

**Supplementary Table 1.** The association of hePRS-IR, mePRS-IR, IGF-1, IGFBP-1, and -3 in a subsample in older adults

Dependent variable	Men					Women				
	No.	Crude		Adjusted		No.	Crude		Adjusted	
		b (95% CI)	P value	b (95% CI)	P value		b (95% CI)	P value	b (95% CI)	P value
<b>hePRS-IR</b>										
IGF-1, ng/mL	233	-0.02 (-7.2 to 7.2)	1.00	-0.5 (-7.9 to 6.9)	0.89	221	3.8 (-4.8 to 12.5)	0.39	2.8 (-6.6 to 12.2)	0.56
IGFBP-1, ng/mL	233	0.6 (-9.8 to 11)	0.91	0.002 (-9.8 to 9.8)	1	221	-19.4 (-30.6 to -8.2)	0.001	-17.6 (-29 to -6.1)	0.003
IGFBP-3, ng/mL	233	40.7 (-390.5 to 471.9)	0.85	46.2 (-385.3 to 477.7)	0.83	221	176.2 (-346.6 to 698.9)	0.51	128.7 (-394.3 to 651.6)	0.63
<b>mePRS-IR</b>										
IGF-1, ng/mL	233	-1.5 (-8.4 to 5.5)	0.68	-2.3 (-9.6 to 5.1)	0.55	221	-12.3 (-21.2 to -3.4)	0.01	-10.6 (-19.5 to -1.8)	0.02
IGFBP-1, ng/mL	233	-10.6 (-22.6 to 1.3)	0.08	-11.1 (-21.2 to -0.9)	0.03	221	7.2 (-5.2 to 19.6)	0.26	7.4 (-5.7 to 20.5)	0.27
IGFBP-3, ng/mL	233	-144.4 (-549.5 to 260.7)	0.48	-122.8 (-543.5 to 297.9)	0.57	221	-74.7 (-585.2 to 435.7)	0.77	-56.4 (-552.9 to 440)	0.82

Crude models are adjusted for age and population stratification. Fully adjusted models are additionally adjusted for smoking, alcohol consumption, socioeconomic status, presence of chronic diseases, birth weight, and leisure-time physical activity.

hePRS-IR, polygenic risk score for the hippocampal-insulin receptor; mePRS-IR, polygenic risk score for the mesocorticolimbic-insulin receptor; IGF-1, insulin growth factor 1; IGFBP-1, insulin growth factor-binding protein 1; IGFBP-3, insulin growth factor-binding protein 3; CI, confidence interval.