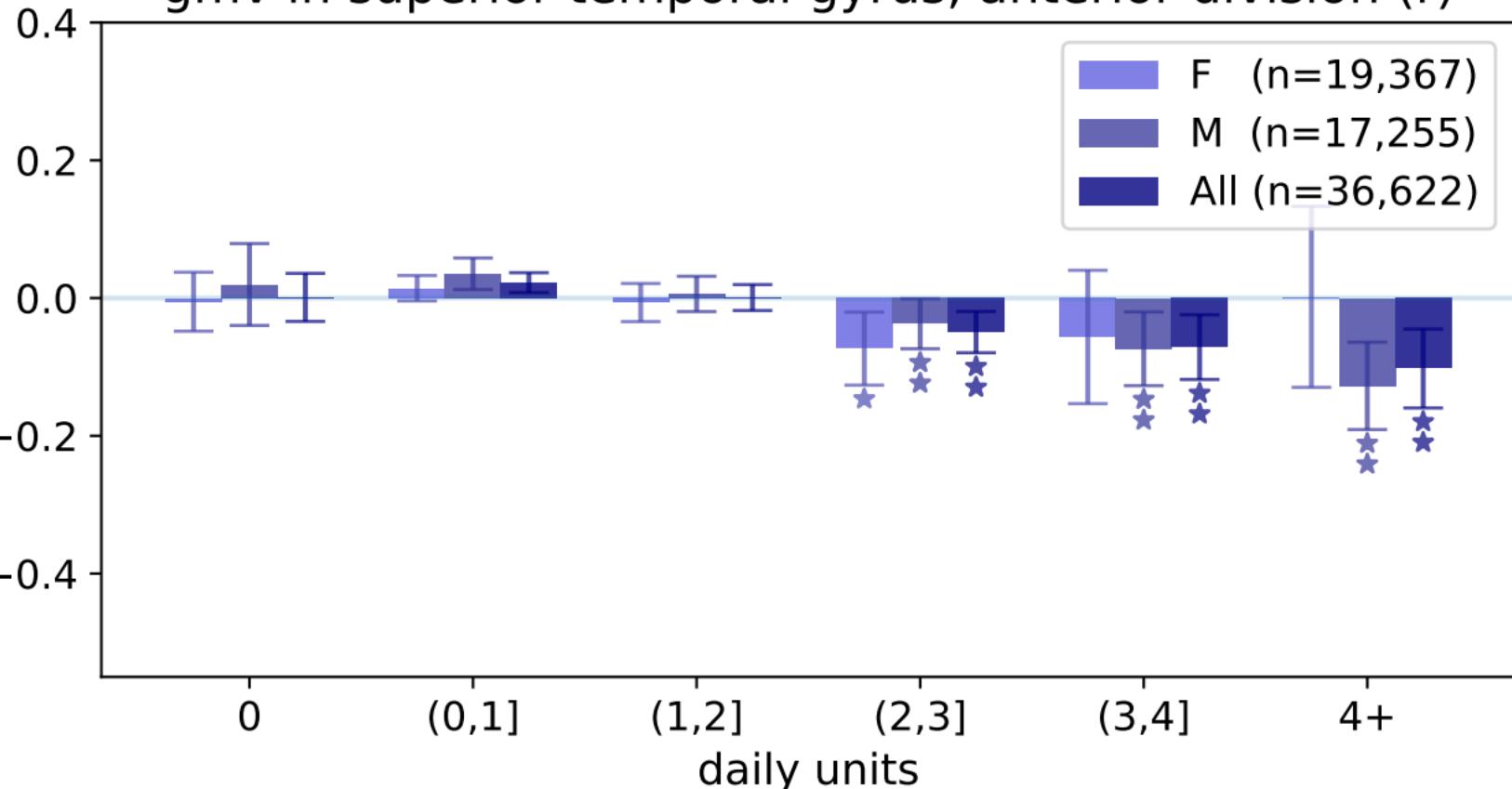
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in superior temporal gyrus, anterior division (r)

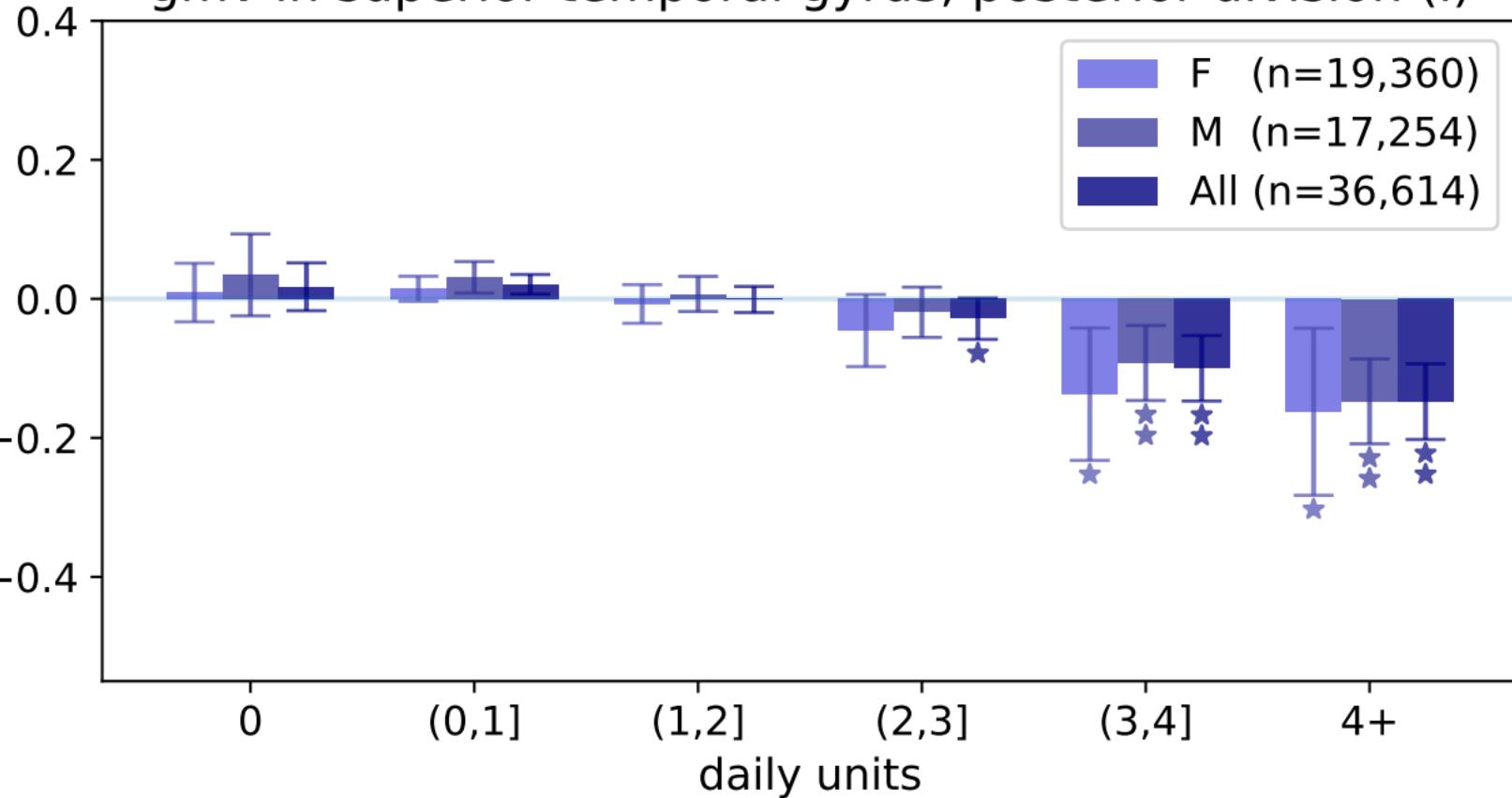
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in superior temporal gyrus, posterior division (l)

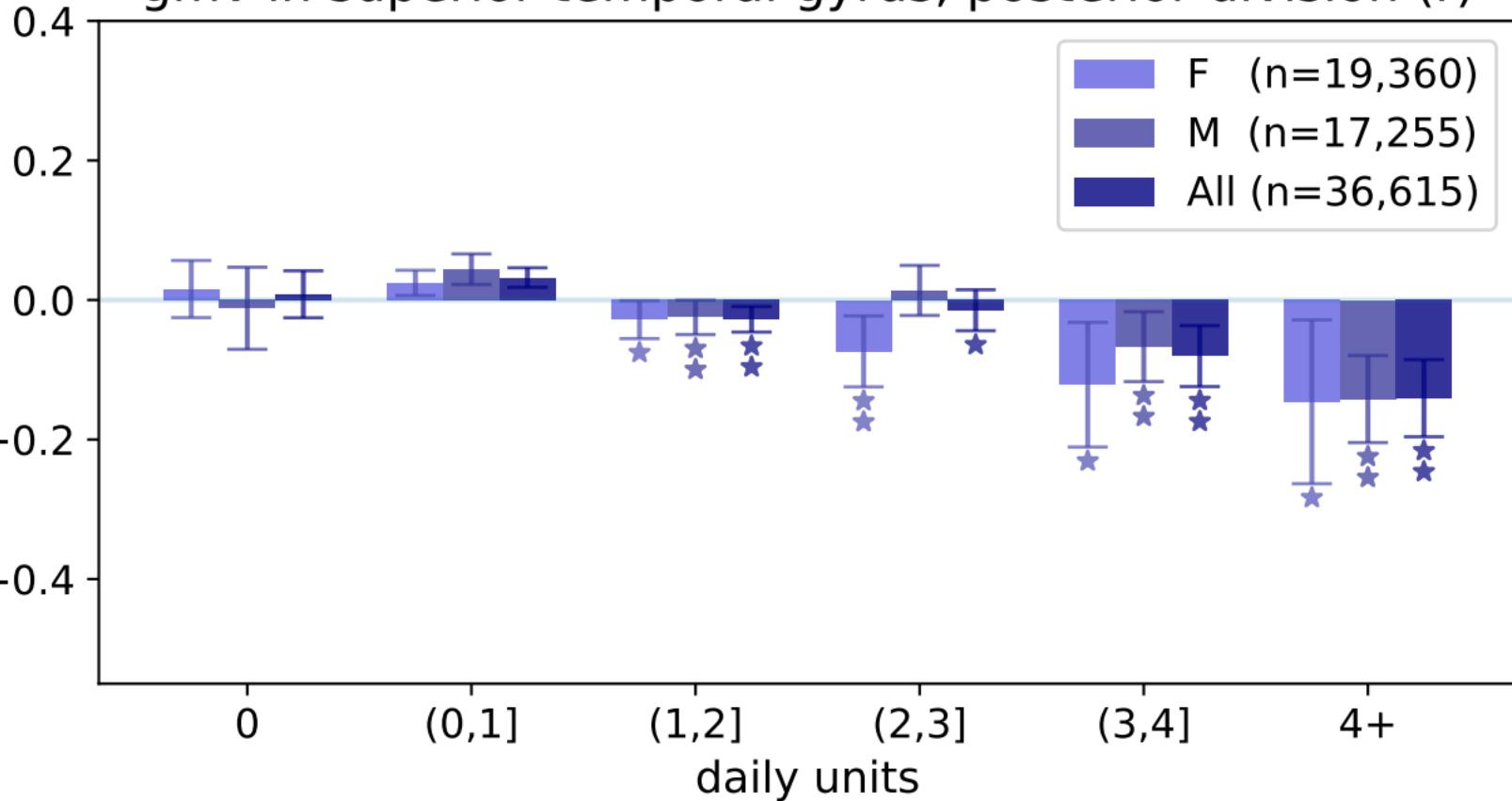
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in superior temporal gyrus, posterior division (r)

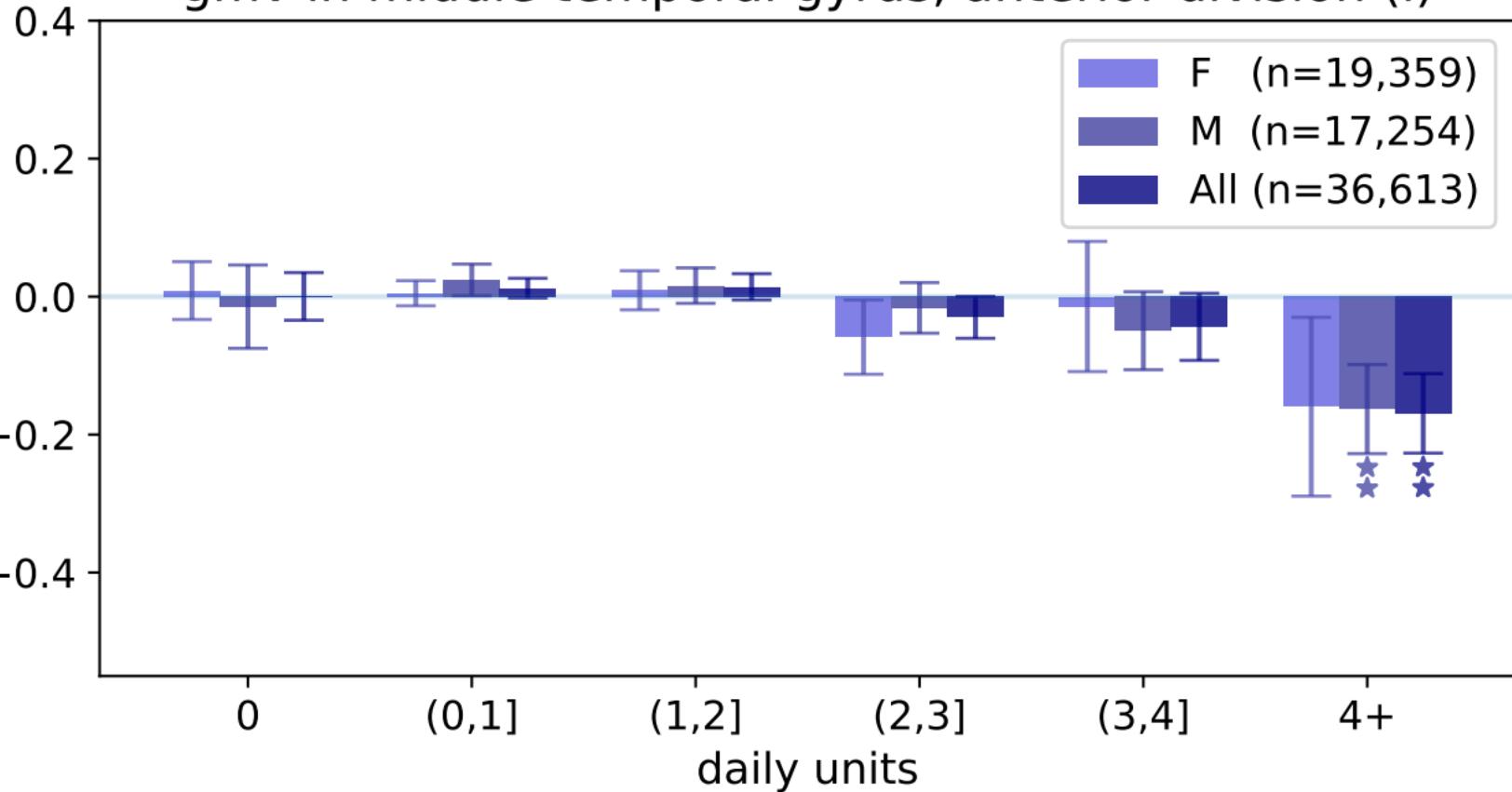
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in middle temporal gyrus, anterior division (I)

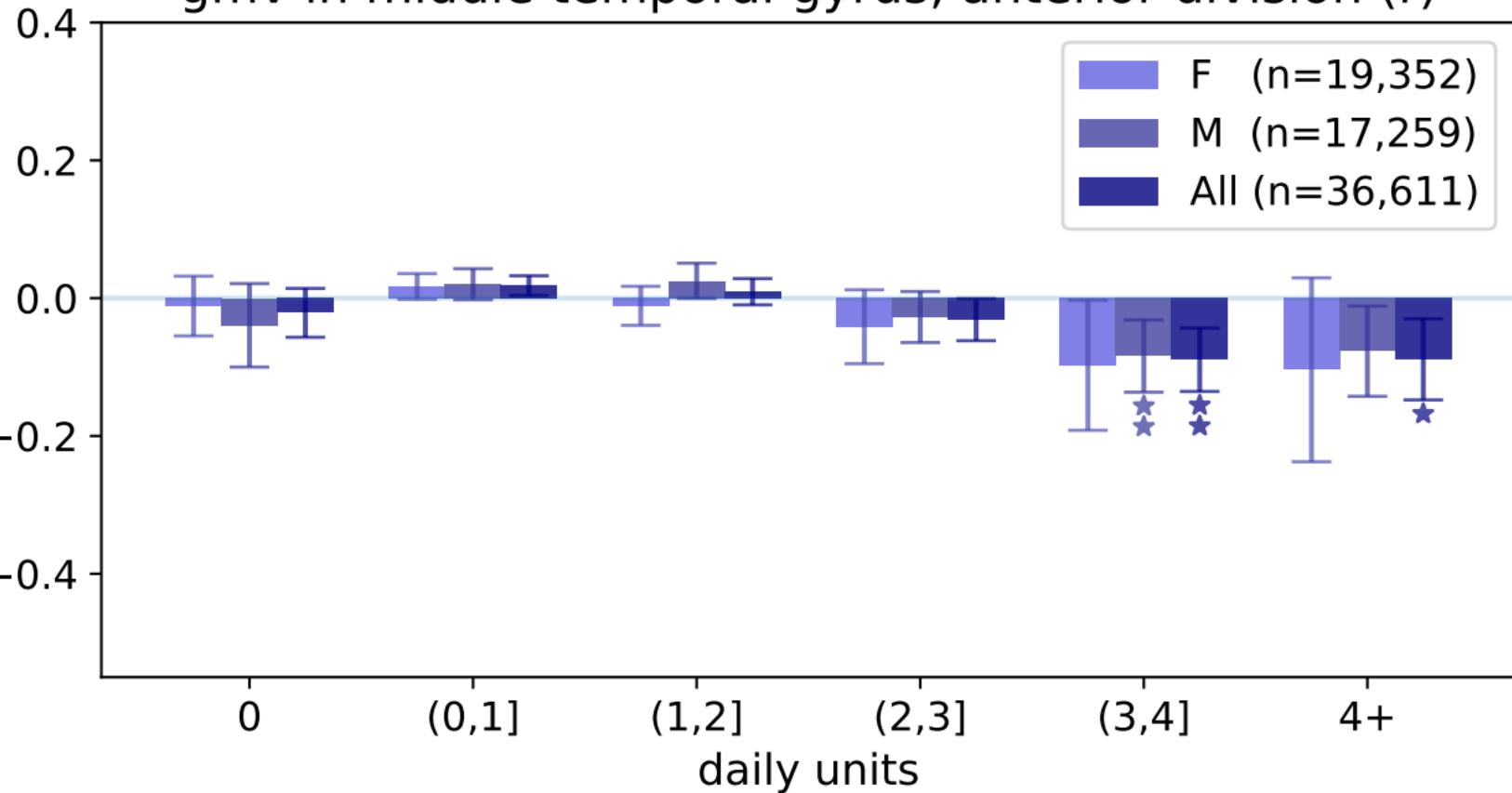
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in middle temporal gyrus, anterior division (r)

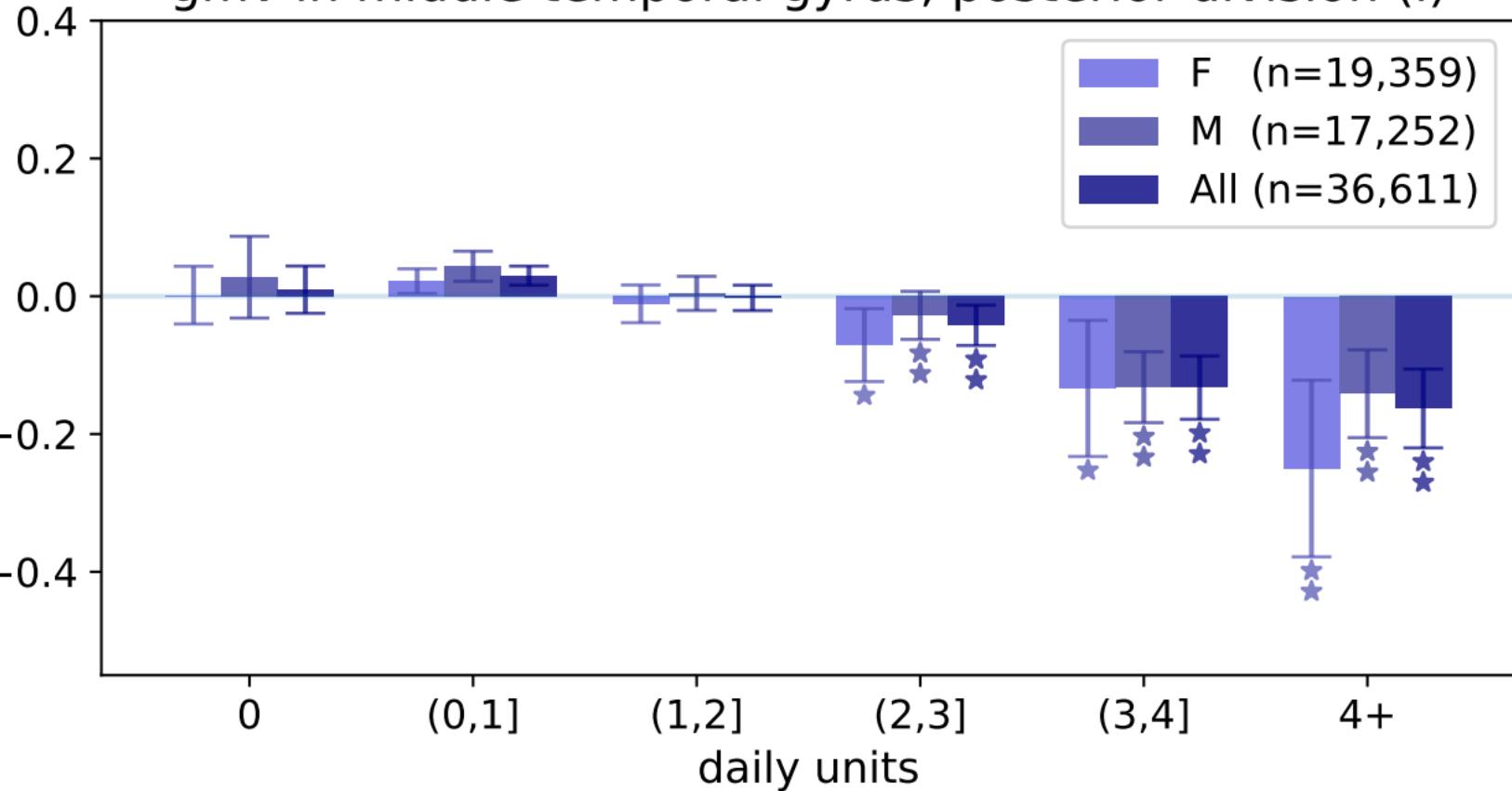
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in middle temporal gyrus, posterior division (I)

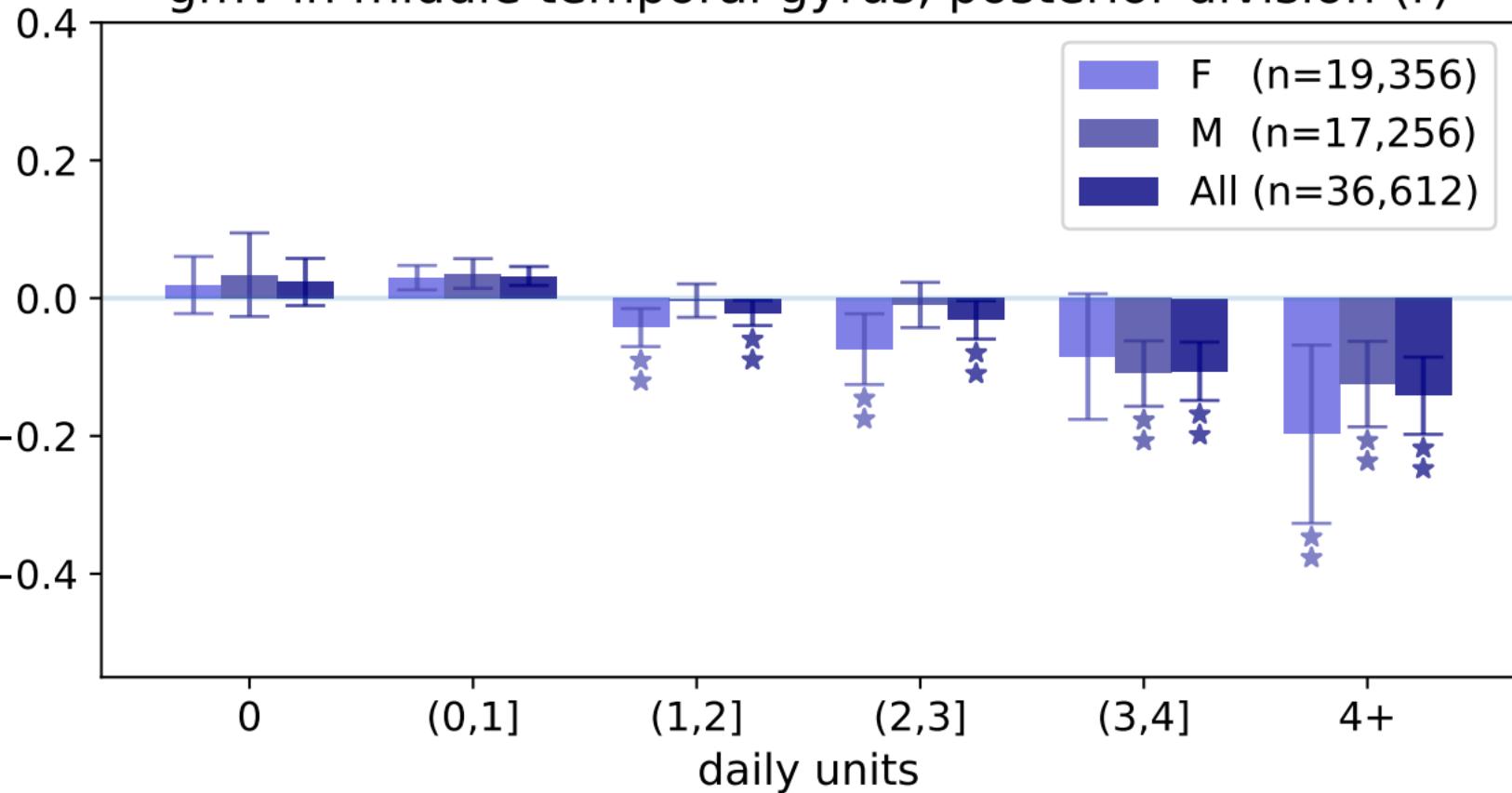
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in middle temporal gyrus, posterior division (r)

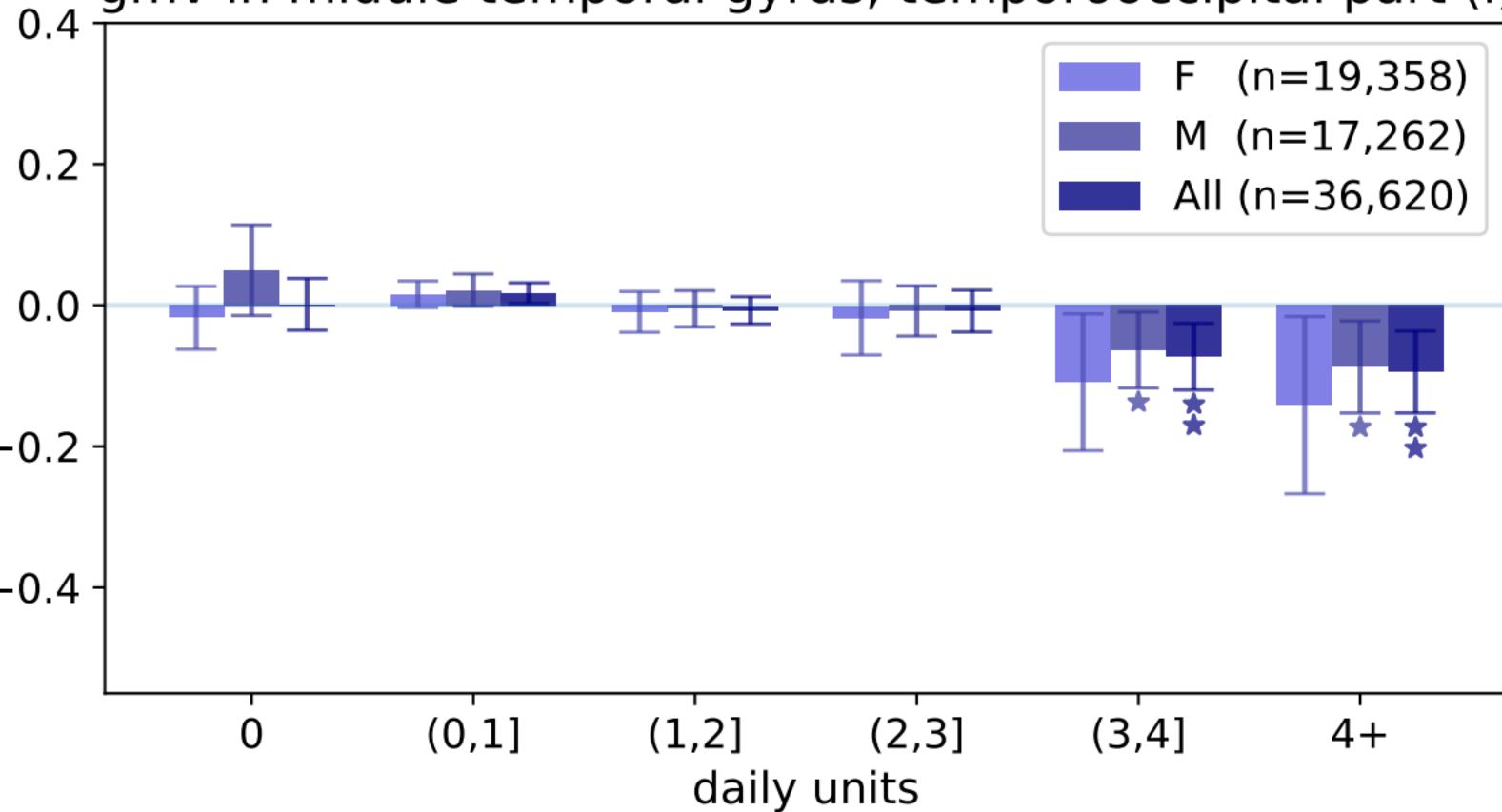
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in middle temporal gyrus, temporooccipital part (I)

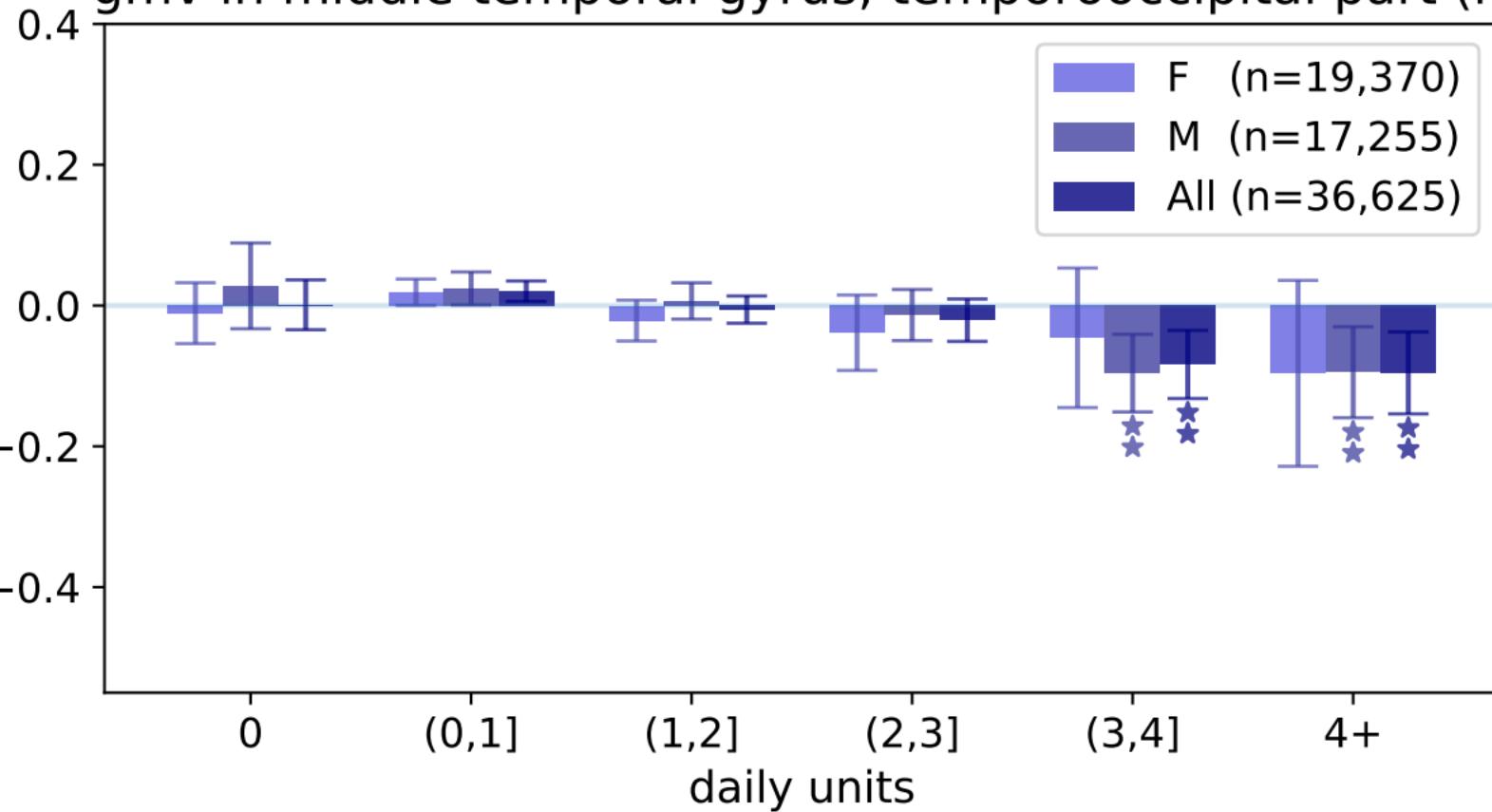
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in middle temporal gyrus, temporooccipital part (r)

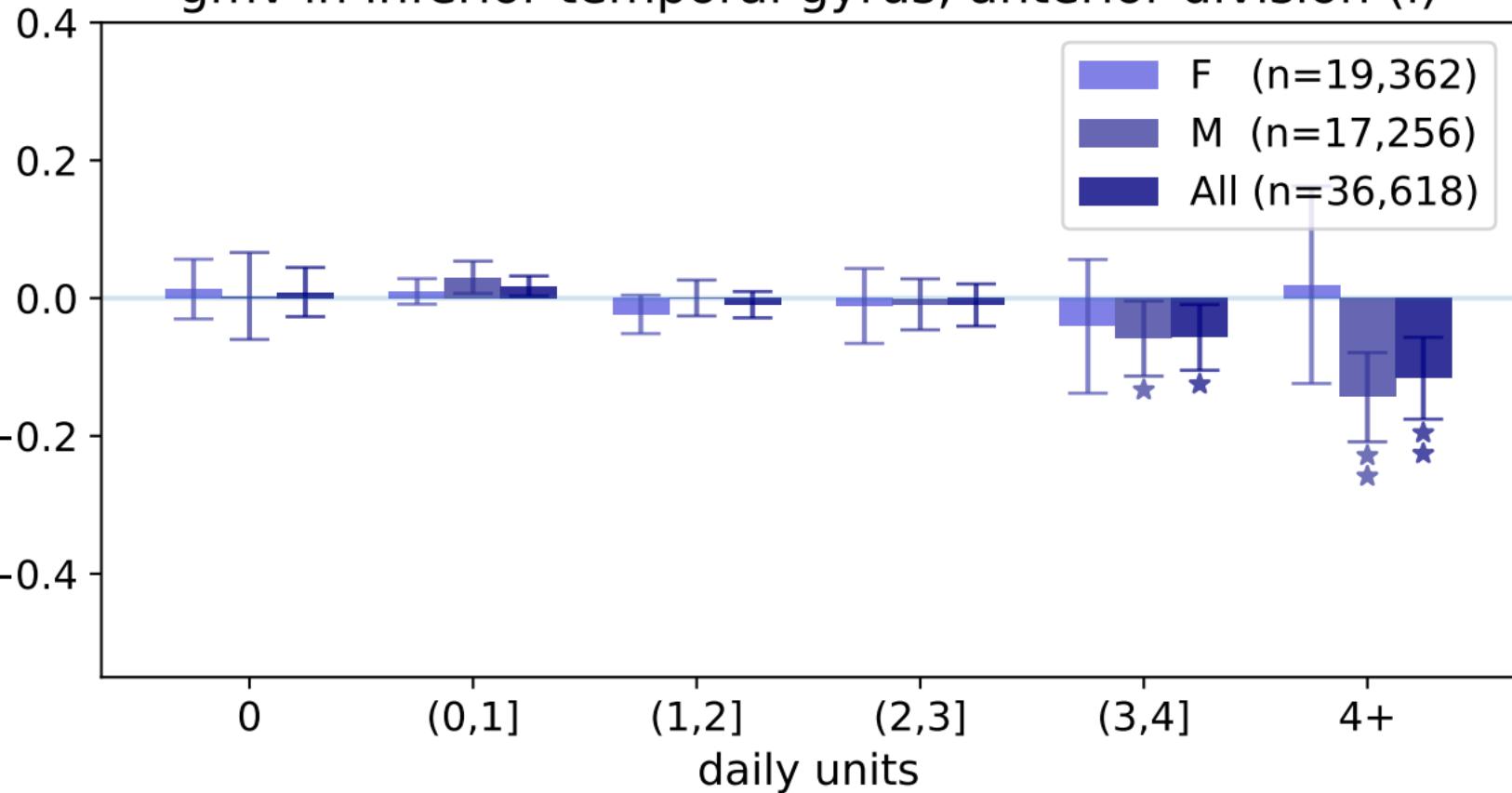
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in inferior temporal gyrus, anterior division (I)

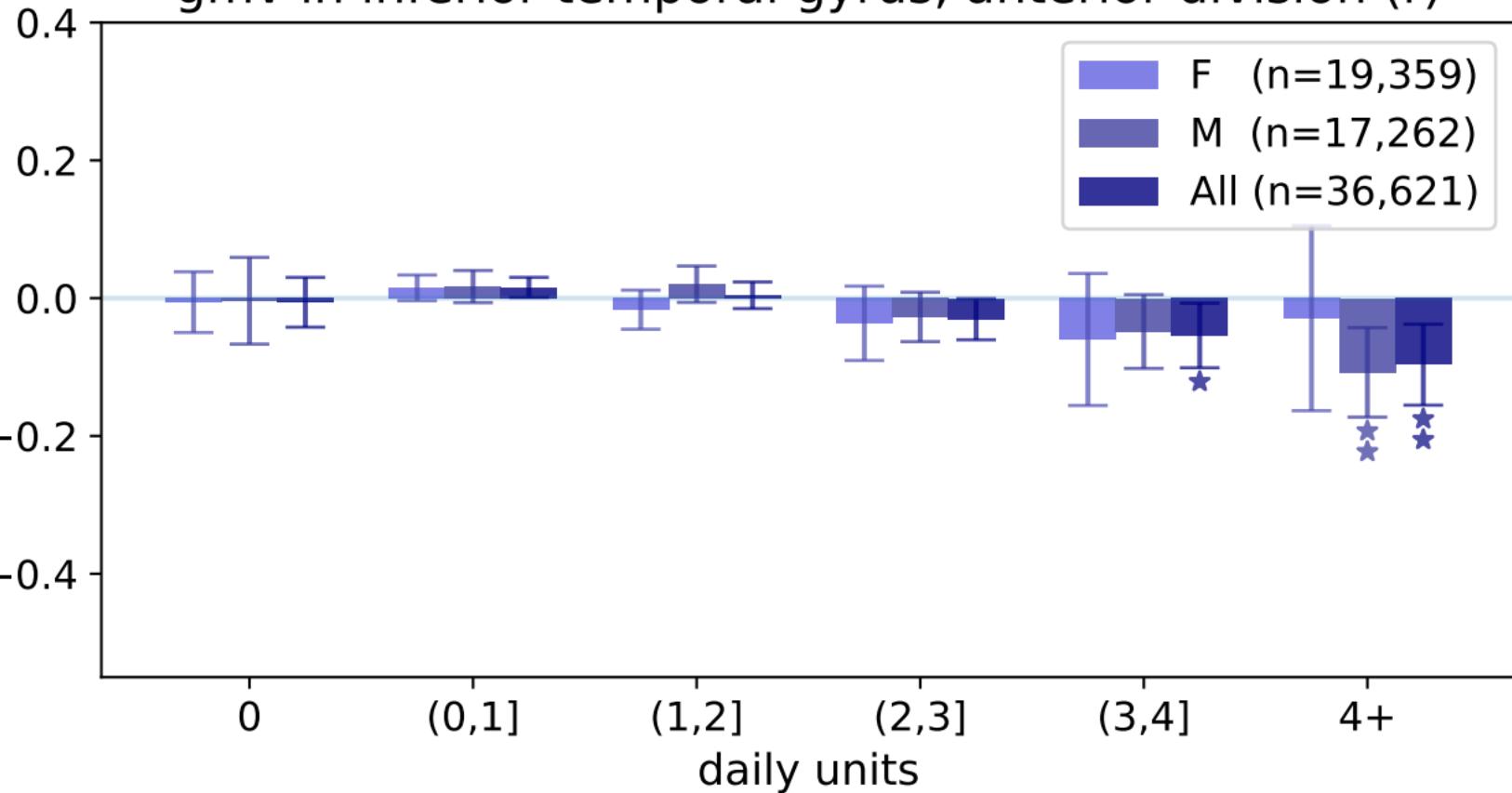
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in inferior temporal gyrus, anterior division (r)

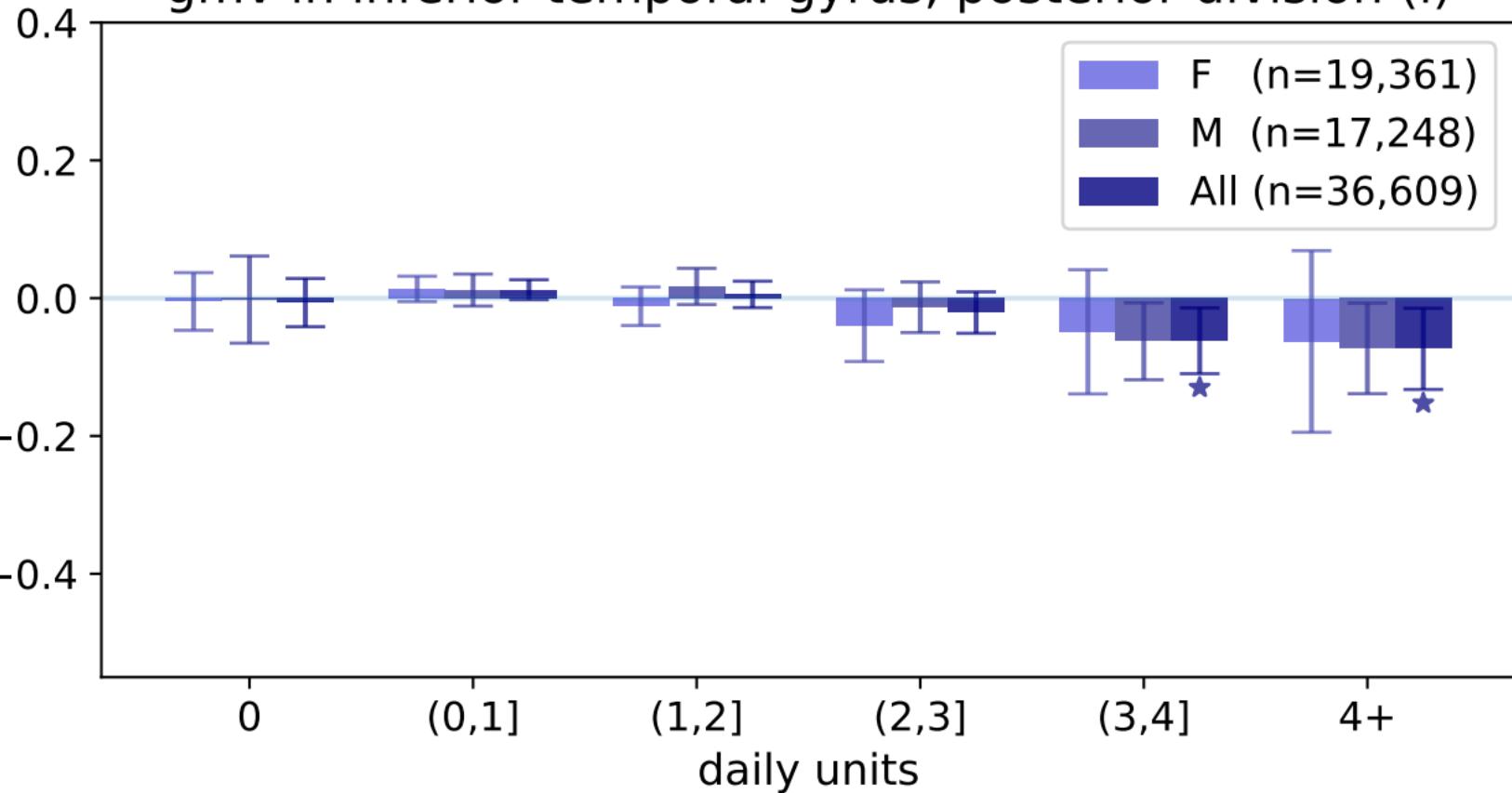
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in inferior temporal gyrus, posterior division (I)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in inferior temporal gyrus, posterior division (r)

mean residual (CI: 95%)

0.4

0.2

-0.2

-0.4

0

(0,1]

(1,2]

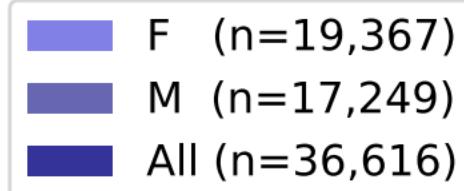
(2,3]

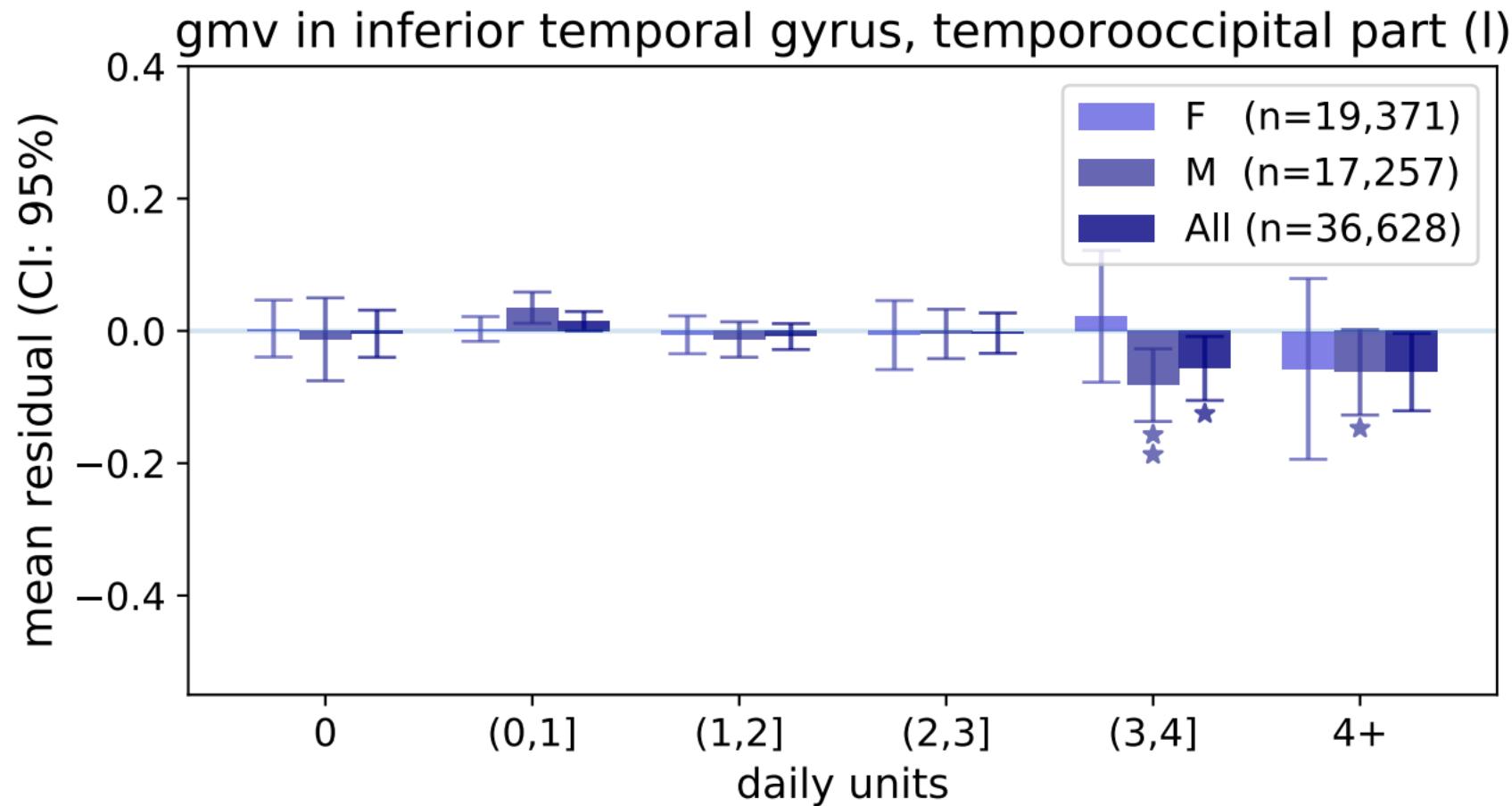
(3,4]

4+

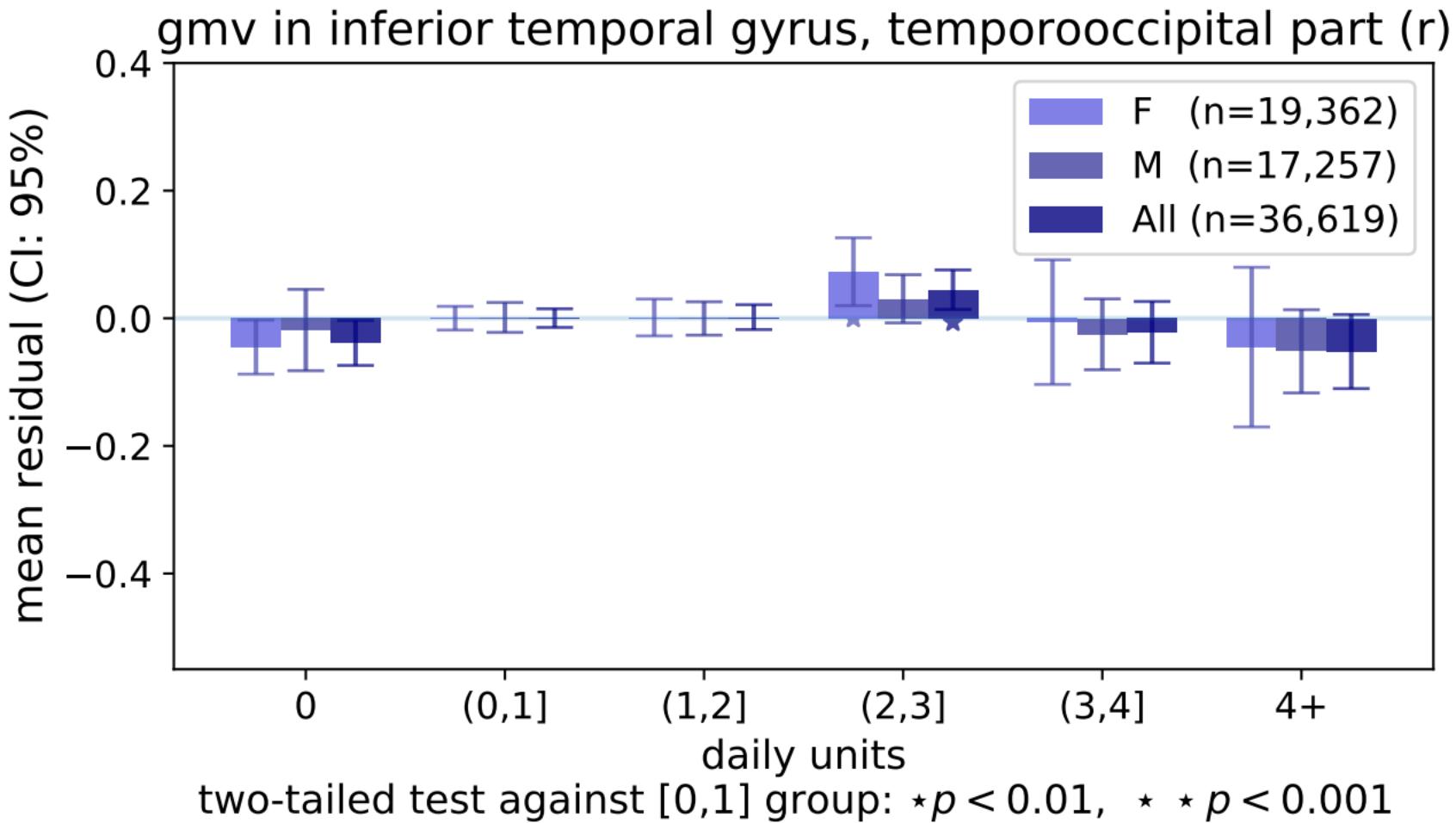
daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$



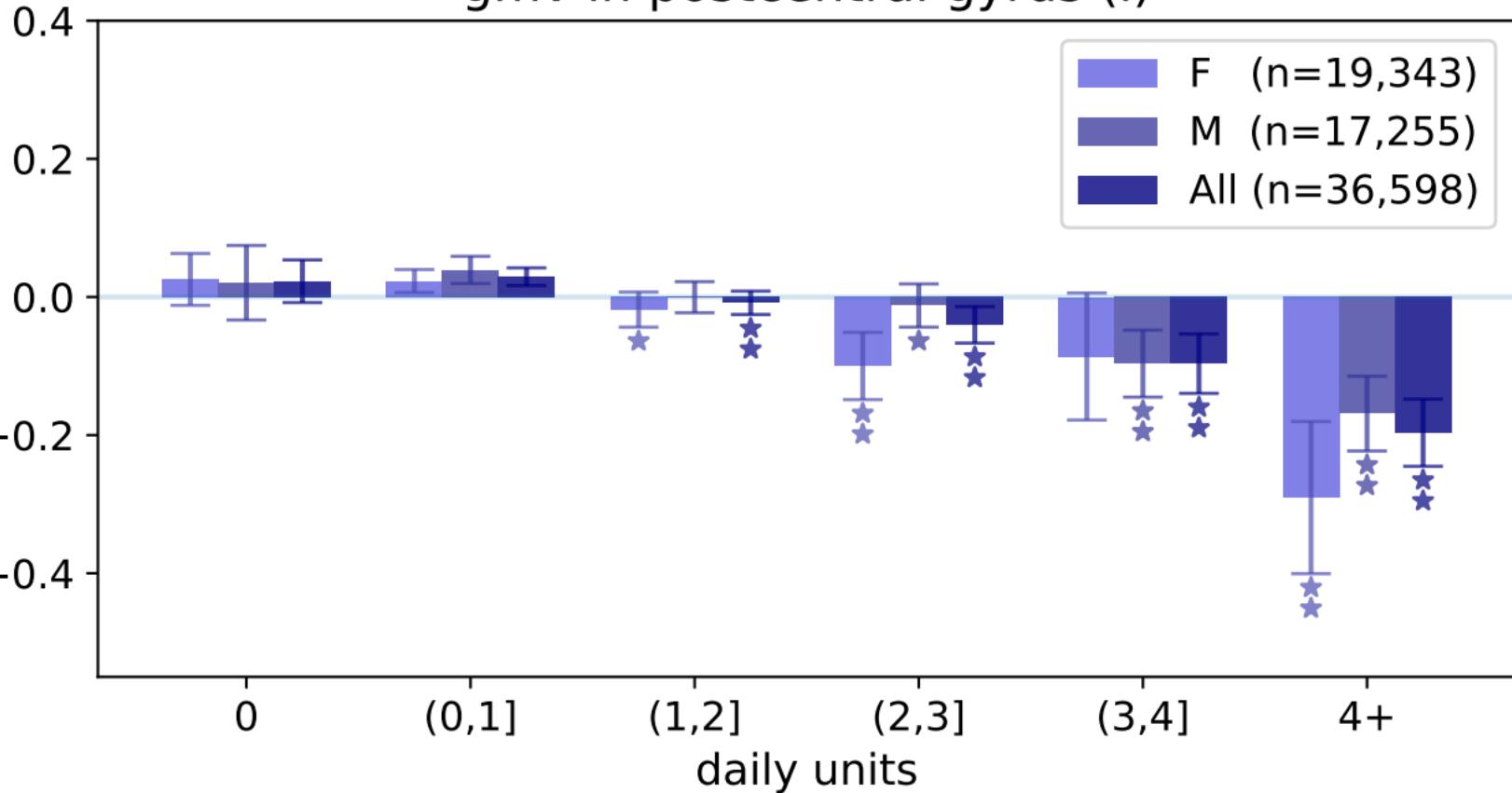


two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$



gmv in postcentral gyrus (I)

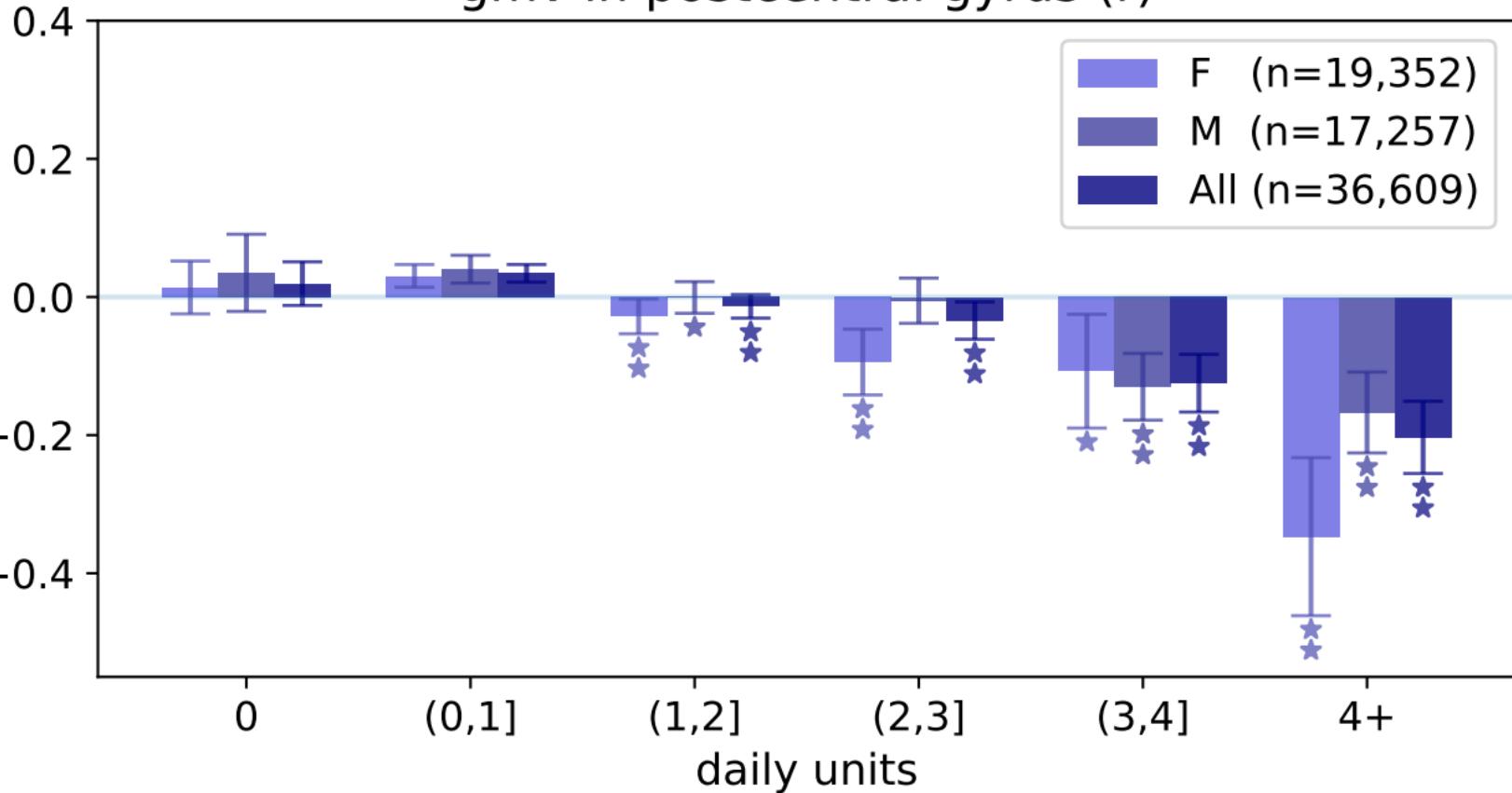
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

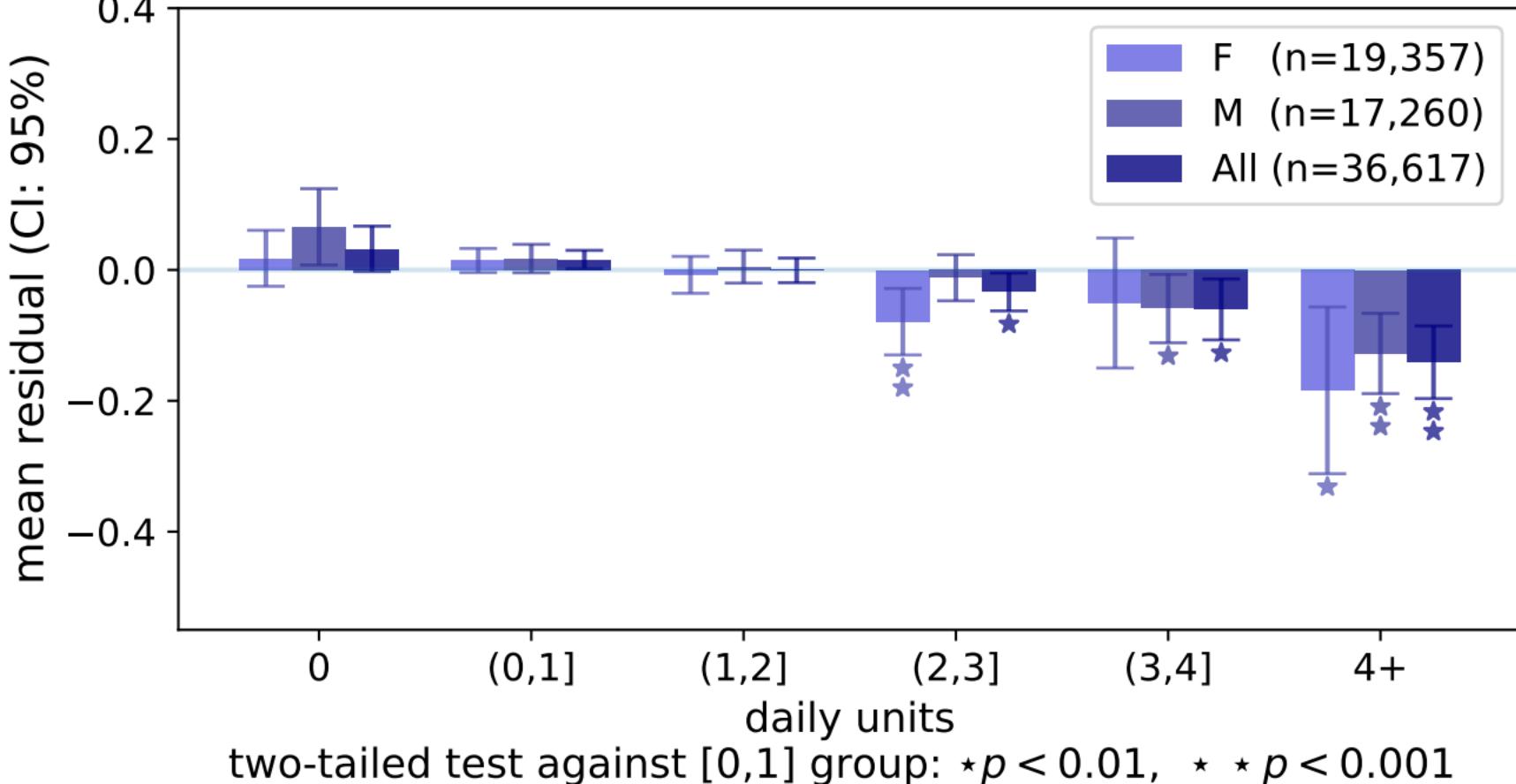
gmv in postcentral gyrus (r)

mean residual (CI: 95%)



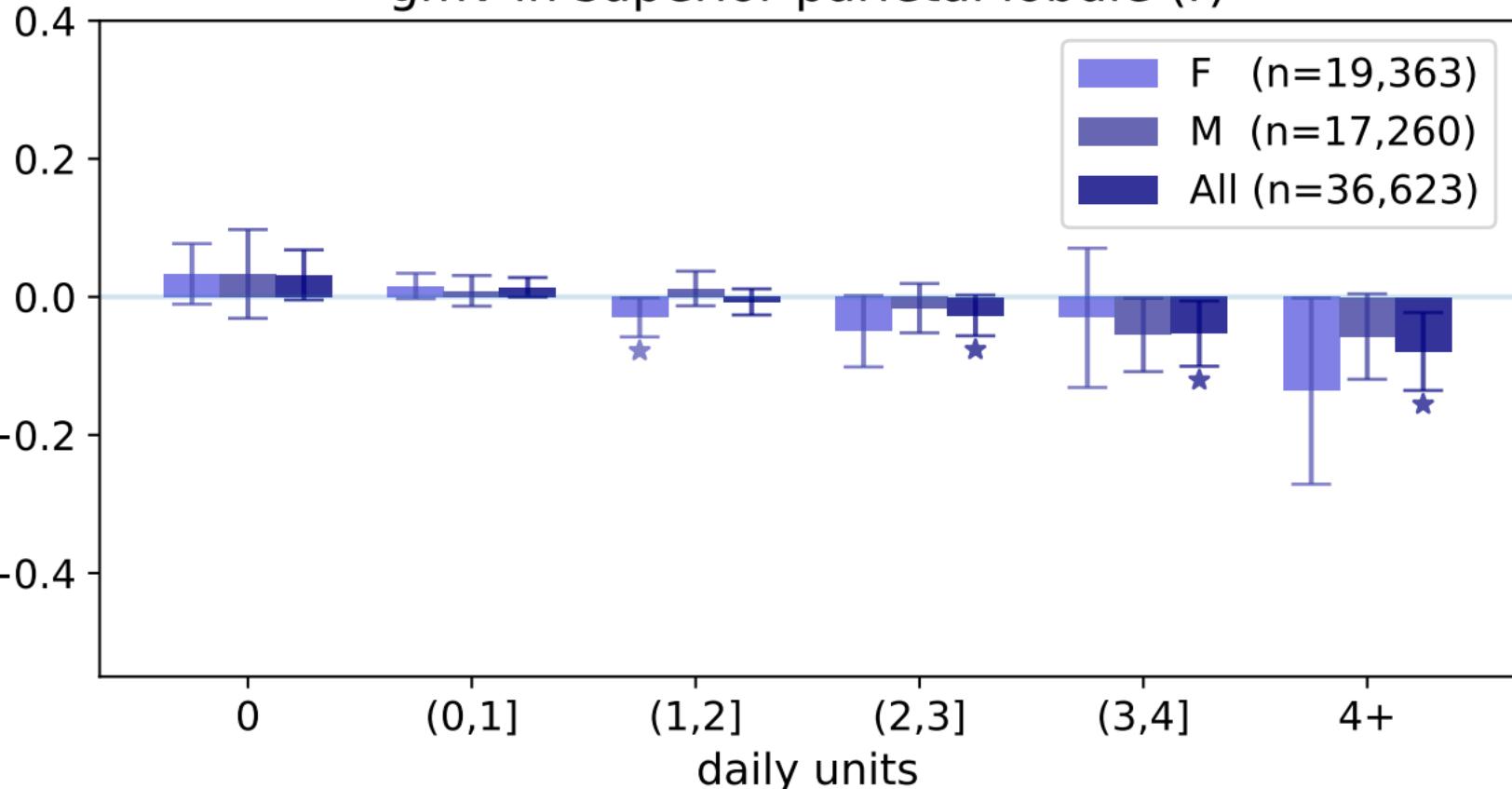
two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in superior parietal lobule (I)



gmv in superior parietal lobule (r)

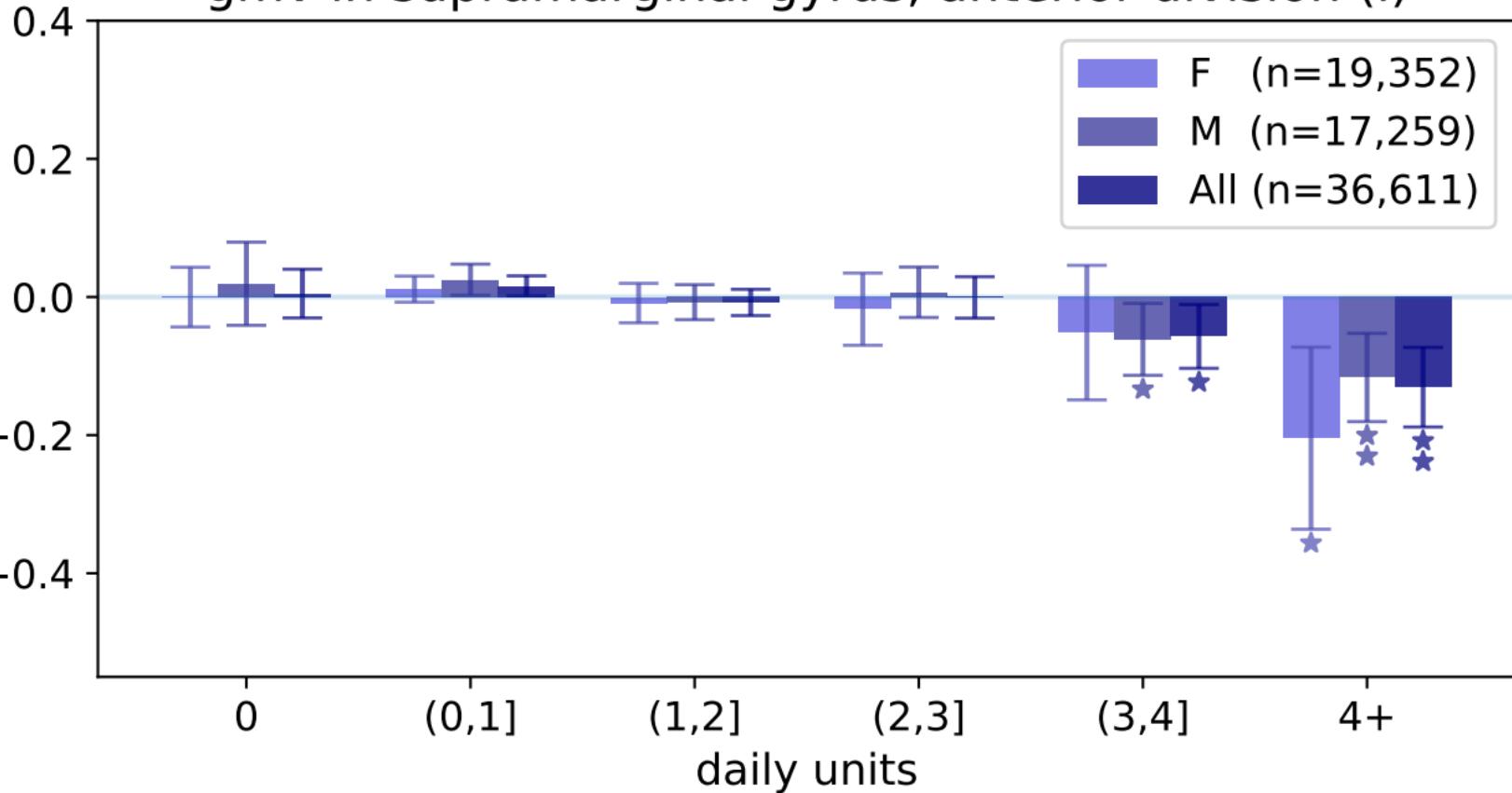
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in supramarginal gyrus, anterior division (I)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in supramarginal gyrus, anterior division (r)

mean residual (CI: 95%)

0.4

0.2

0.0

-0.2

-0.4

F (n=19,355)
M (n=17,257)
All (n=36,612)

0

(0,1]

(1,2]

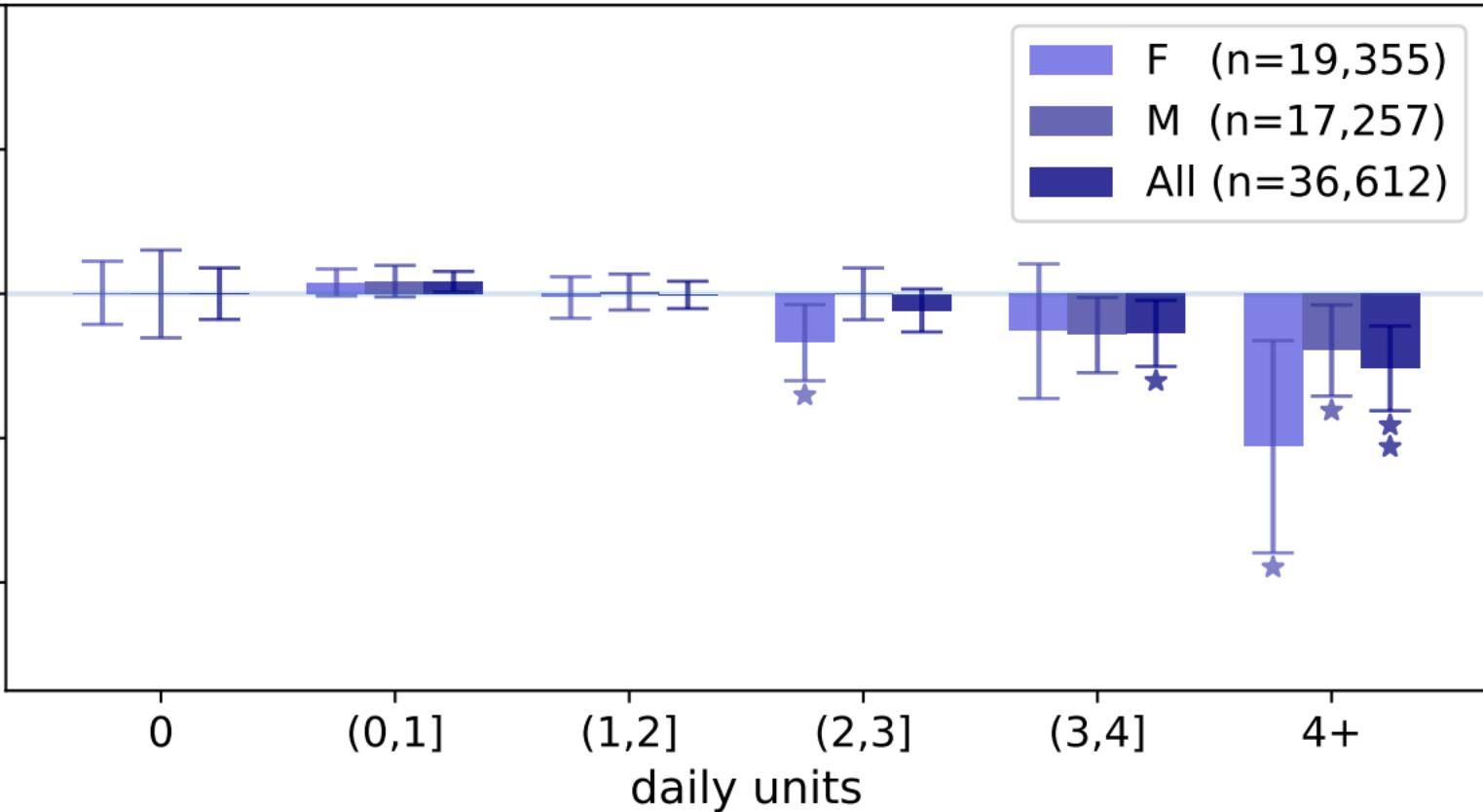
(2,3]

(3,4]

4+

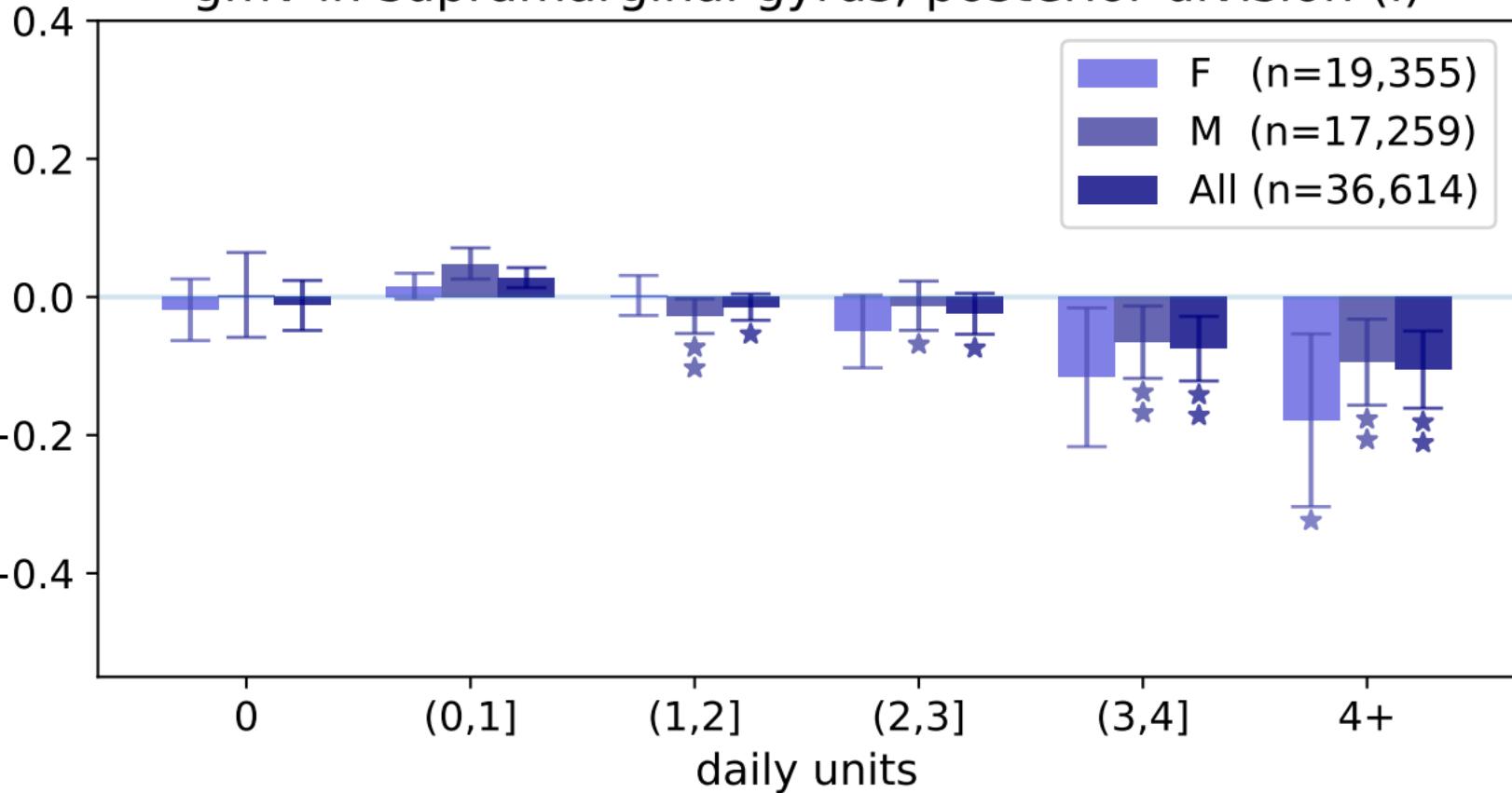
daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$



gmv in supramarginal gyrus, posterior division (I)

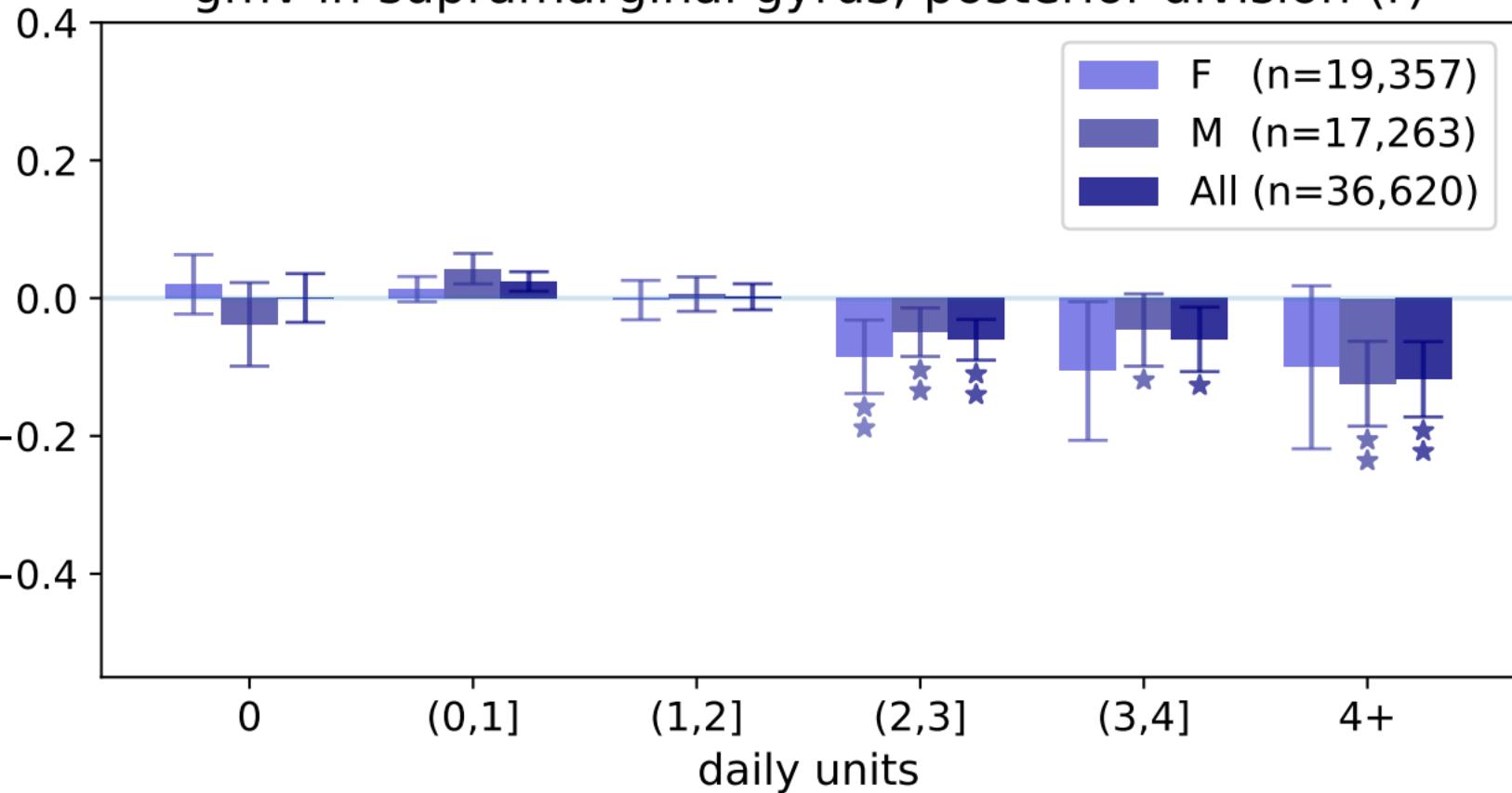
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

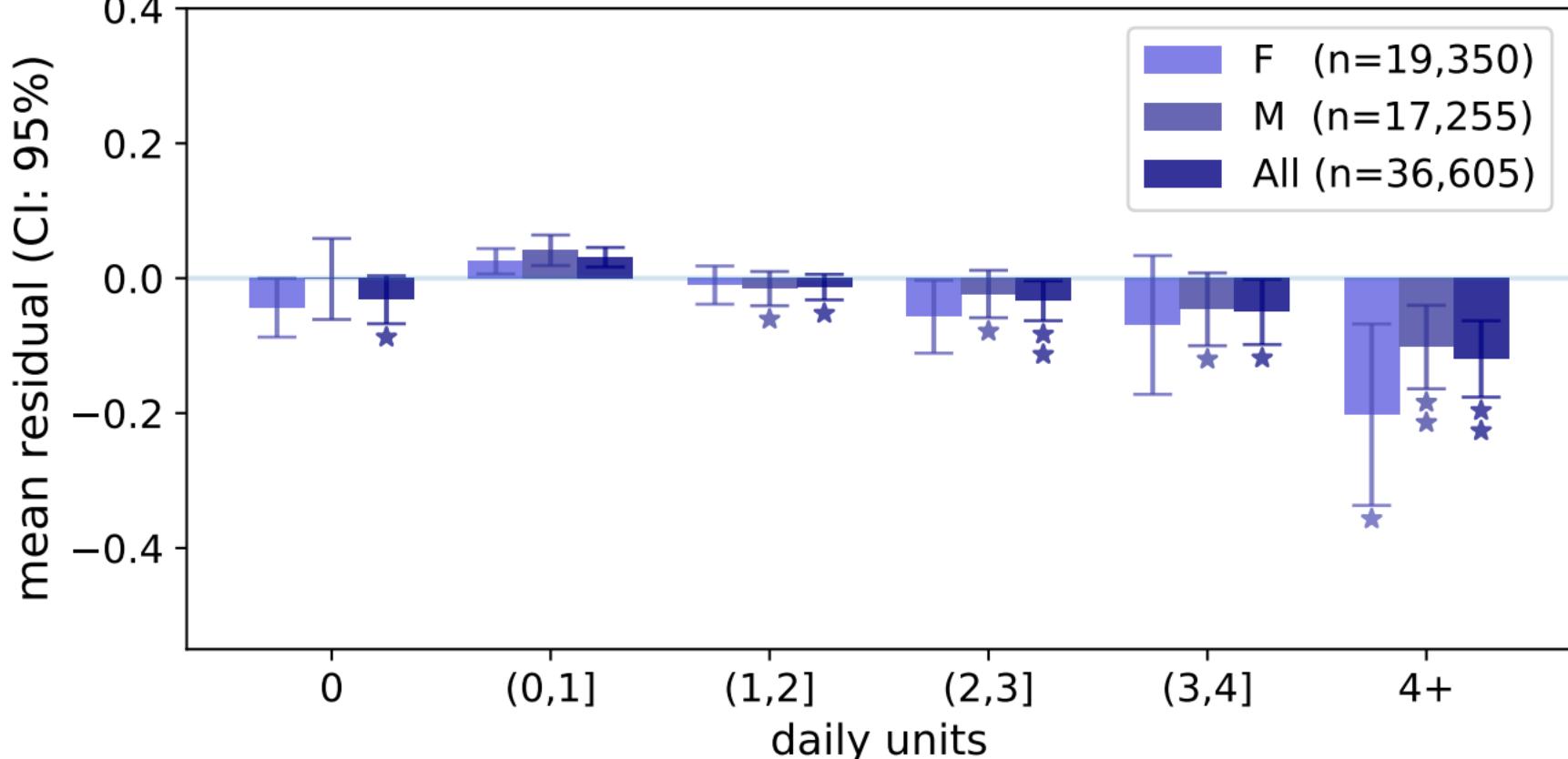
gmv in supramarginal gyrus, posterior division (r)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

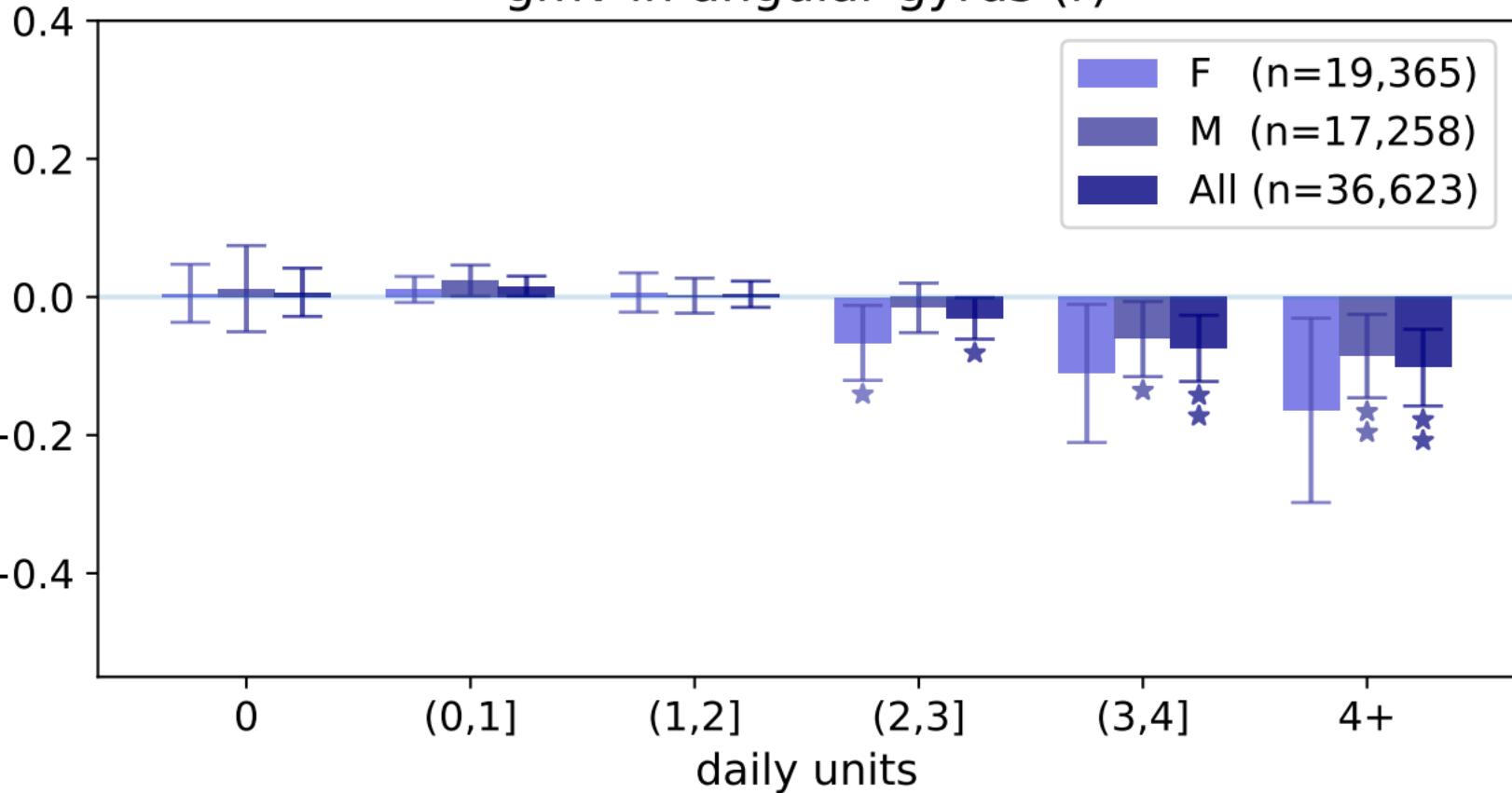
gmv in angular gyrus (l)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in angular gyrus (r)

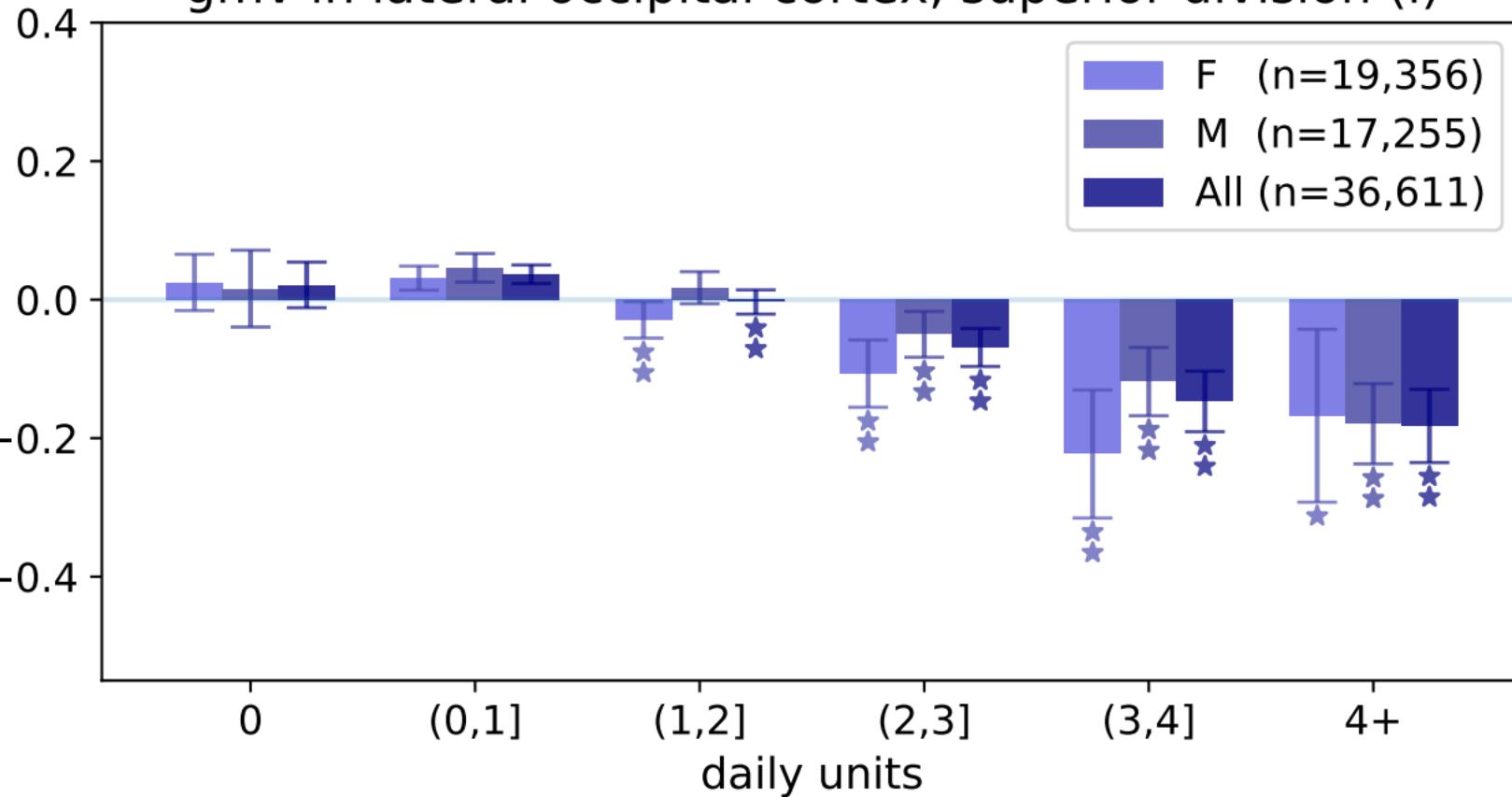
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in lateral occipital cortex, superior division (I)

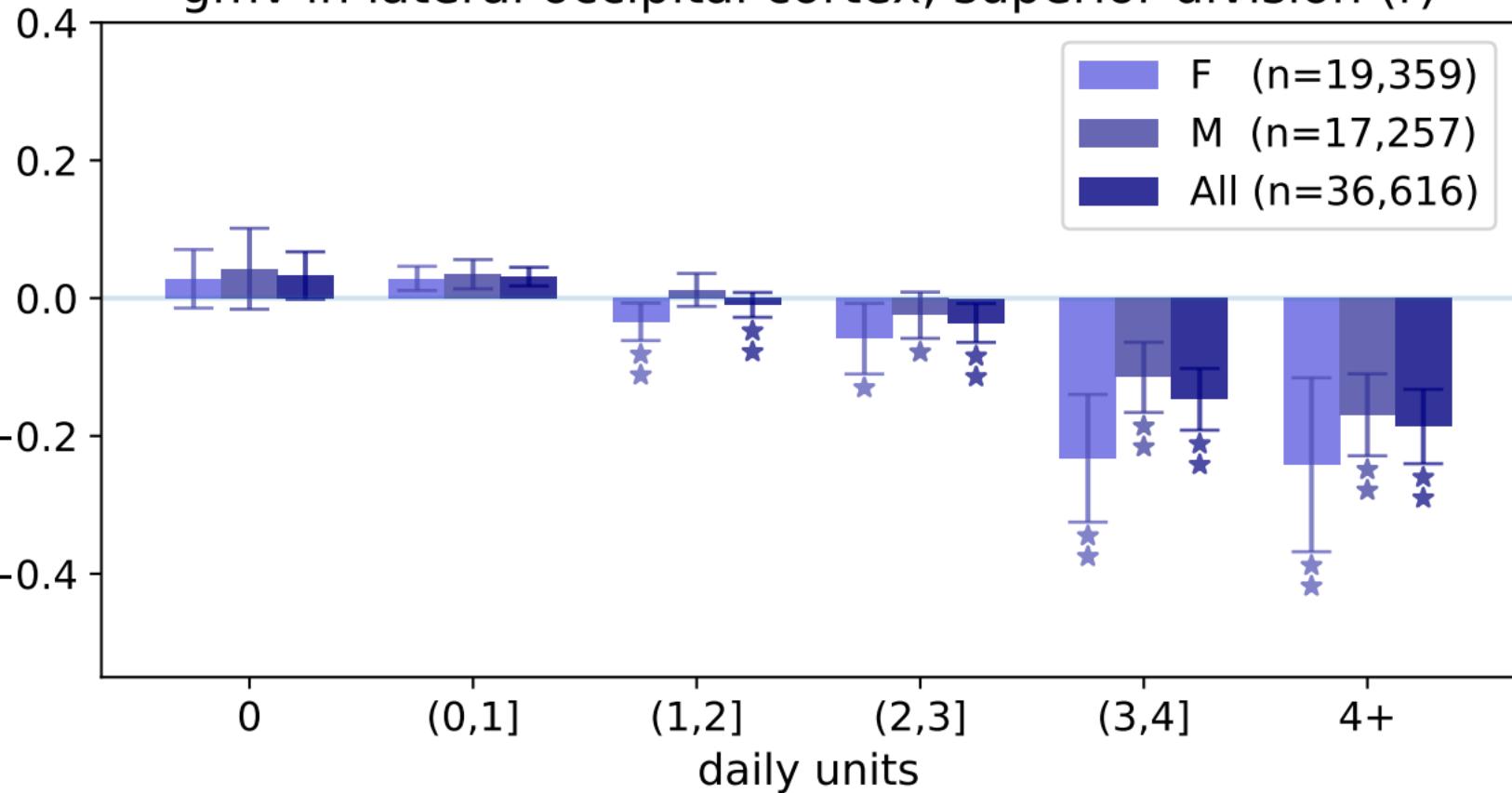
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in lateral occipital cortex, superior division (r)

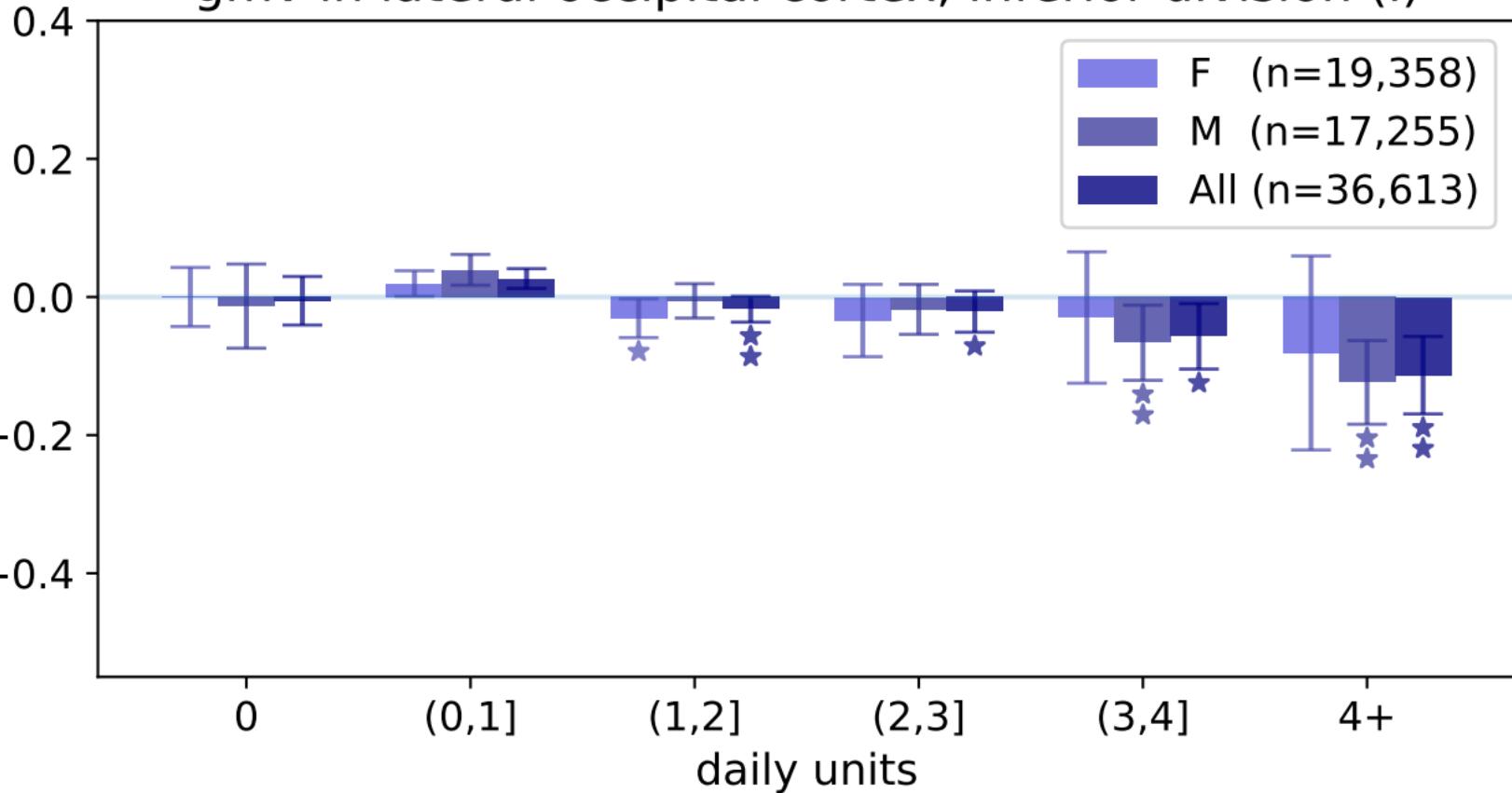
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in lateral occipital cortex, inferior division (I)

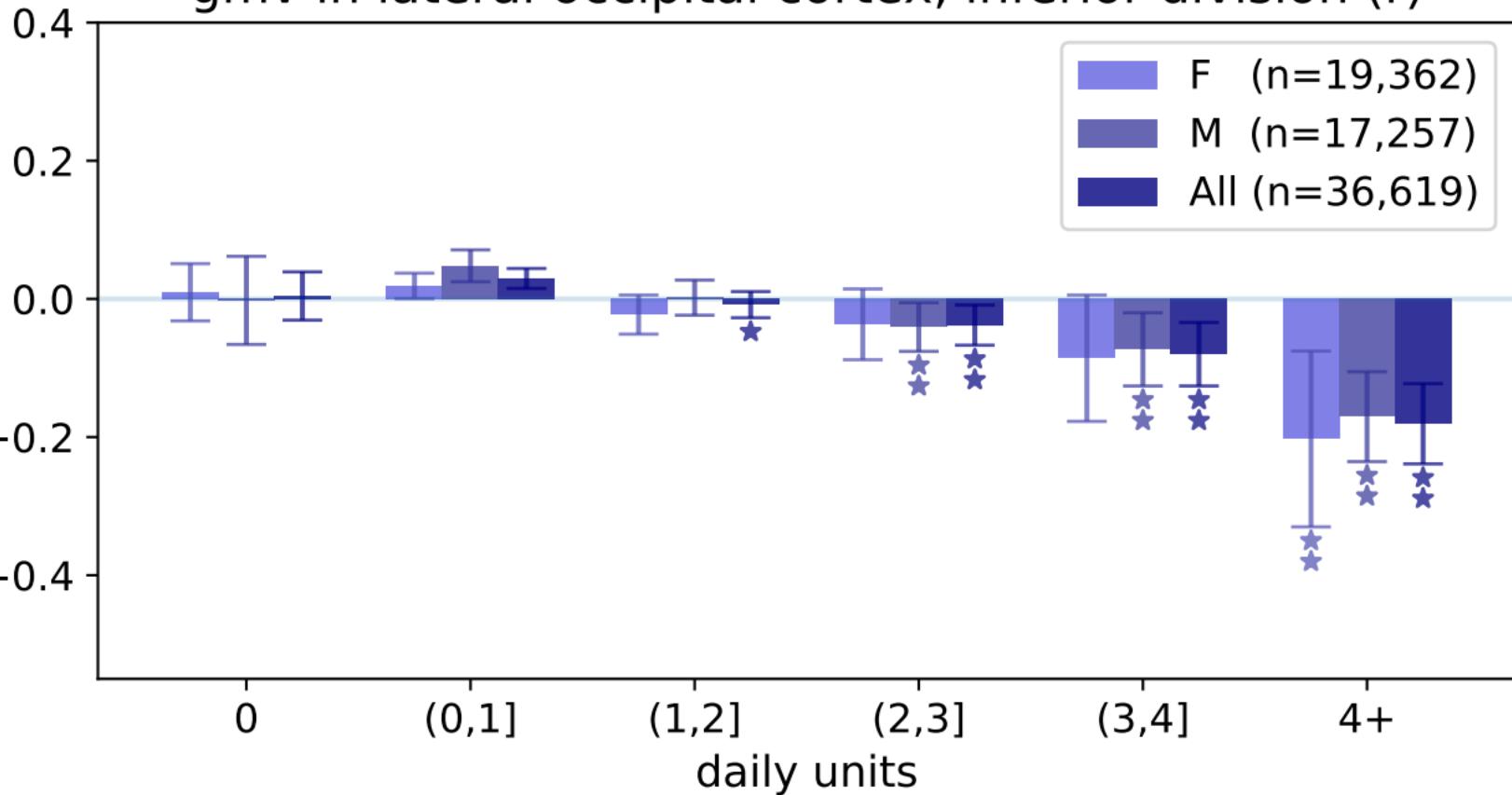
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in lateral occipital cortex, inferior division (r)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in intracalcarine cortex (I)

mean residual (CI: 95%)

0.4

0.2

-0.2

-0.4

0

(0,1]

(1,2]

(2,3]

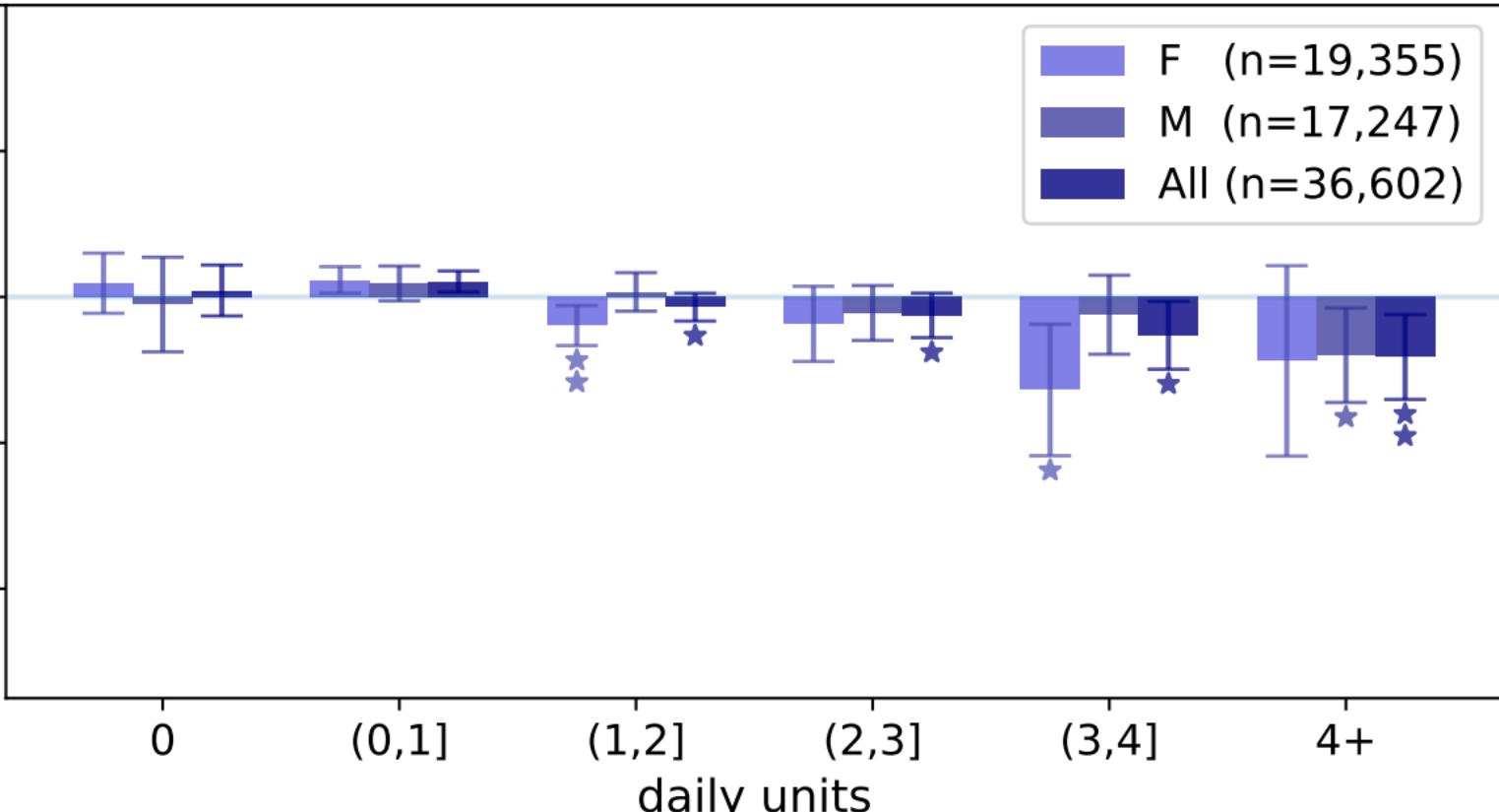
(3,4]

4+

daily units

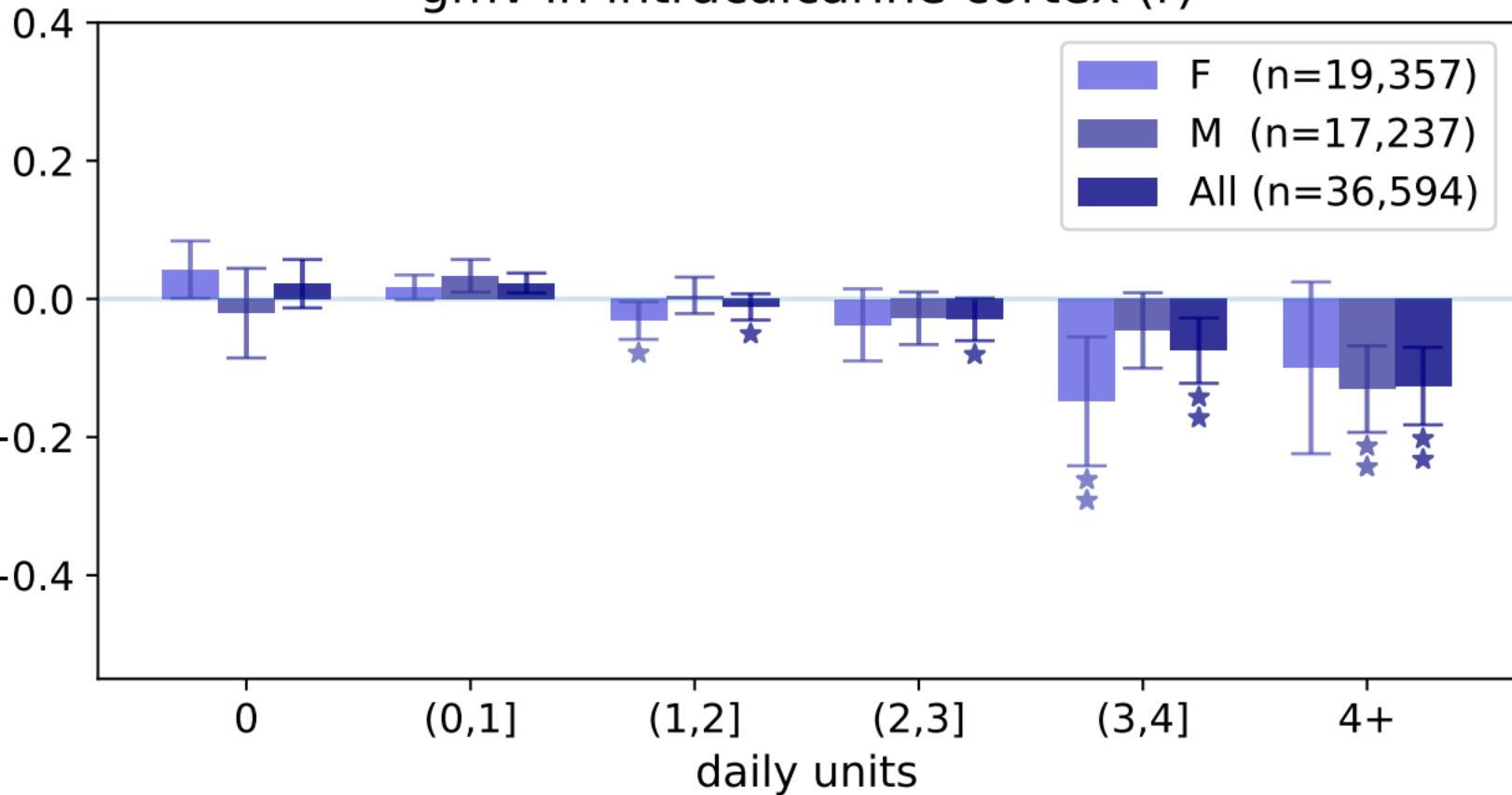
F (n=19,355)
M (n=17,247)
All (n=36,602)

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$



gmv in intracalcarine cortex (r)

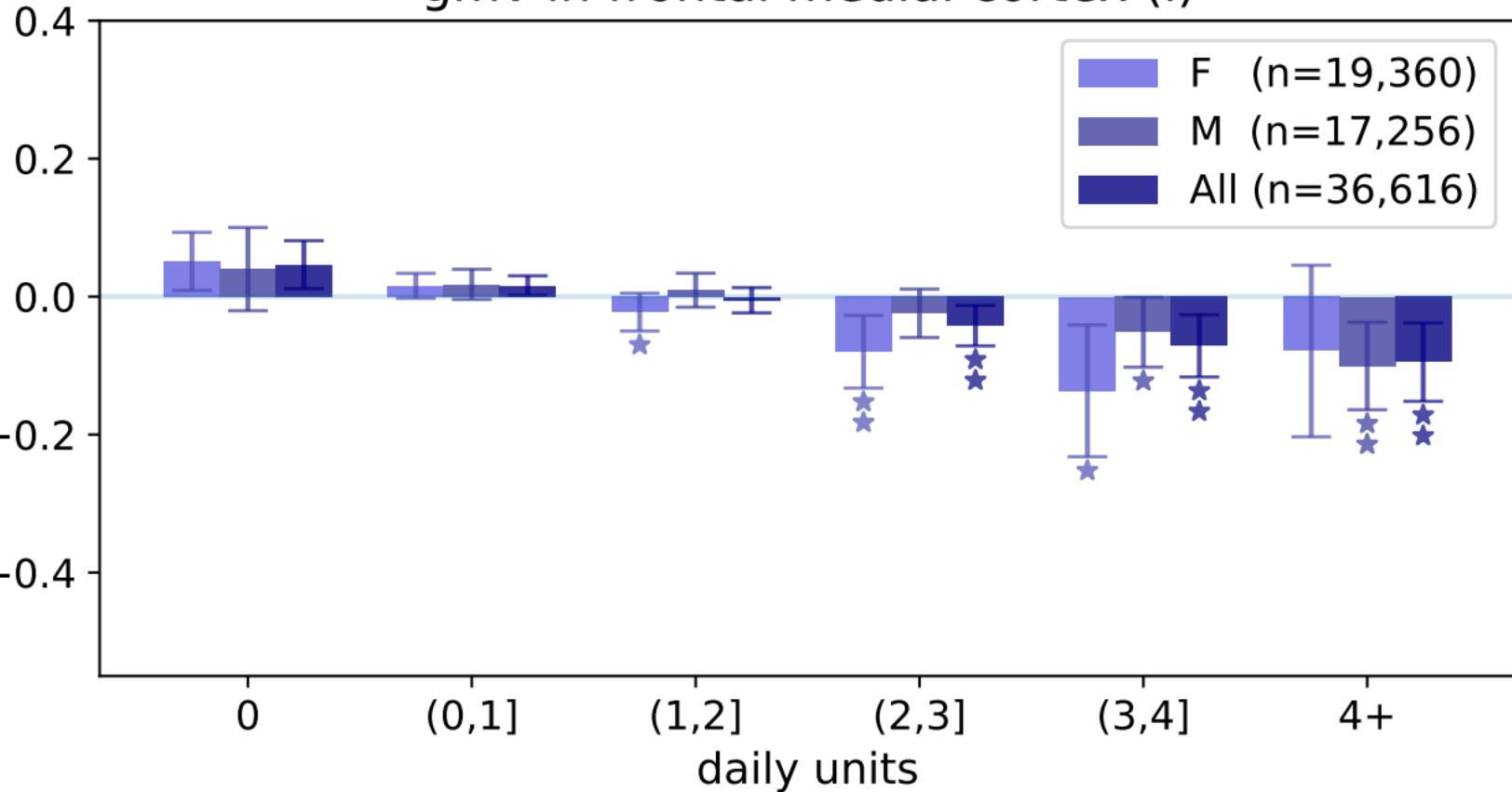
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

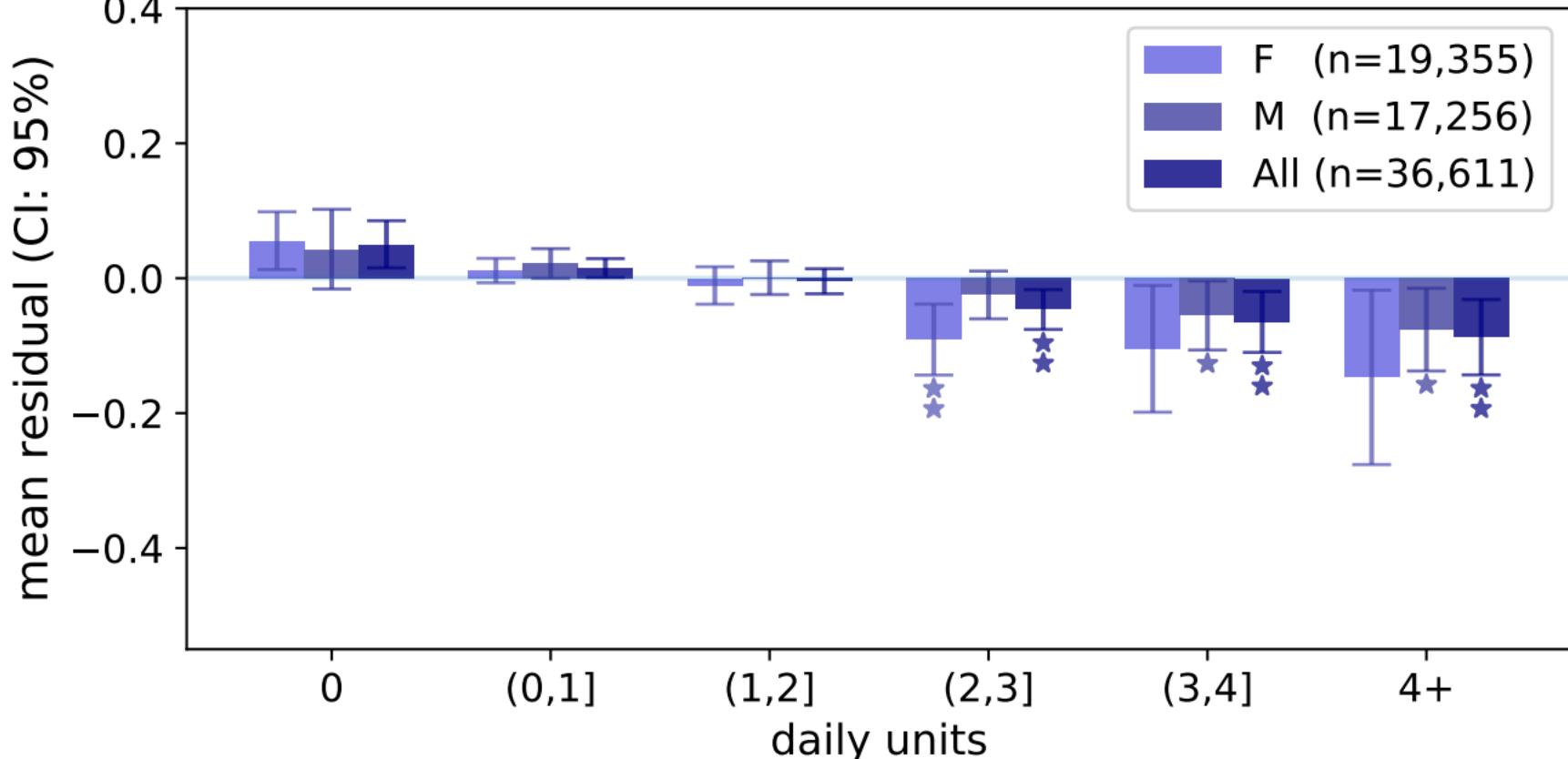
gmv in frontal medial cortex (I)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

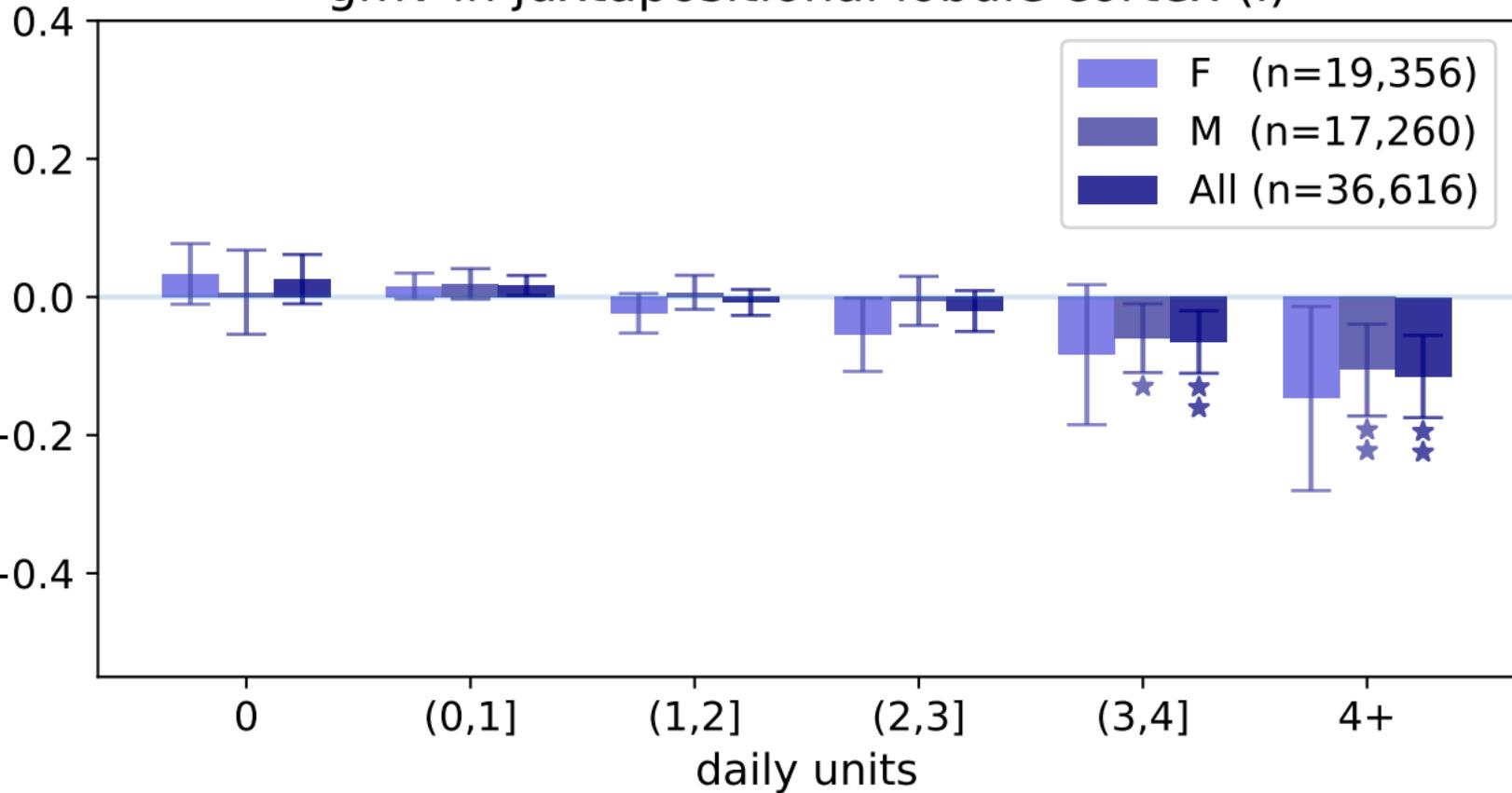
gmv in frontal medial cortex (r)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in juxtapositional lobule cortex (I)

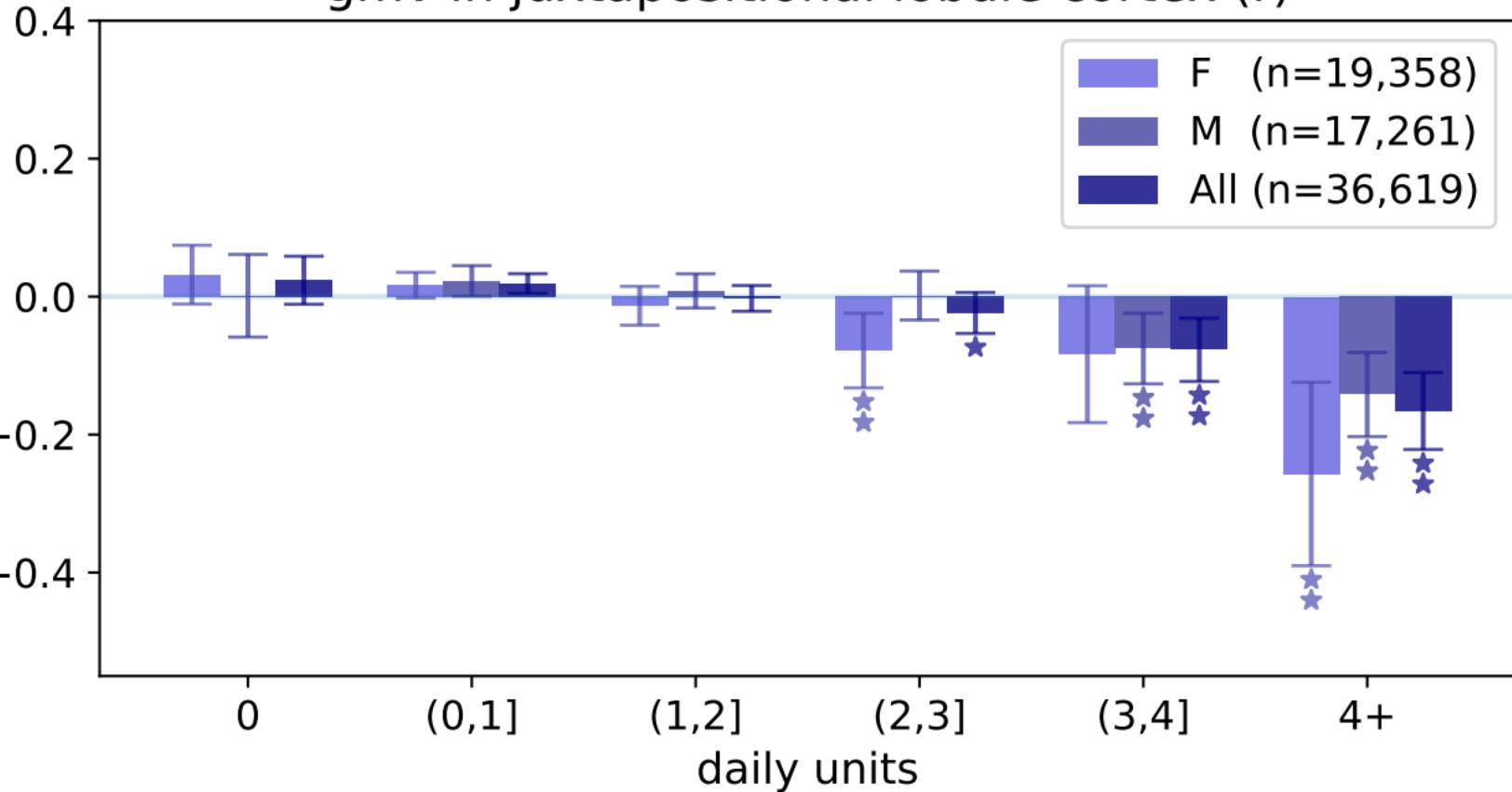
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in juxtapositional lobule cortex (r)

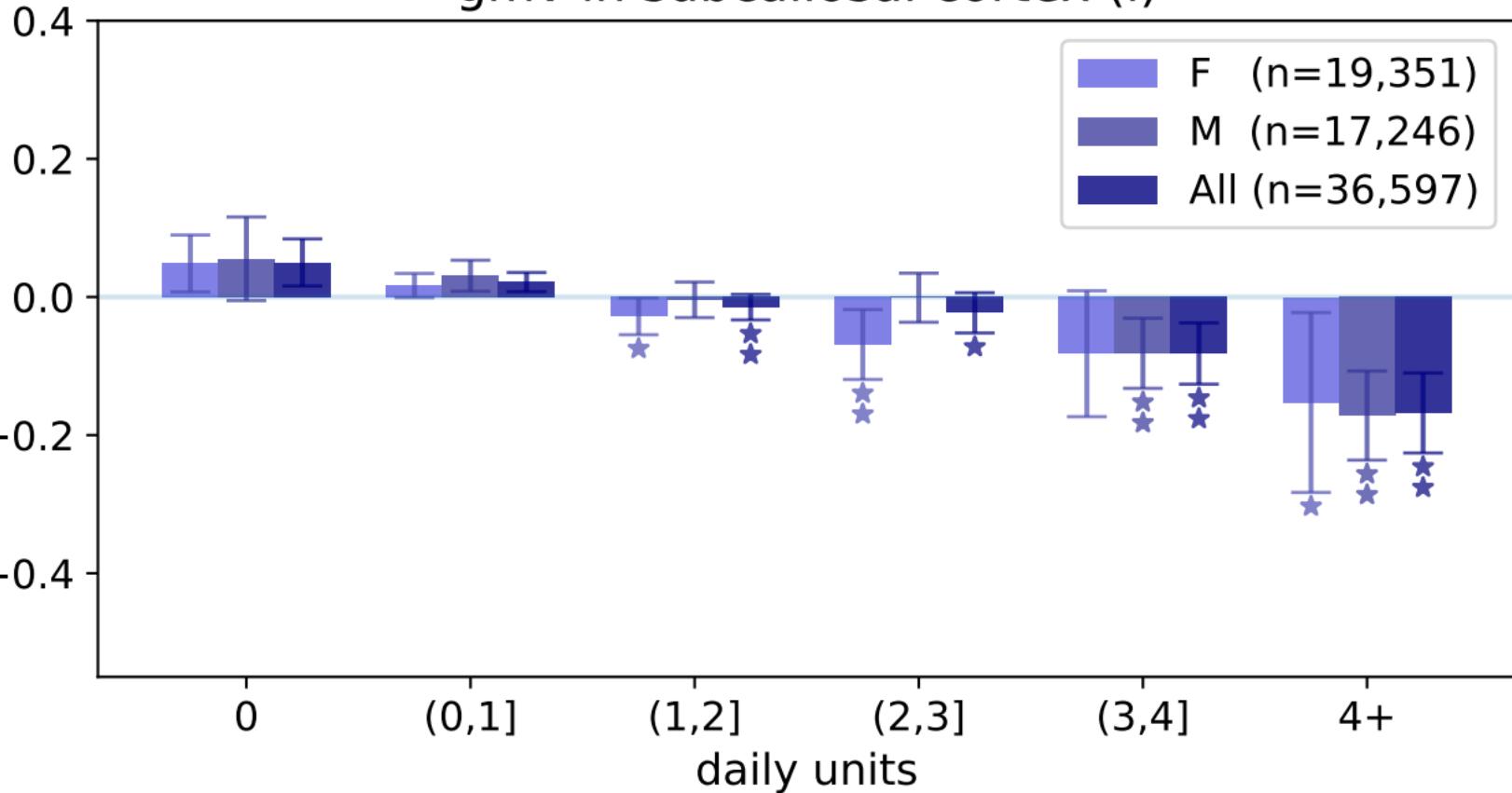
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in subcallosal cortex (I)

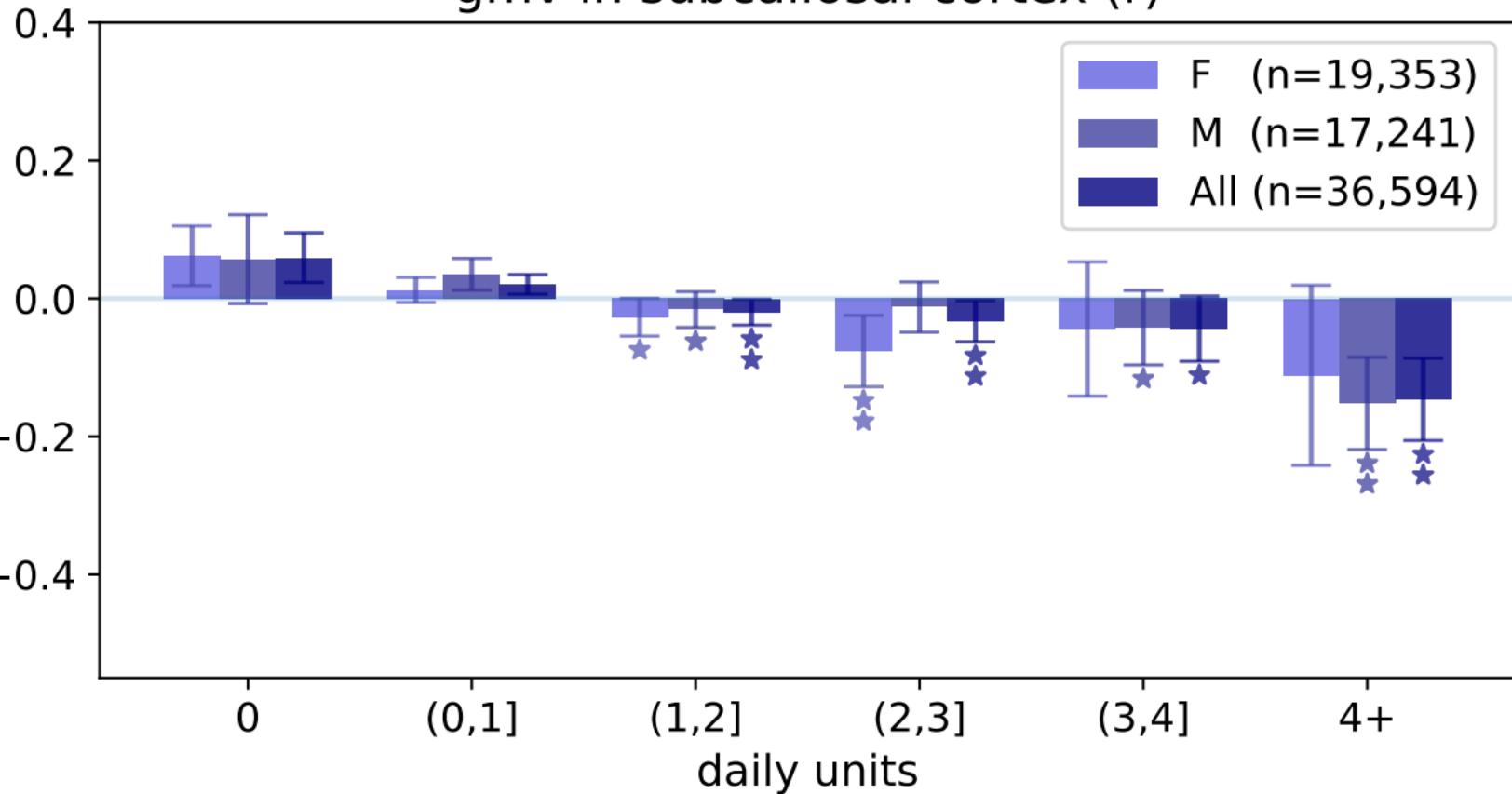
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in subcallosal cortex (r)

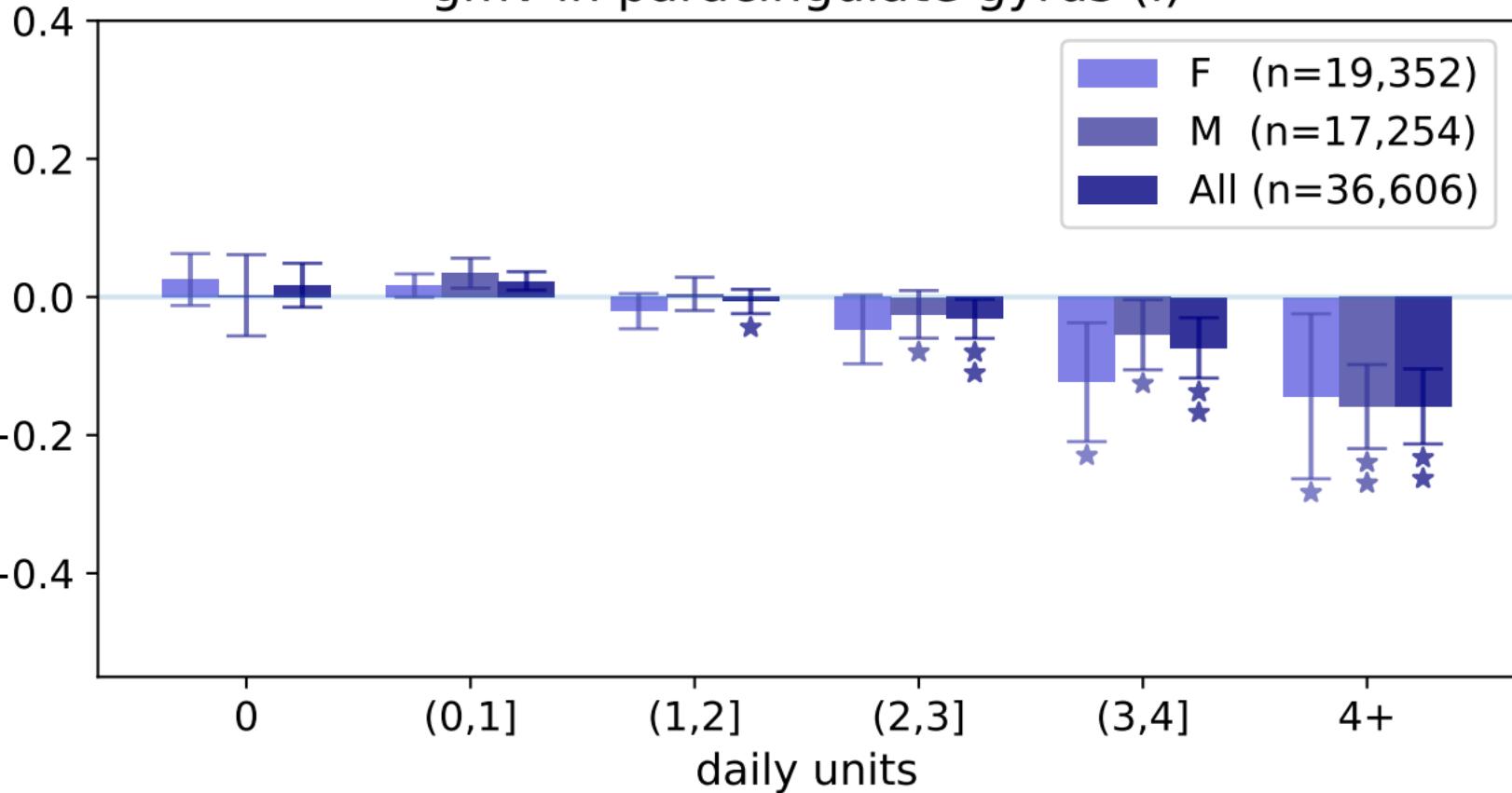
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in paracingulate gyrus (I)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in paracingulate gyrus (r)

mean residual (CI: 95%)

0.4

0.2

-0.2

-0.4

0

(0,1]

(1,2]

(2,3]

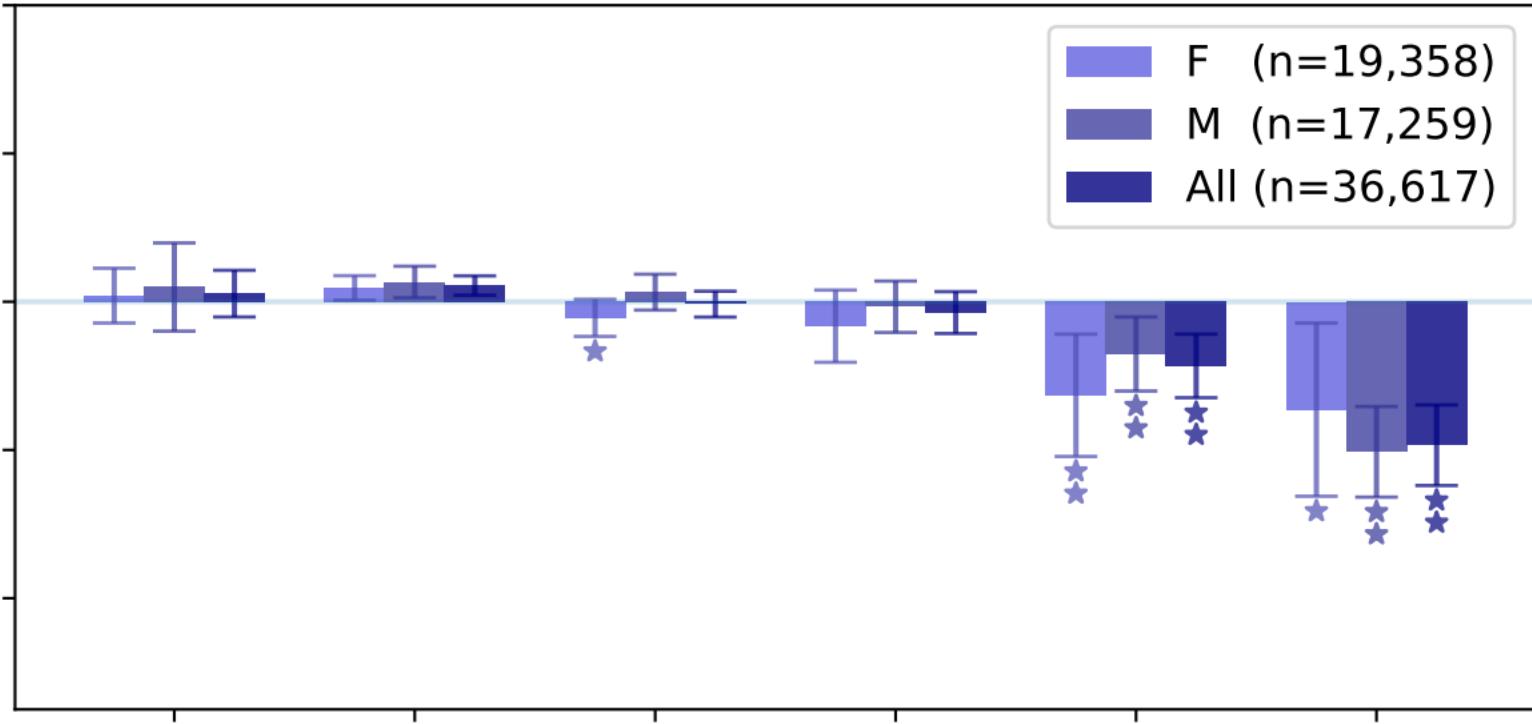
(3,4]

4+

daily units

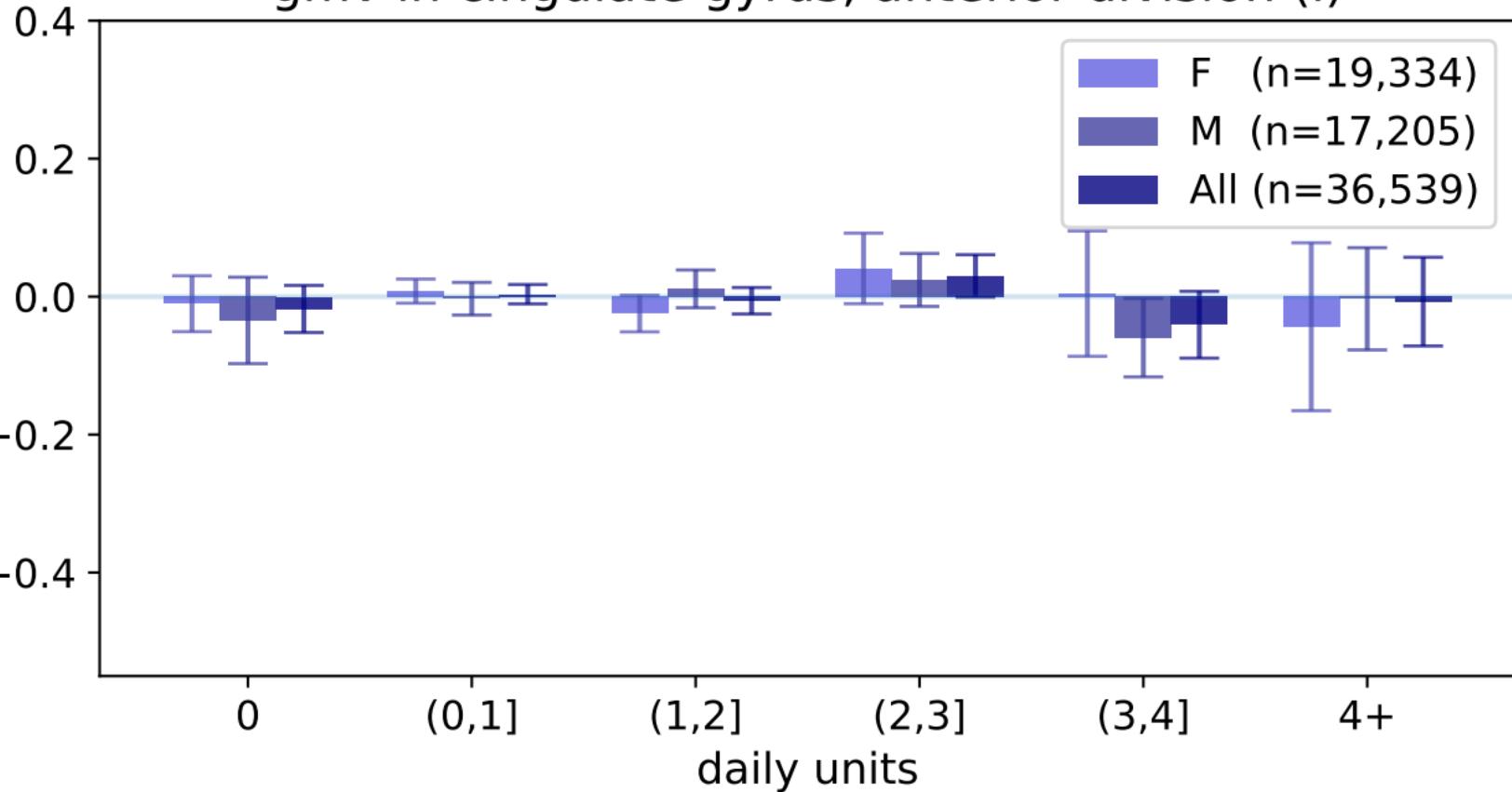
two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

F (n=19,358)
M (n=17,259)
All (n=36,617)



gmv in cingulate gyrus, anterior division (I)

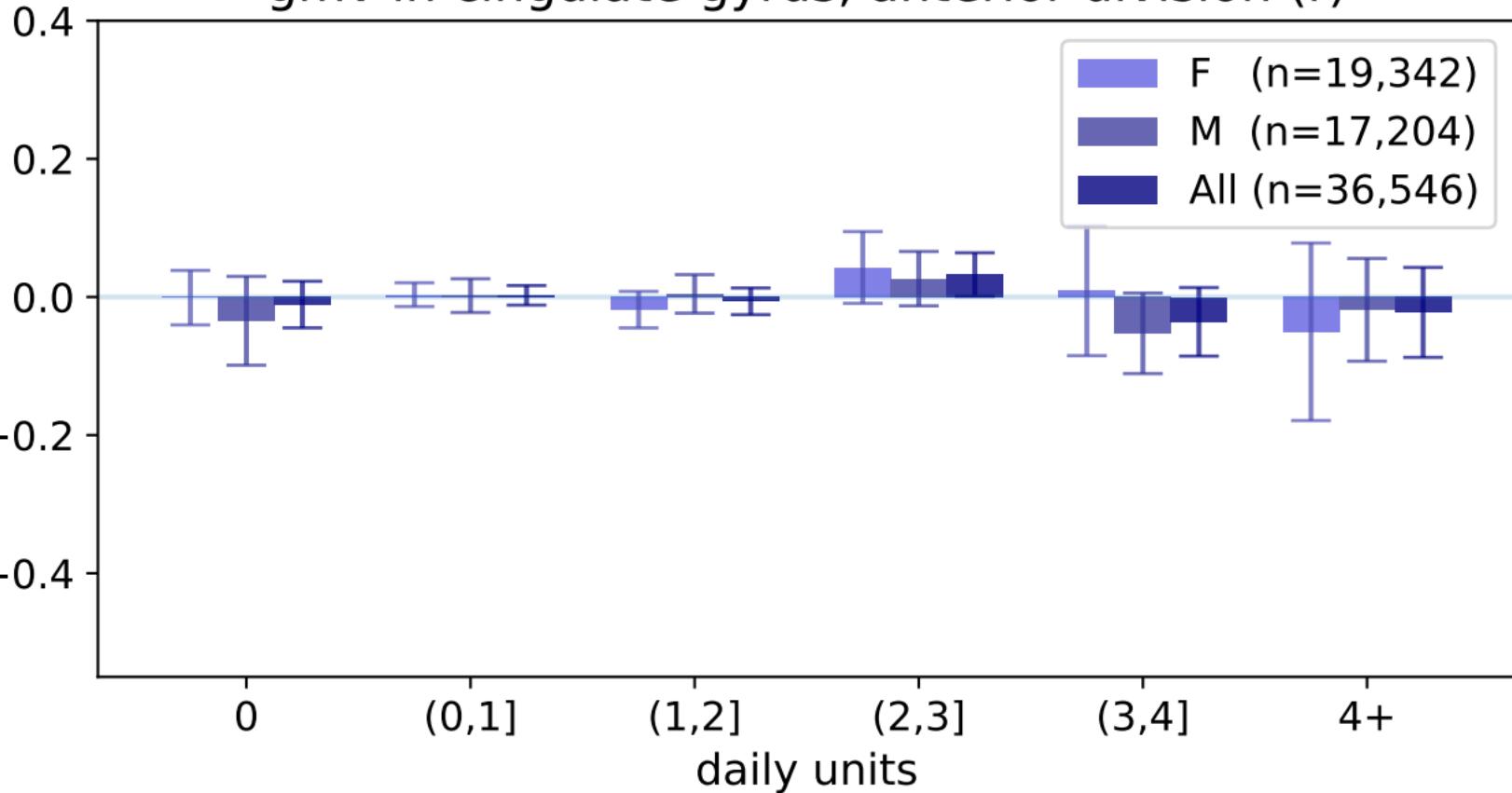
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in cingulate gyrus, anterior division (r)

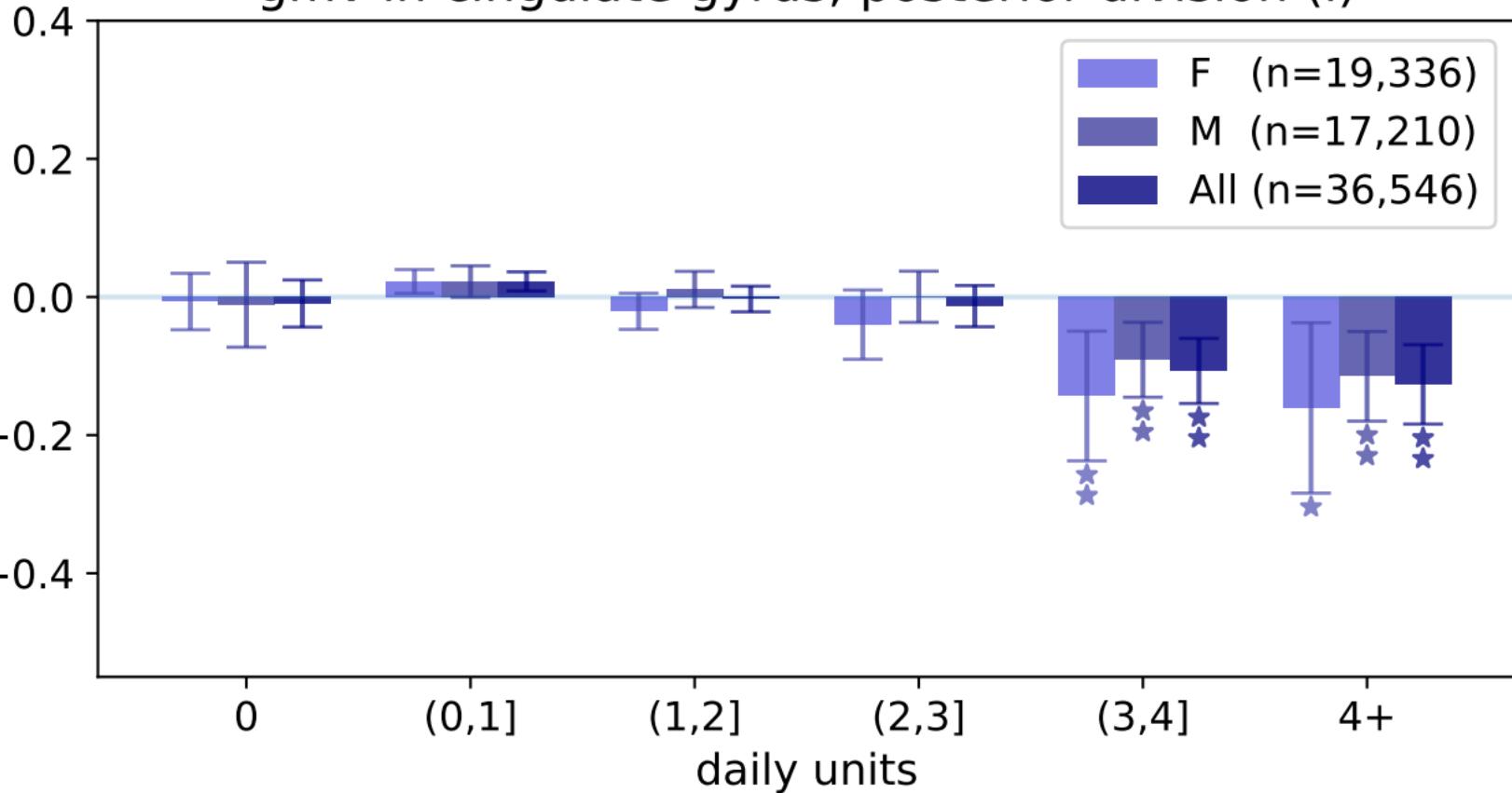
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in cingulate gyrus, posterior division (I)

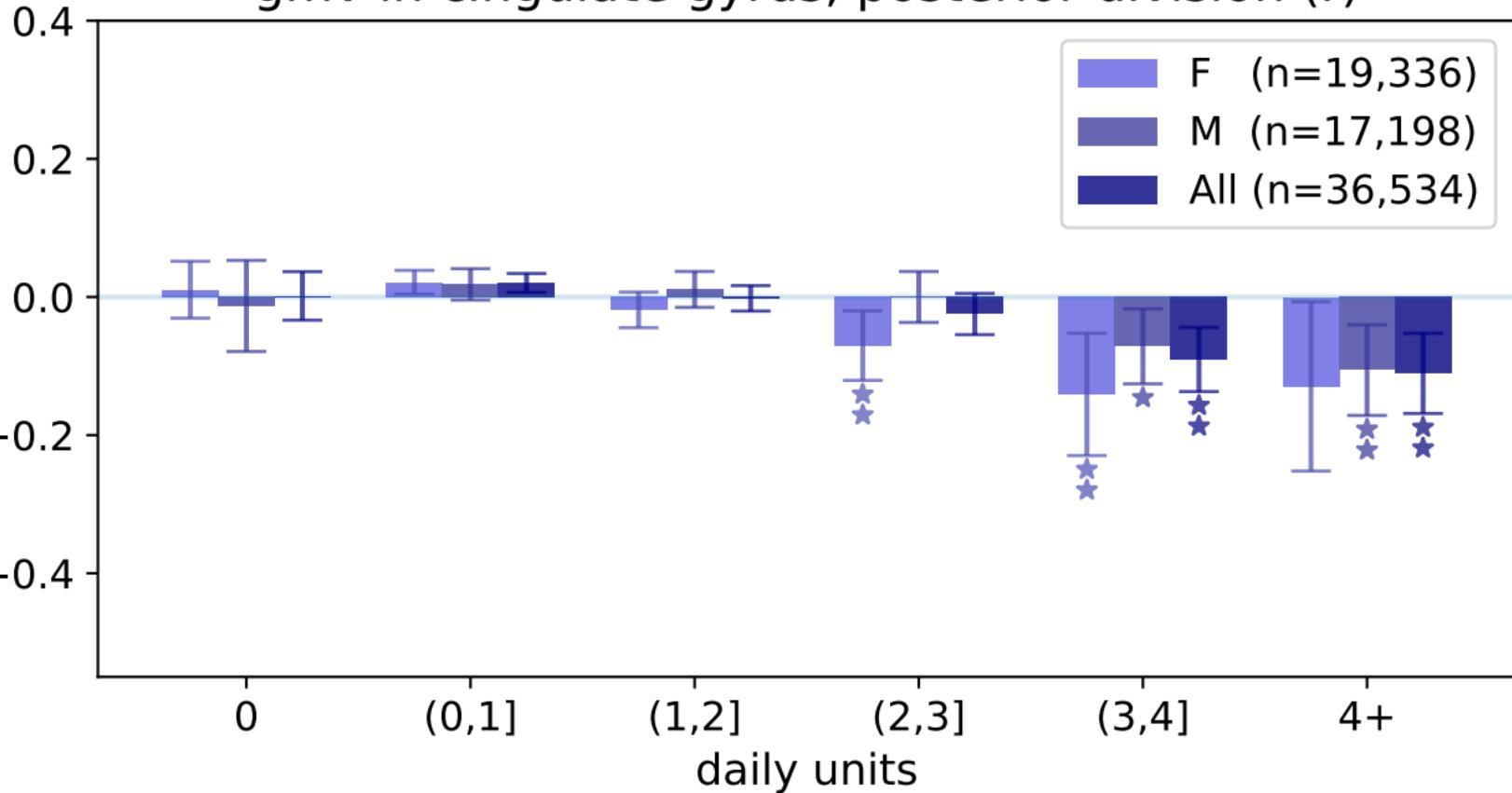
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in cingulate gyrus, posterior division (r)

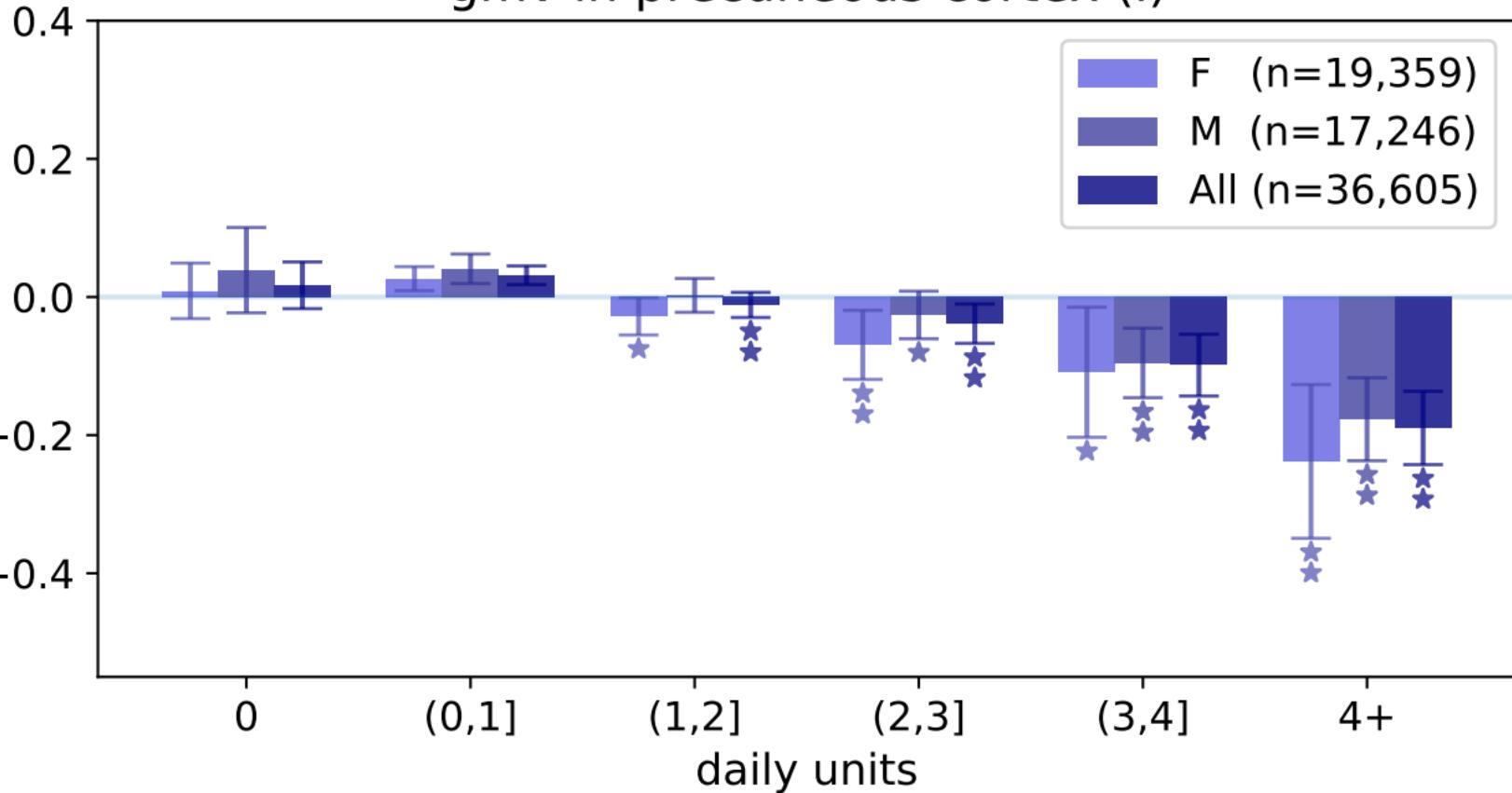
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in precuneous cortex (I)

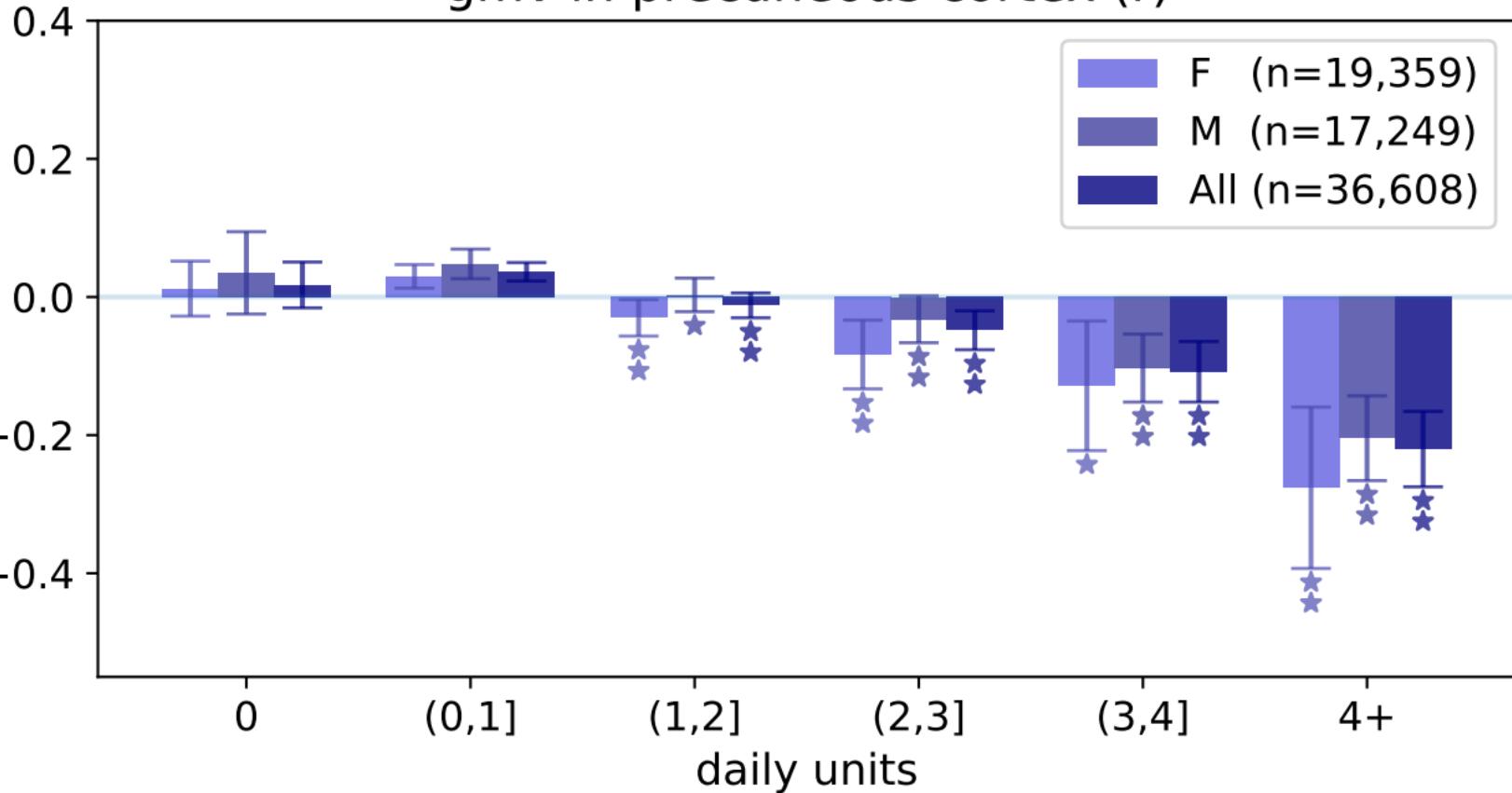
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in precuneous cortex (r)

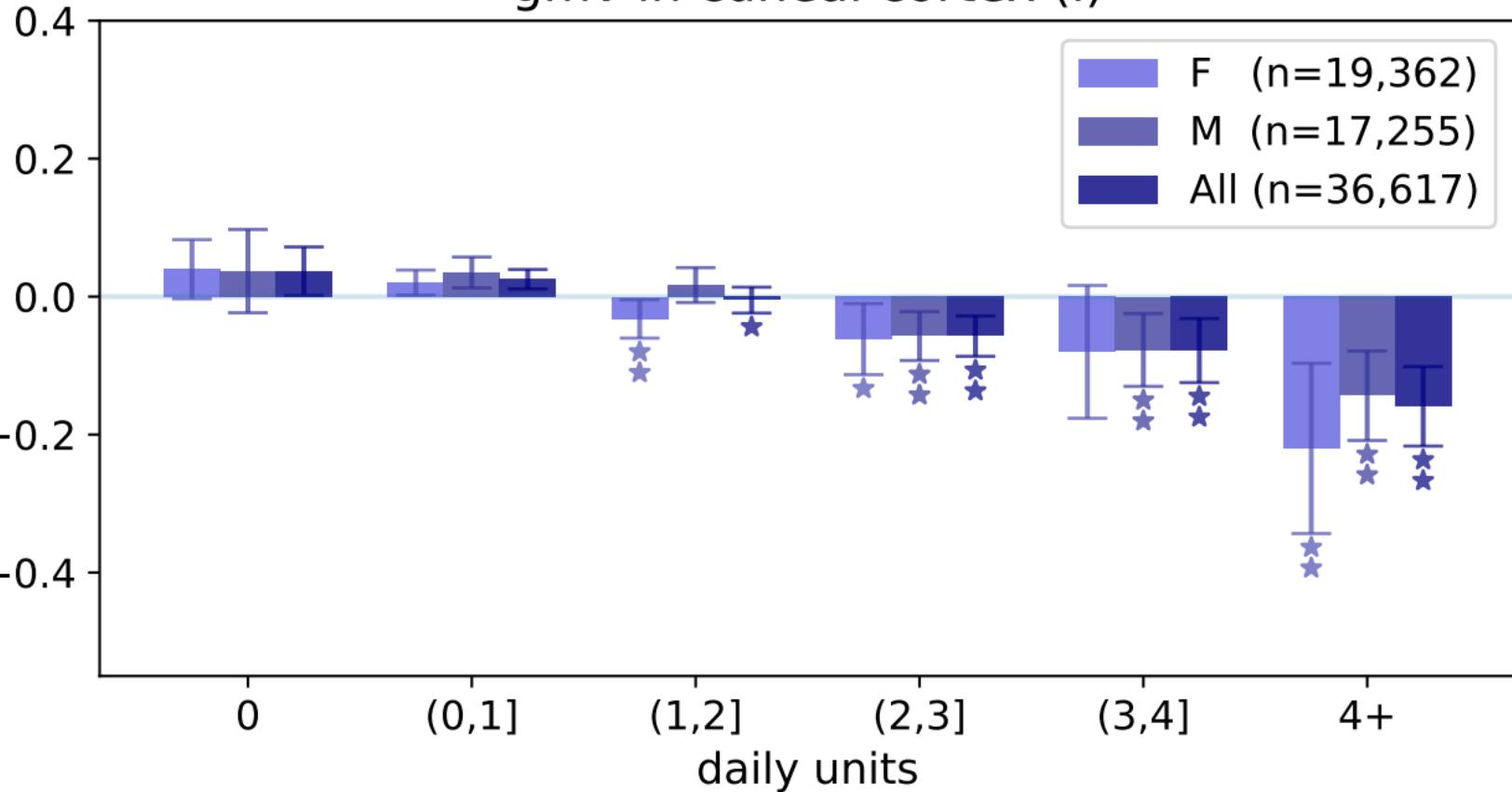
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in cuneal cortex (I)

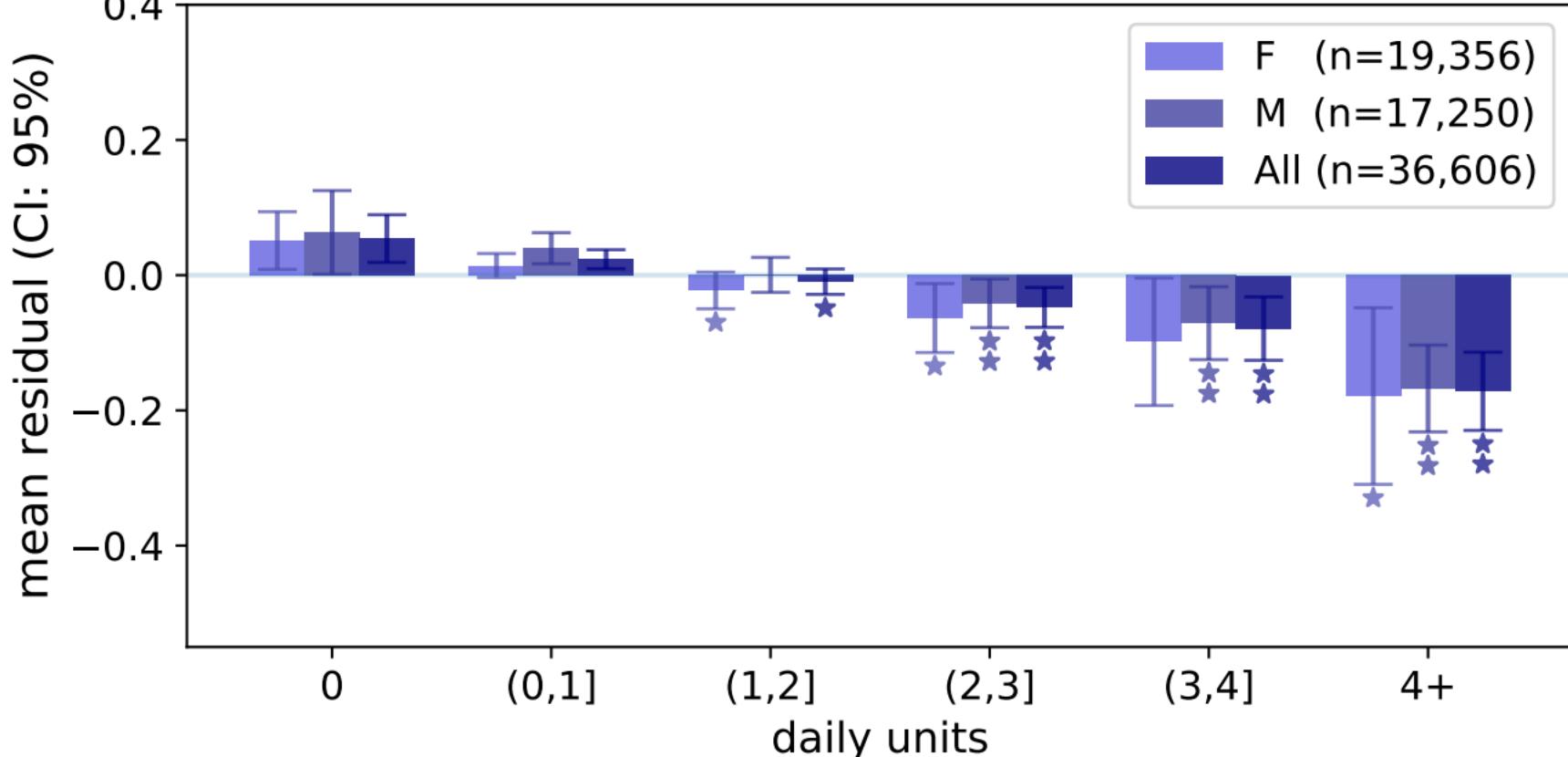
mean residual (CI: 95%)



daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

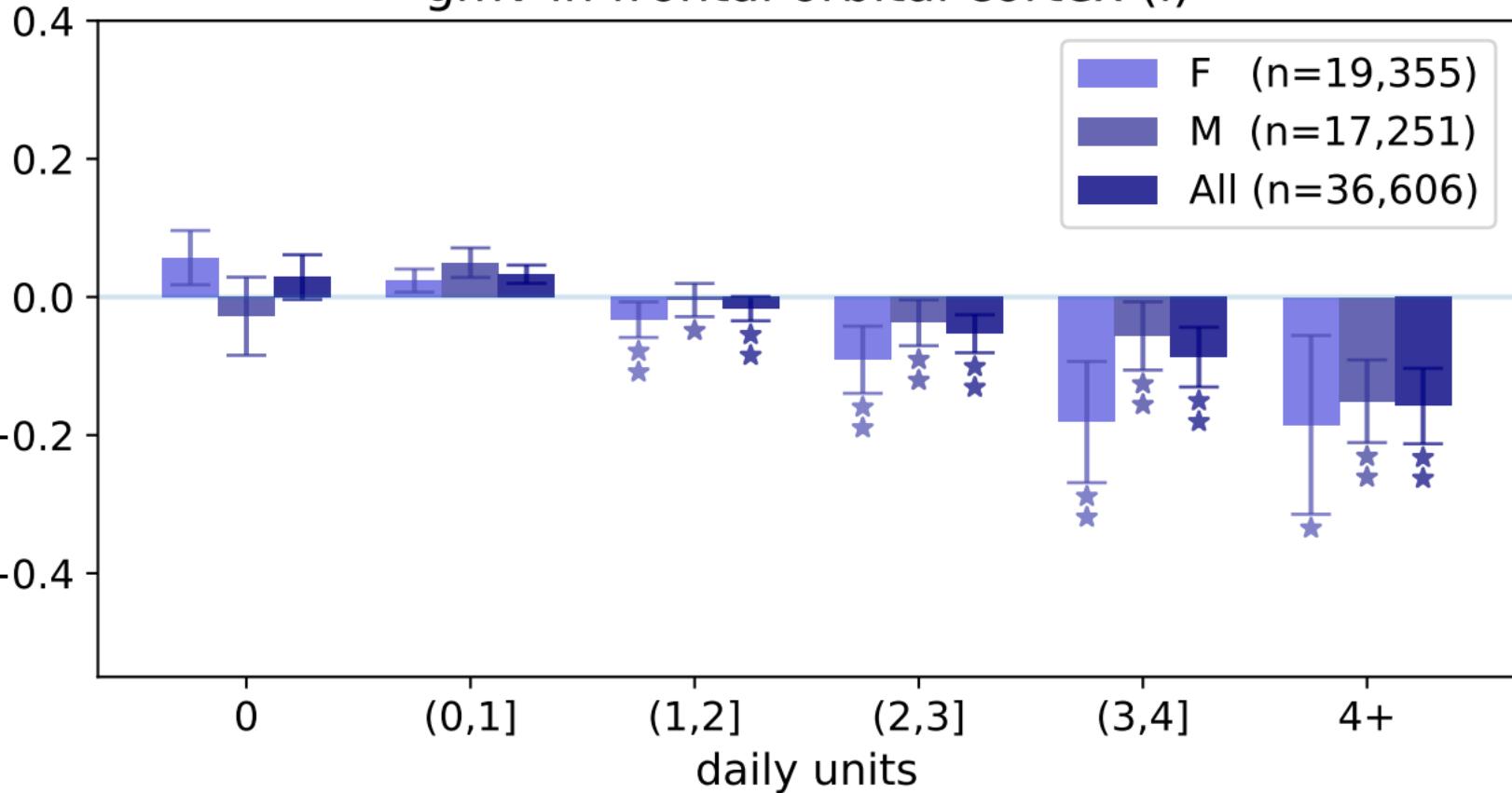
gmv in cuneal cortex (r)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in frontal orbital cortex (I)

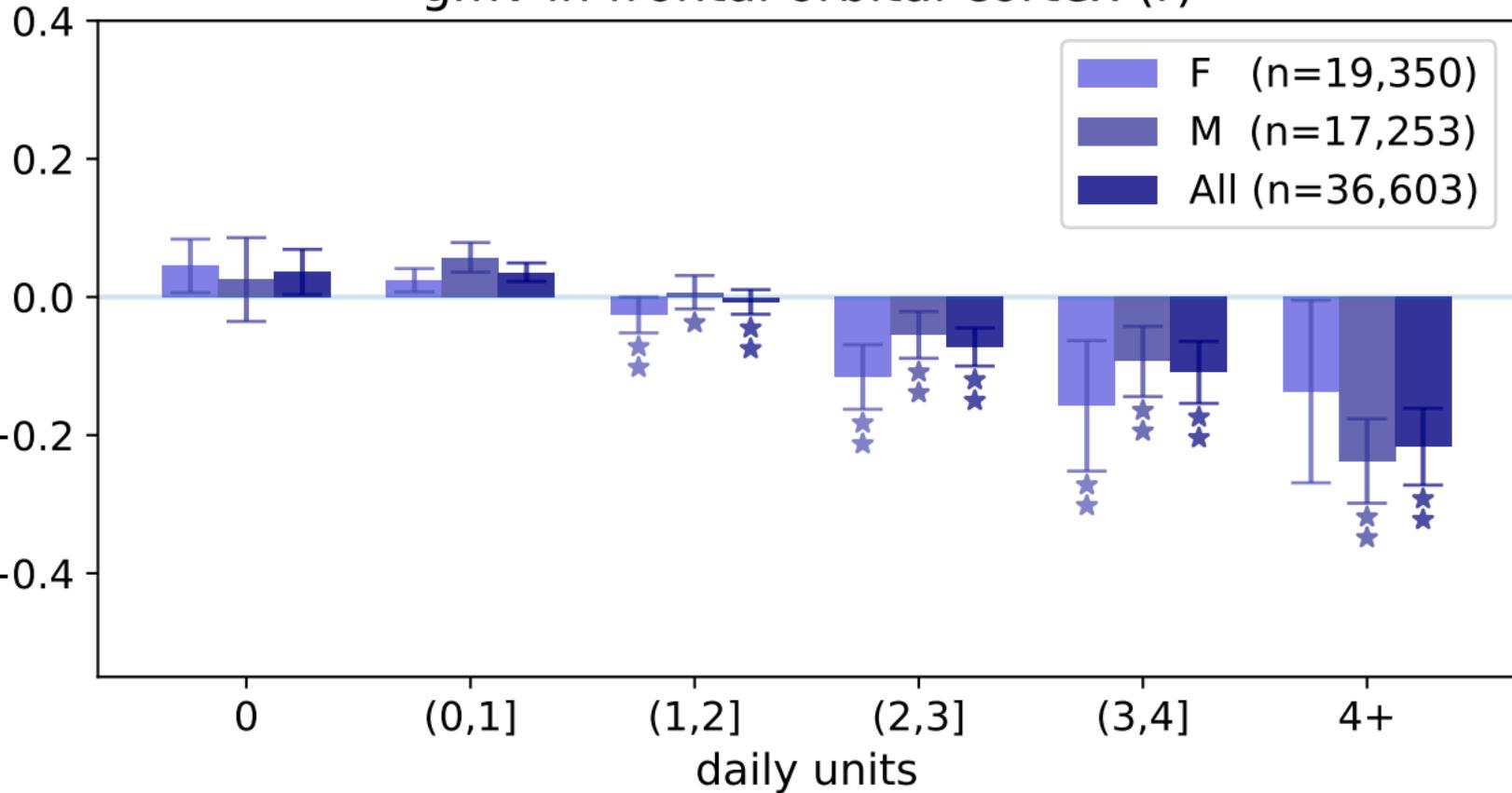
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in frontal orbital cortex (r)

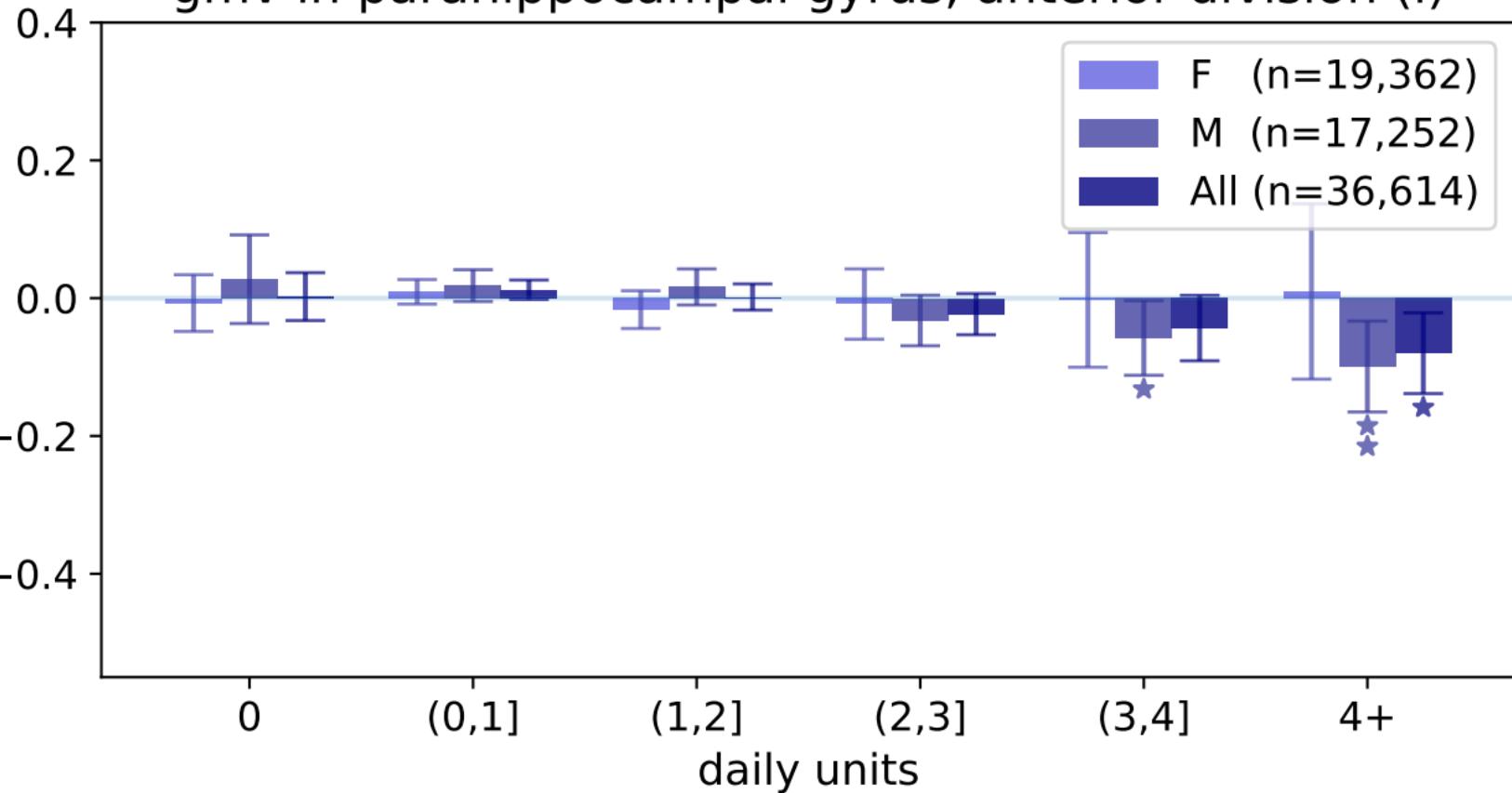
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in parahippocampal gyrus, anterior division (I)

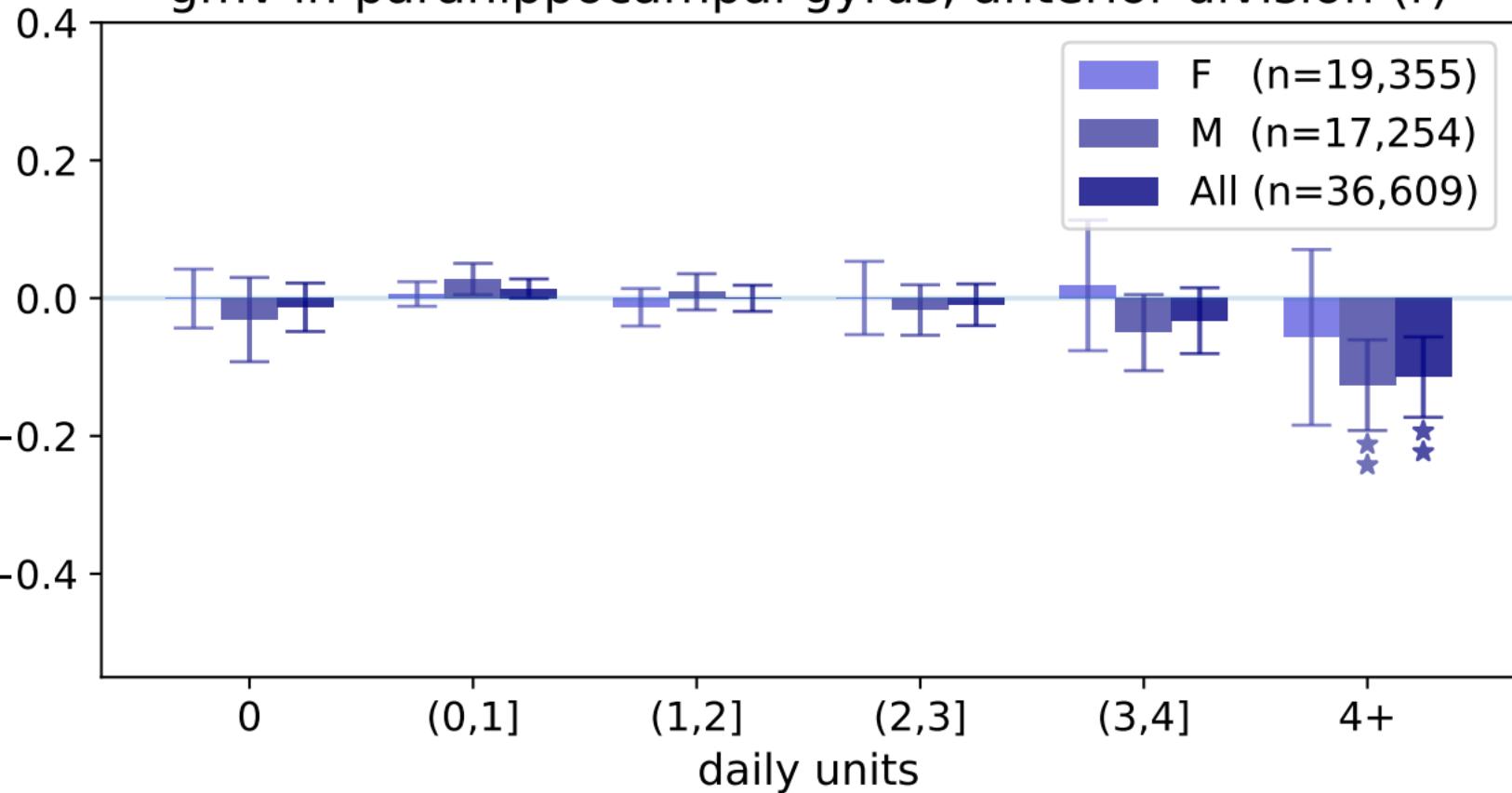
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in parahippocampal gyrus, anterior division (r)

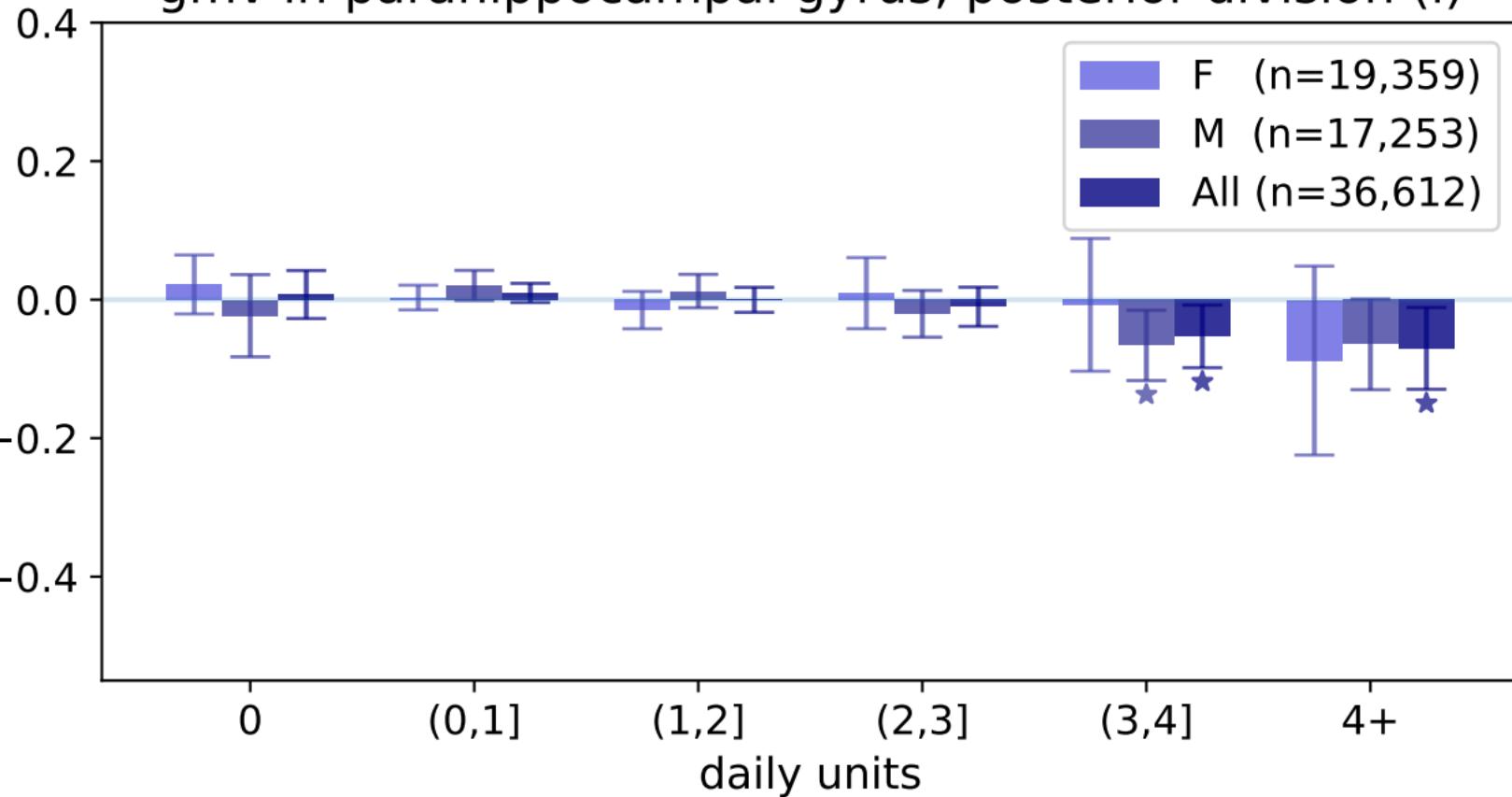
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in parahippocampal gyrus, posterior division (l)

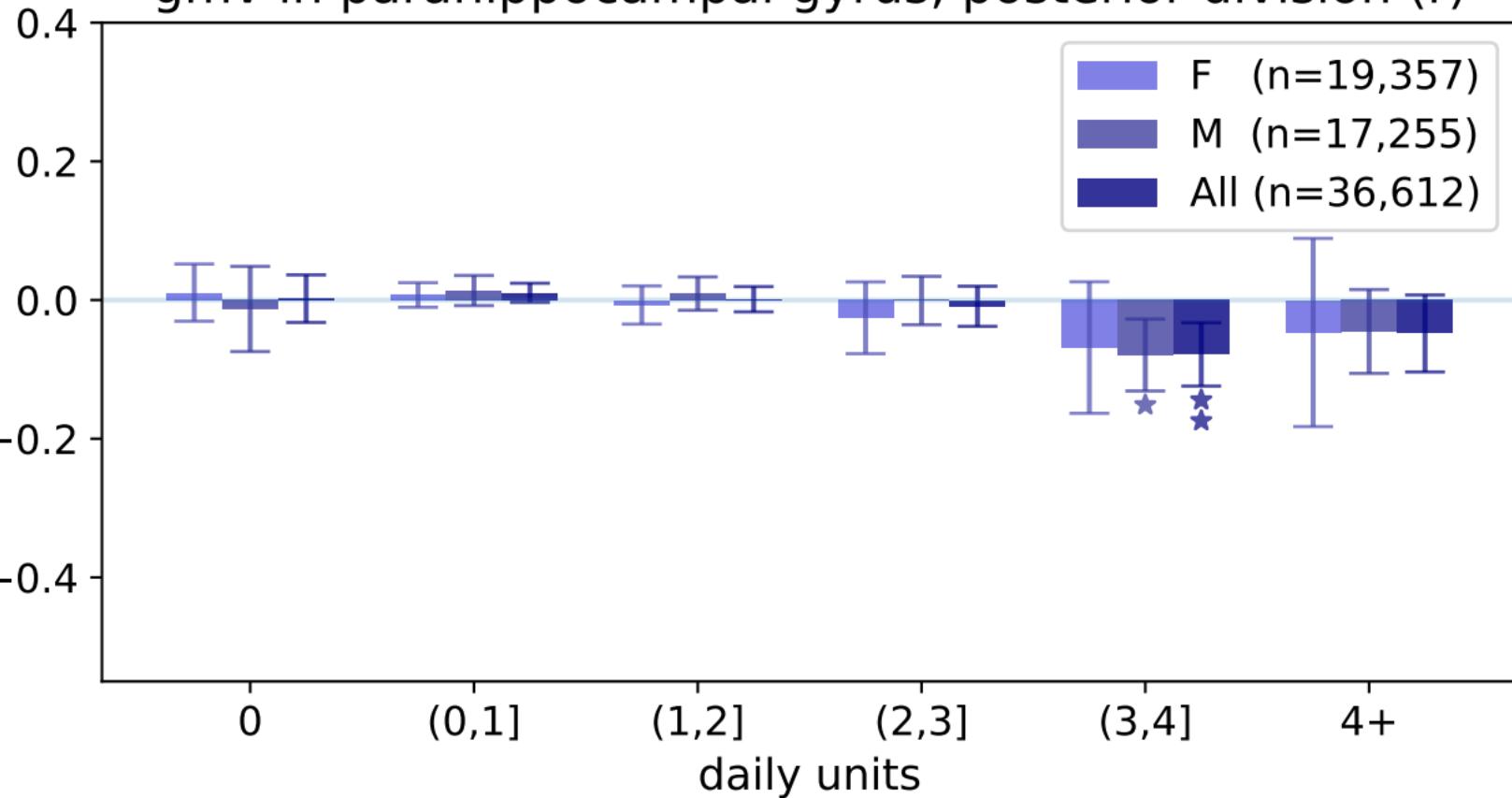
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

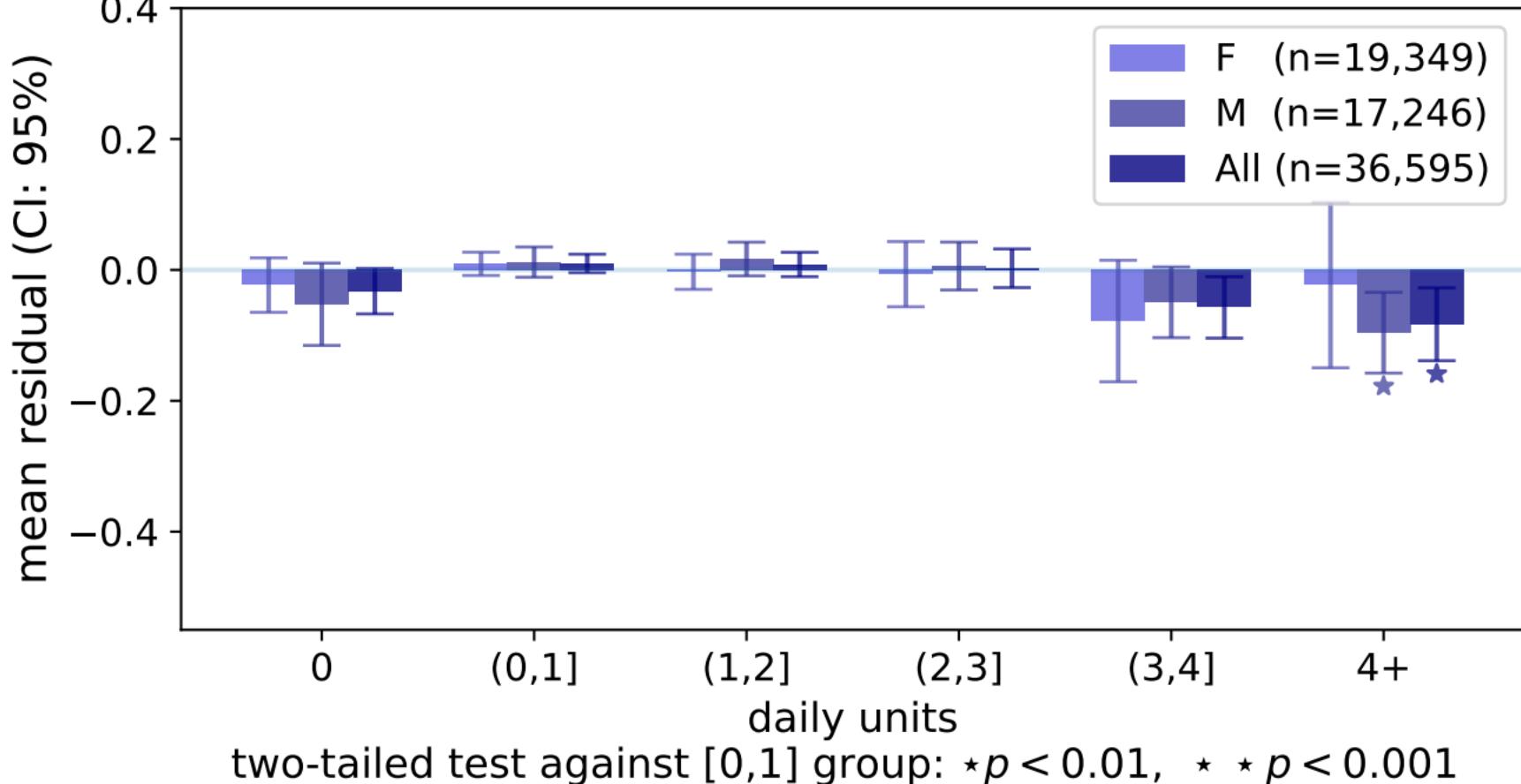
gmv in parahippocampal gyrus, posterior division (r)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in lingual gyrus (l)



gmv in lingual gyrus (r)

mean residual (CI: 95%)

0.4

0.2

-0.2

-0.4

F (n=19,354)
M (n=17,246)
All (n=36,600)

0

(0,1]

(1,2]

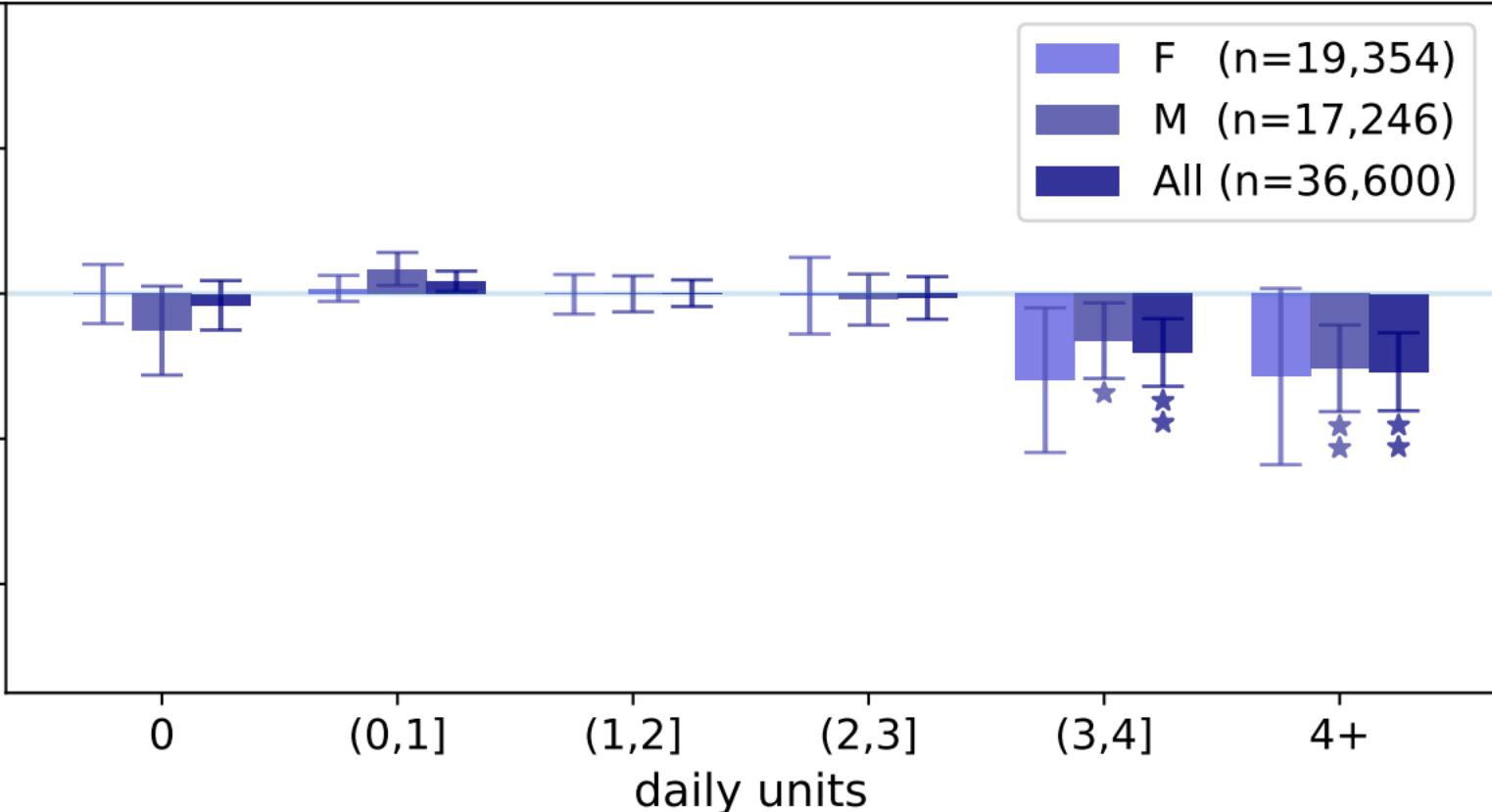
(2,3]

(3,4]

4+

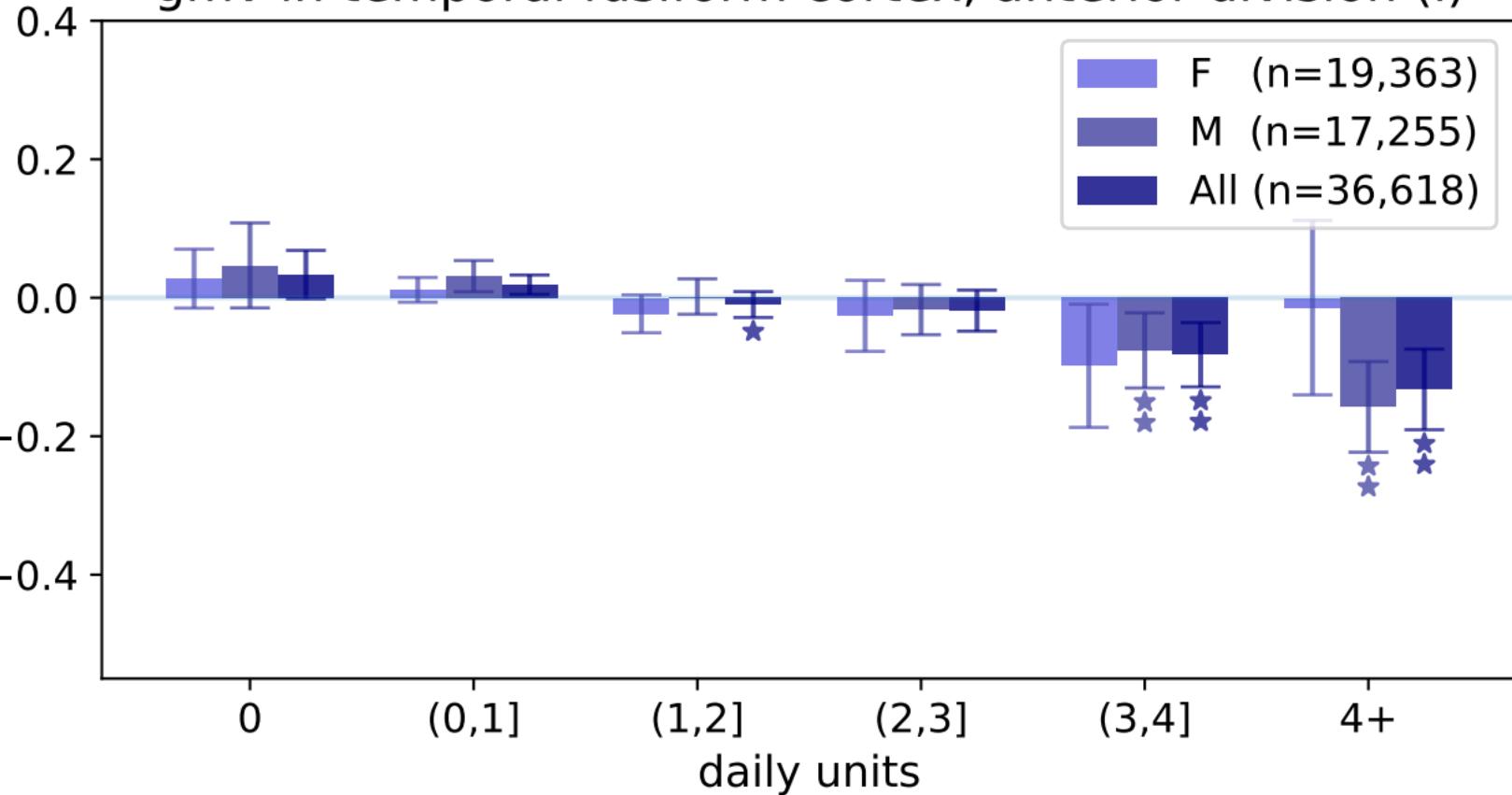
daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$



gmv in temporal fusiform cortex, anterior division (I)

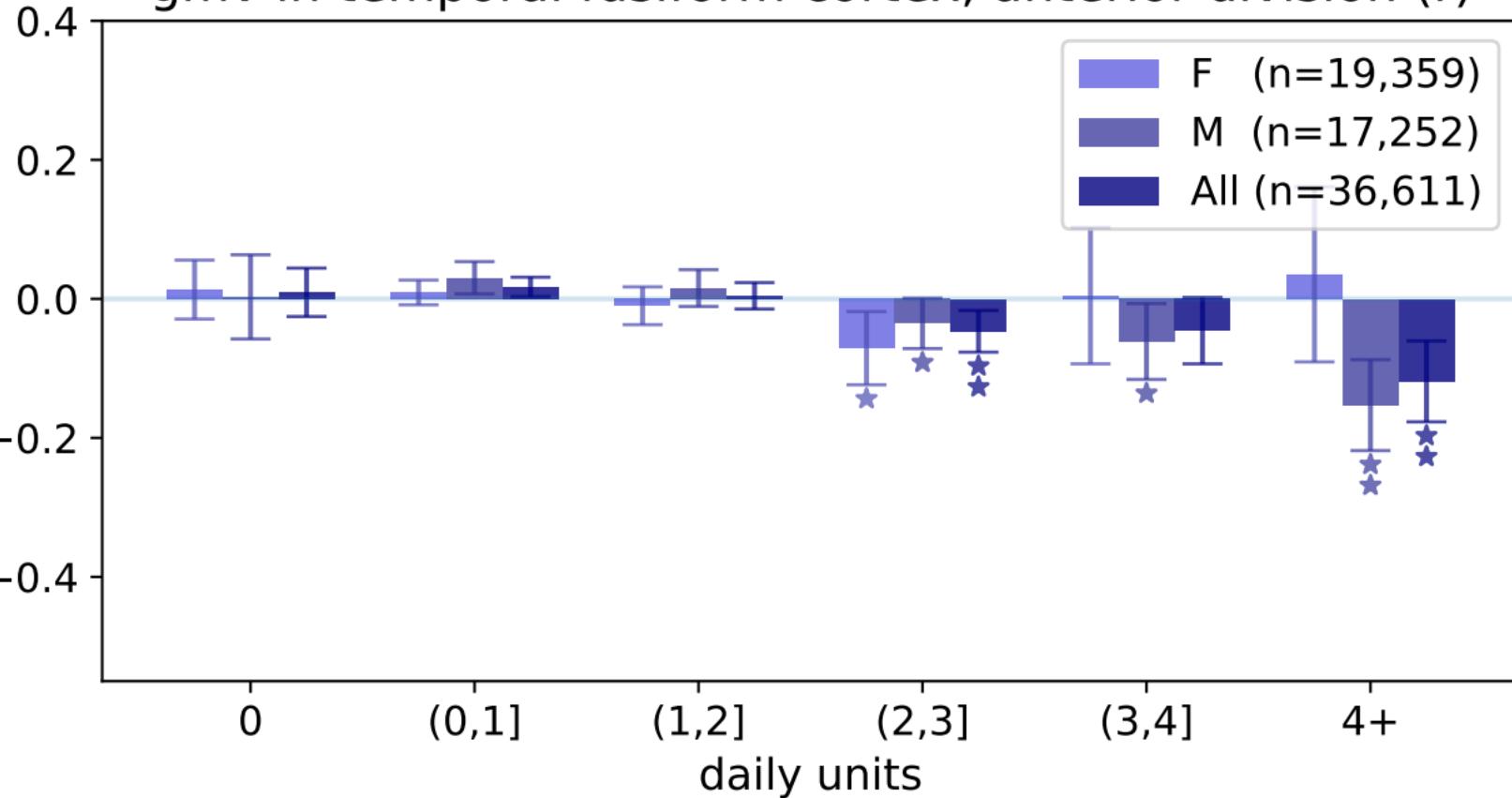
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in temporal fusiform cortex, anterior division (r)

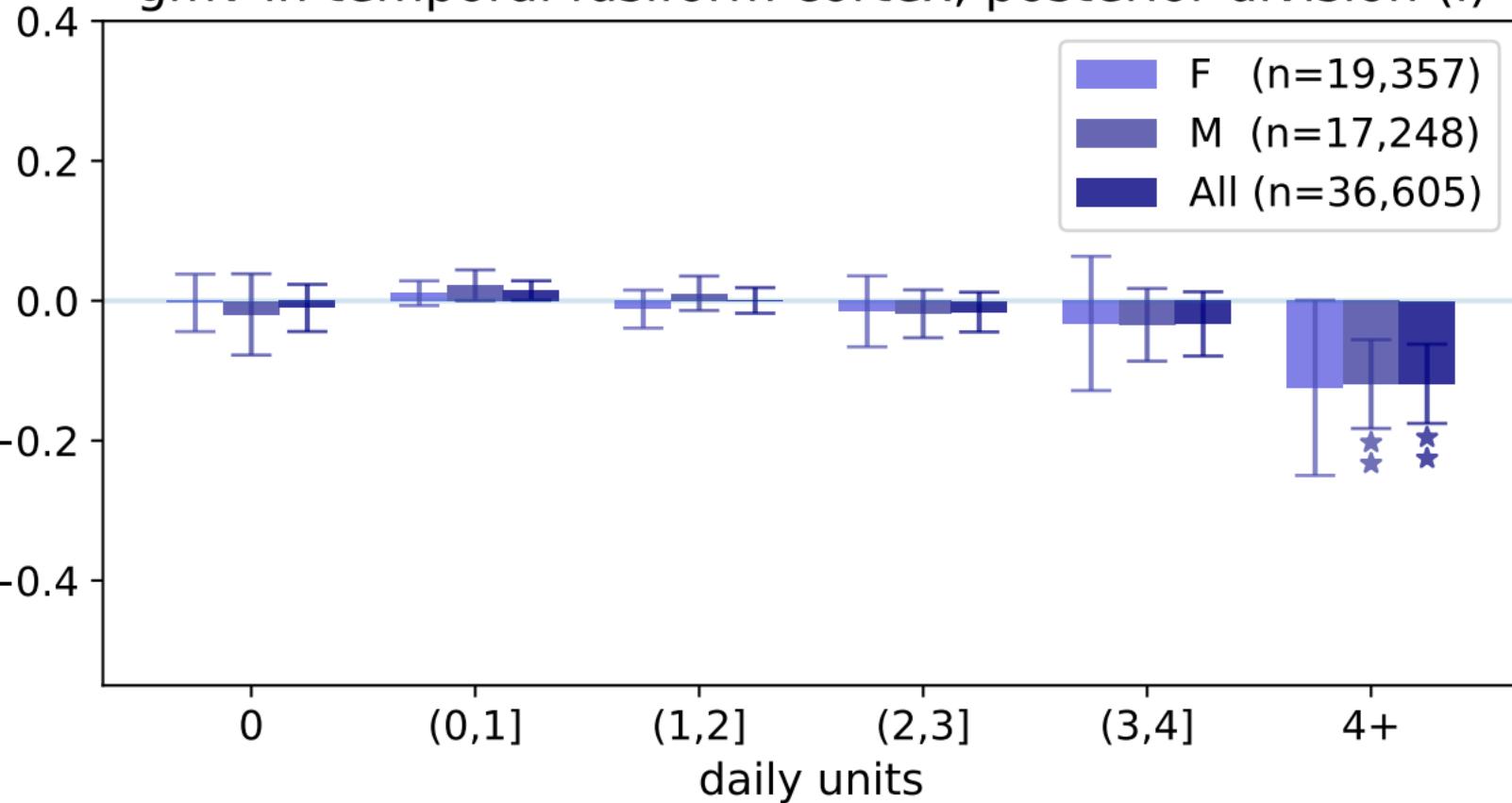
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in temporal fusiform cortex, posterior division (I)

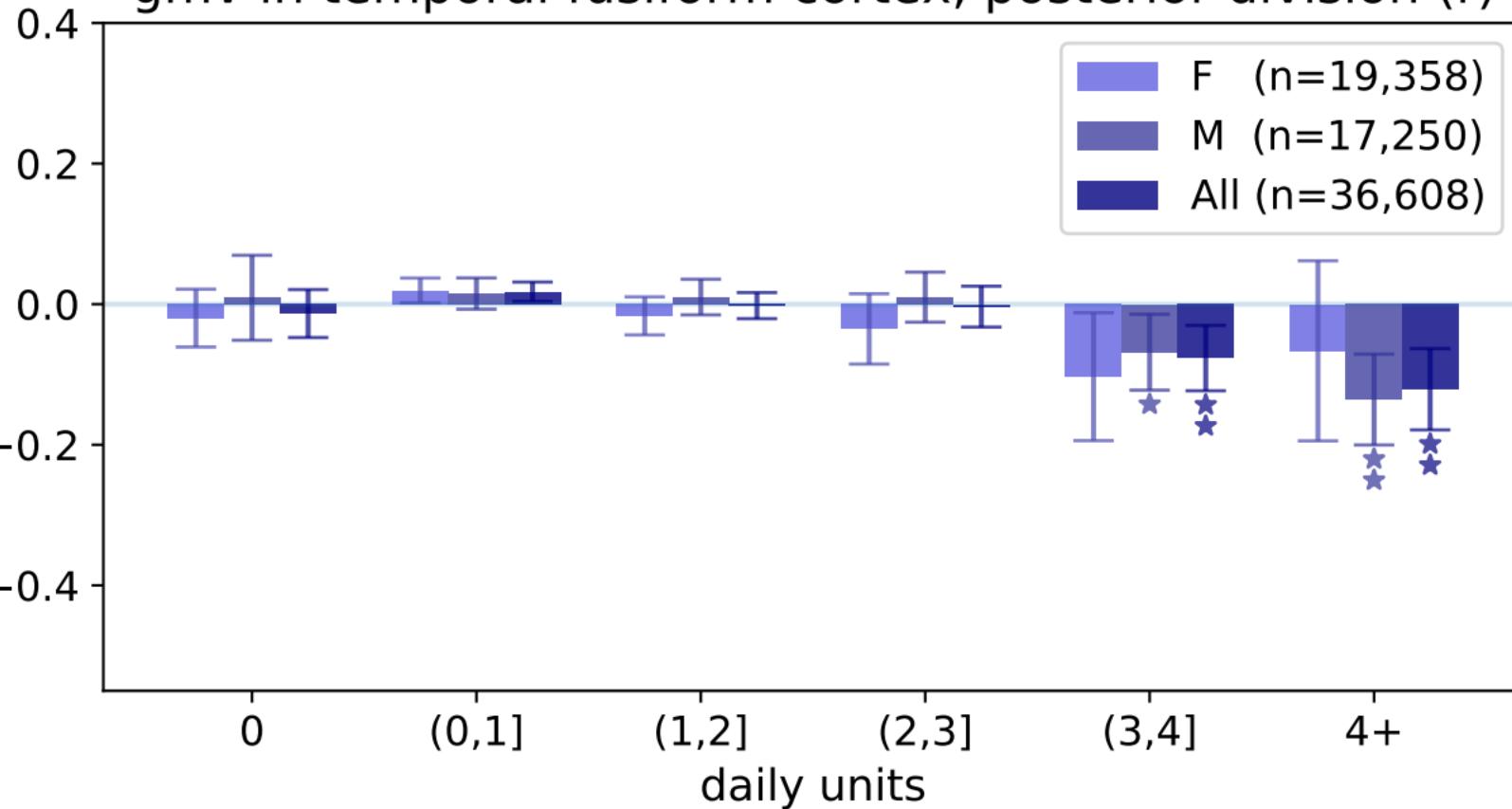
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in temporal fusiform cortex, posterior division (r)

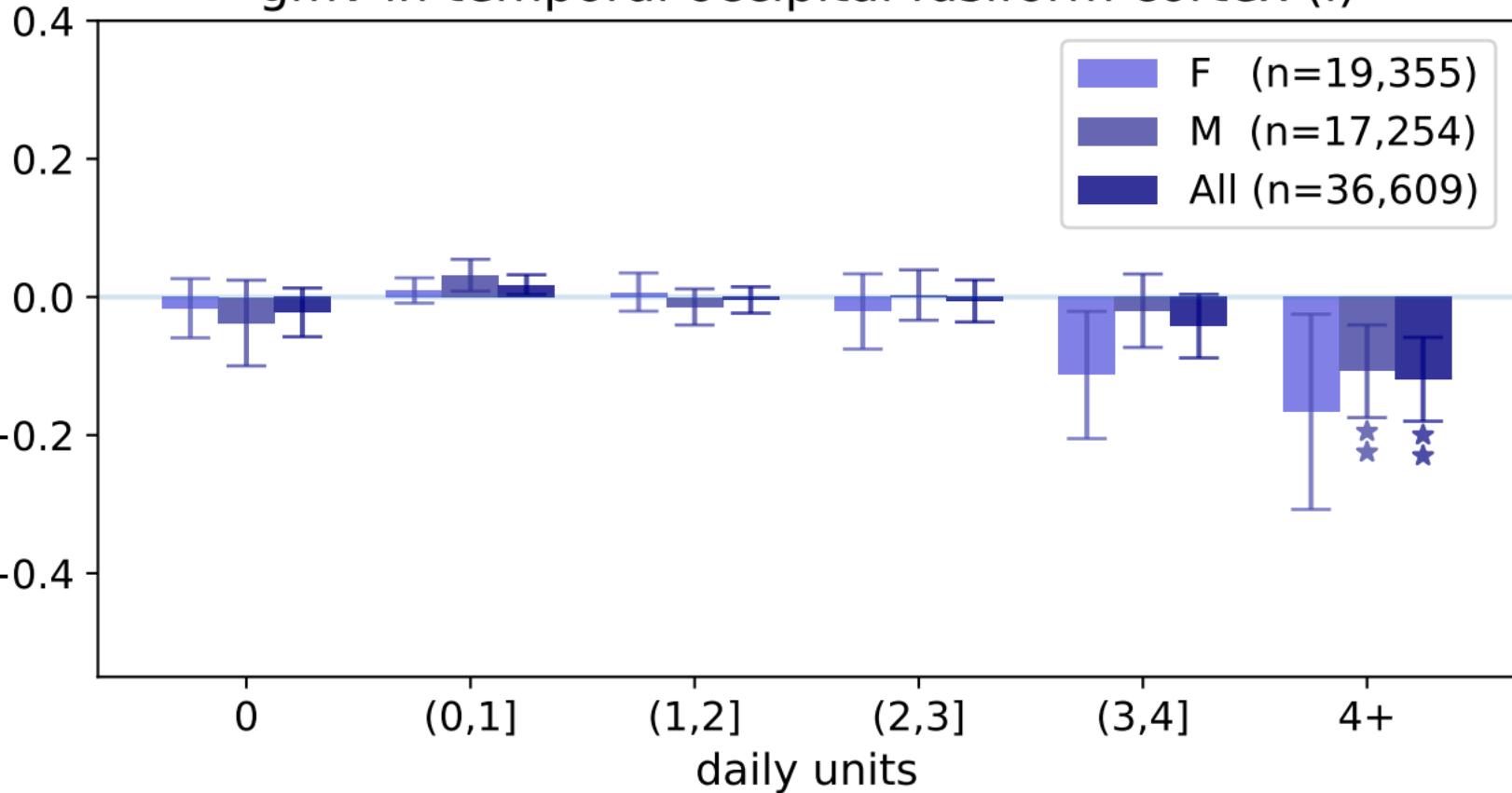
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in temporal occipital fusiform cortex (I)

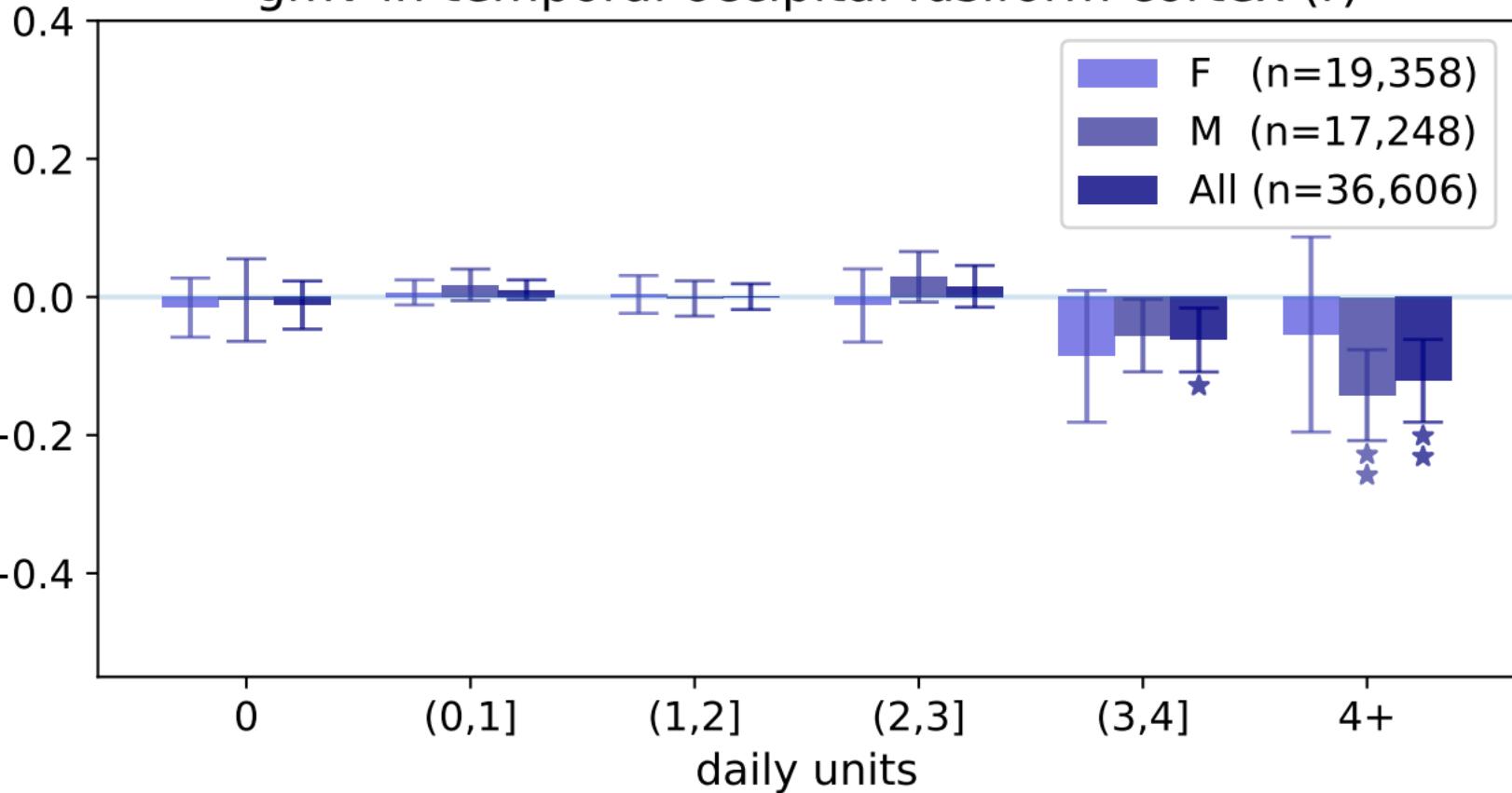
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in temporal occipital fusiform cortex (r)

mean residual (CI: 95%)

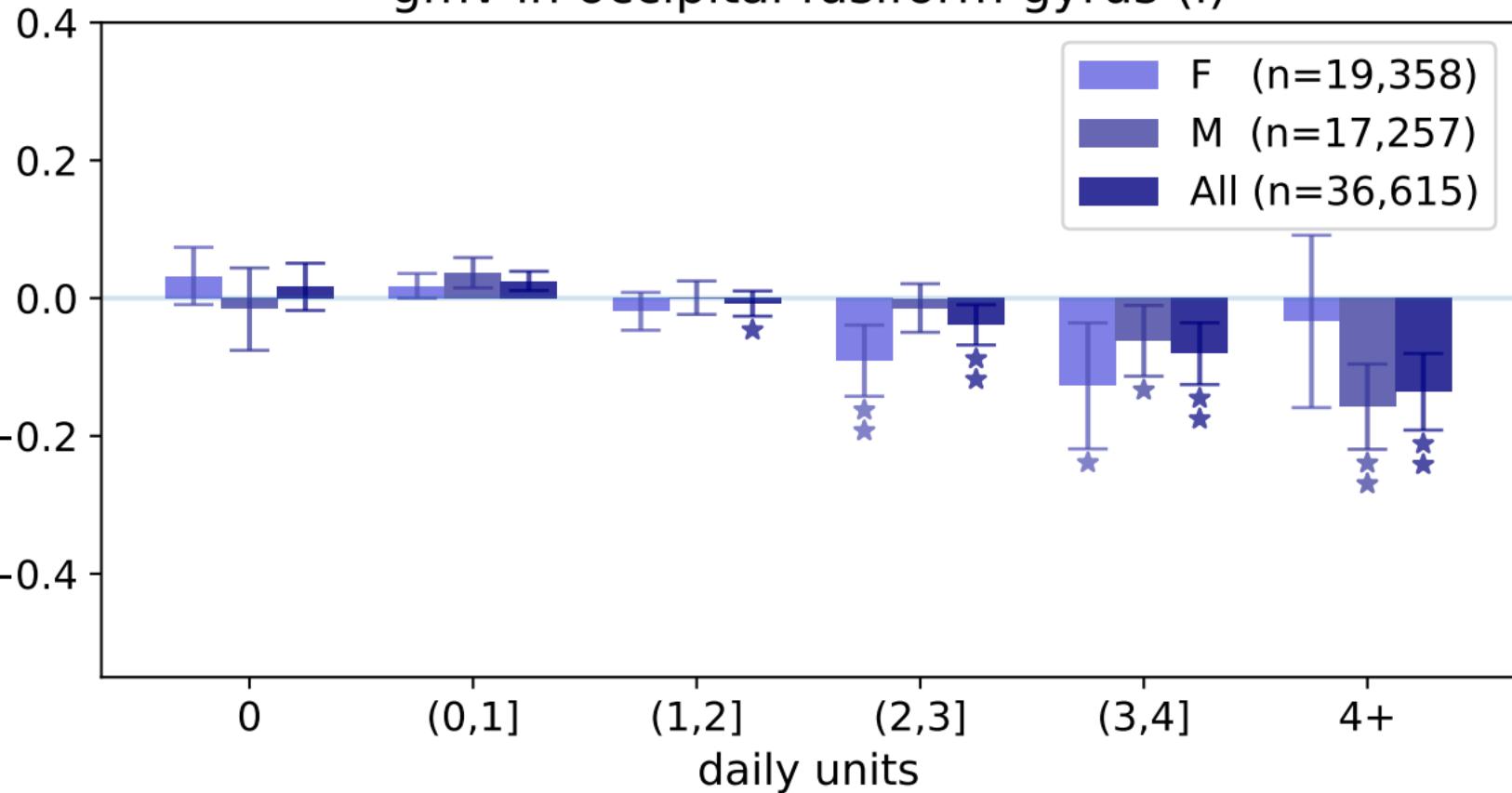


daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in occipital fusiform gyrus (I)

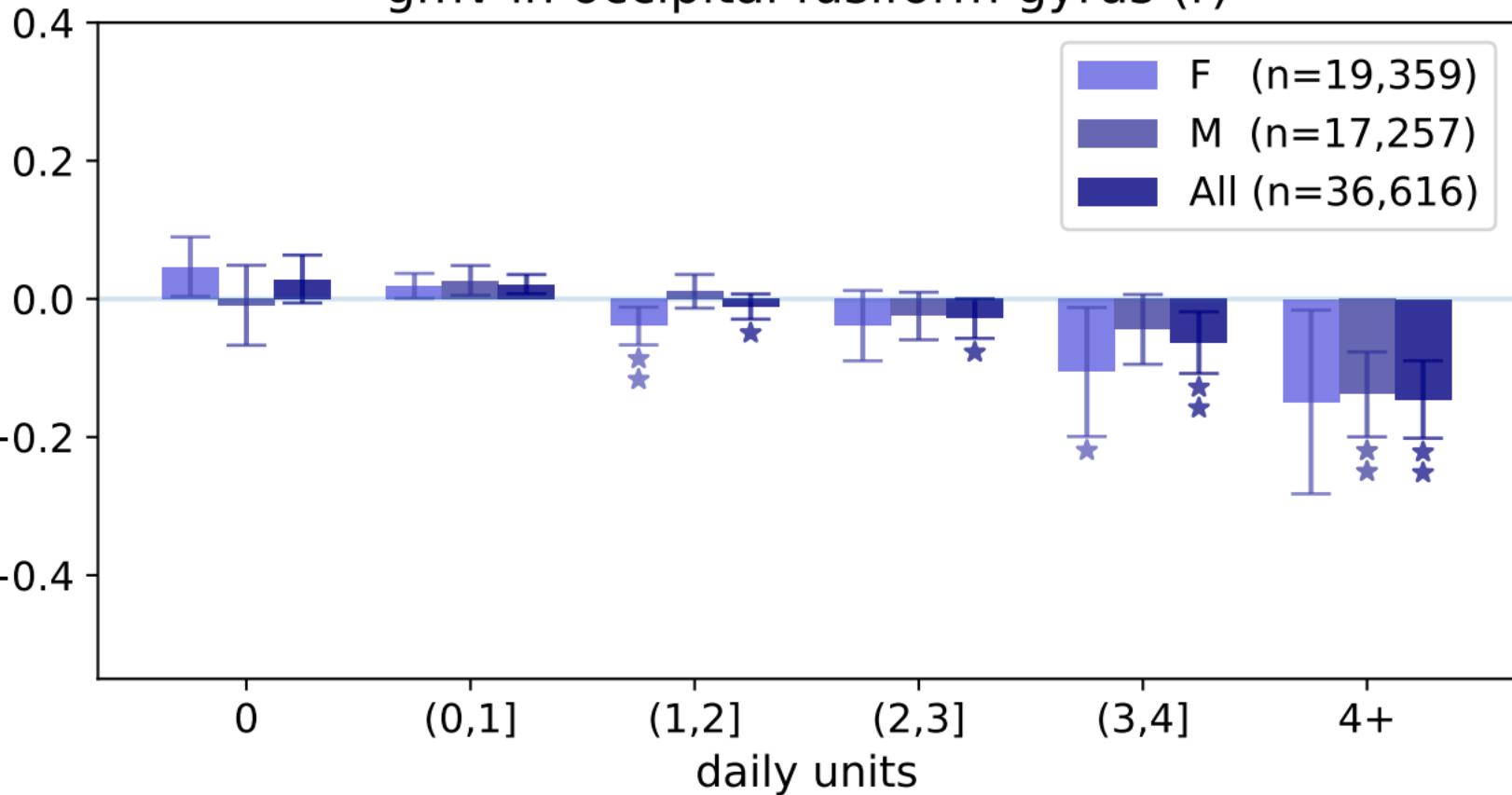
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in occipital fusiform gyrus (r)

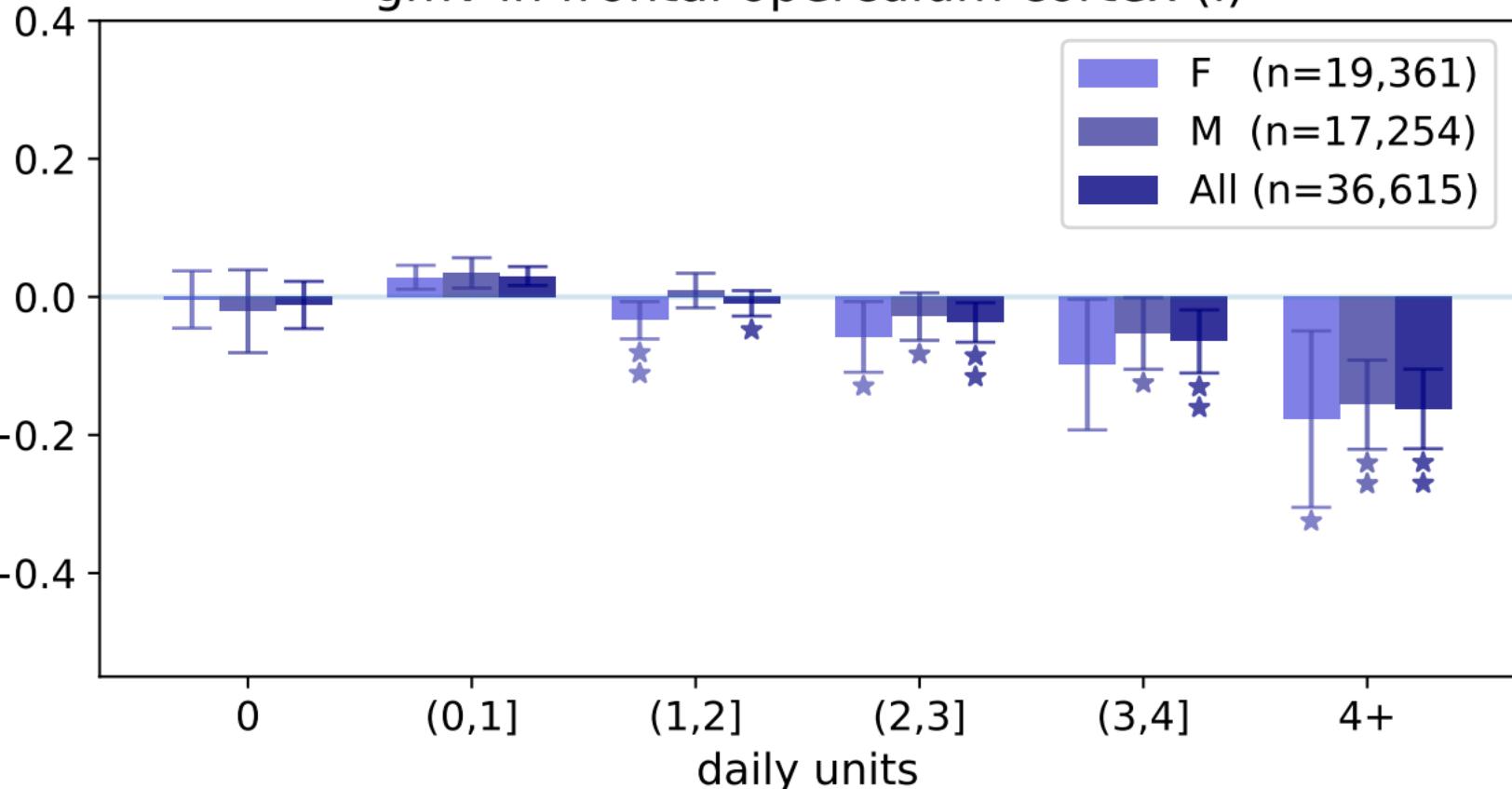
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in frontal operculum cortex (I)

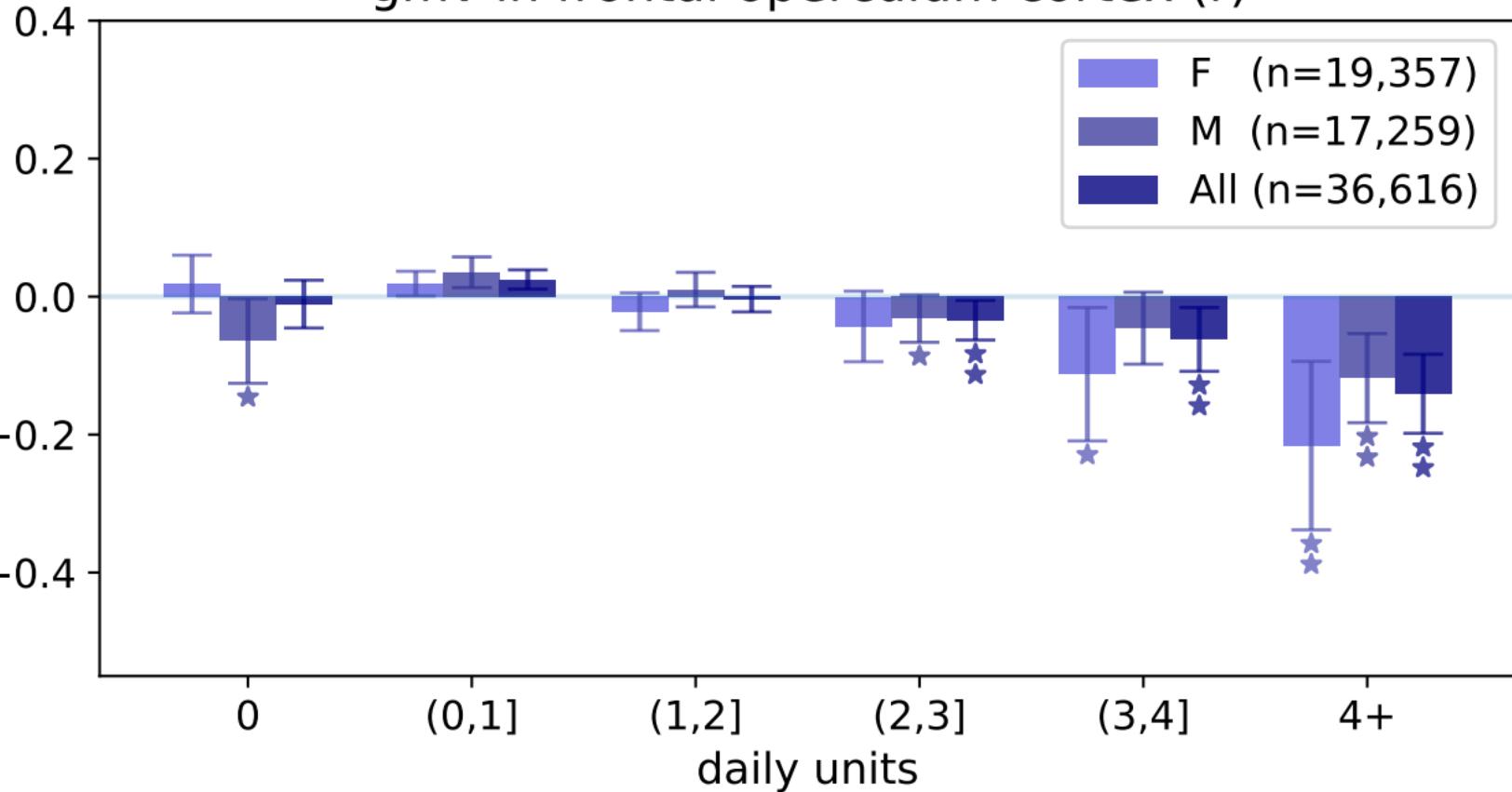
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in frontal operculum cortex (r)

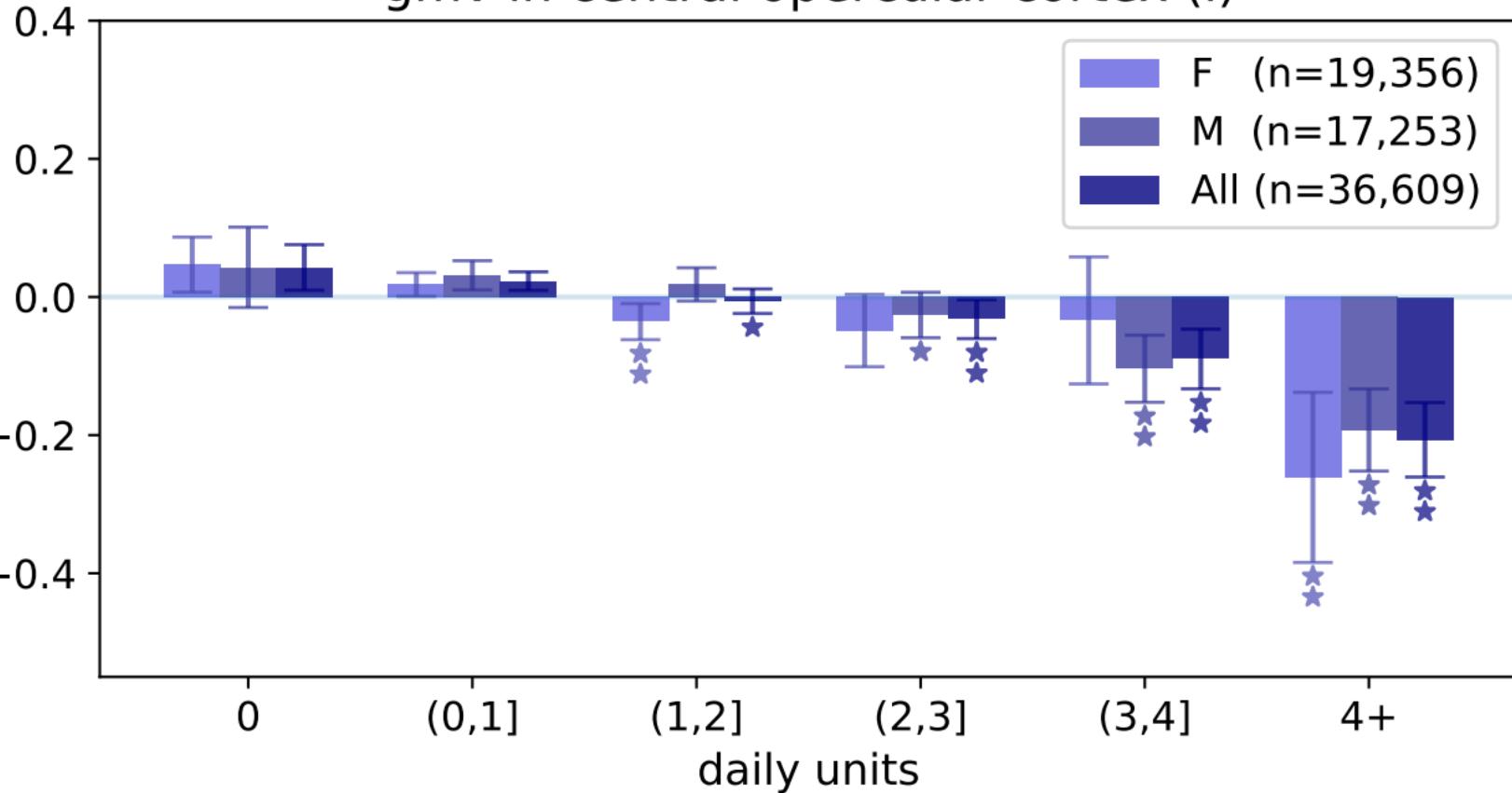
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in central opercular cortex (I)

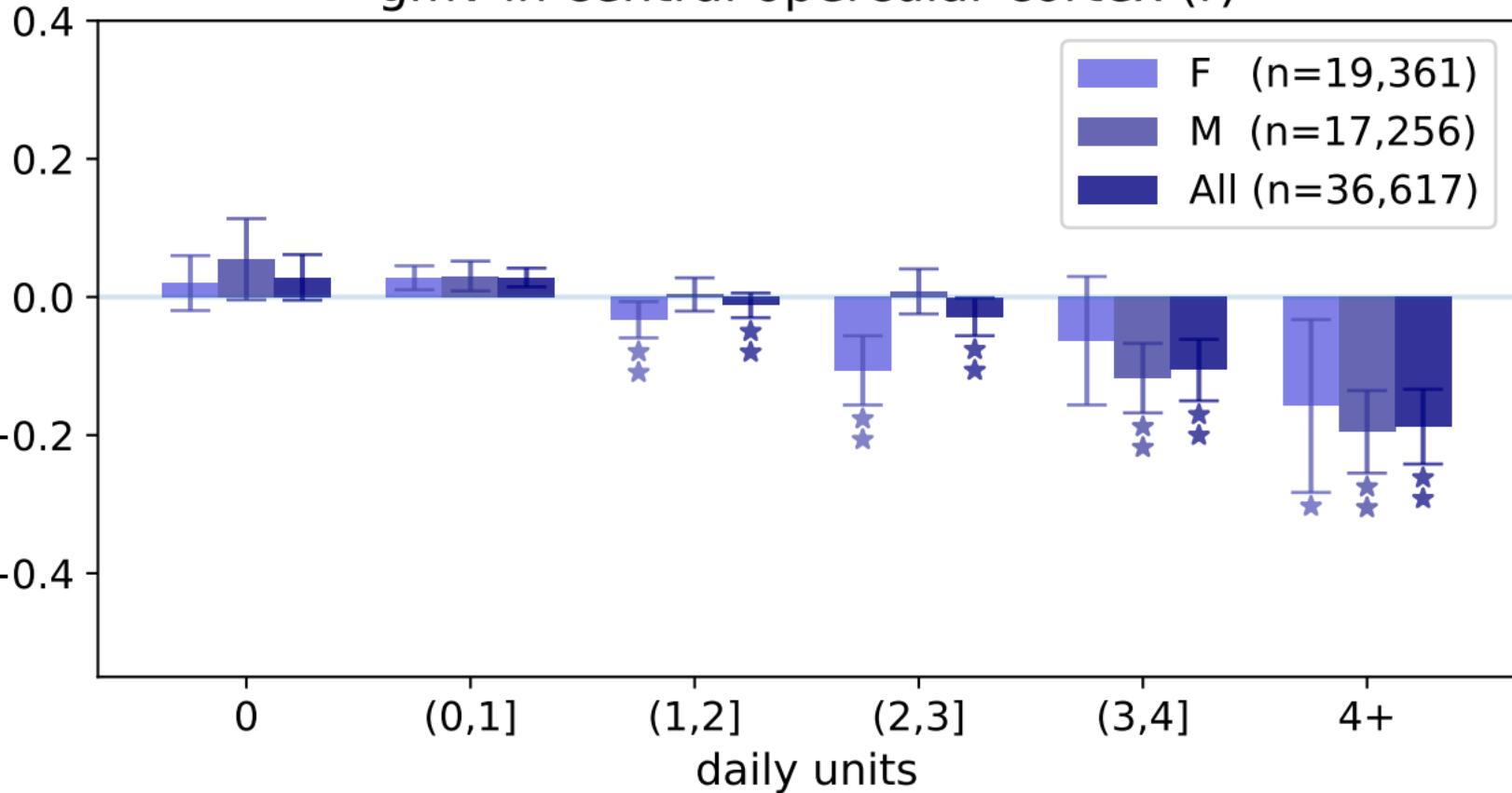
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in central opercular cortex (r)

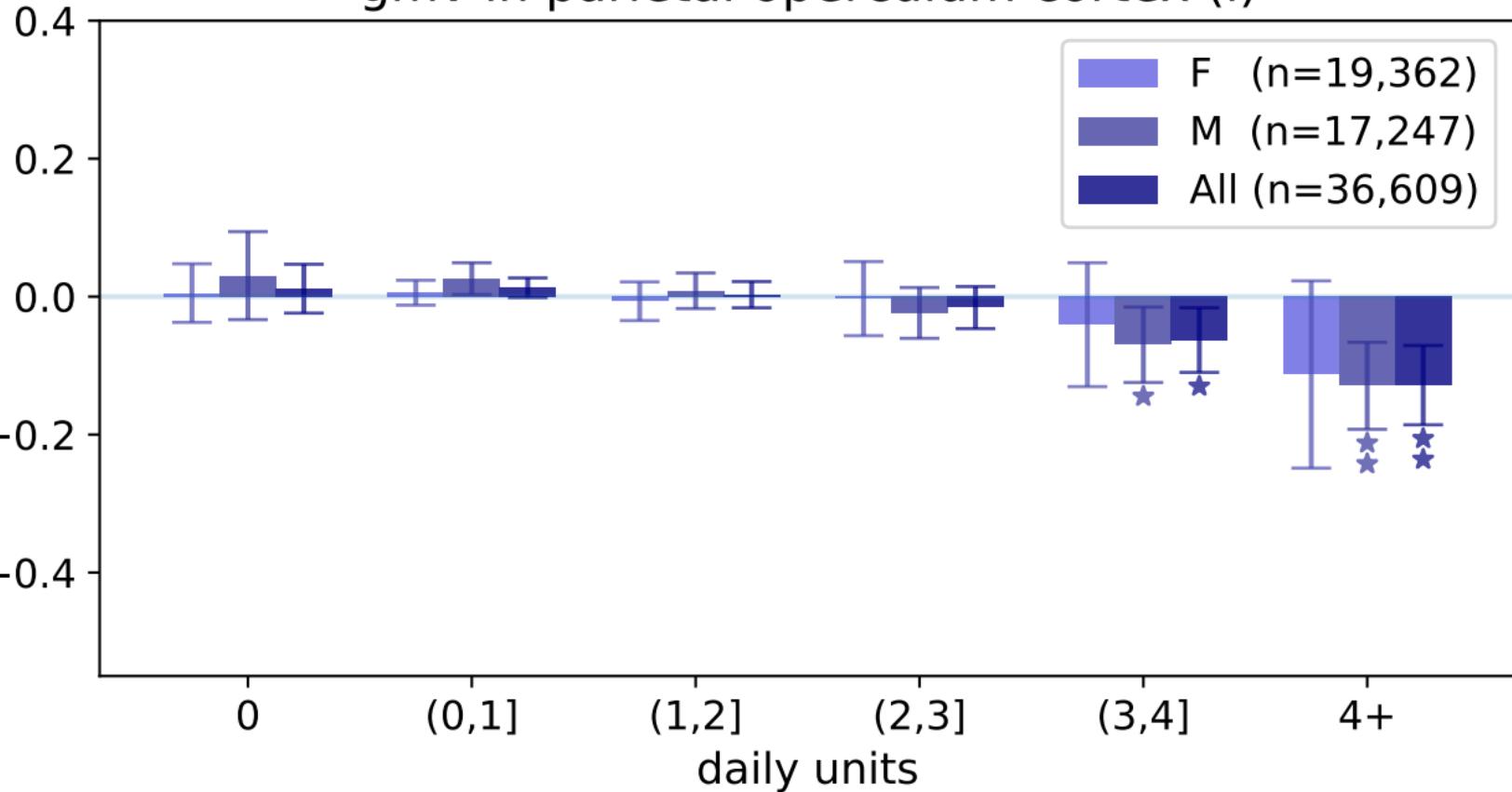
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in parietal operculum cortex (I)

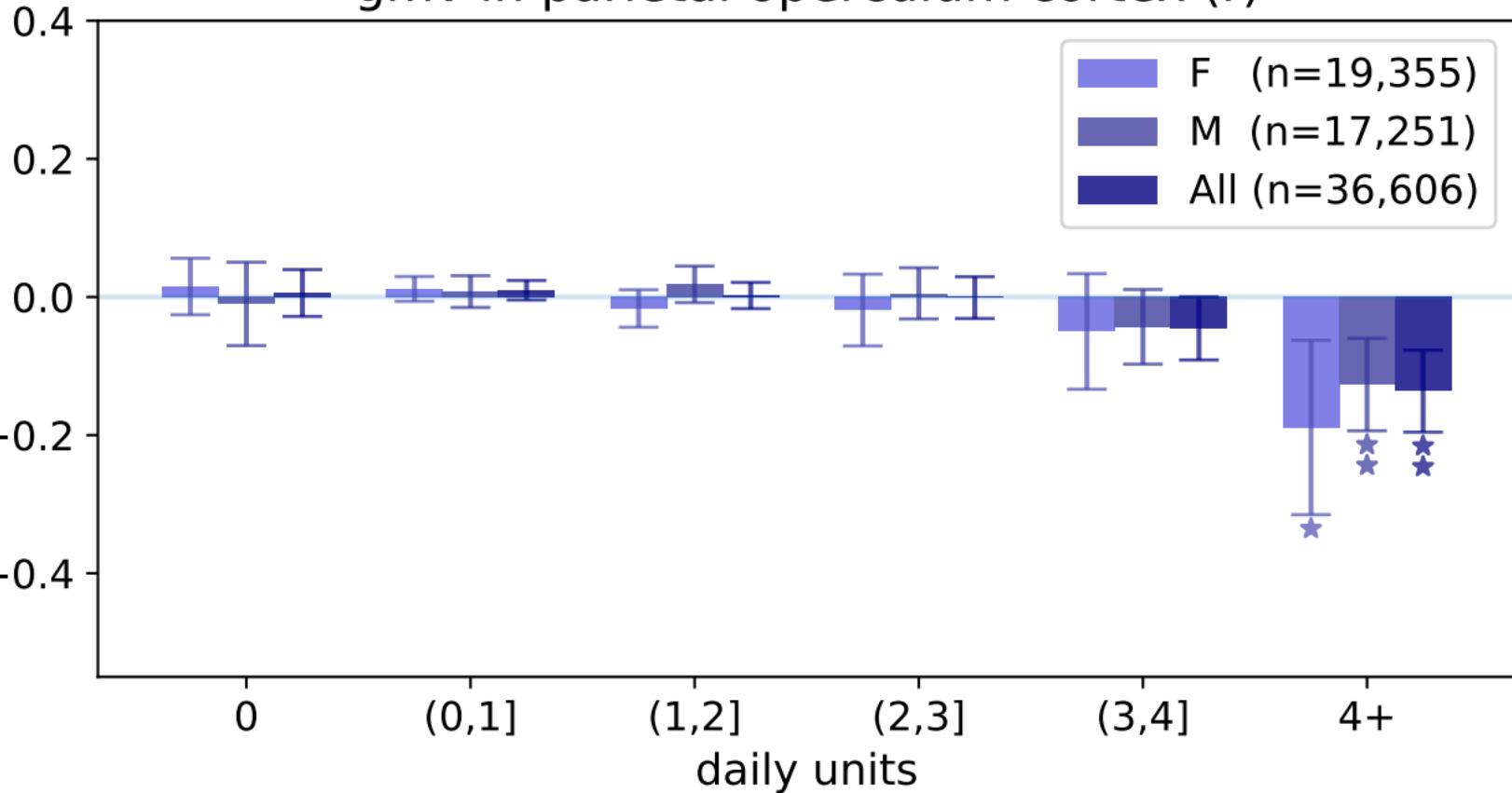
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in parietal operculum cortex (r)

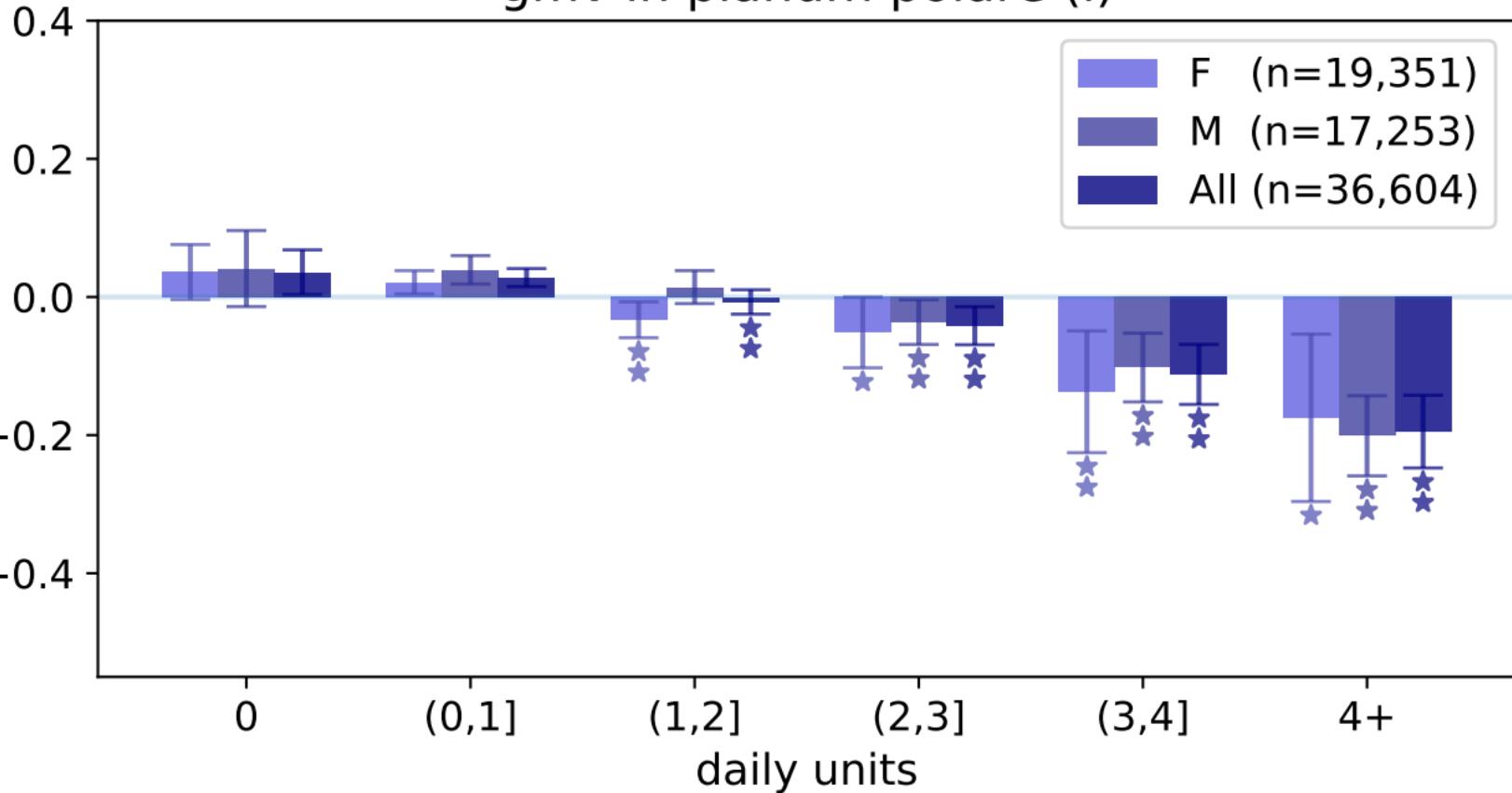
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in planum polare (I)

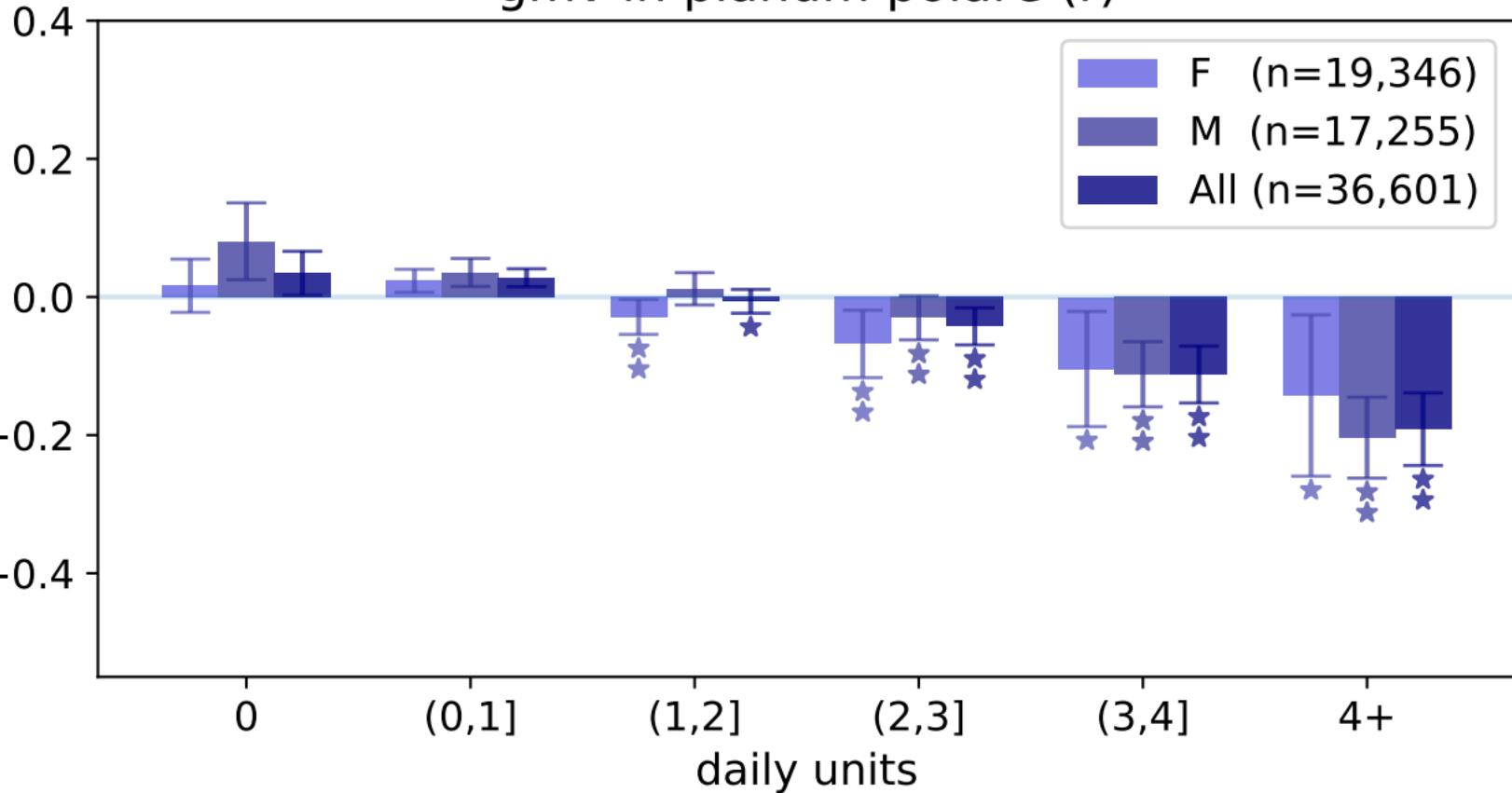
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in planum polare (r)

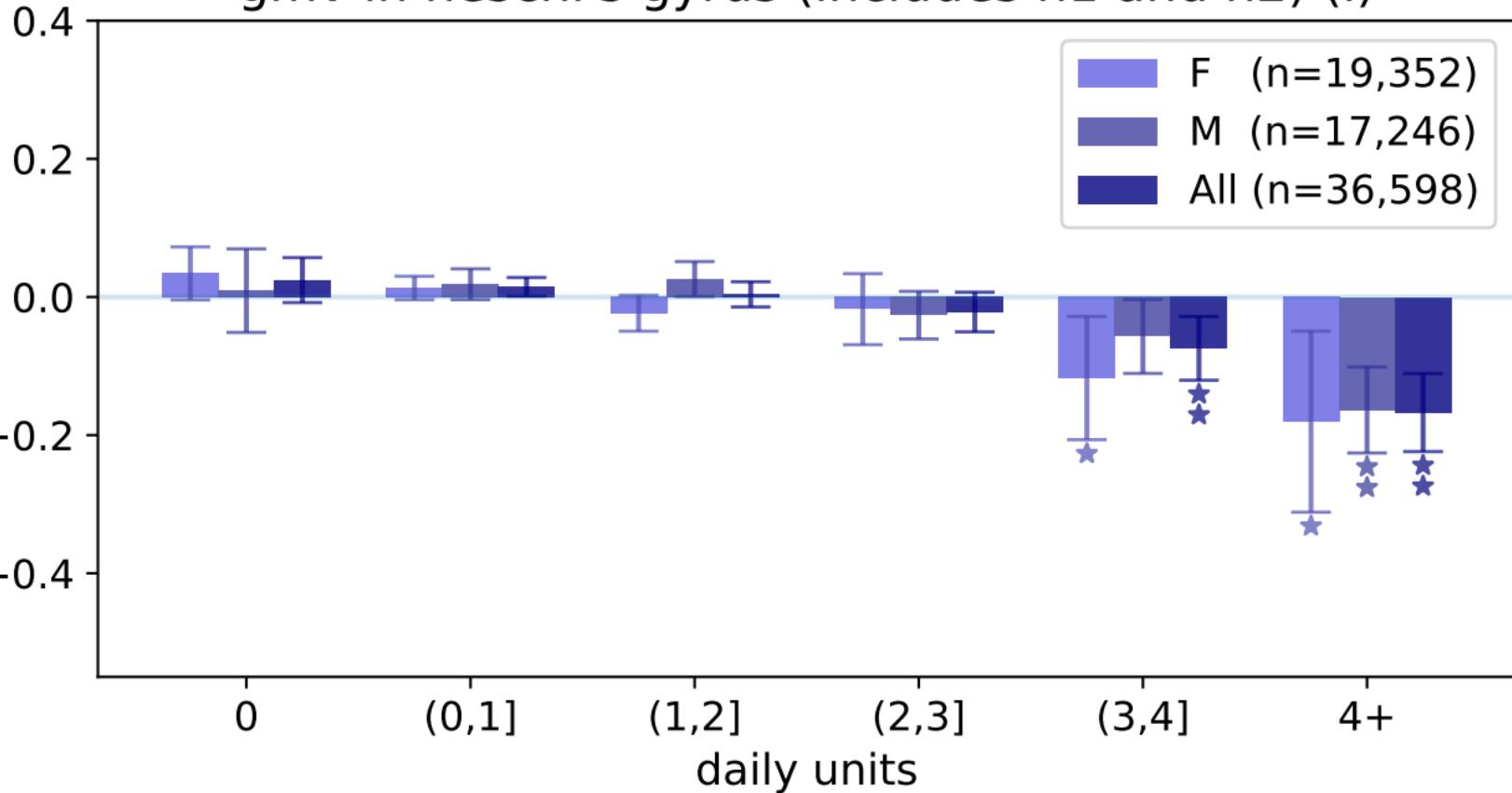
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in heschl's gyrus (includes h1 and h2) (I)

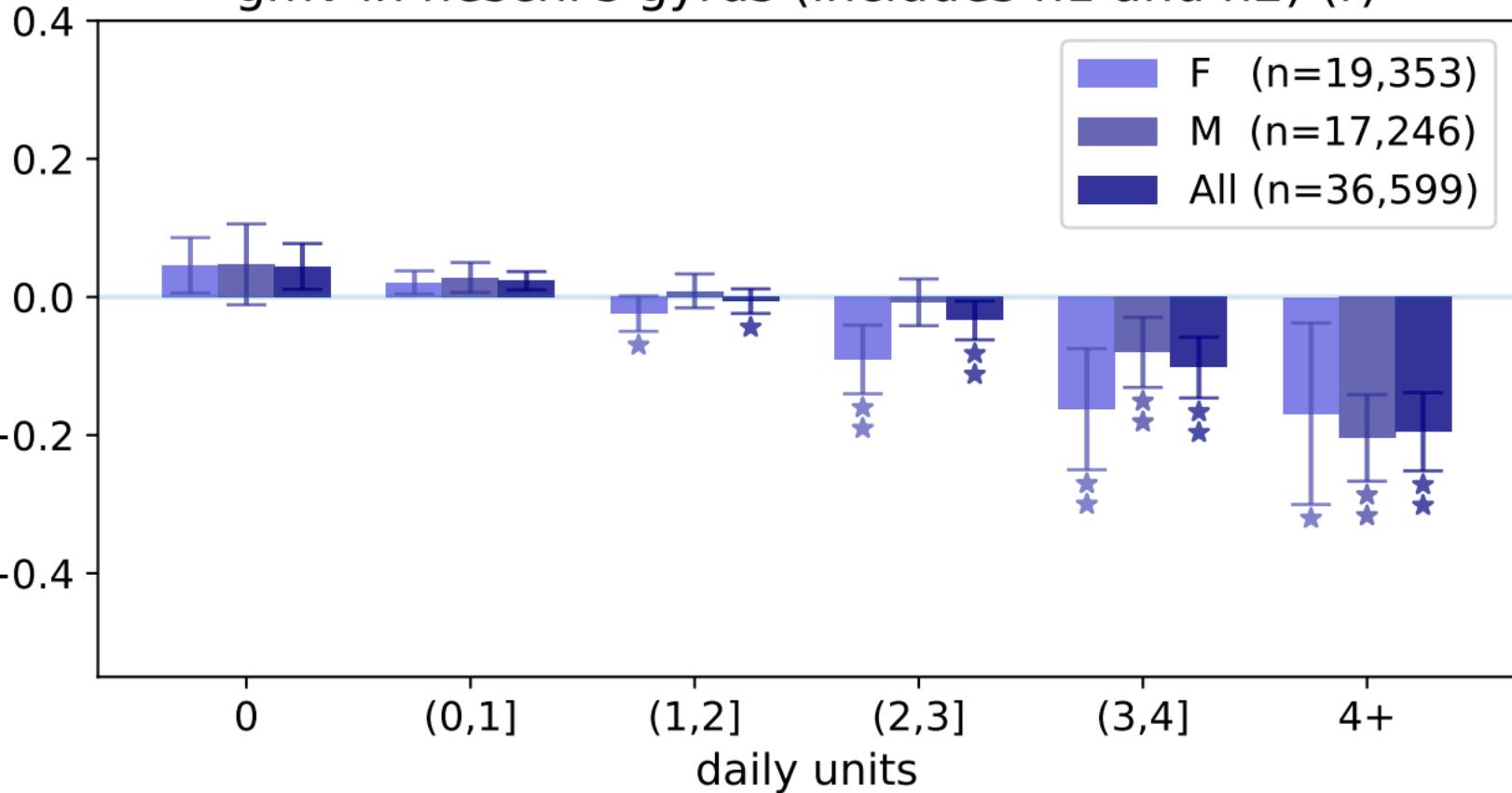
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

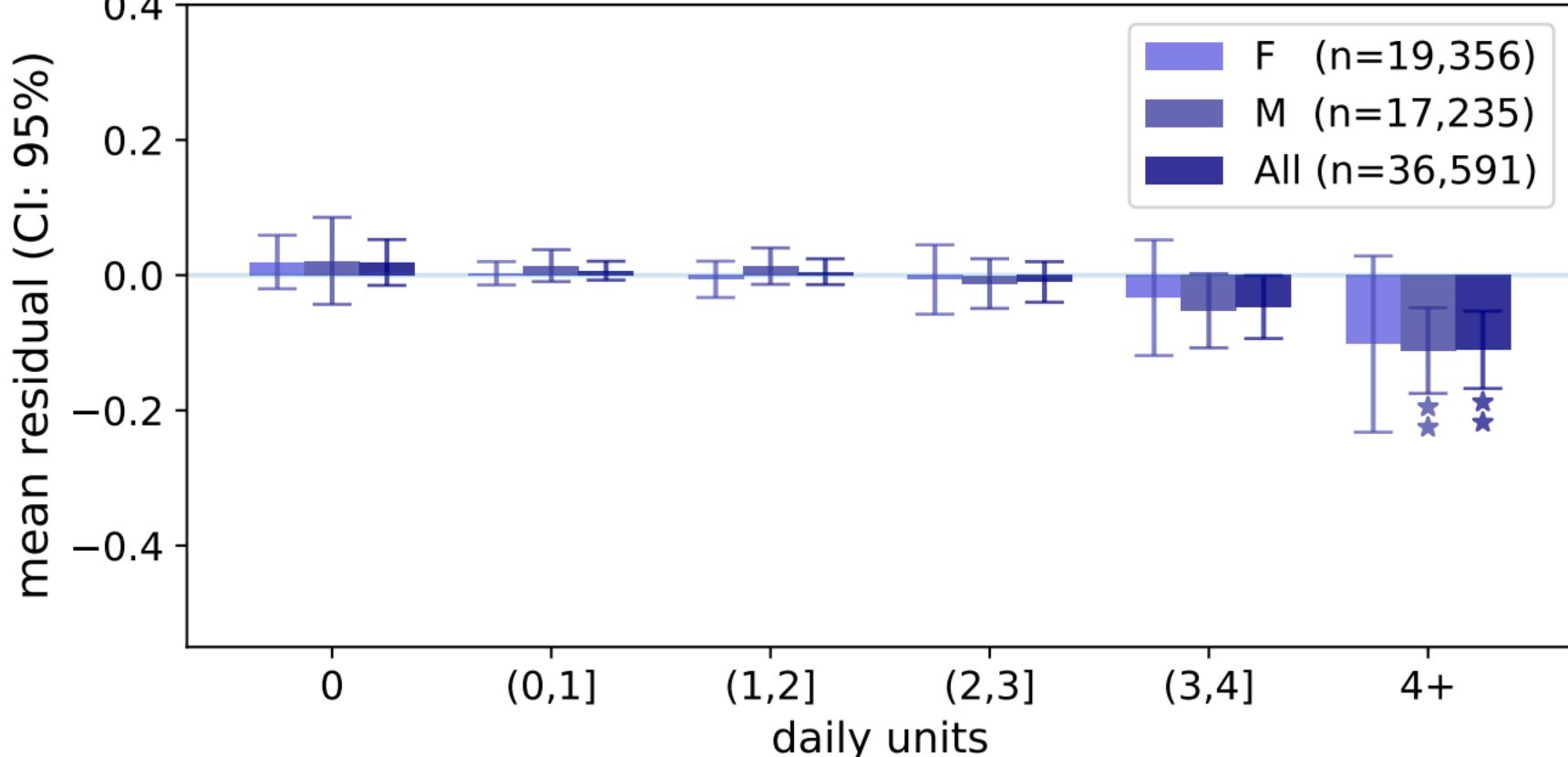
gmv in heschl's gyrus (includes h1 and h2) (r)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in planum temporale (I)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in planum temporale (r)

mean residual (CI: 95%)

0.4

0.2

0.0

-0.2

-0.4

F (n=19,360)
M (n=17,247)
All (n=36,607)

0

(0,1]

(1,2]

(2,3]

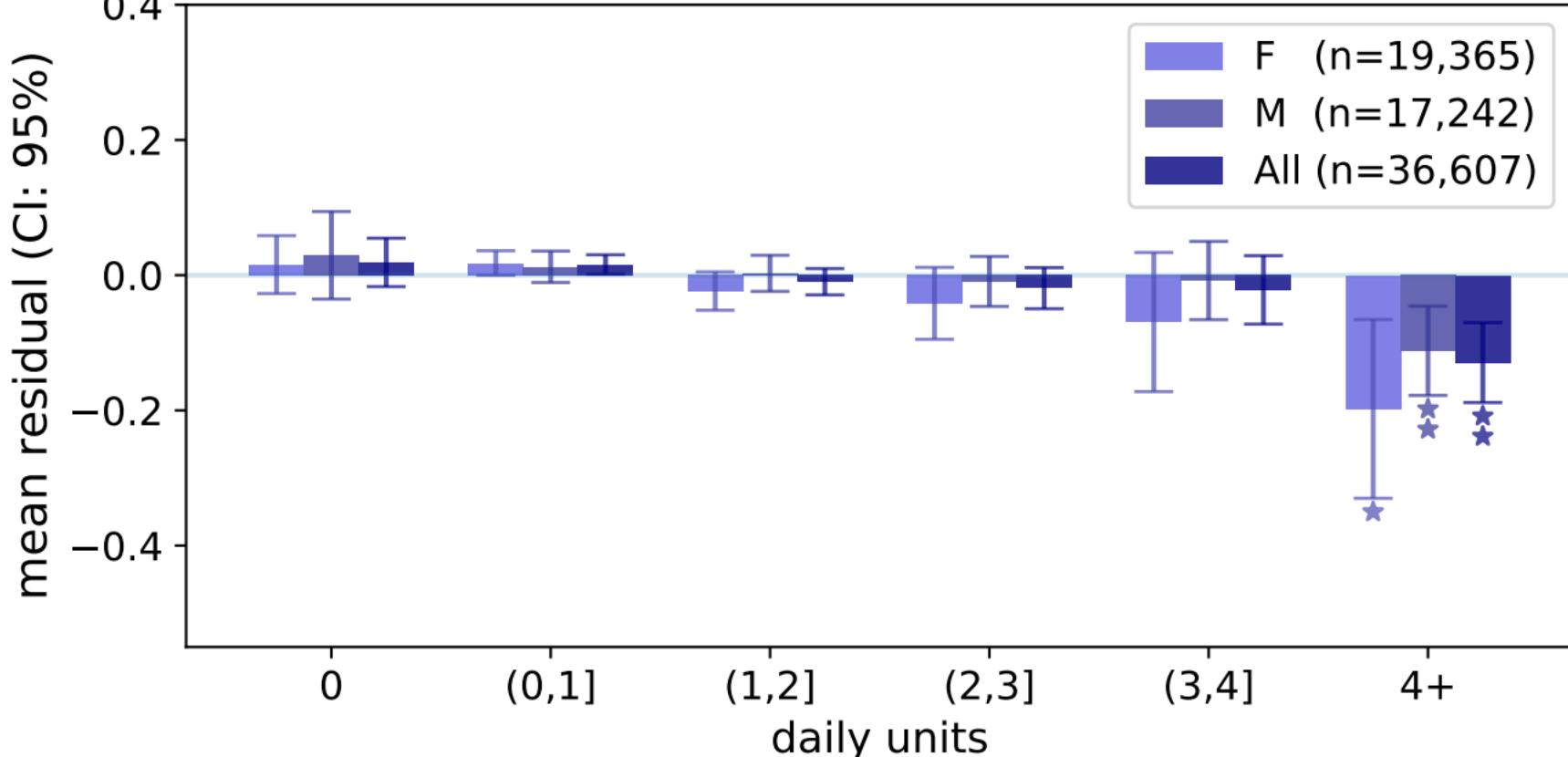
(3,4]

4+

daily units

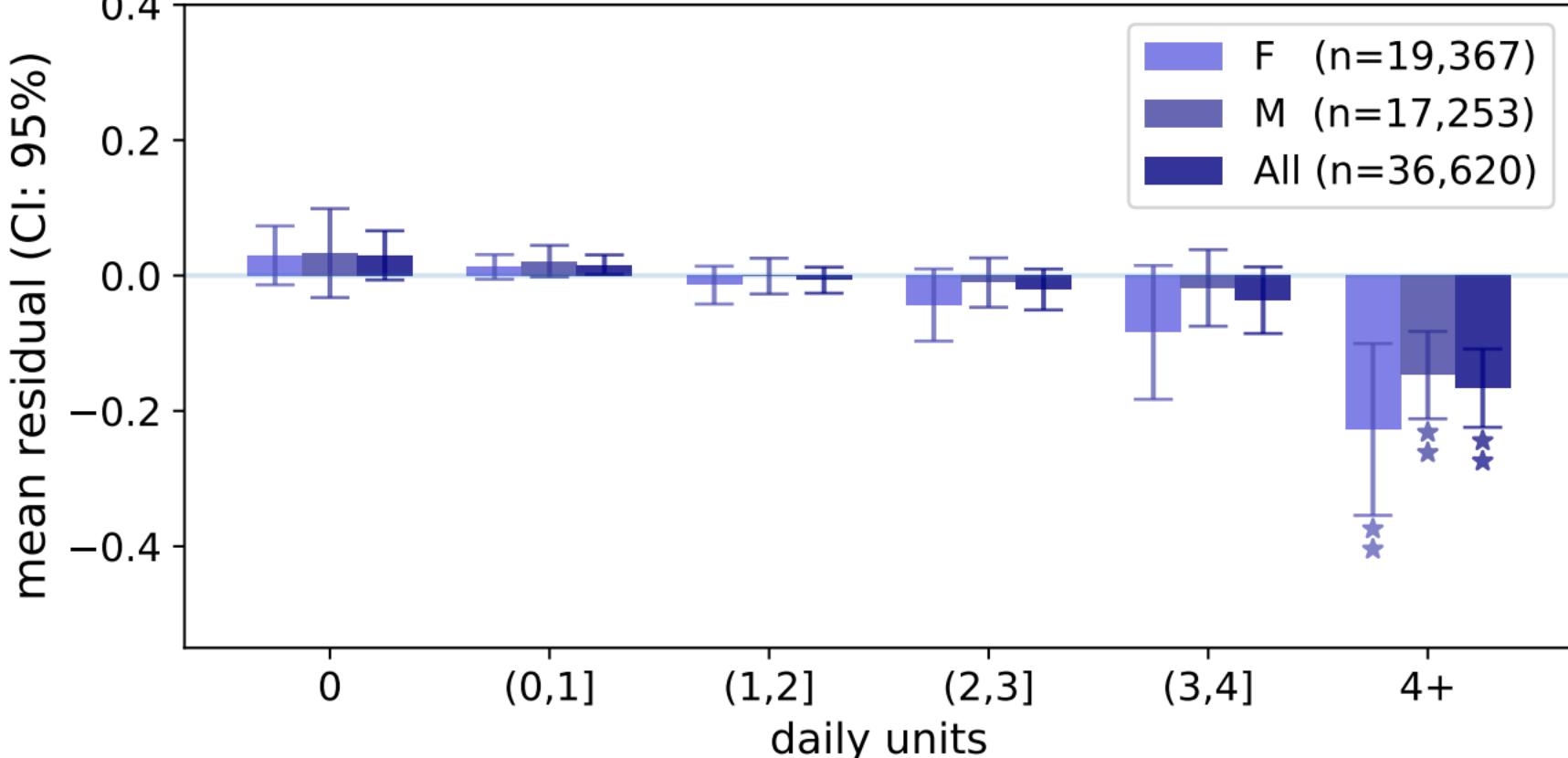
two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in supracingulate cortex (I)



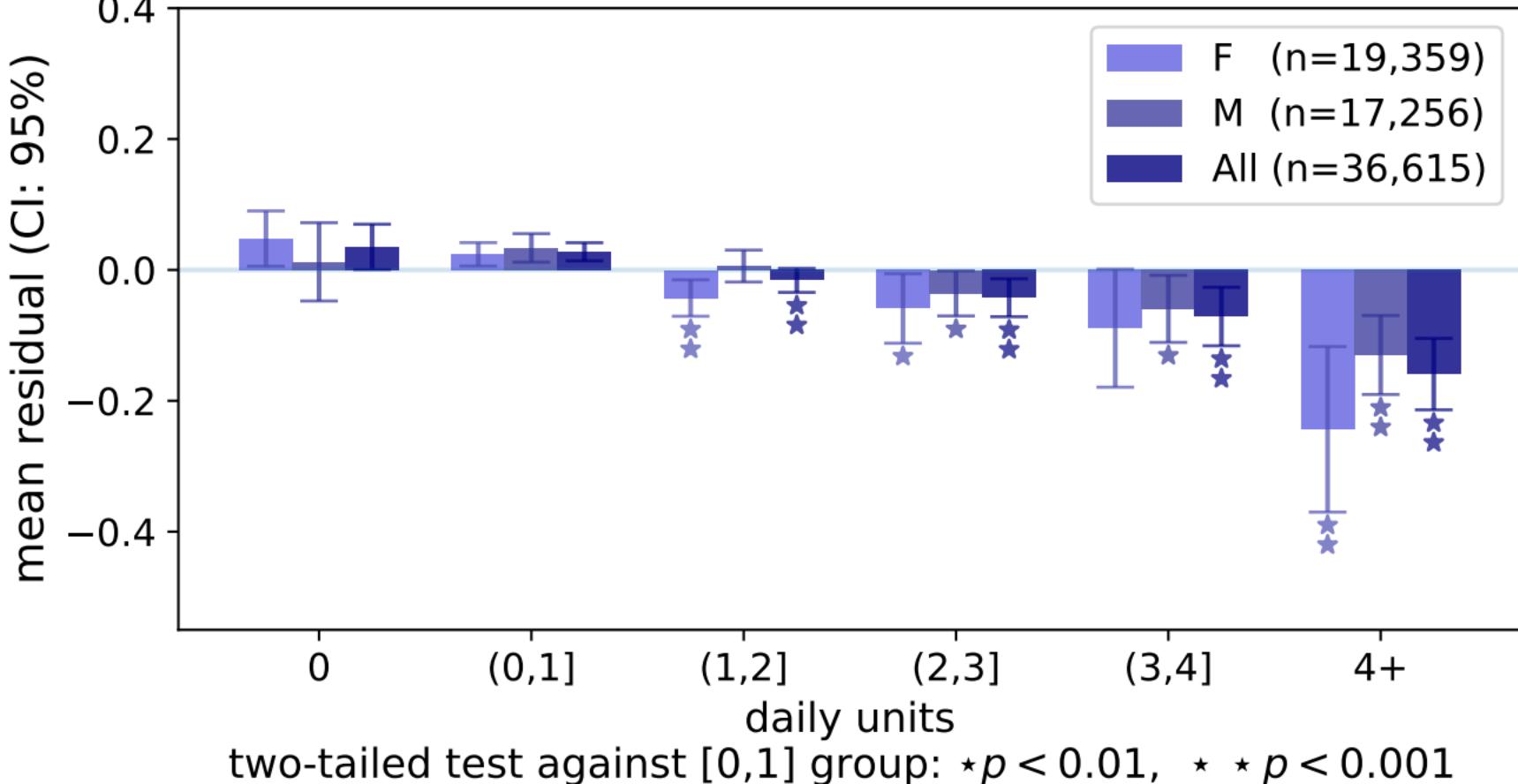
two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in supracingulate cortex (r)

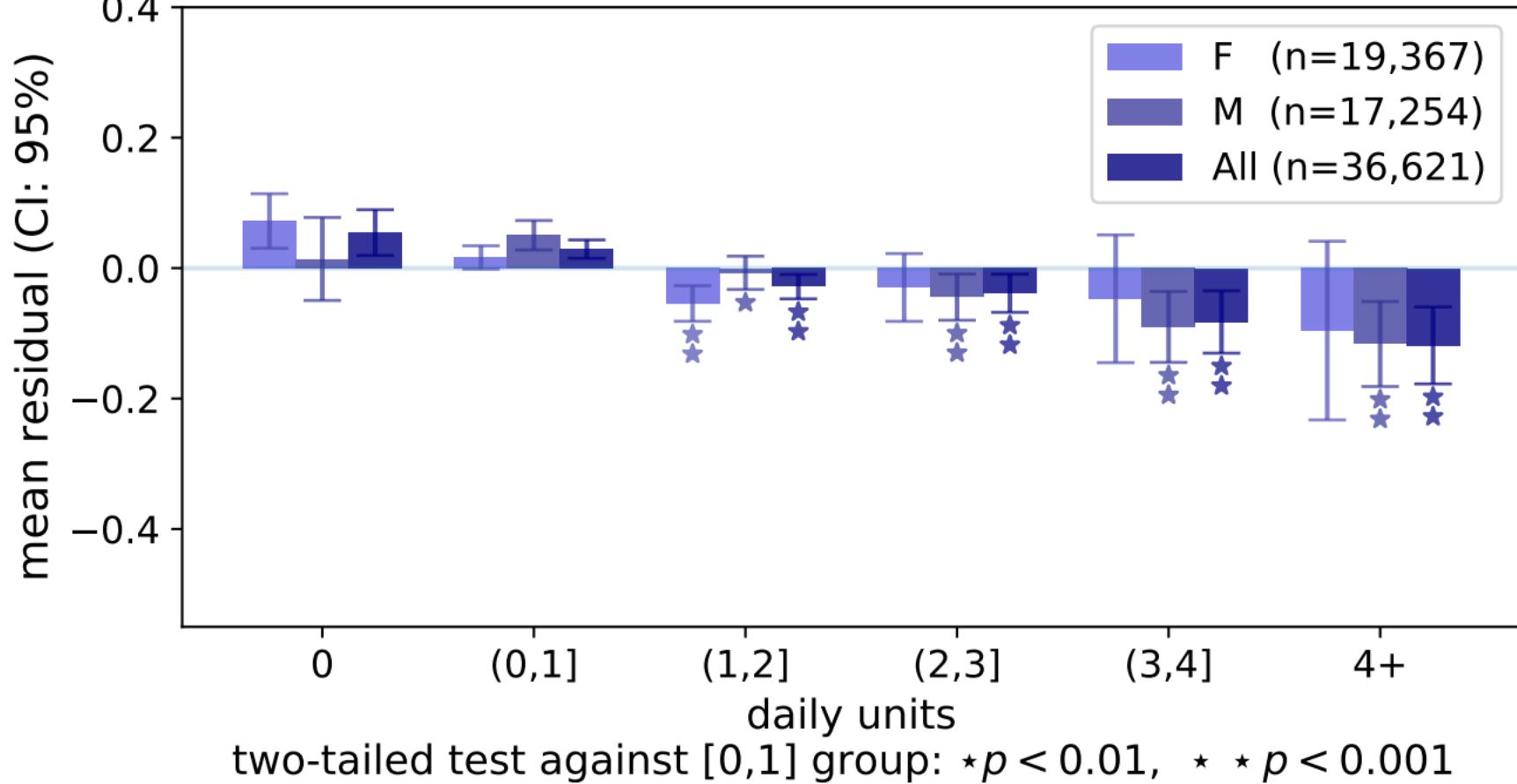


two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

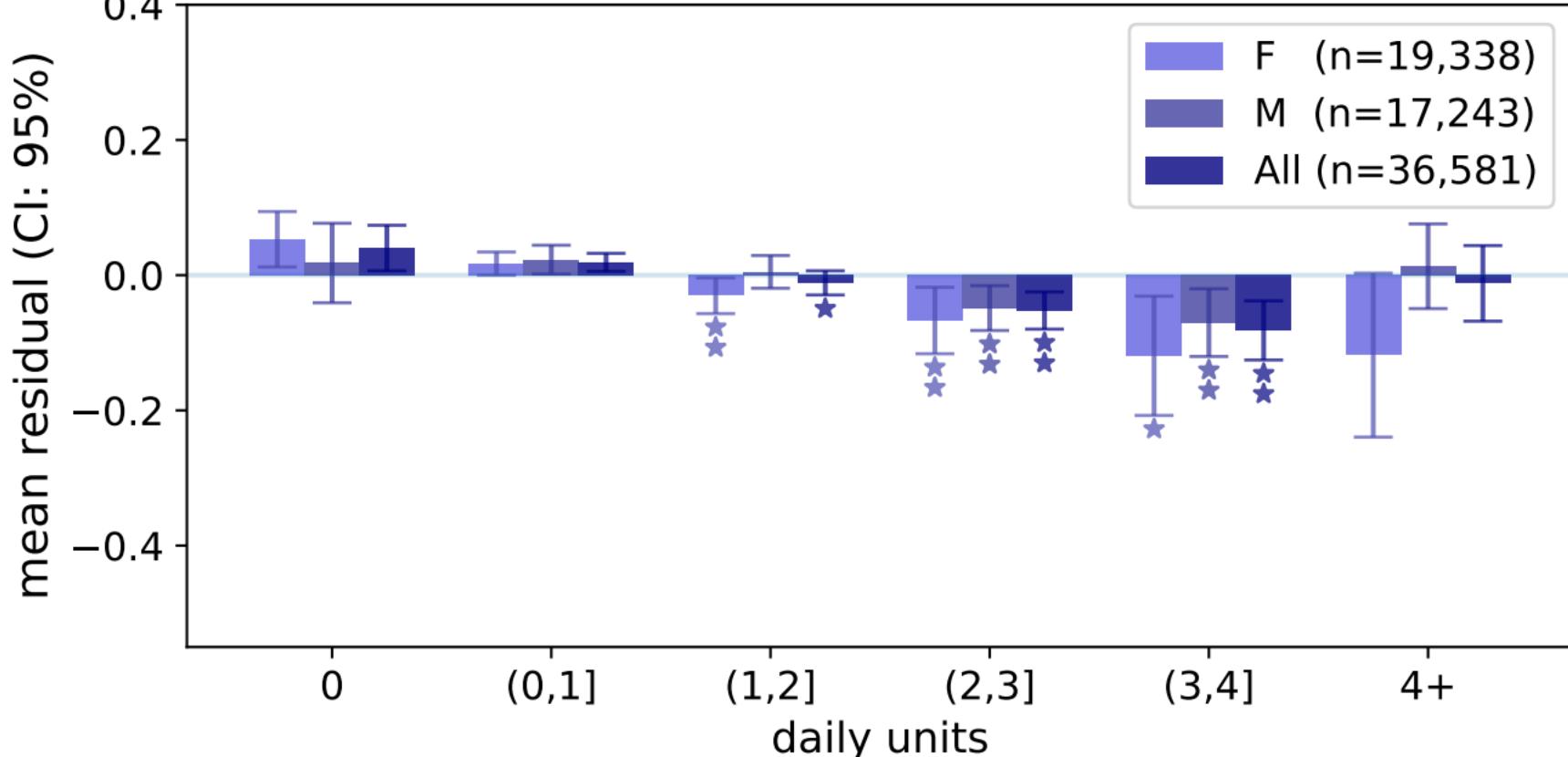
gmv in occipital pole (I)



gmv in occipital pole (r)



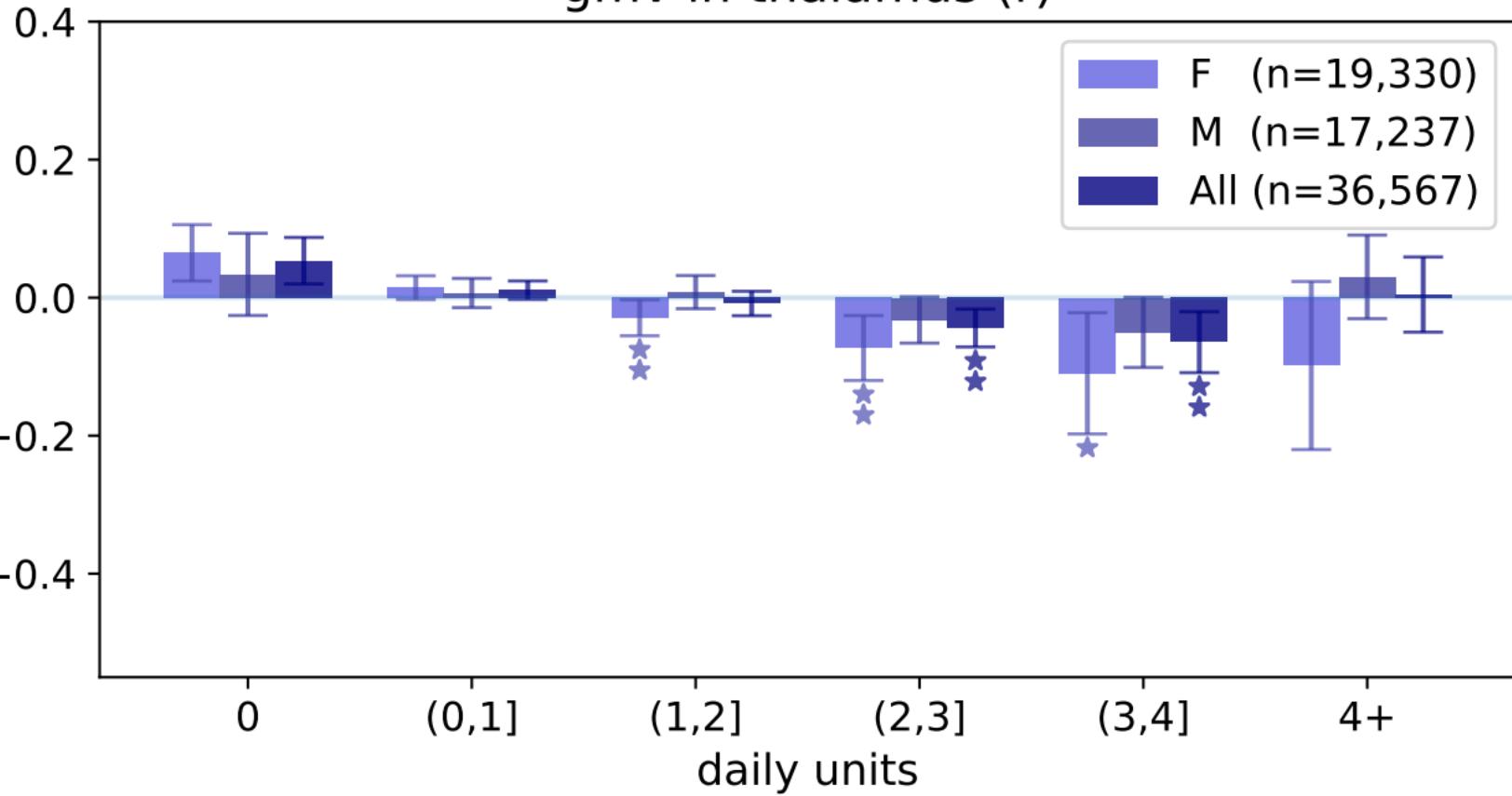
gmv in thalamus (I)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

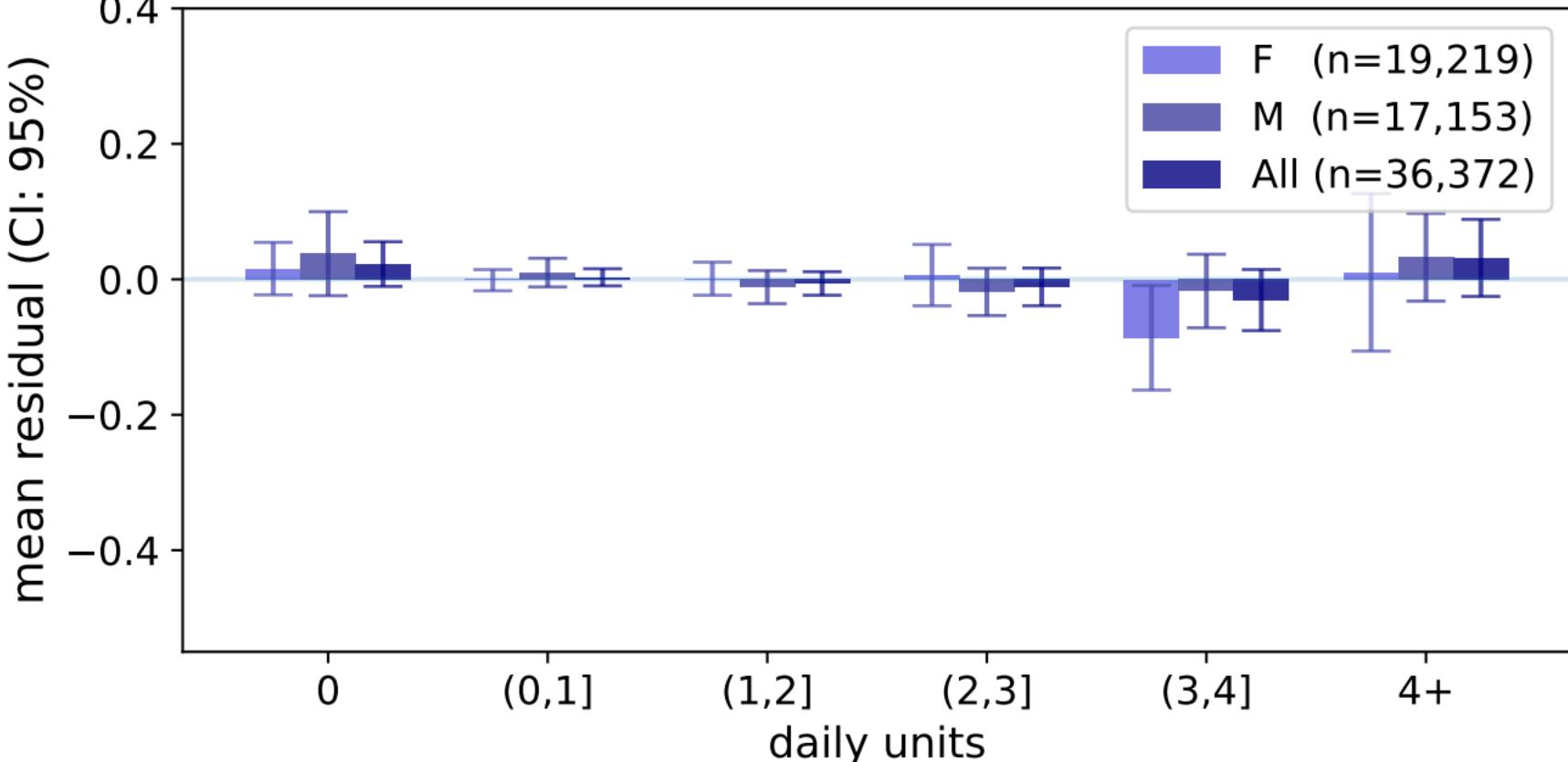
gmv in thalamus (r)

mean residual (CI: 95%)



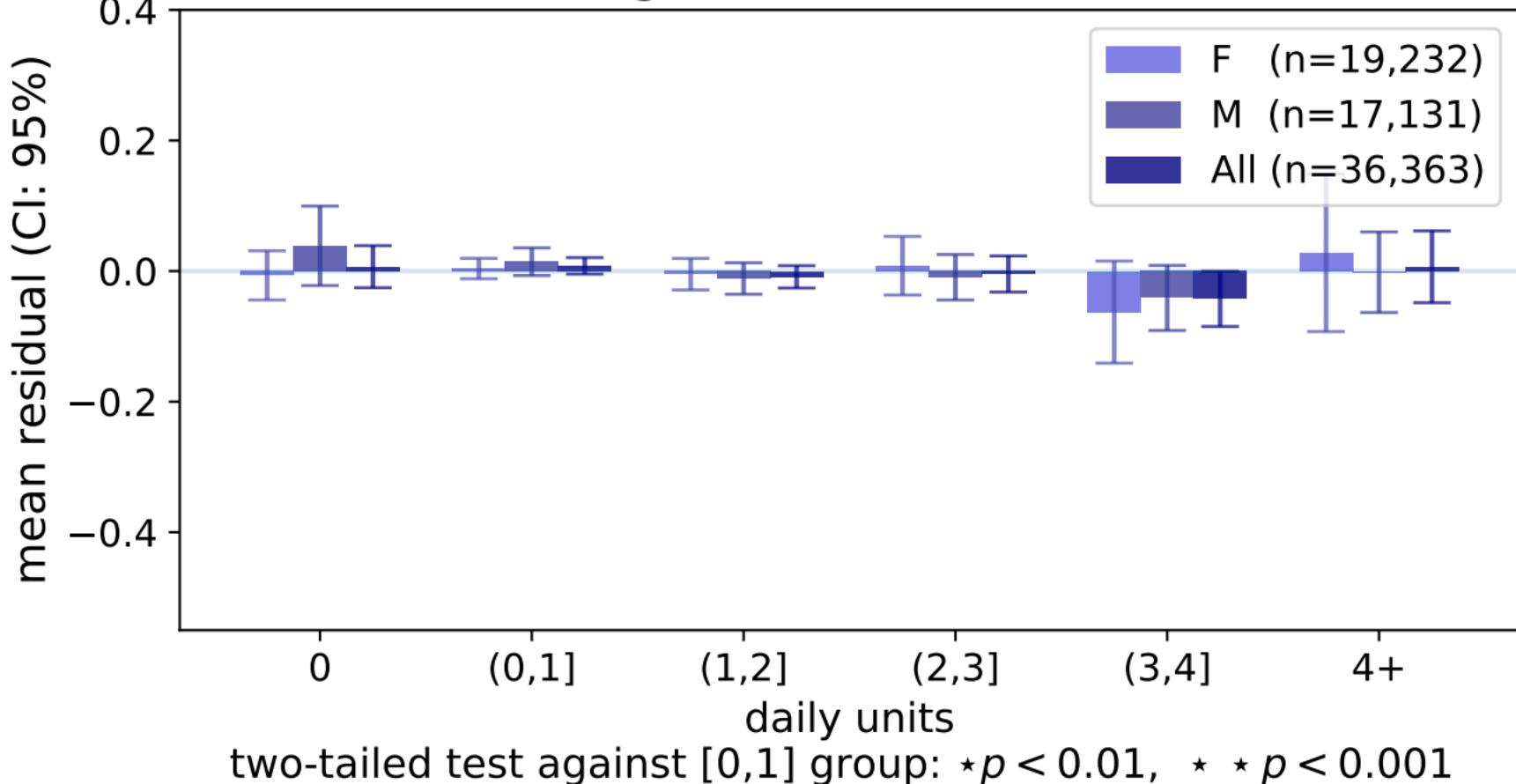
two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in caudate (l)

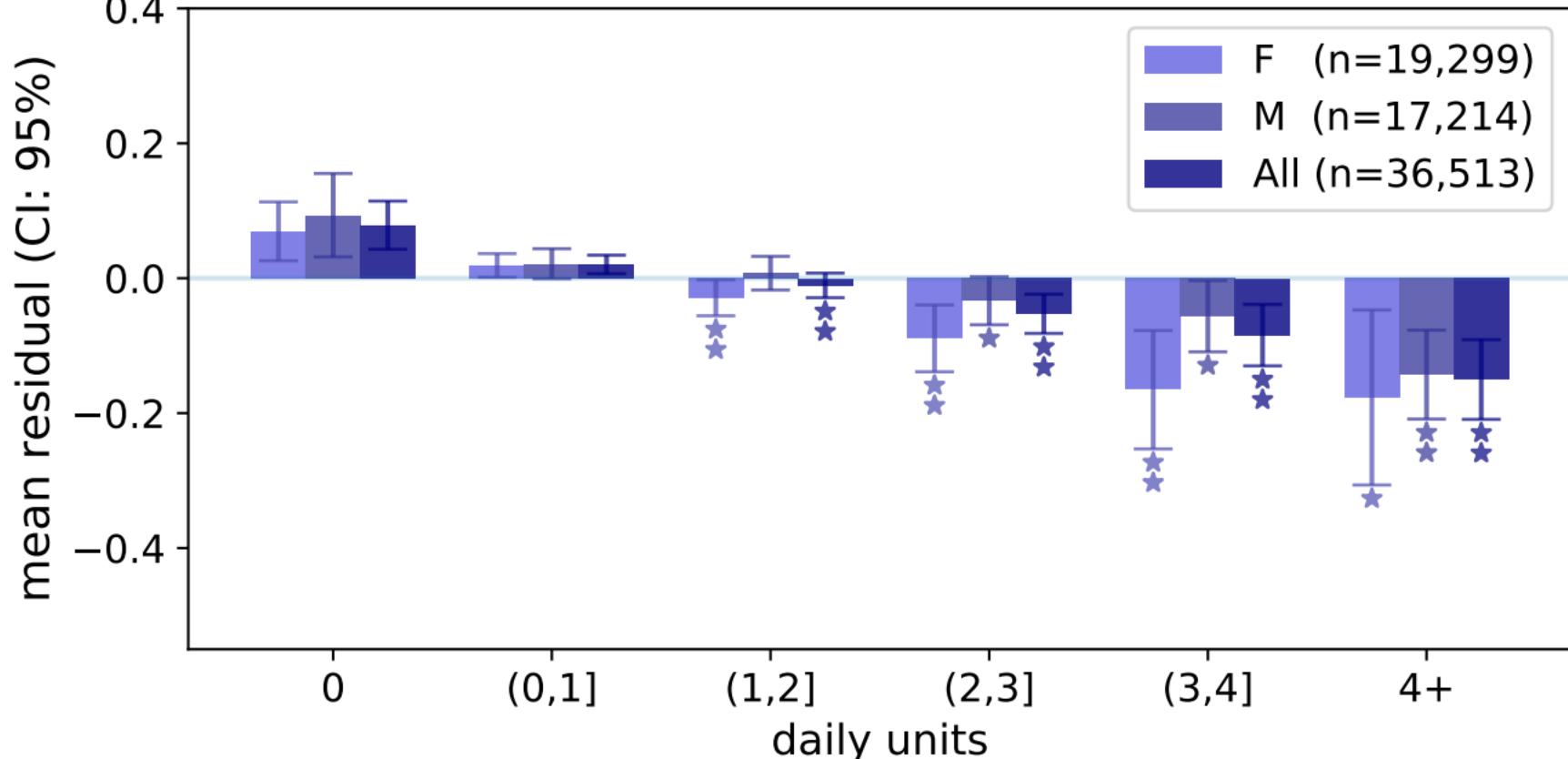


two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in caudate (r)

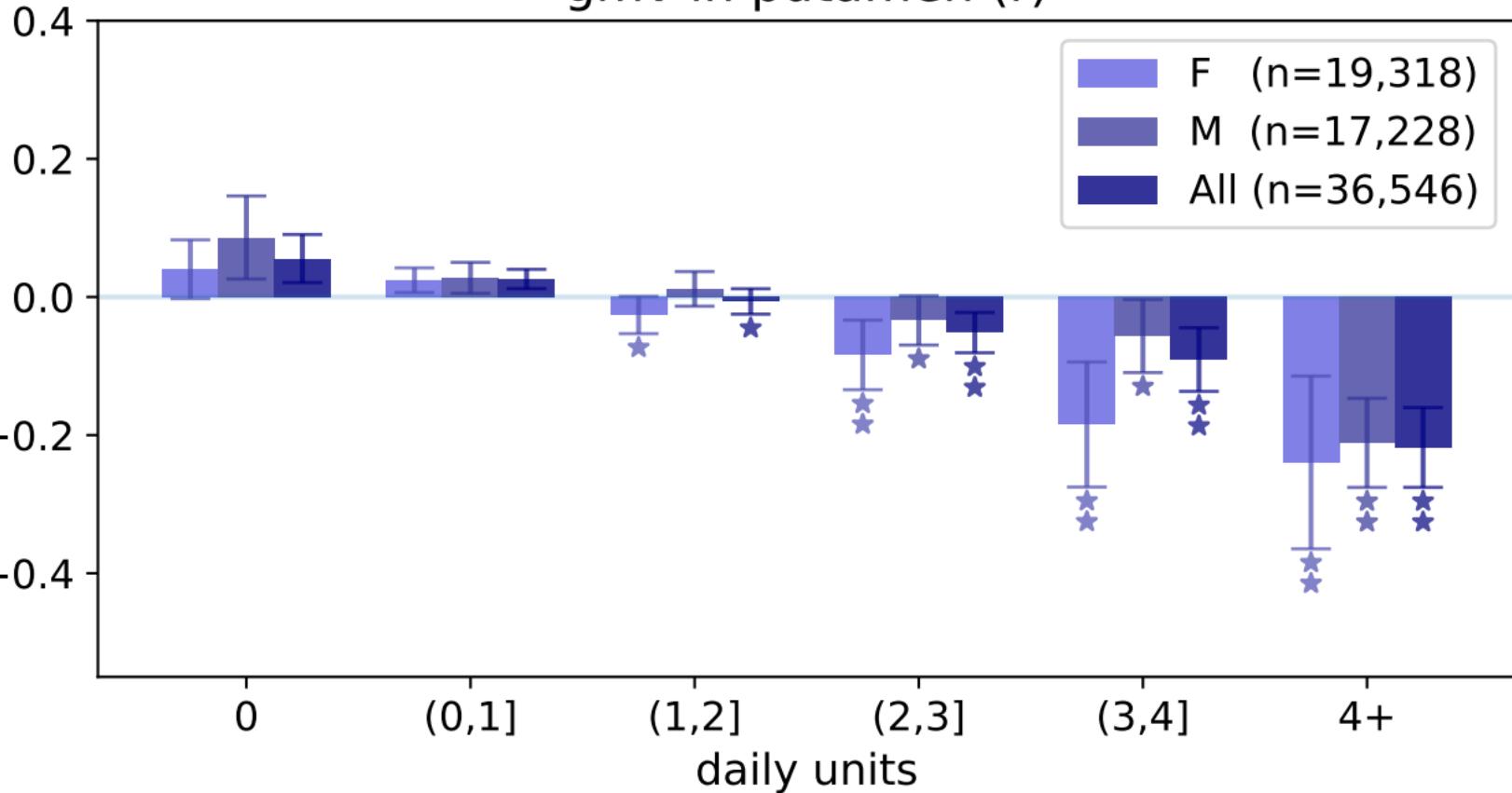


gmv in putamen (l)



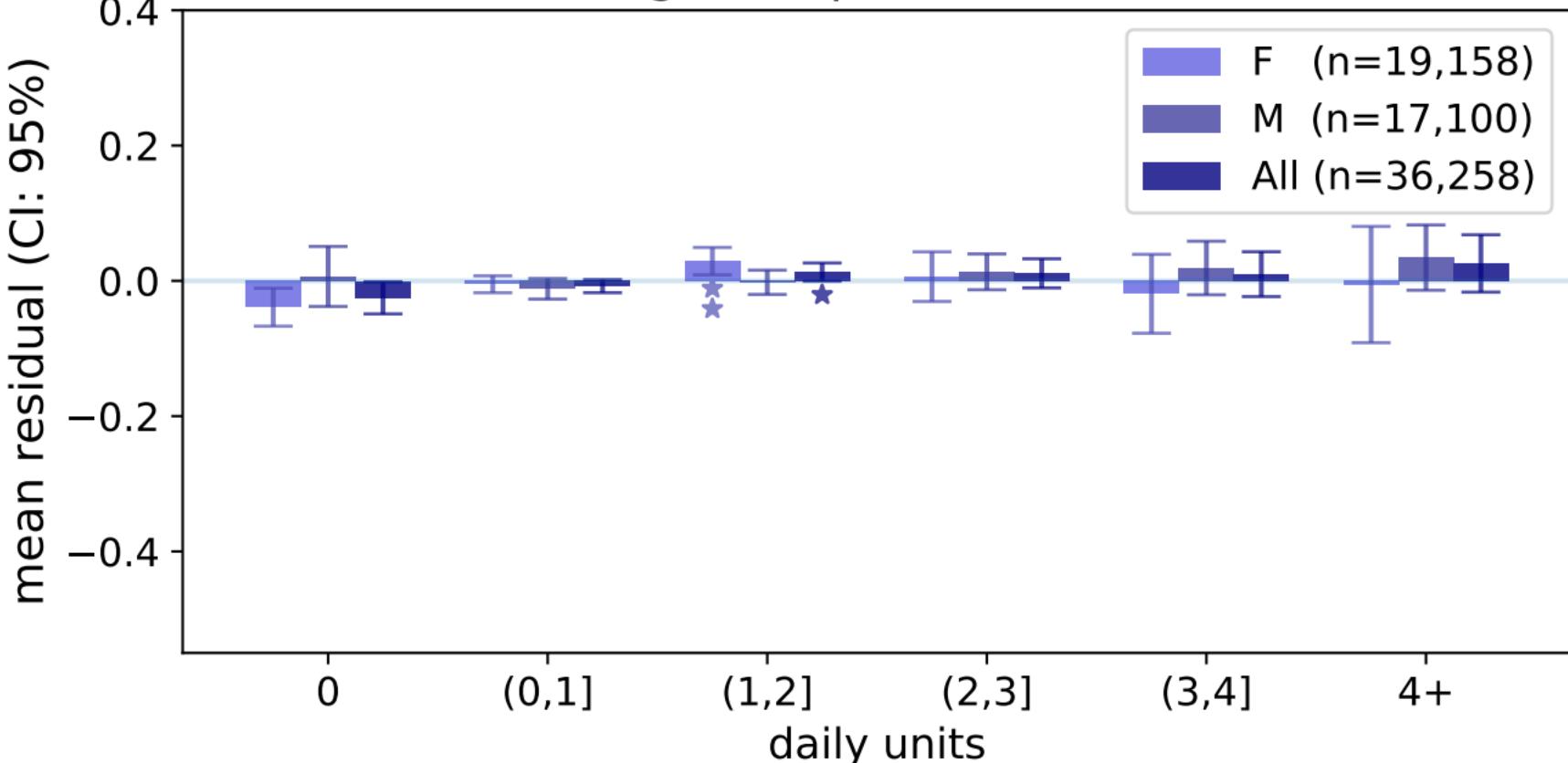
gmv in putamen (r)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in pallidum (l)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in pallidum (r)

mean residual (CI: 95%)

0.4

0.2

-0.2

-0.4

F (n=19,158)
M (n=17,073)
All (n=36,231)

0

(0,1]

(1,2]

(2,3]

(3,4]

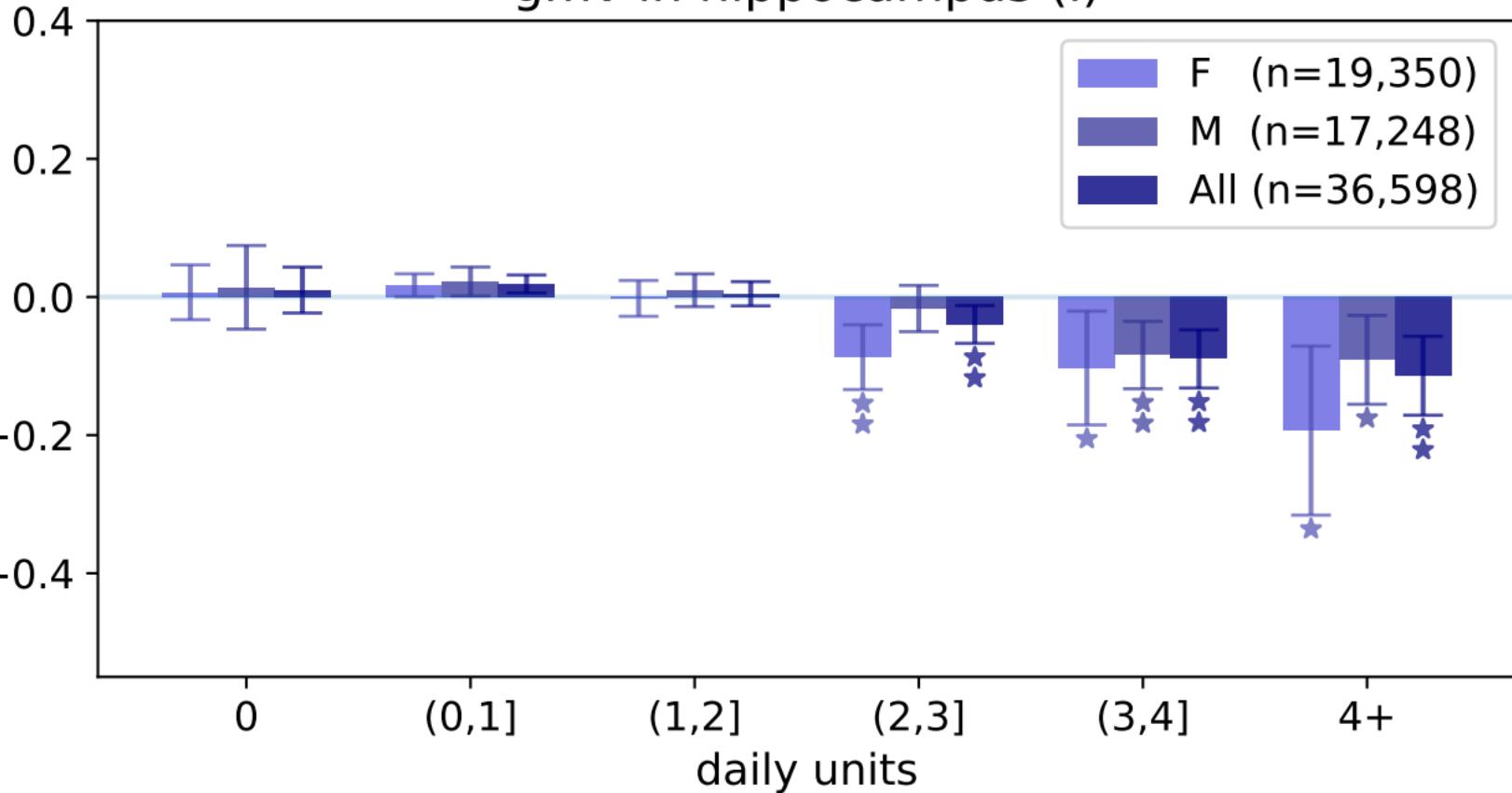
4+

daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in hippocampus (I)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in hippocampus (r)

mean residual (CI: 95%)

0.4

0.2

0.0

-0.2

-0.4

F (n=19,351)
M (n=17,247)
All (n=36,598)

0

(0,1]

(1,2]

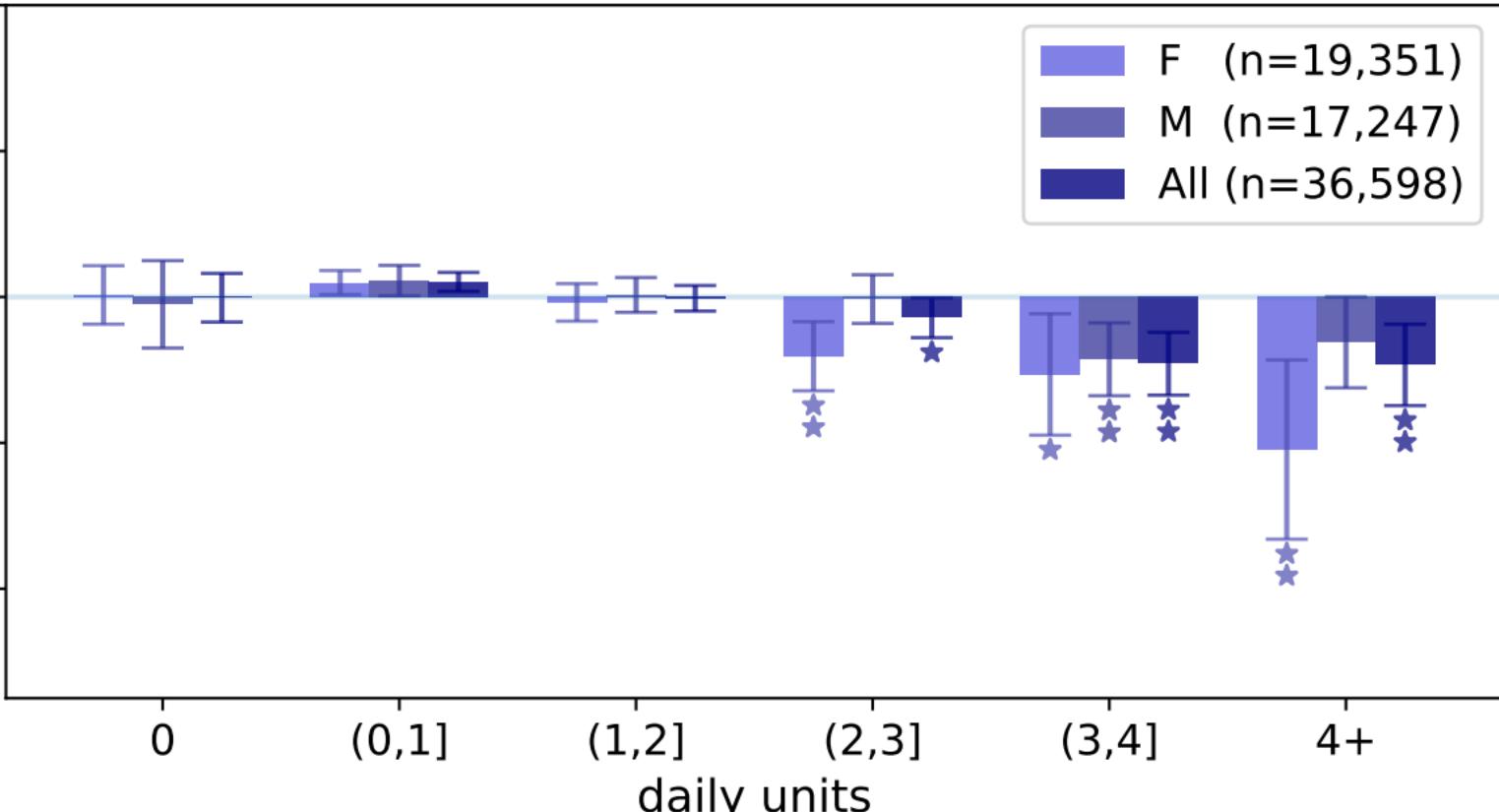
(2,3]

(3,4]

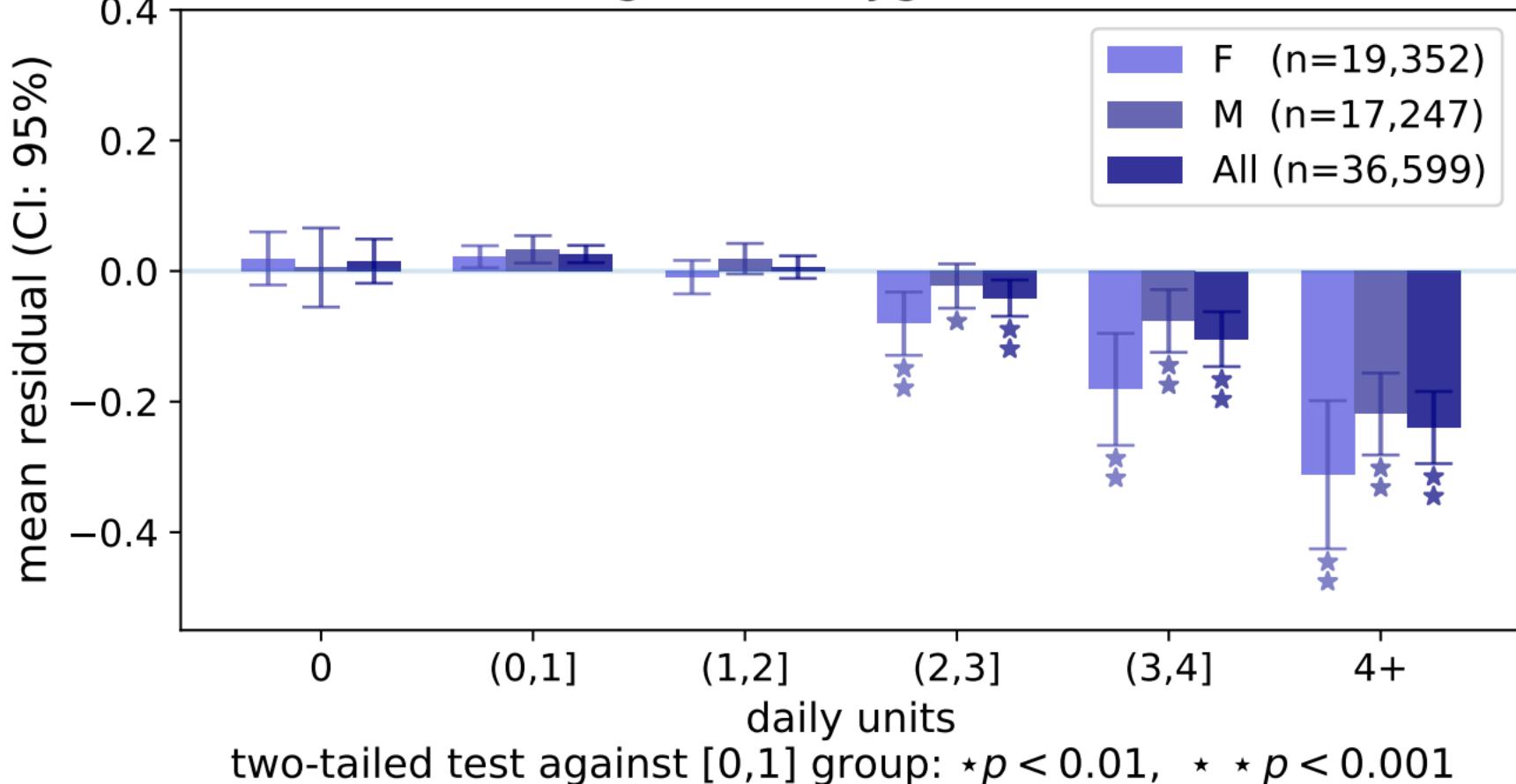
4+

daily units

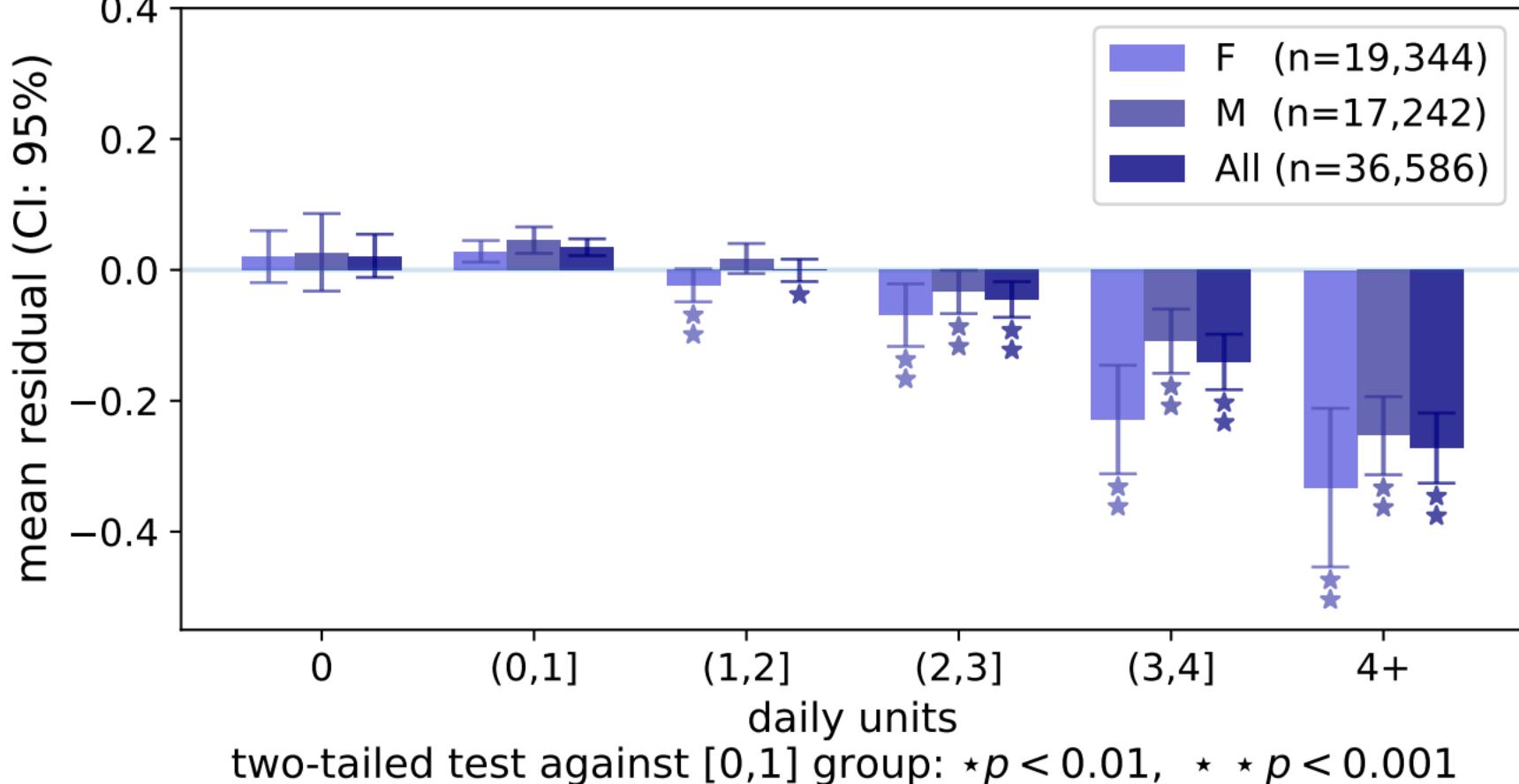
two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$



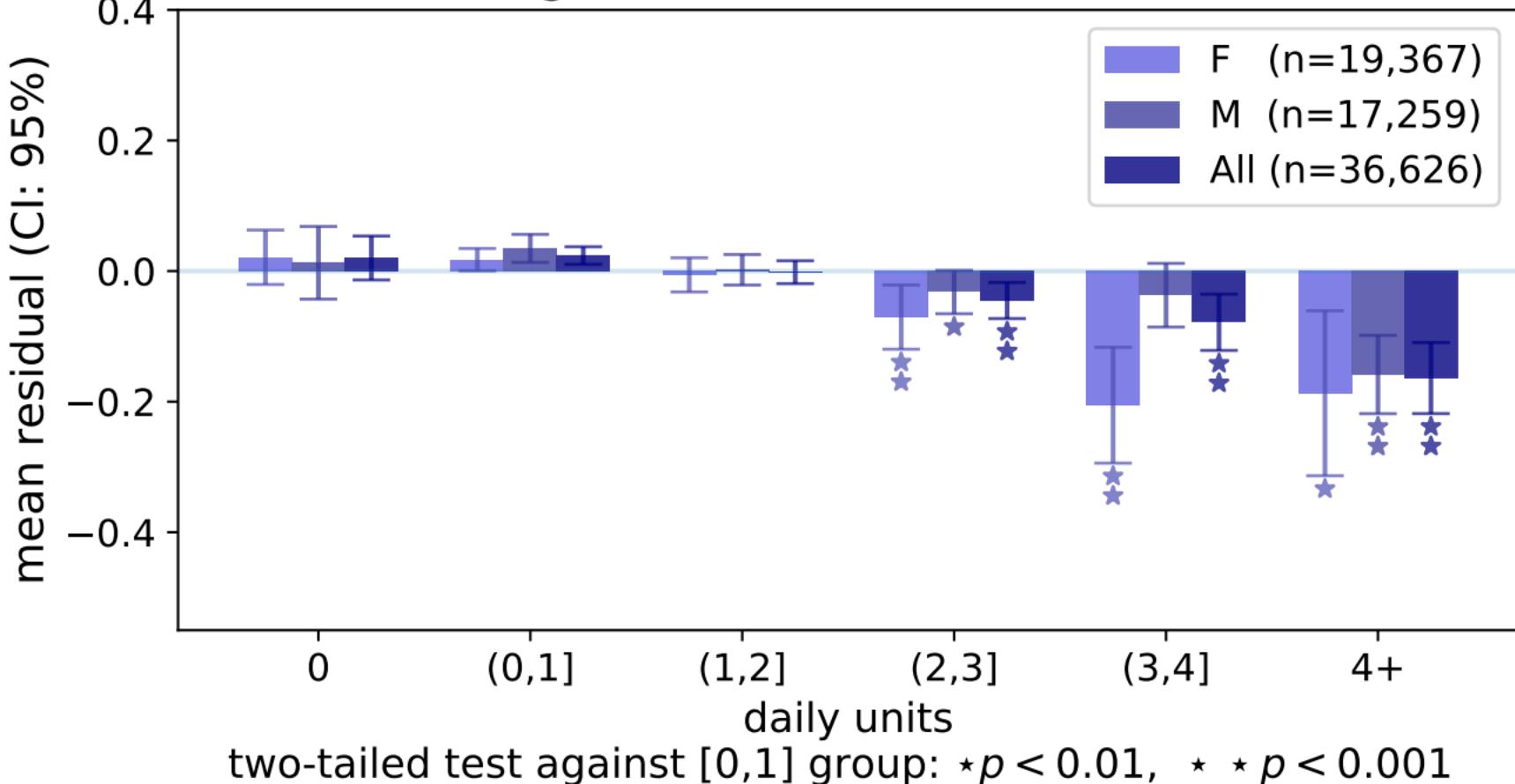
gmv in amygdala (I)



gmv in amygdala (r)

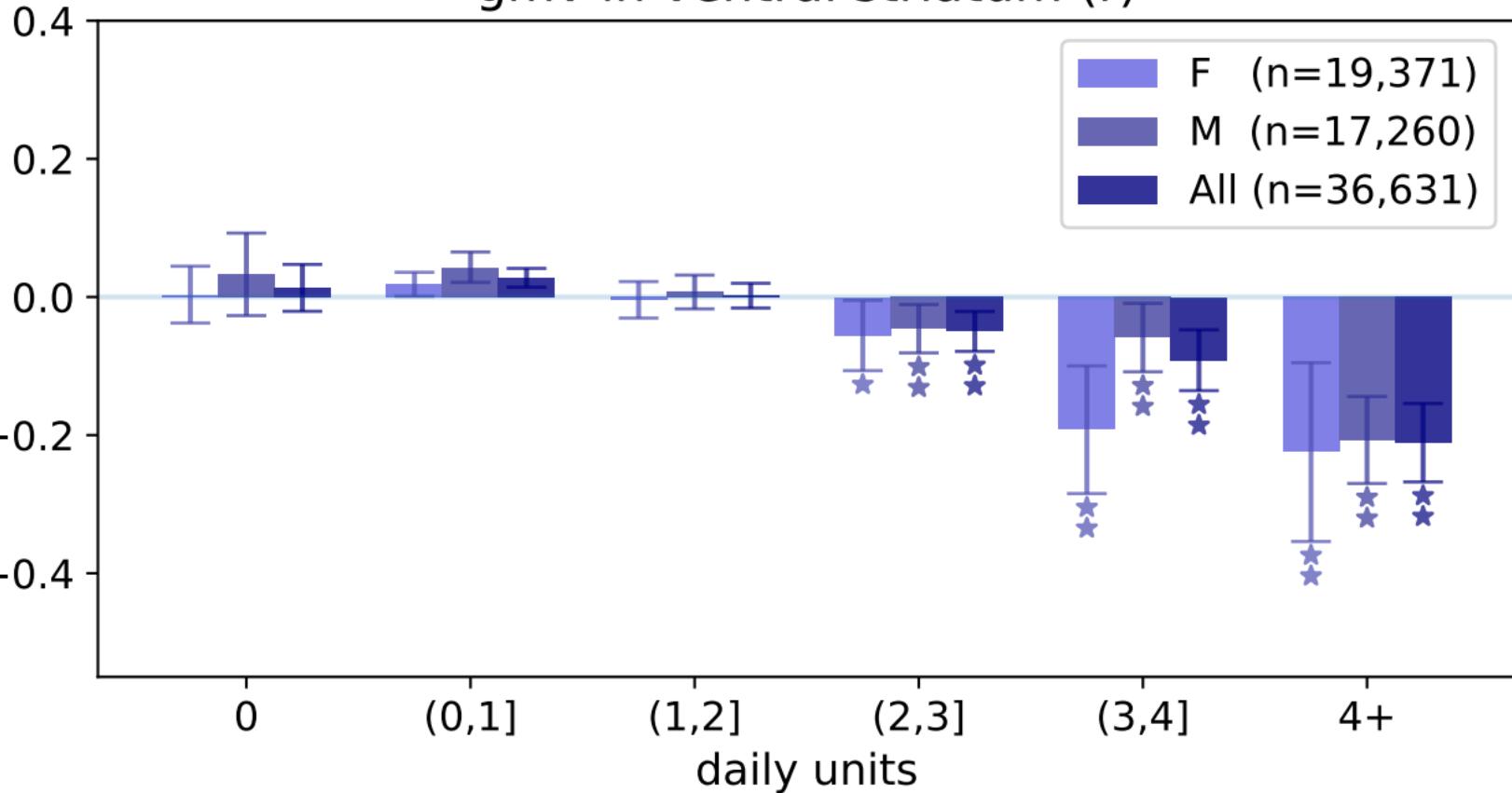


gmv in ventral striatum (I)



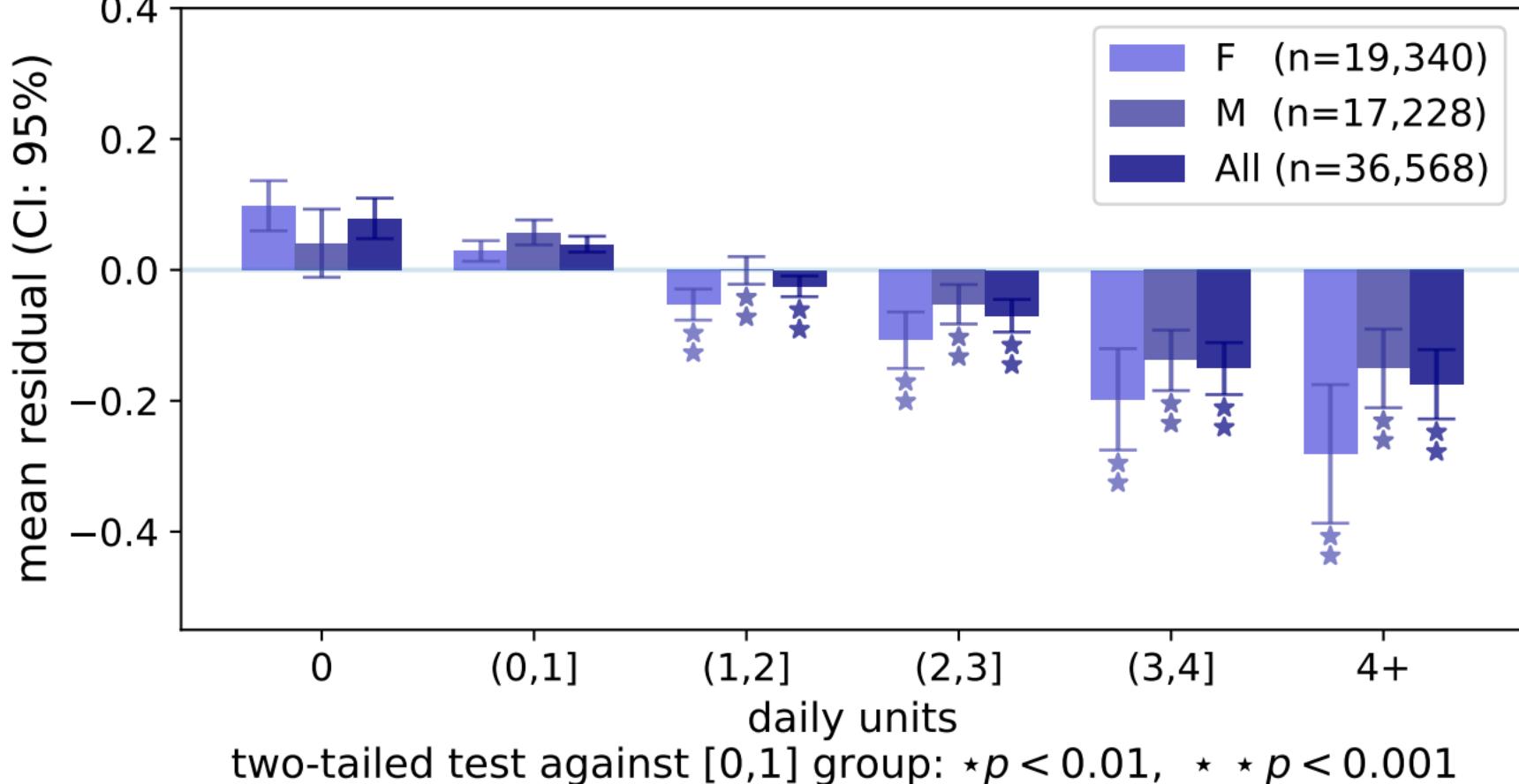
gmv in ventral striatum (r)

mean residual (CI: 95%)

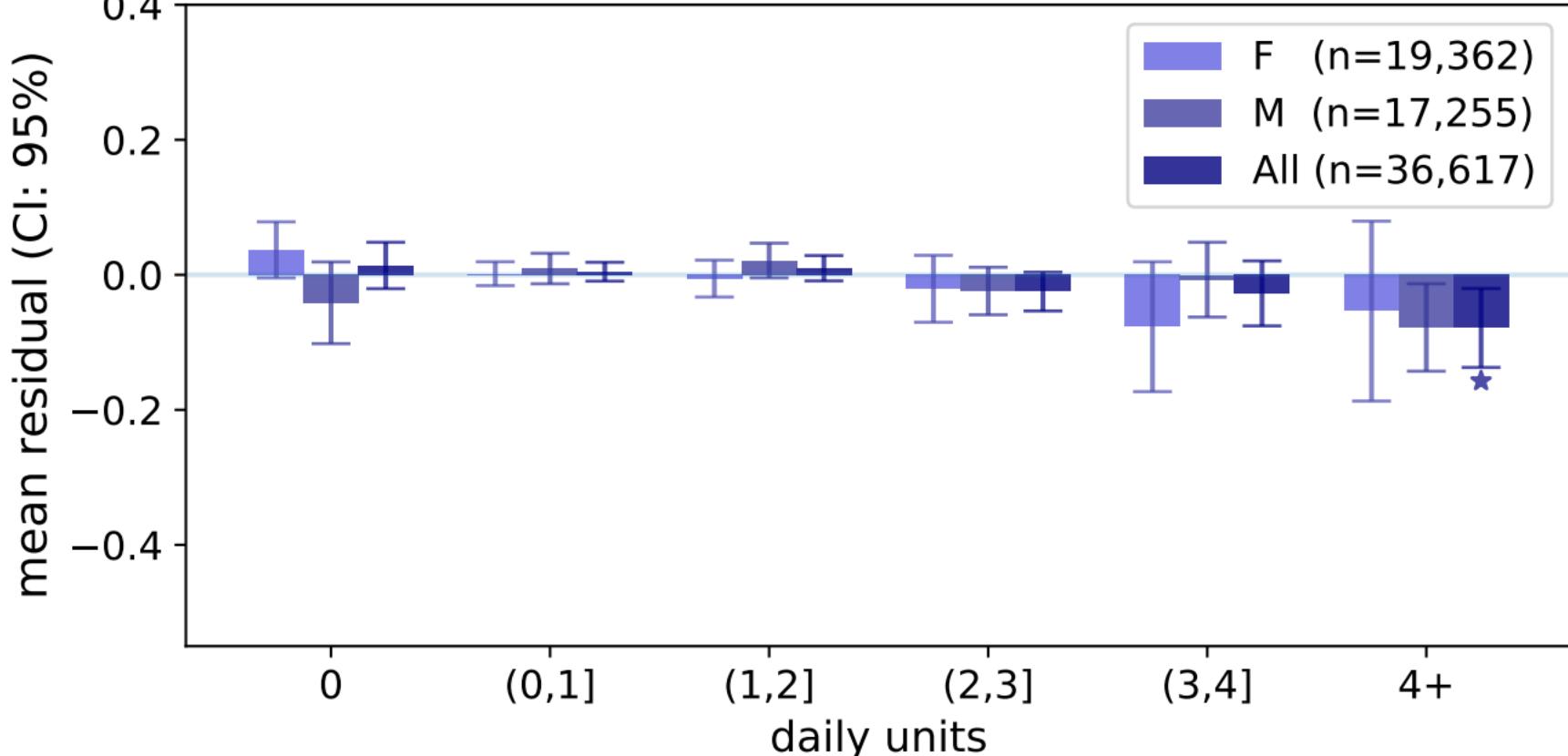


two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in brain-stem



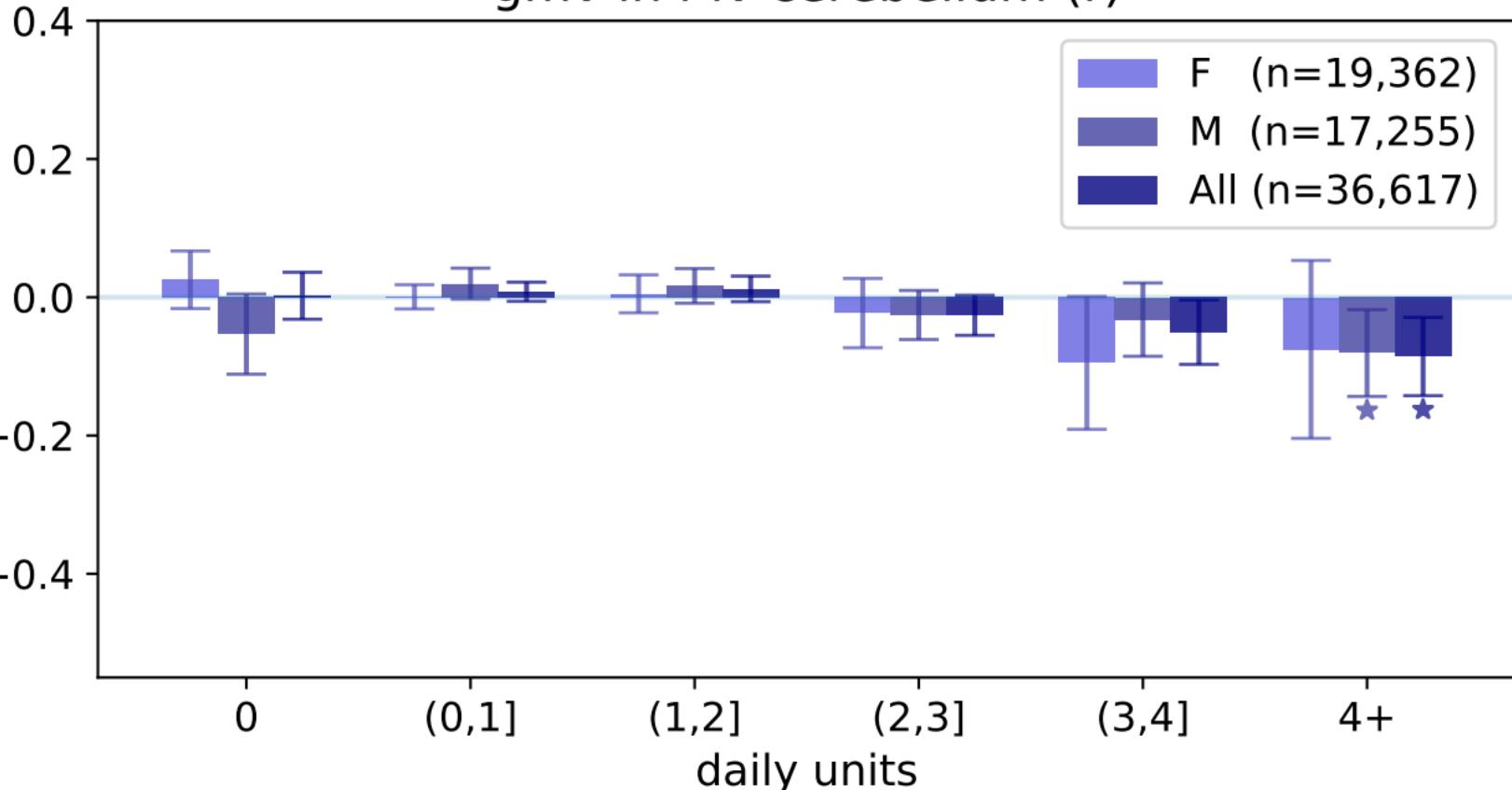
gmv in i-iv cerebellum (I)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in i-iv cerebellum (r)

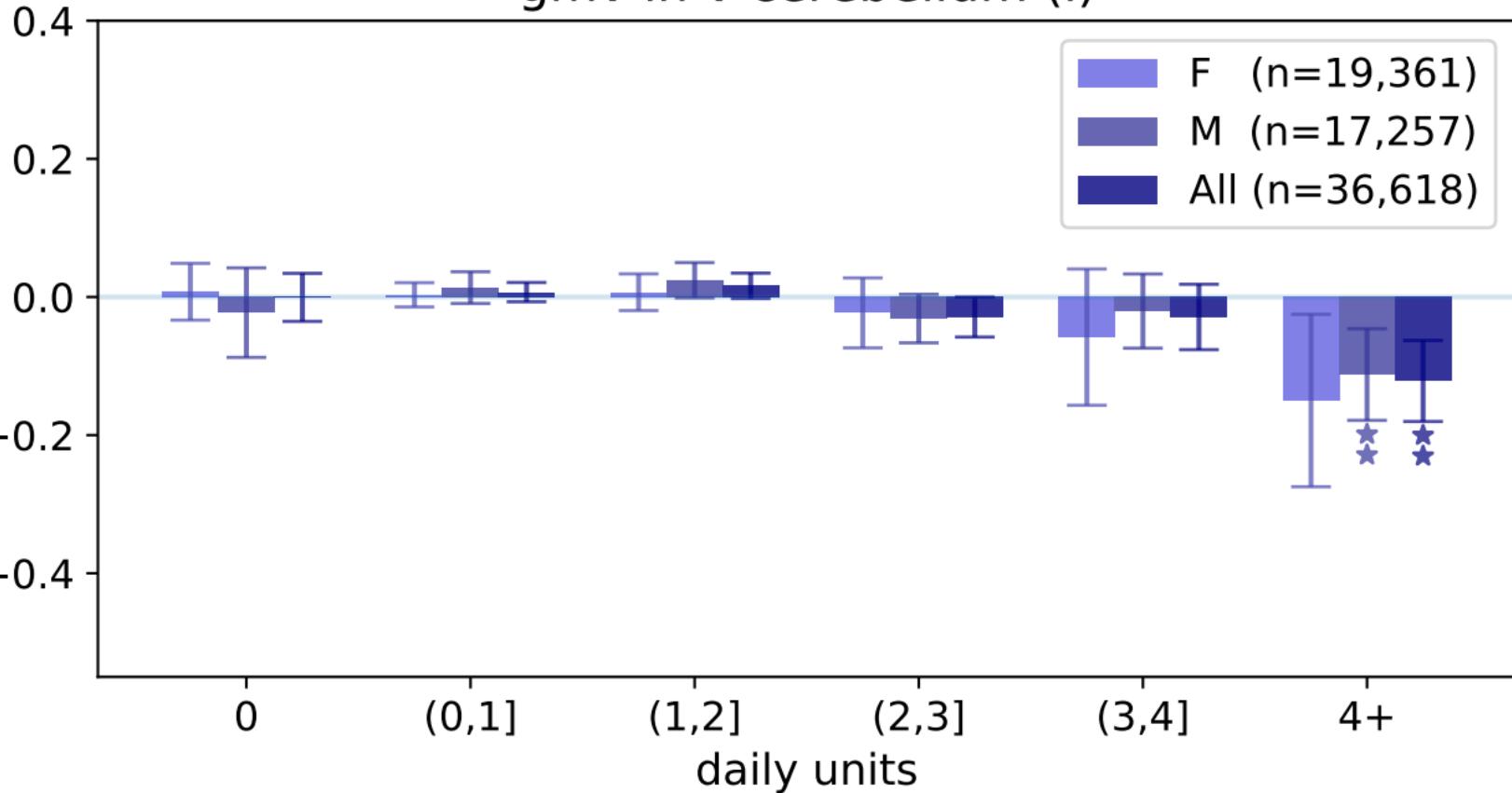
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in v cerebellum (I)

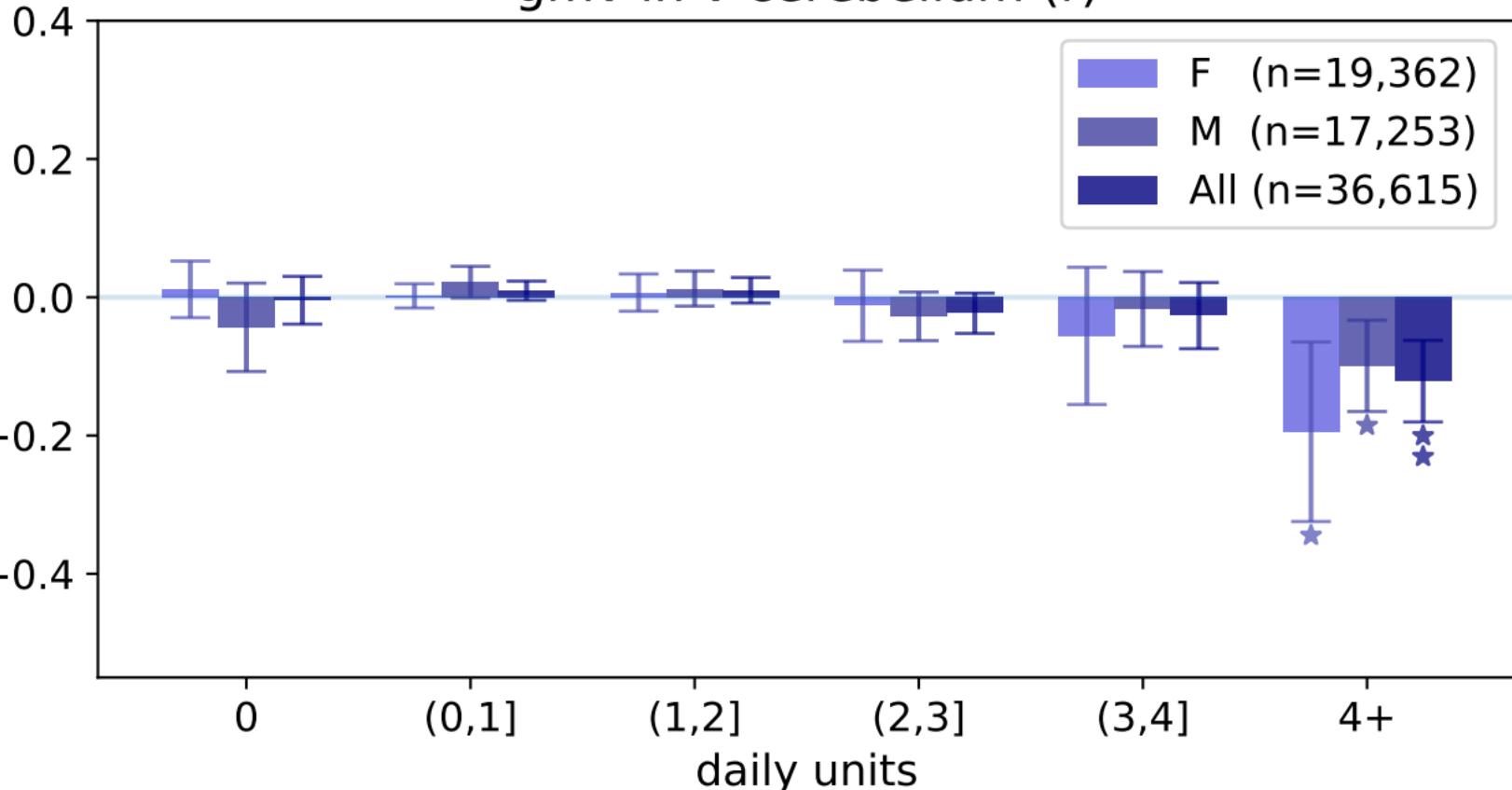
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in v cerebellum (r)

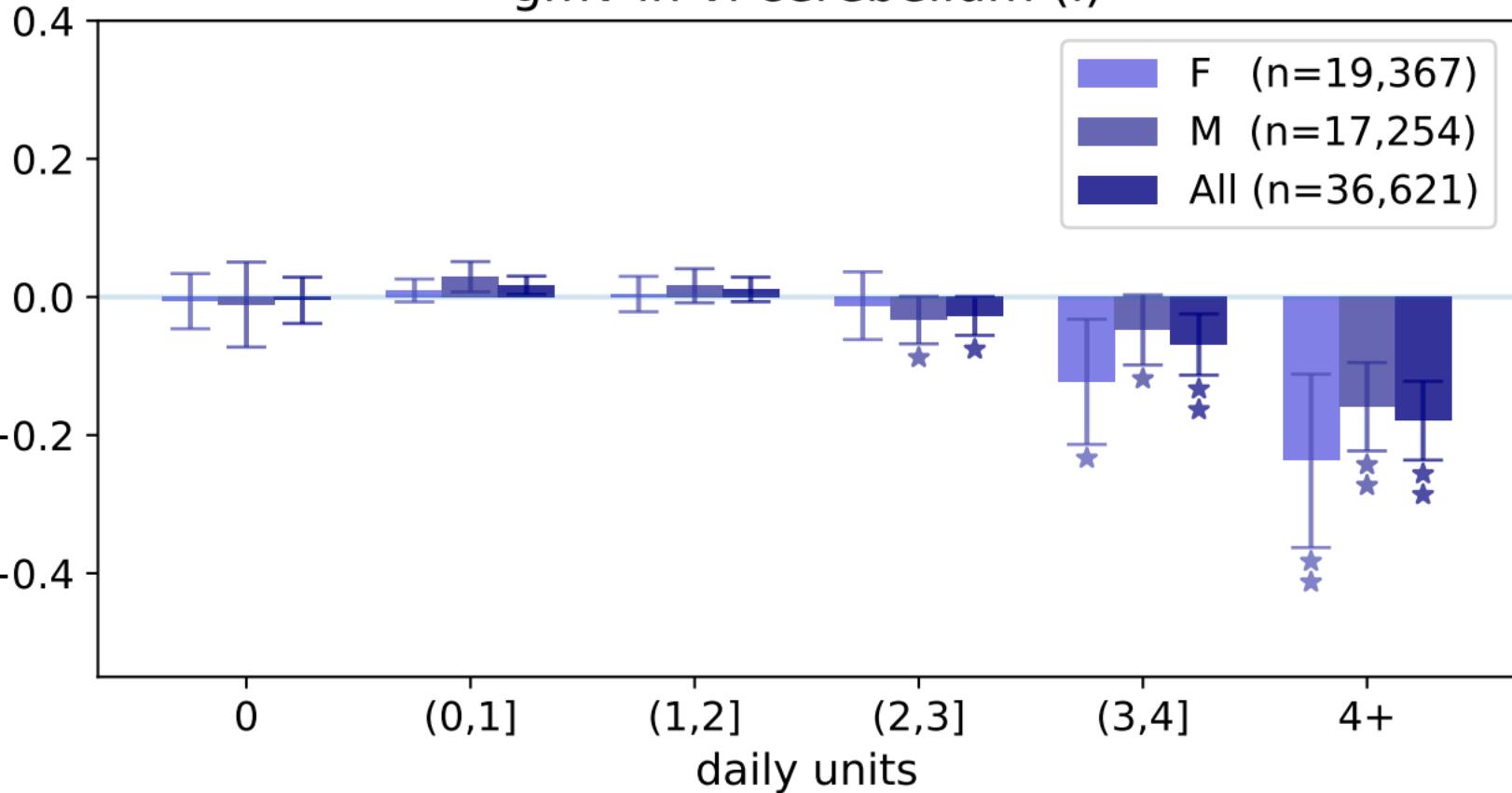
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in vi cerebellum (I)

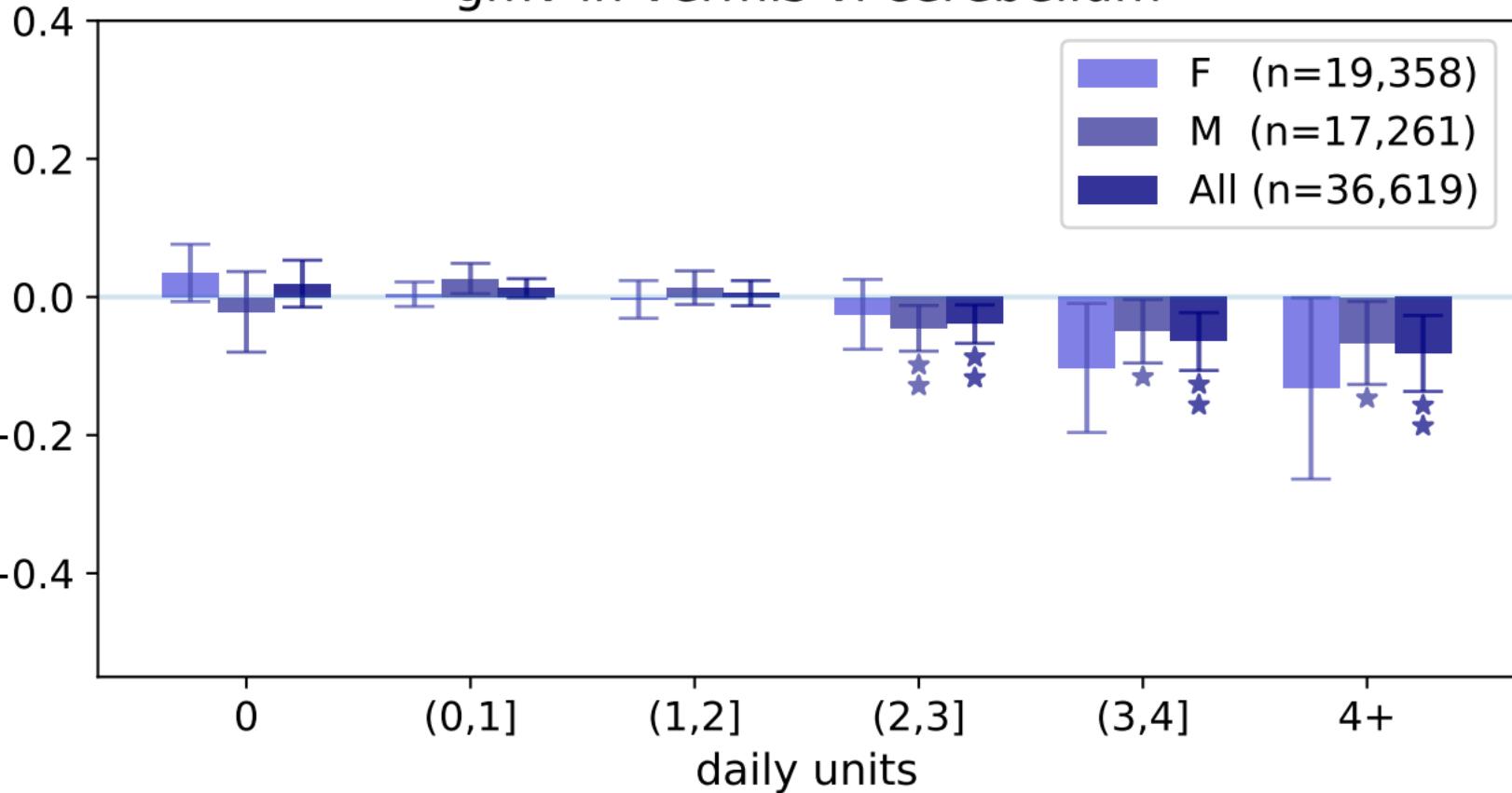
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in vermis vi cerebellum

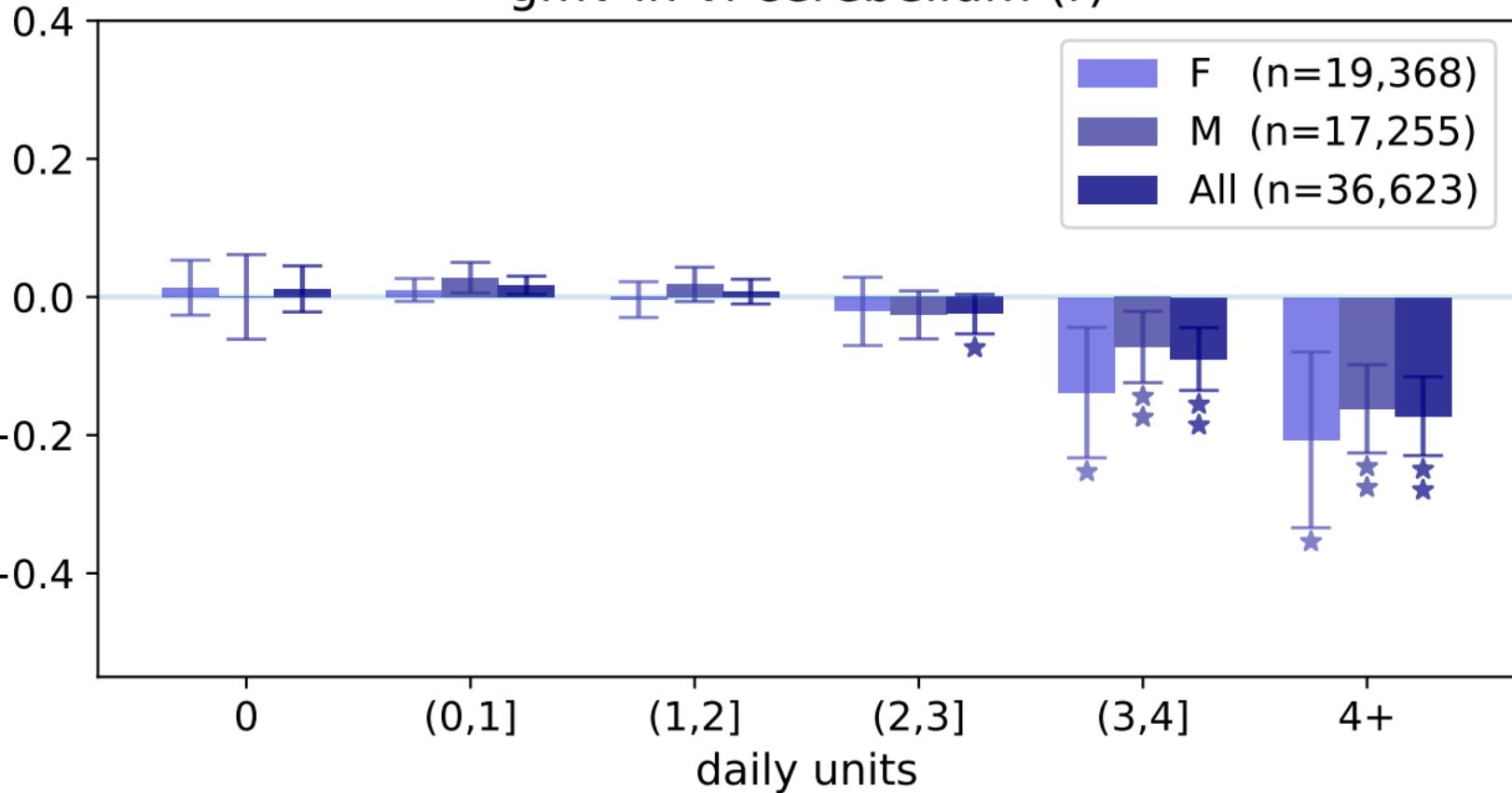
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

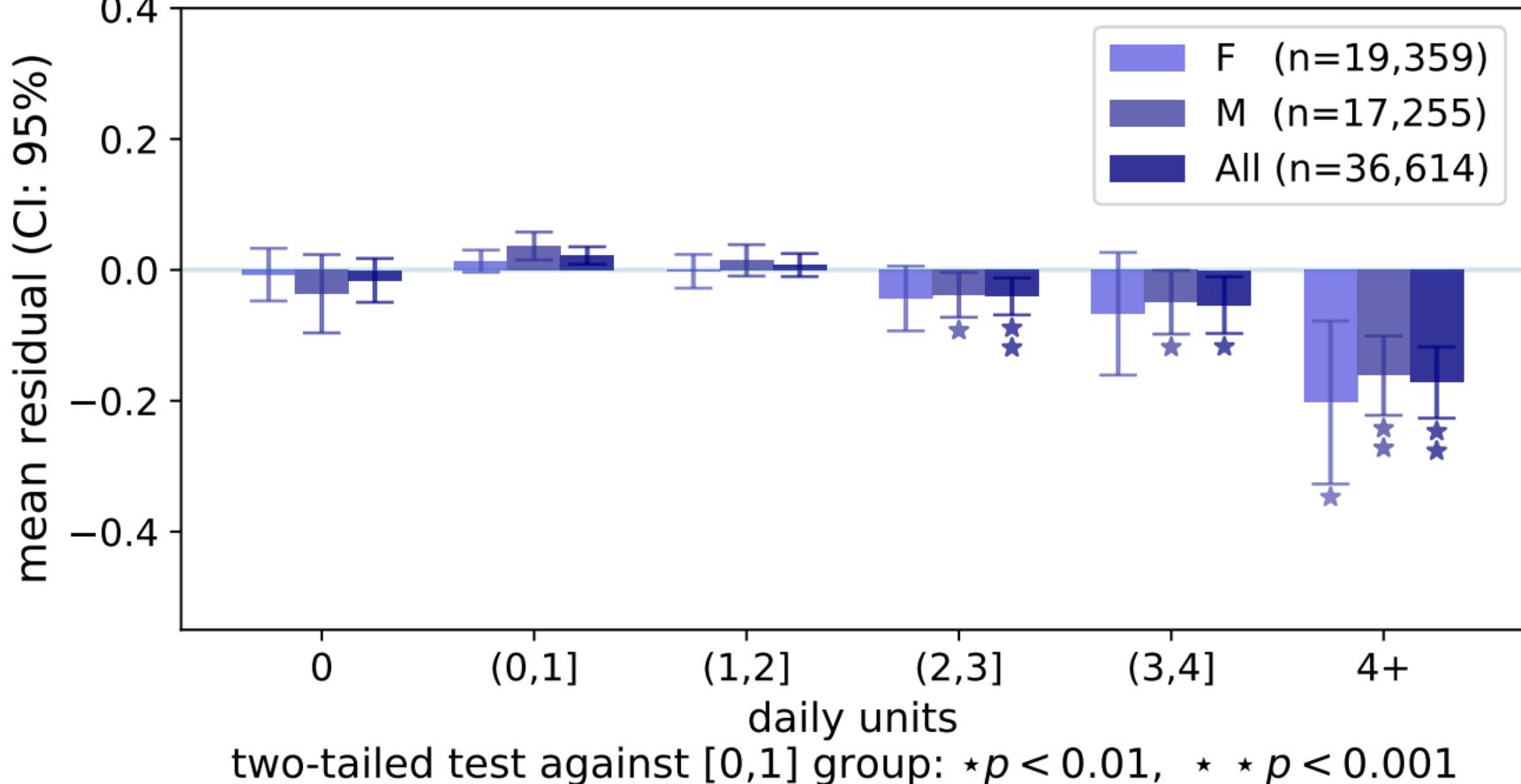
gmv in vi cerebellum (r)

mean residual (CI: 95%)



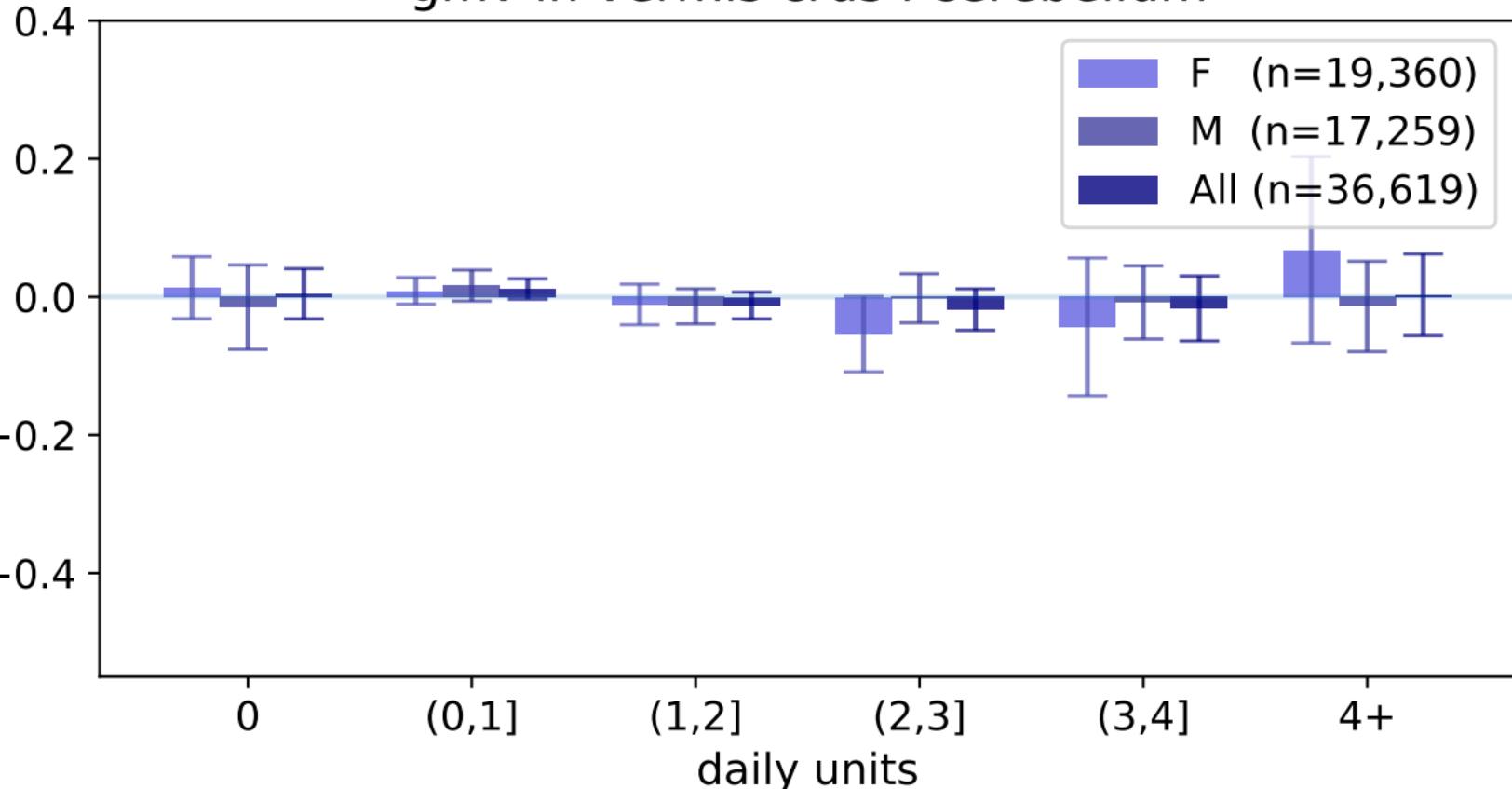
two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in crus i cerebellum (I)



gmv in vermis crus i cerebellum

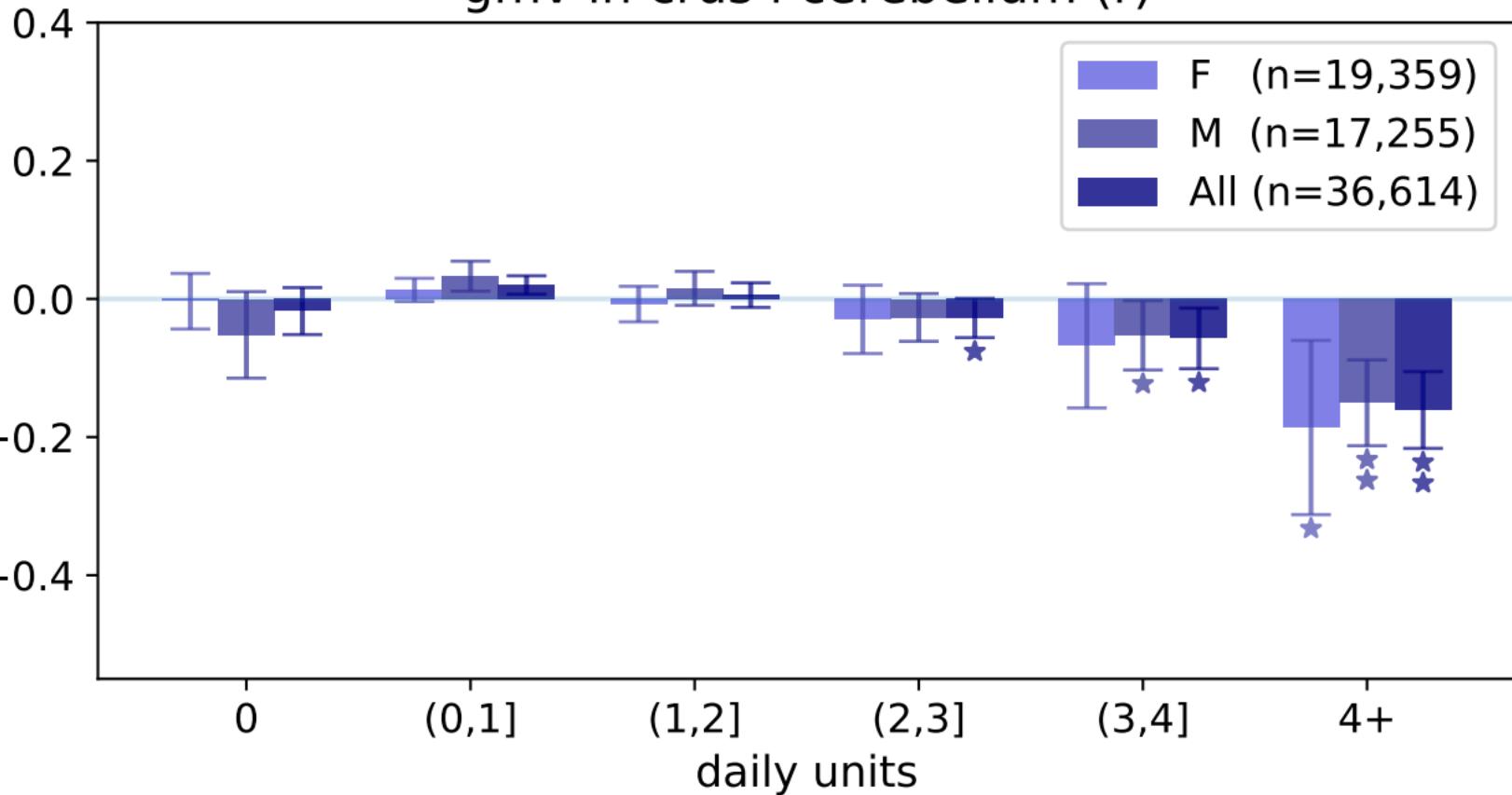
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in crus i cerebellum (r)

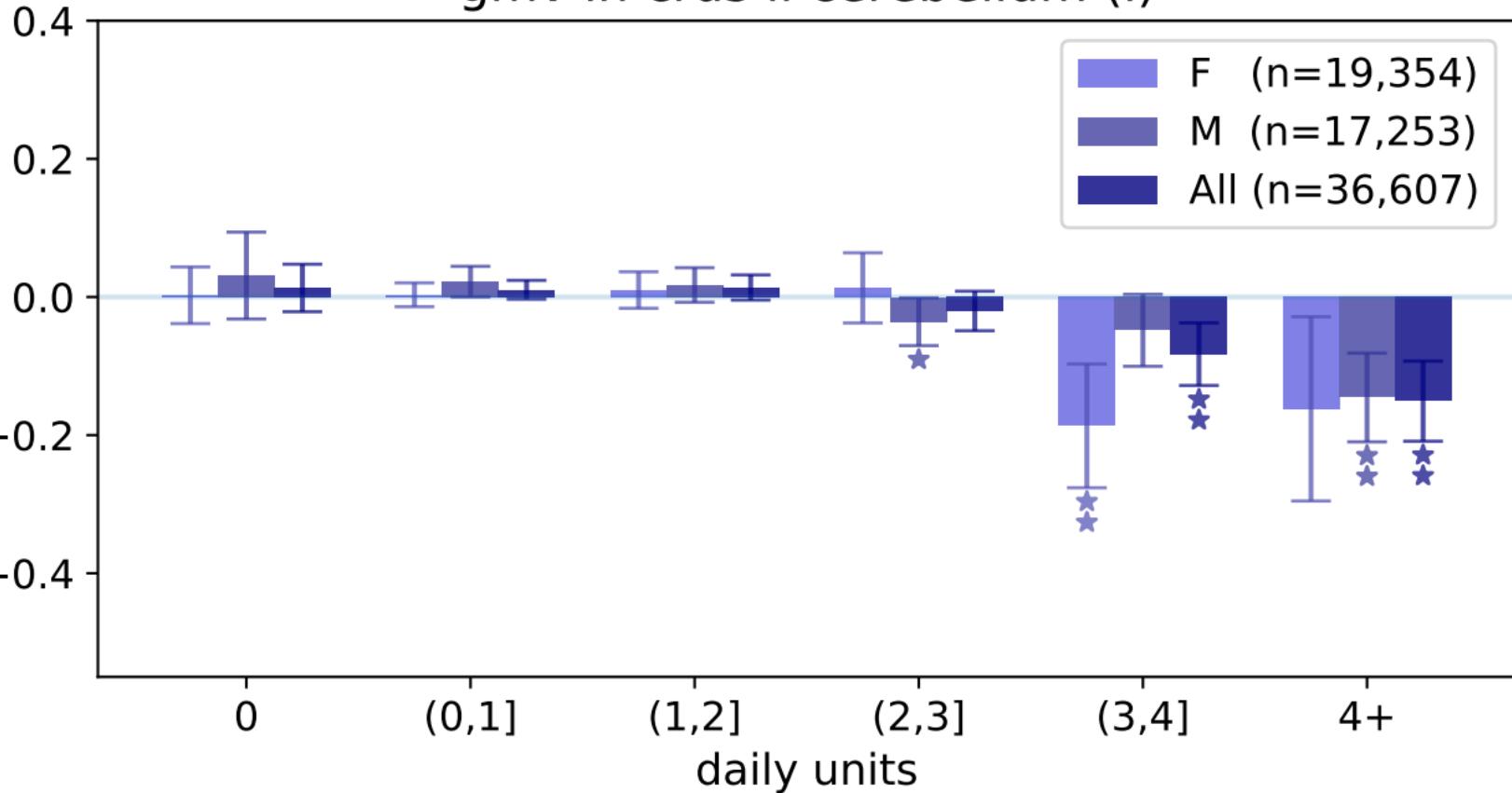
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in crus ii cerebellum (I)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in vermis crus ii cerebellum

mean residual (CI: 95%)

0.4

0.2

-0.2

-0.4

F (n=19,353)
M (n=17,261)
All (n=36,614)

0

(0,1]

(1,2]

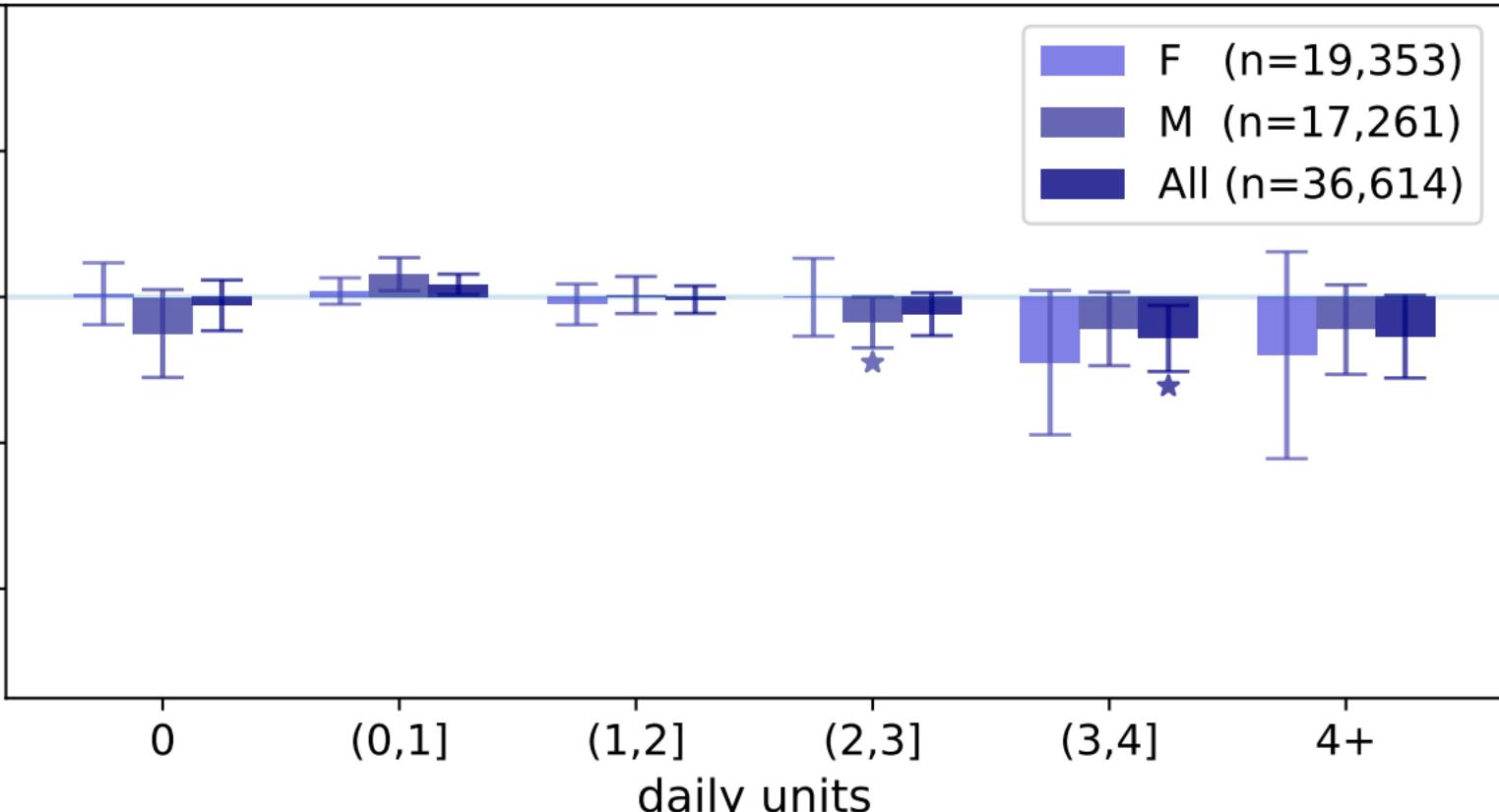
(2,3]

(3,4]

4+

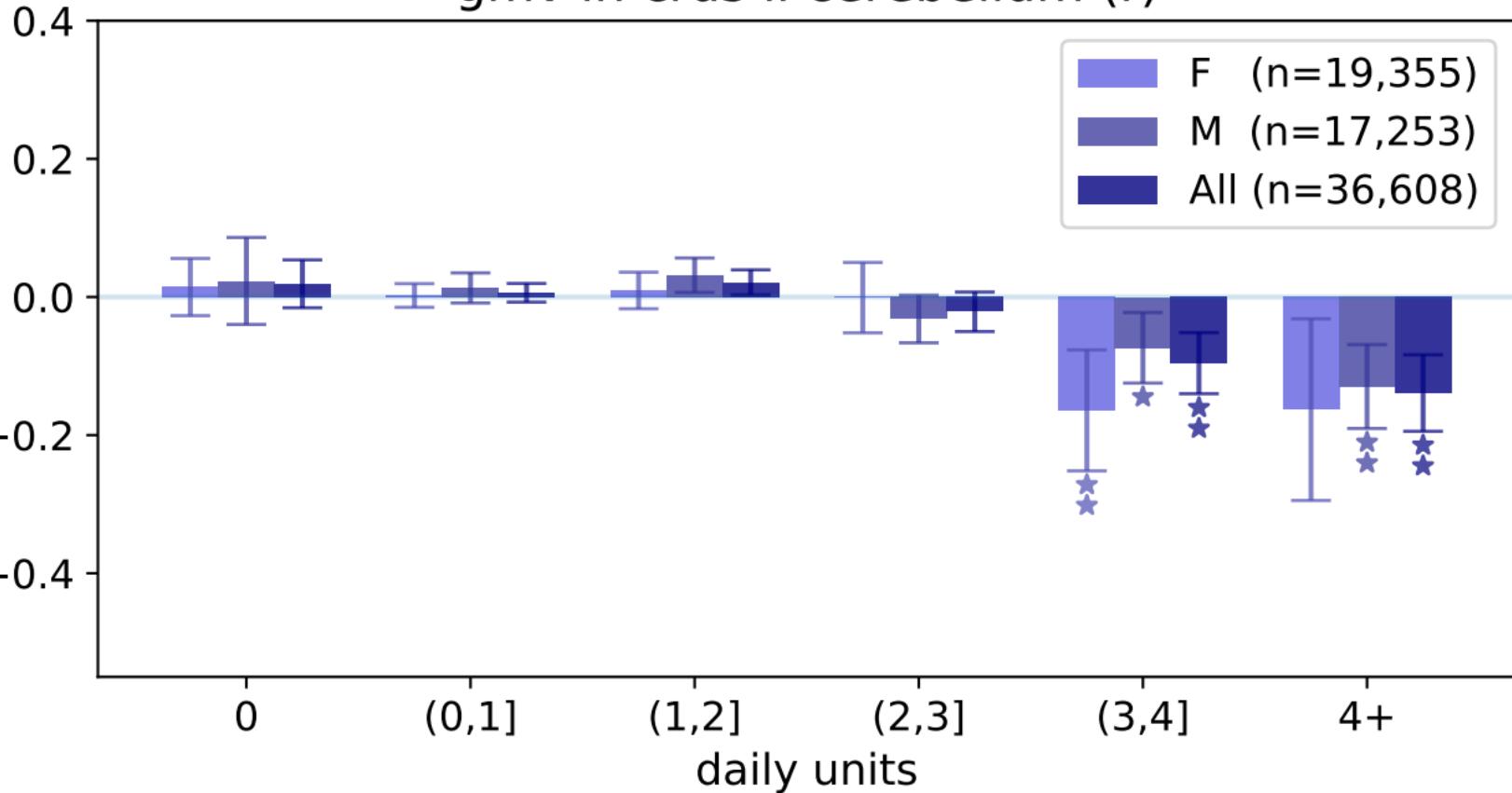
daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$



gmv in crus ii cerebellum (r)

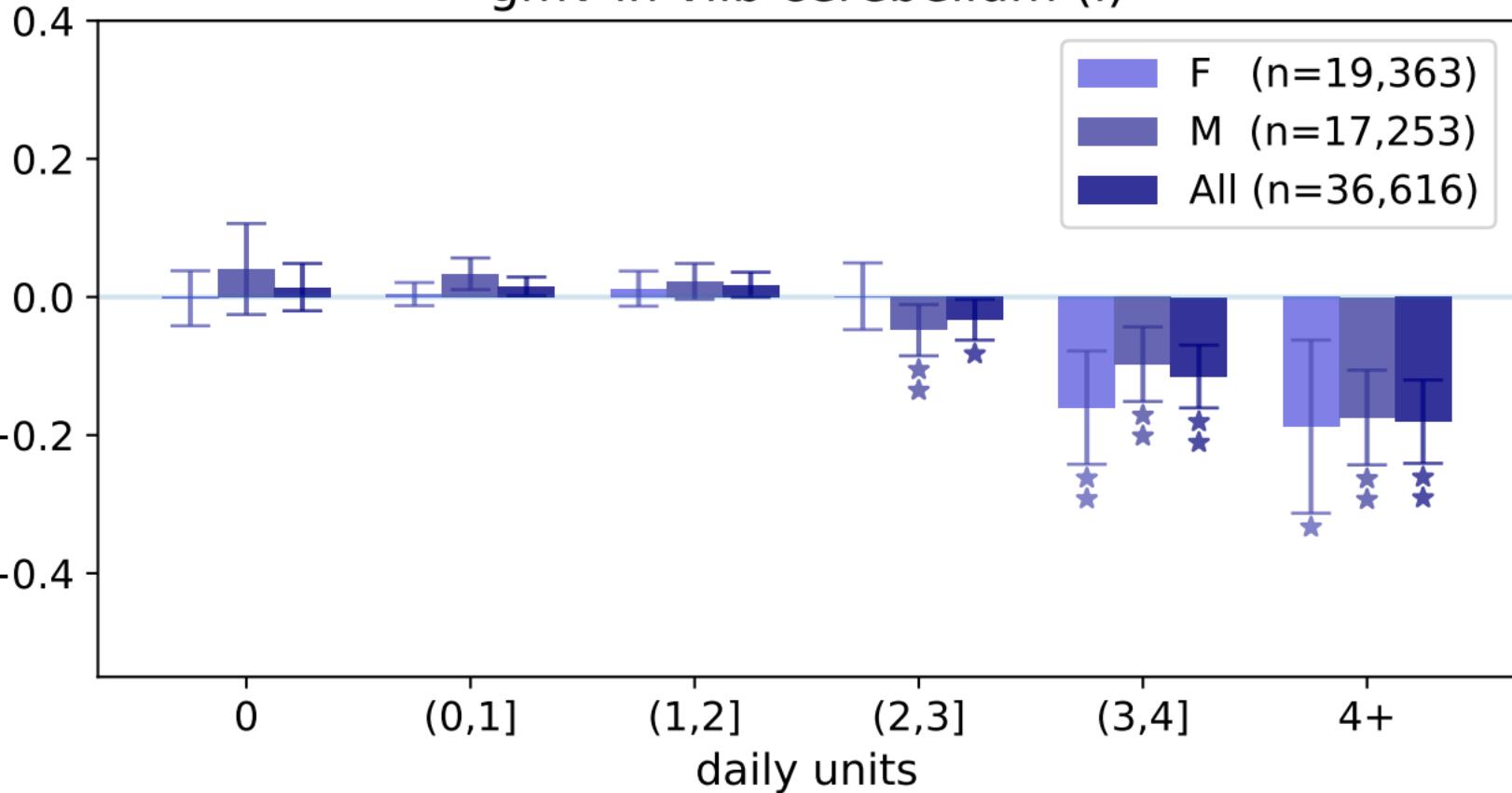
mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in viib cerebellum (I)

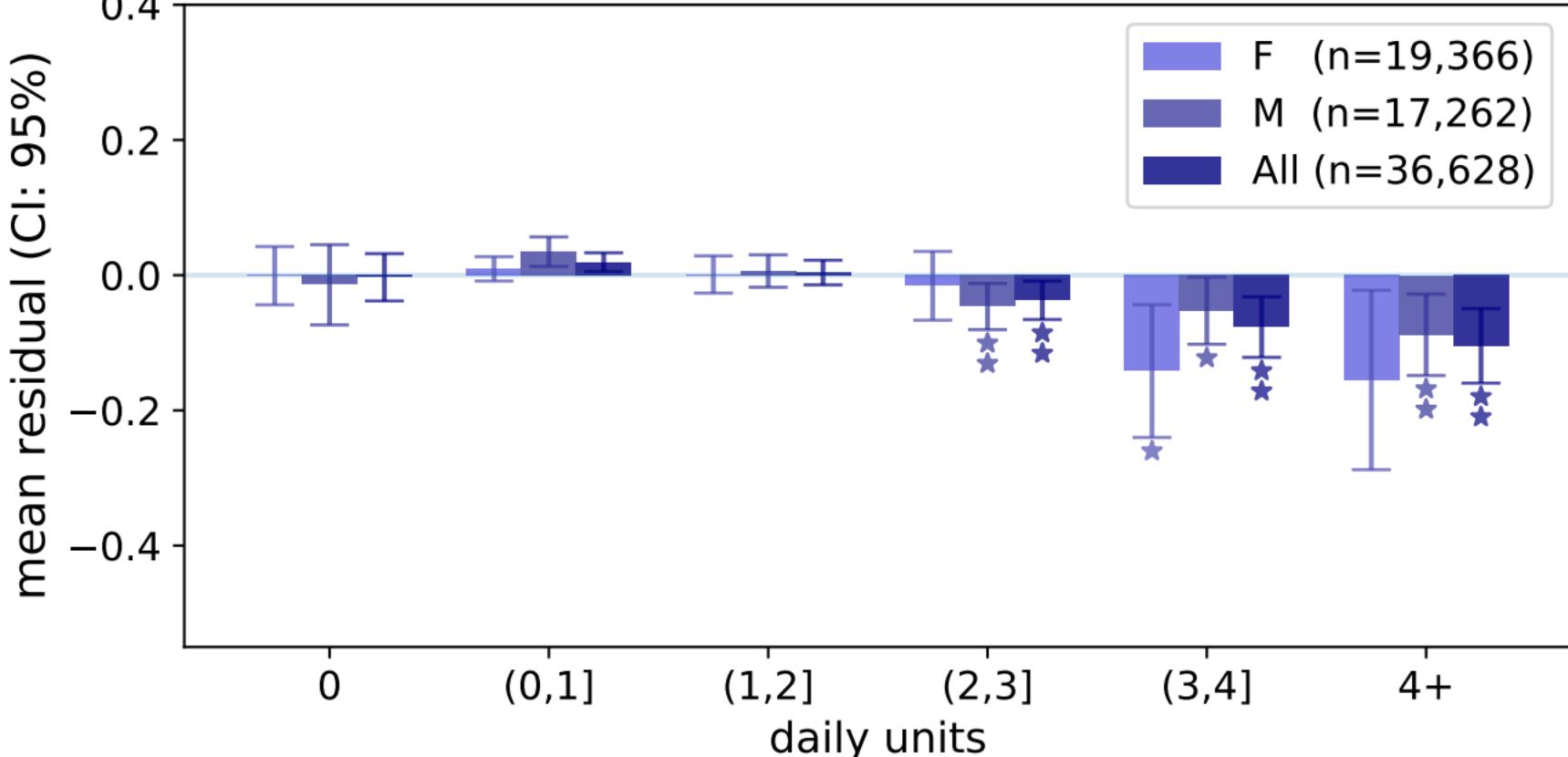
mean residual (CI: 95%)



daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

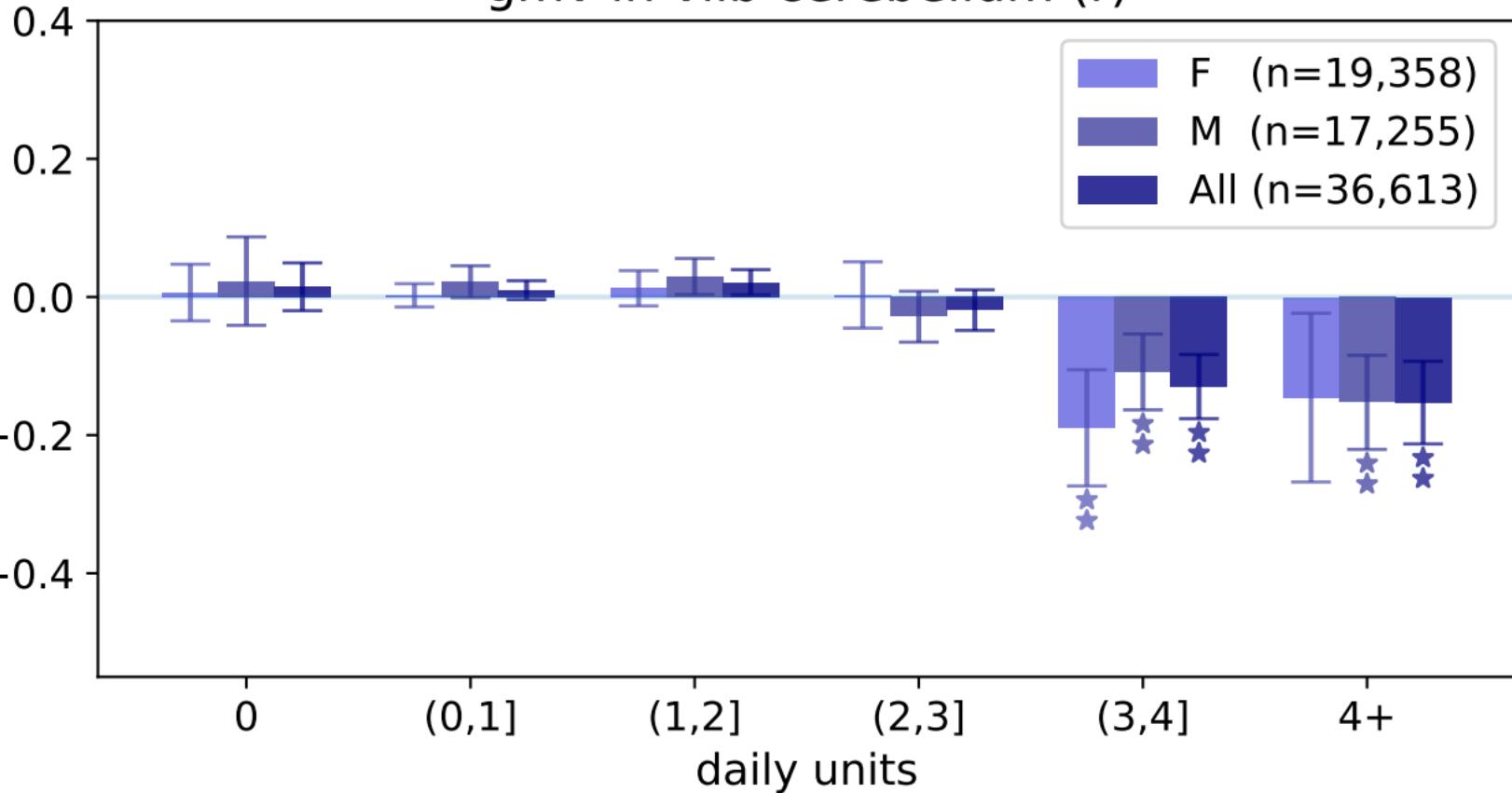
gmv in vermis viib cerebellum



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

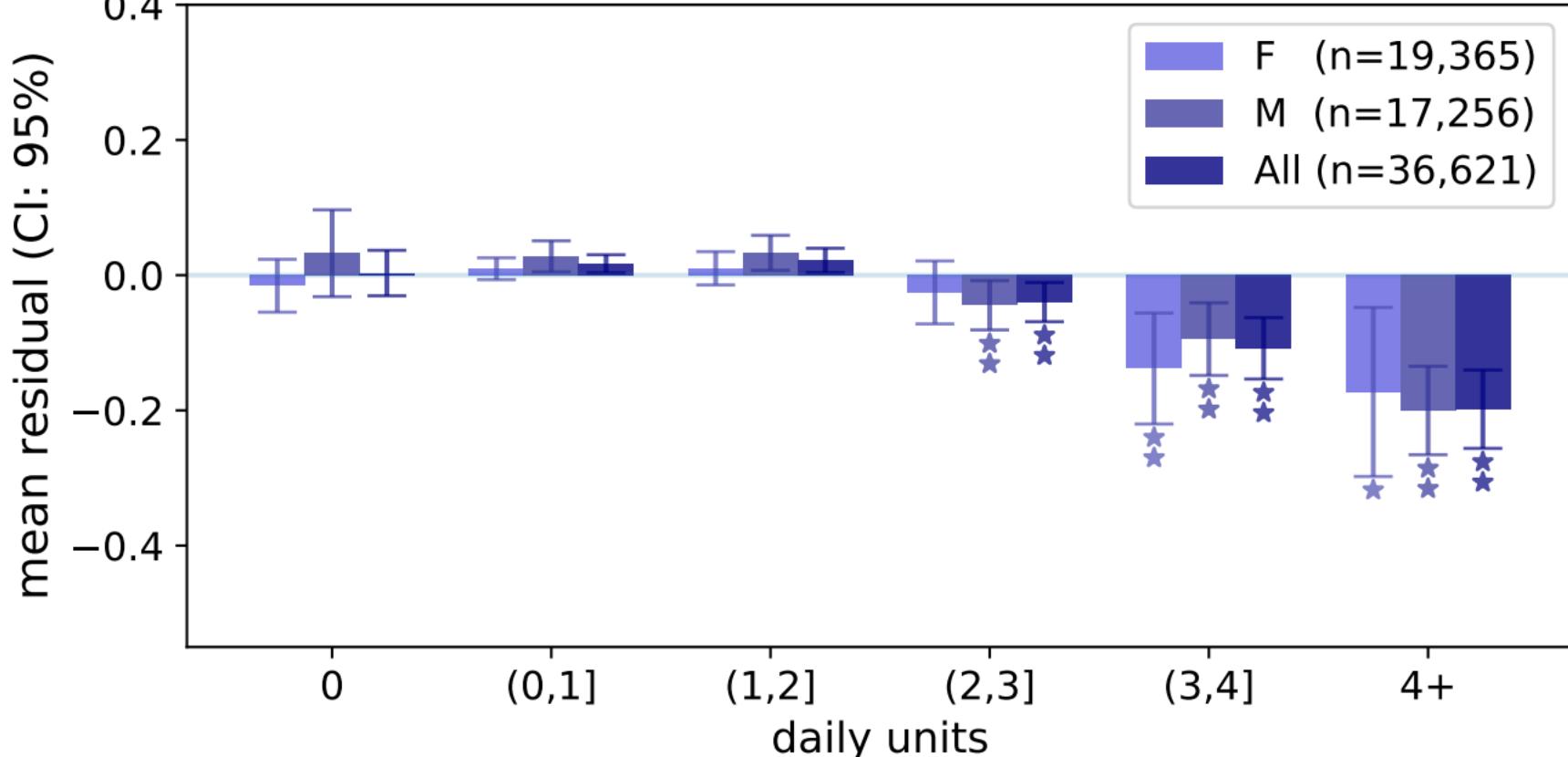
gmv in viib cerebellum (r)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in viiiia cerebellum (I)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in vermis viiiia cerebellum

mean residual (CI: 95%)

0.4

0.2

-0.2

-0.4

F (n=19,366)
M (n=17,262)
All (n=36,628)

0

(0,1]

(1,2]

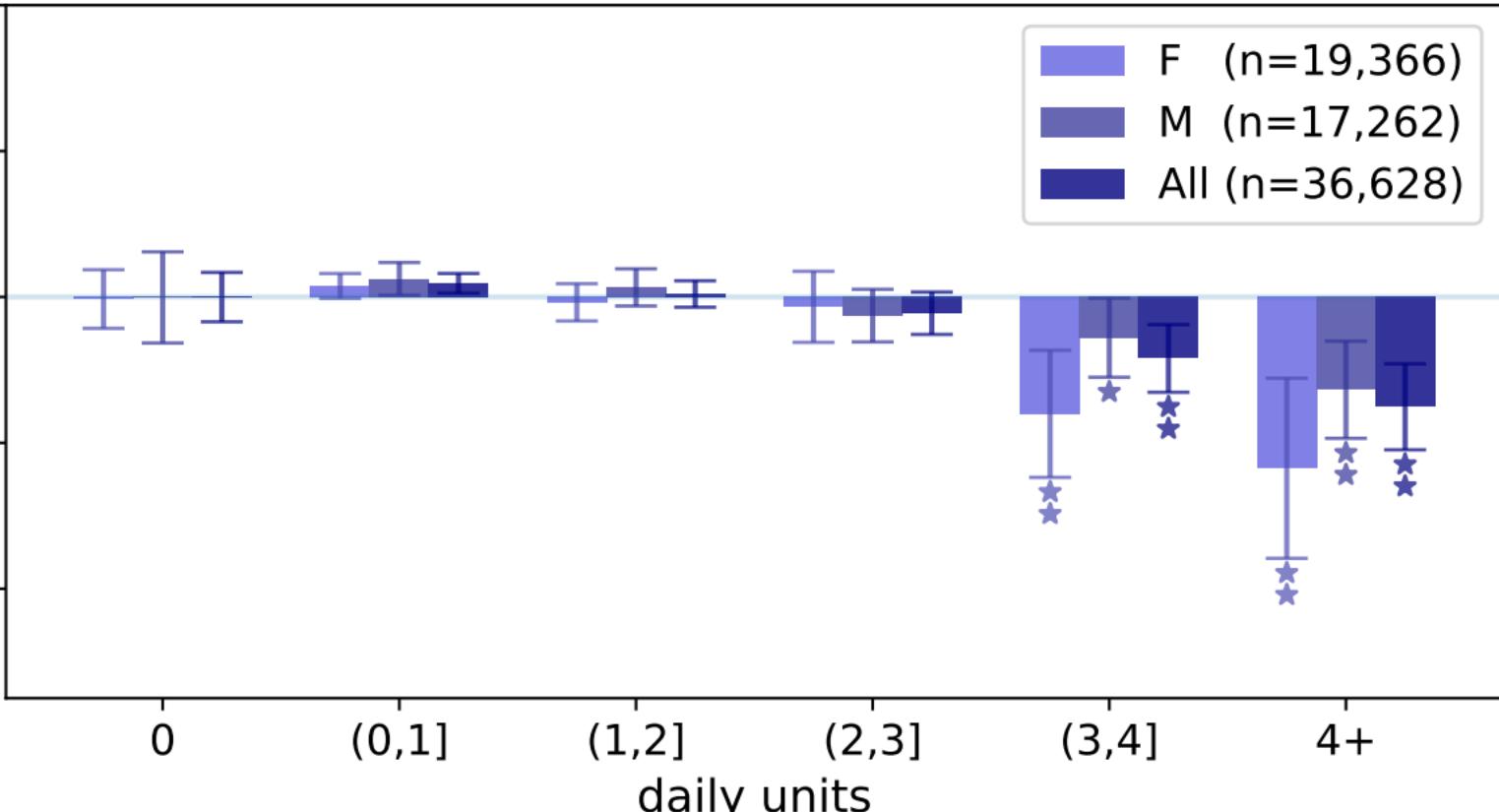
(2,3]

(3,4]

4+

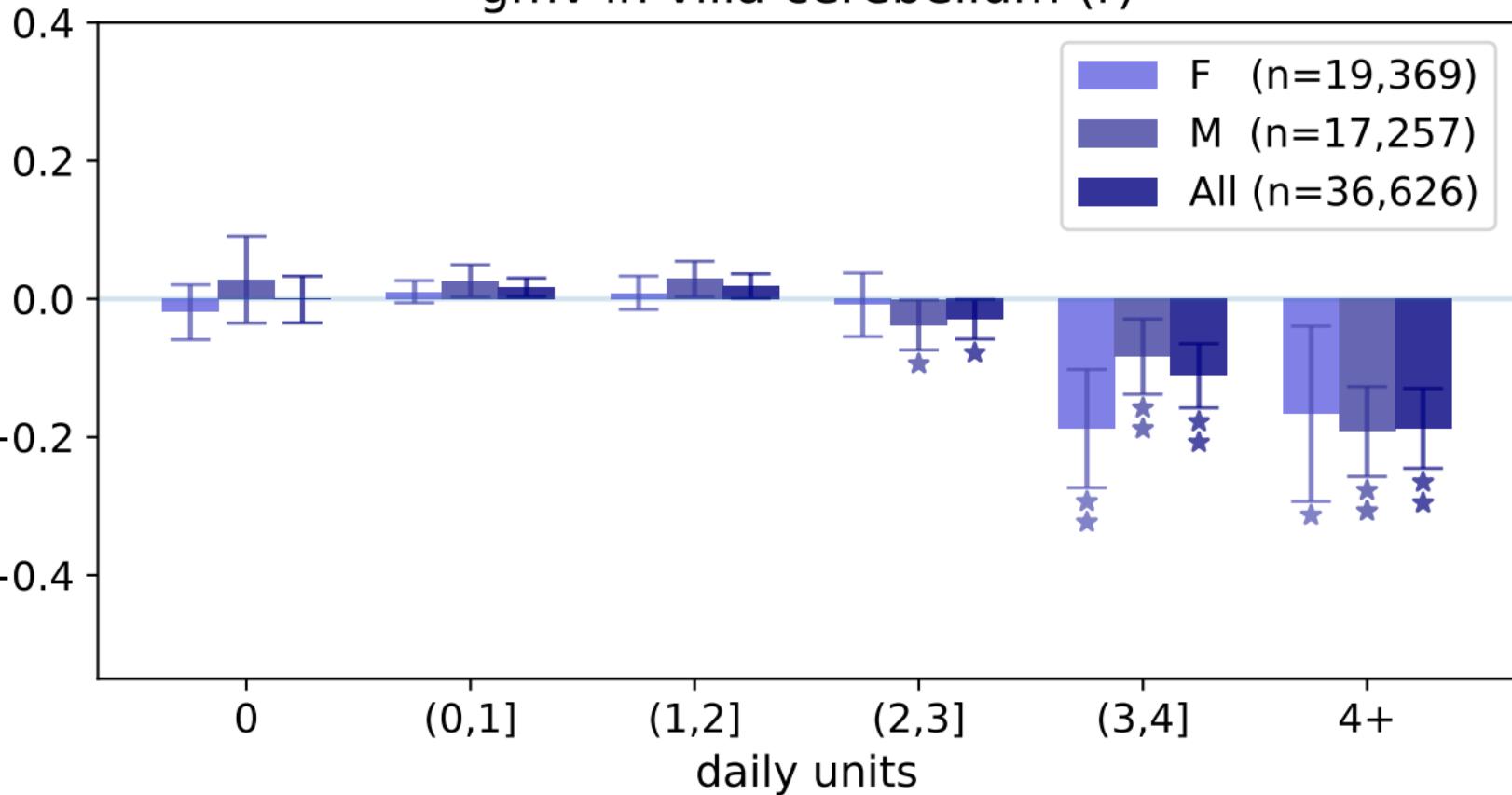
daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$



gmv in viiiia cerebellum (r)

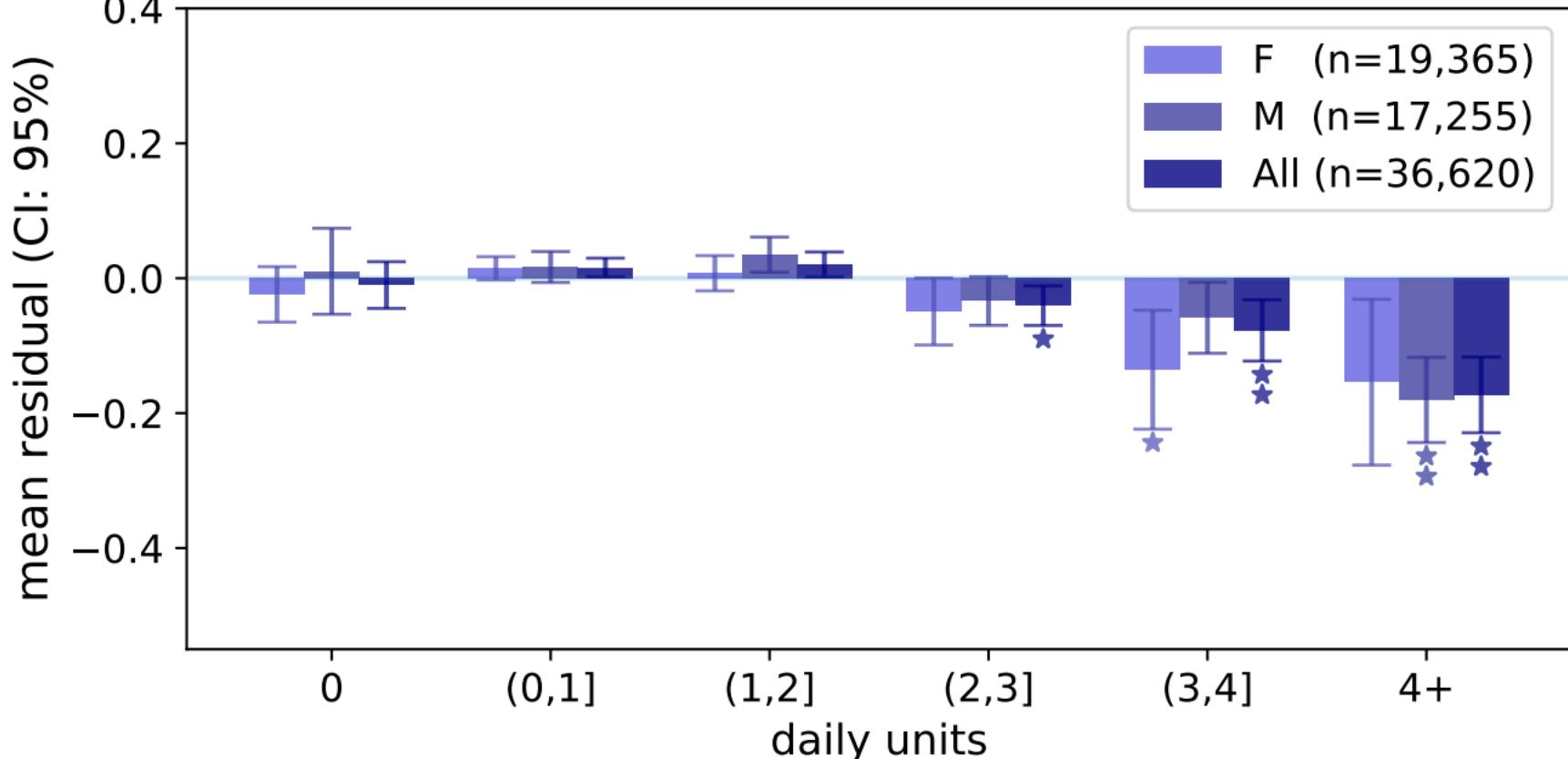
mean residual (CI: 95%)



daily units

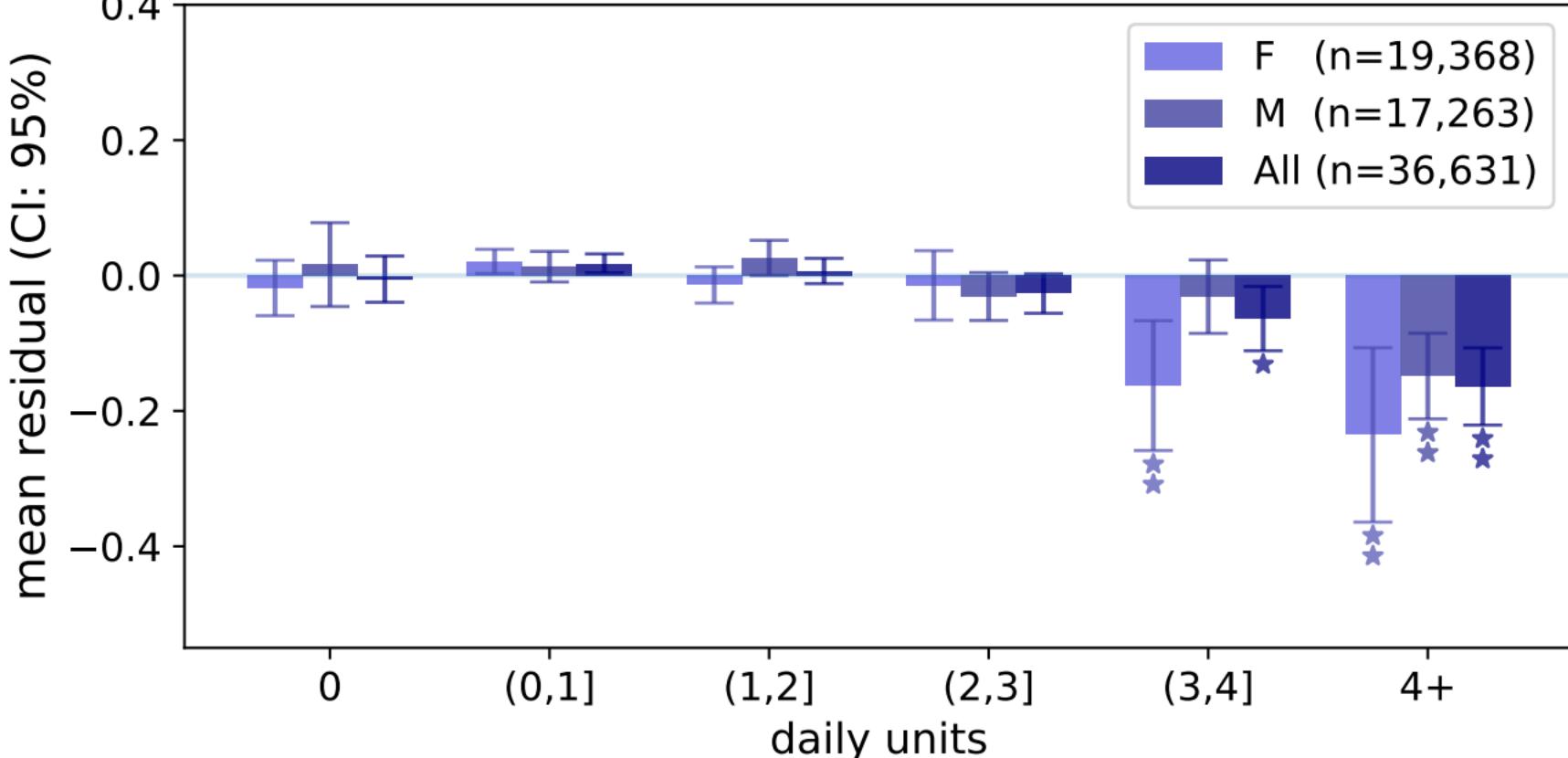
two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in viiib cerebellum (I)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

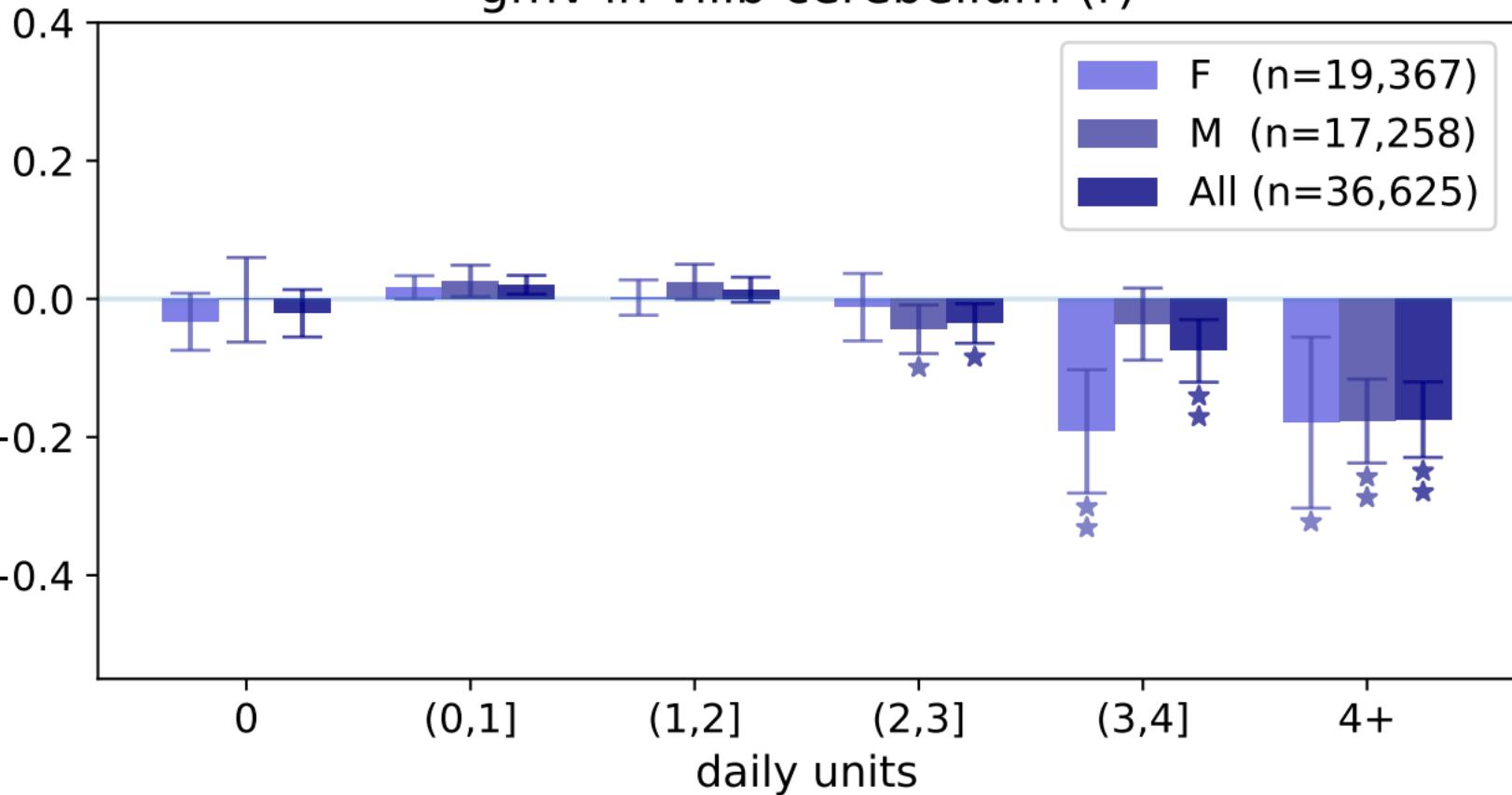
gmv in vermis viiib cerebellum



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

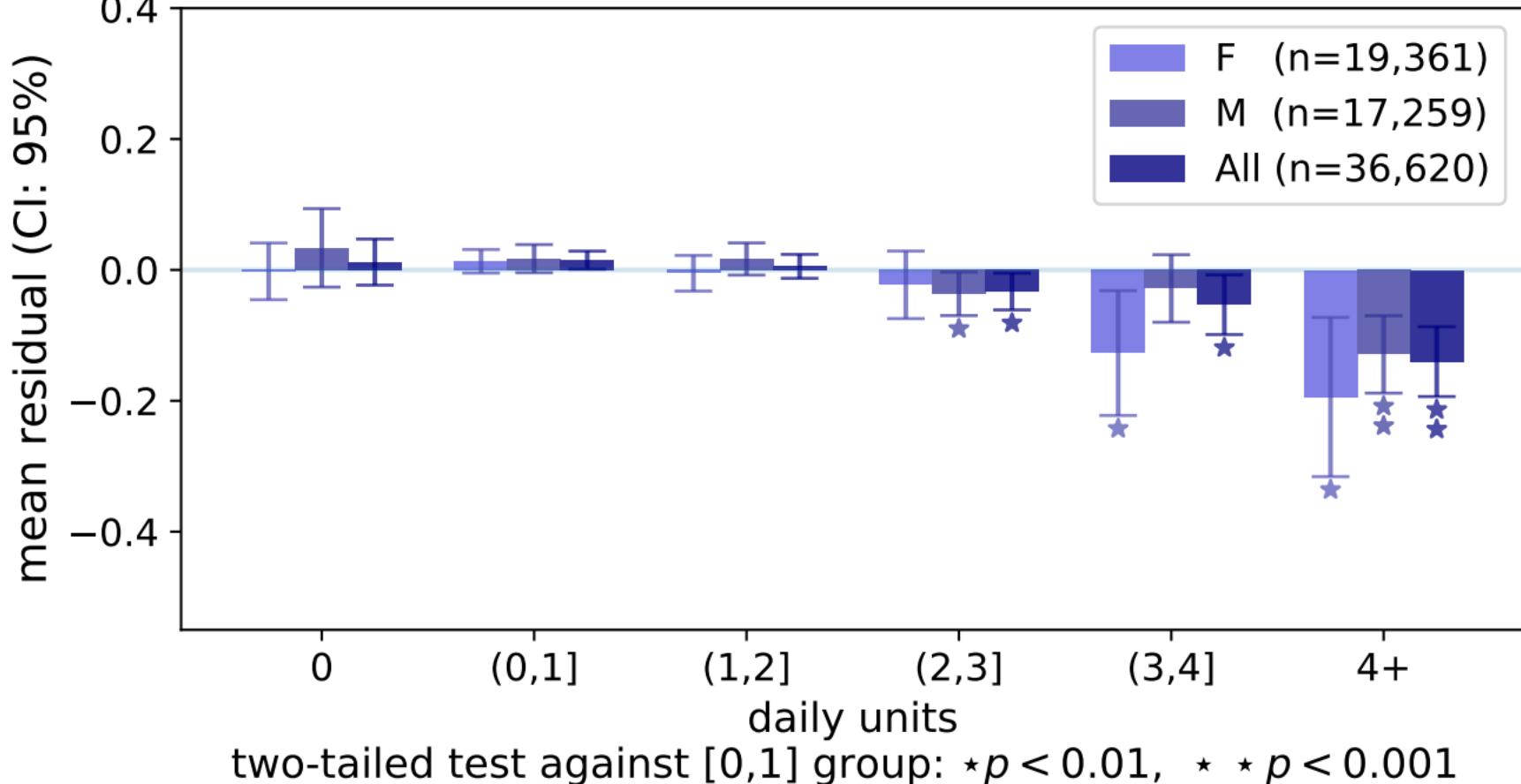
gmv in viiib cerebellum (r)

mean residual (CI: 95%)

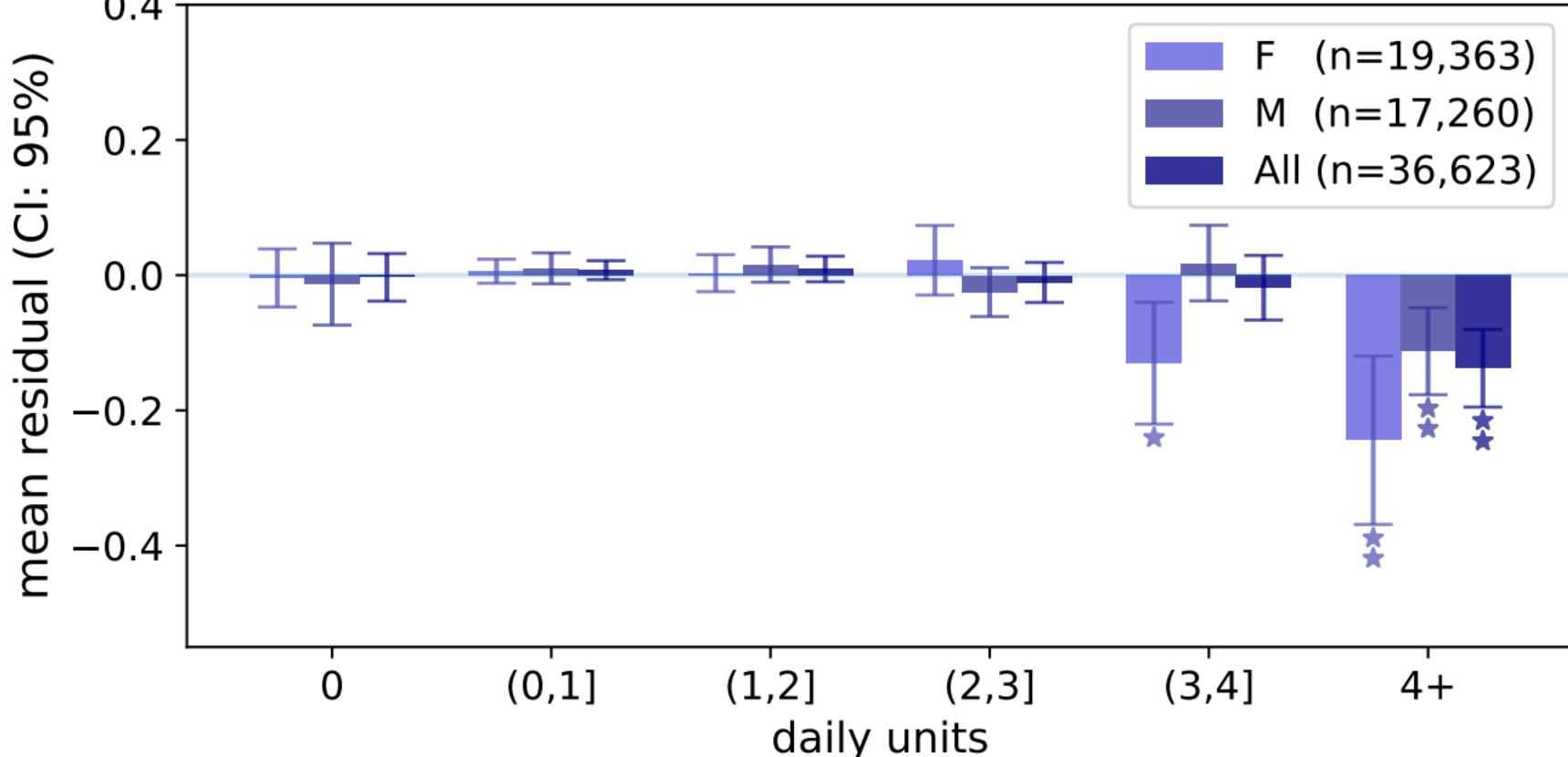


two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in ix cerebellum (I)

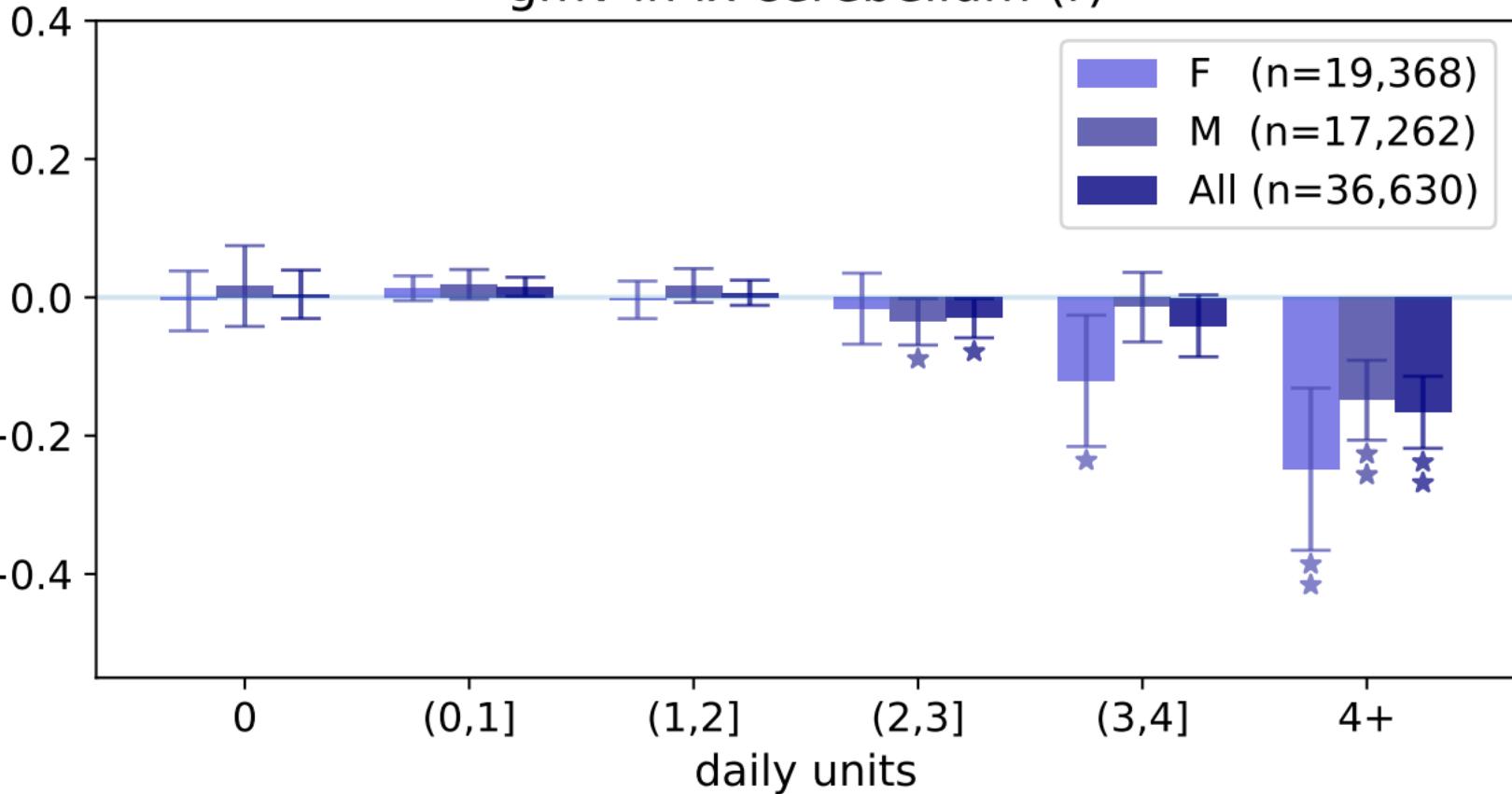


gmv in vermis ix cerebellum



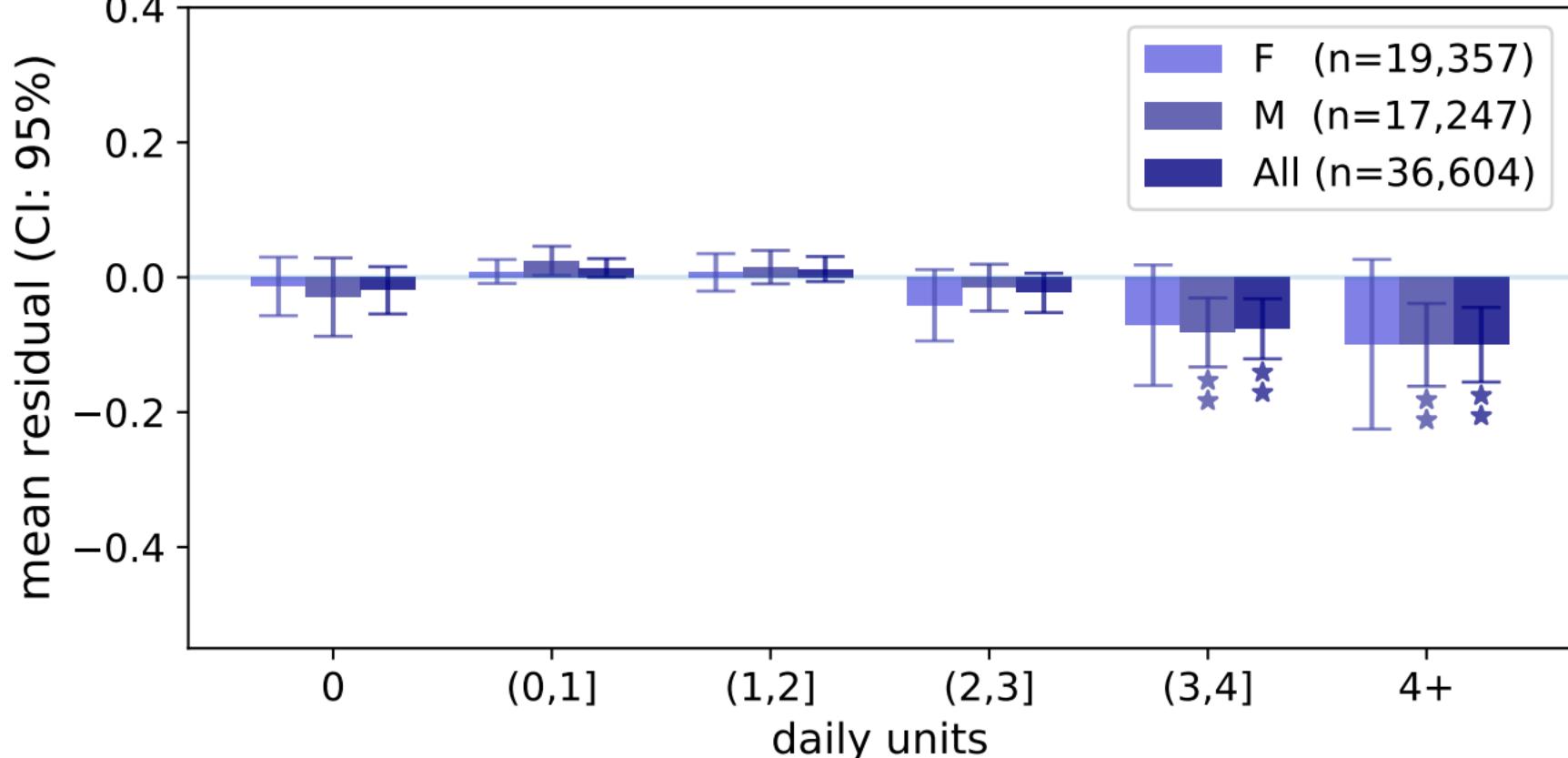
gmv in ix cerebellum (r)

mean residual (CI: 95%)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in x cerebellum (I)



two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in vermis x cerebellum

mean residual (CI: 95%)

0.4

0.2

0.0

-0.2

-0.4

F (n=19,349)
M (n=17,261)
All (n=36,610)

0

(0,1]

(1,2]

(2,3]

(3,4]

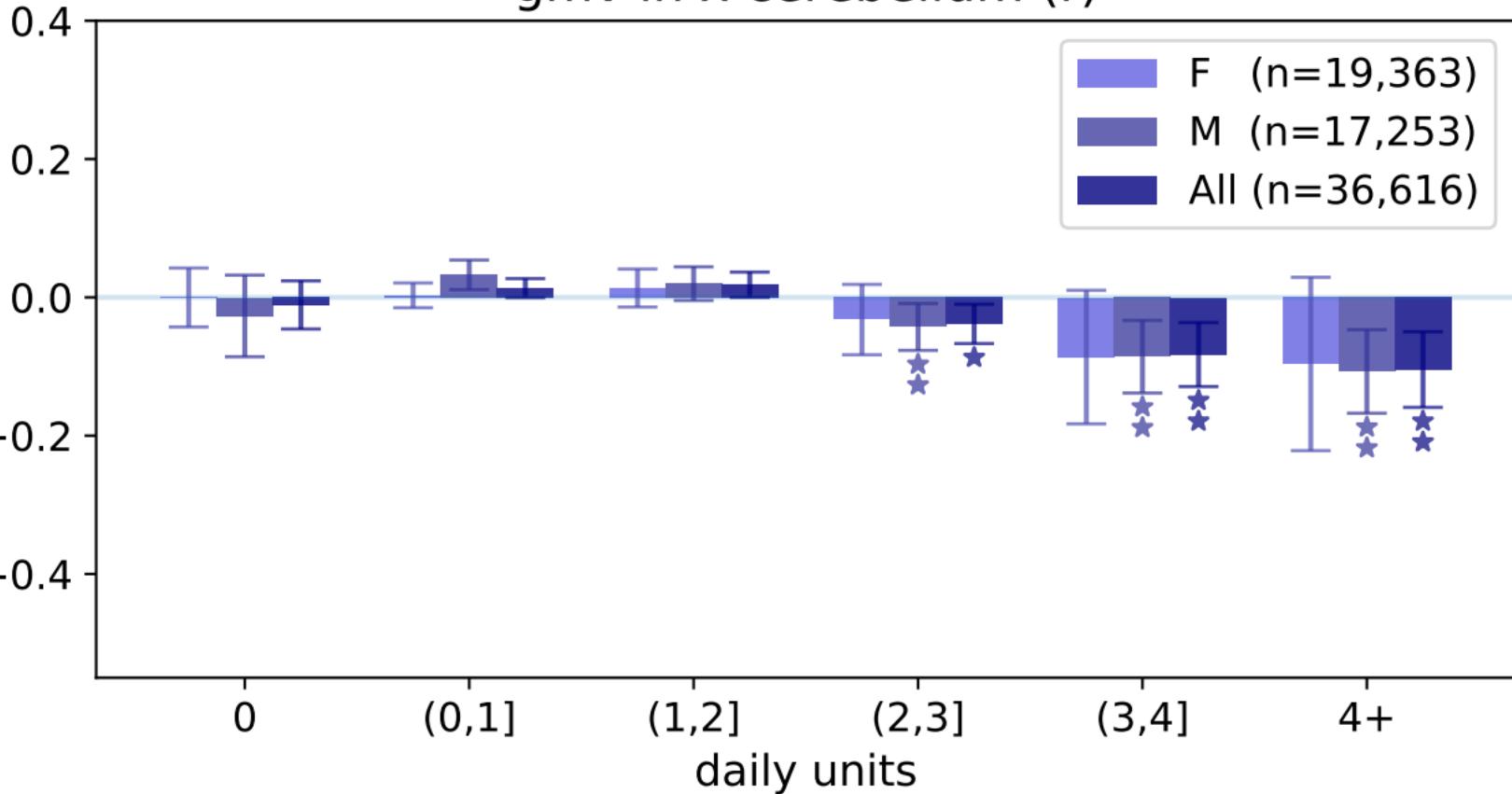
4+

daily units

two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

gmv in x cerebellum (r)

mean residual (CI: 95%)



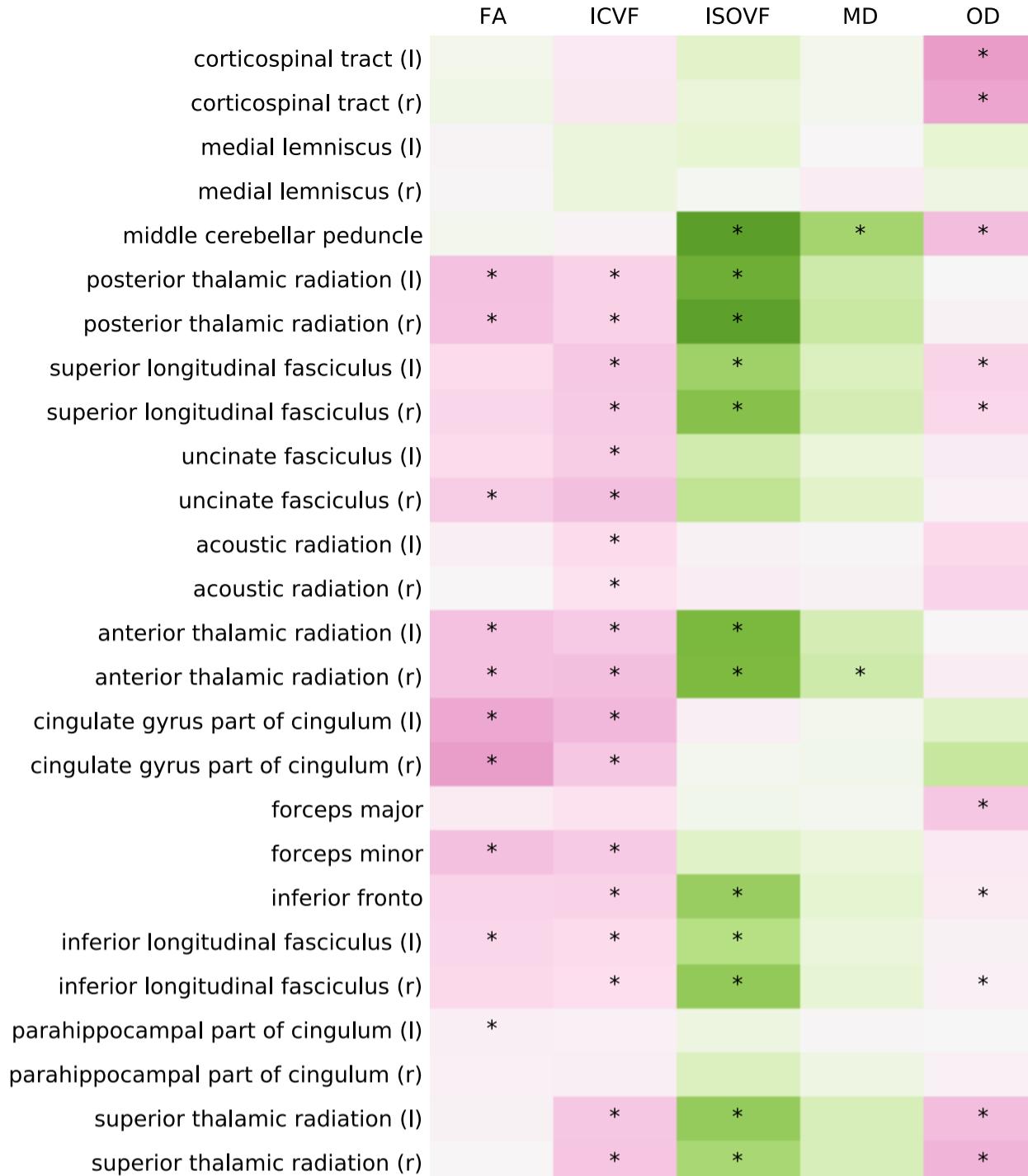
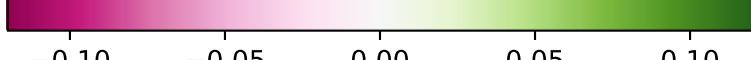
two-tailed test against [0,1] group: * $p < 0.01$, ** $p < 0.001$

Supplementary Figure 4. Associations between daily alcohol units and white matter microstructure indices of interest across white matter tract regions. Asterisks denote statistically significant effects in F-test, corrected for multiple hypothesis testing (Holm method), $p < 1.64 \times 10^{-4}$. Colors represent the expected change in each imaging derived phenotype resulting from the increase in daily consumption from 2 to 3 units, based on the regression model. FA = fractional anisotropy, ICVF = intracellular volume fraction, ISOVF = isotropic volume fraction, MD = mean diffusivity, OD = orientation dispersion, r = right, l = left



* FWER-corrected significance: $p < 1.64 \times 10^{-4}$

effect from 2 to 3 units (in SD)



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