

Supplementary Material

Associations Between Insulin-Like Growth Factor-1 and Resting-State Functional Connectivity in Cognitively Unimpaired Midlife Adults

Papaya viewer was used to examine the 21 non-noise, orthogonalized neural network maps from the 25 Independent Component (IC) solution set originally estimated in 4,181 UK Biobank participants (see https://www.fmrib.ox.ac.uk/ukbiobank/group_means/rfMRI_ICA_d25_good_nodes.html for the link to the viewer and maps). An imaging and neuroanatomy expert (AAW) cross-referenced these maps with established networks in the literature, as UK Biobank neural network have to our knowledge not been extensively described.

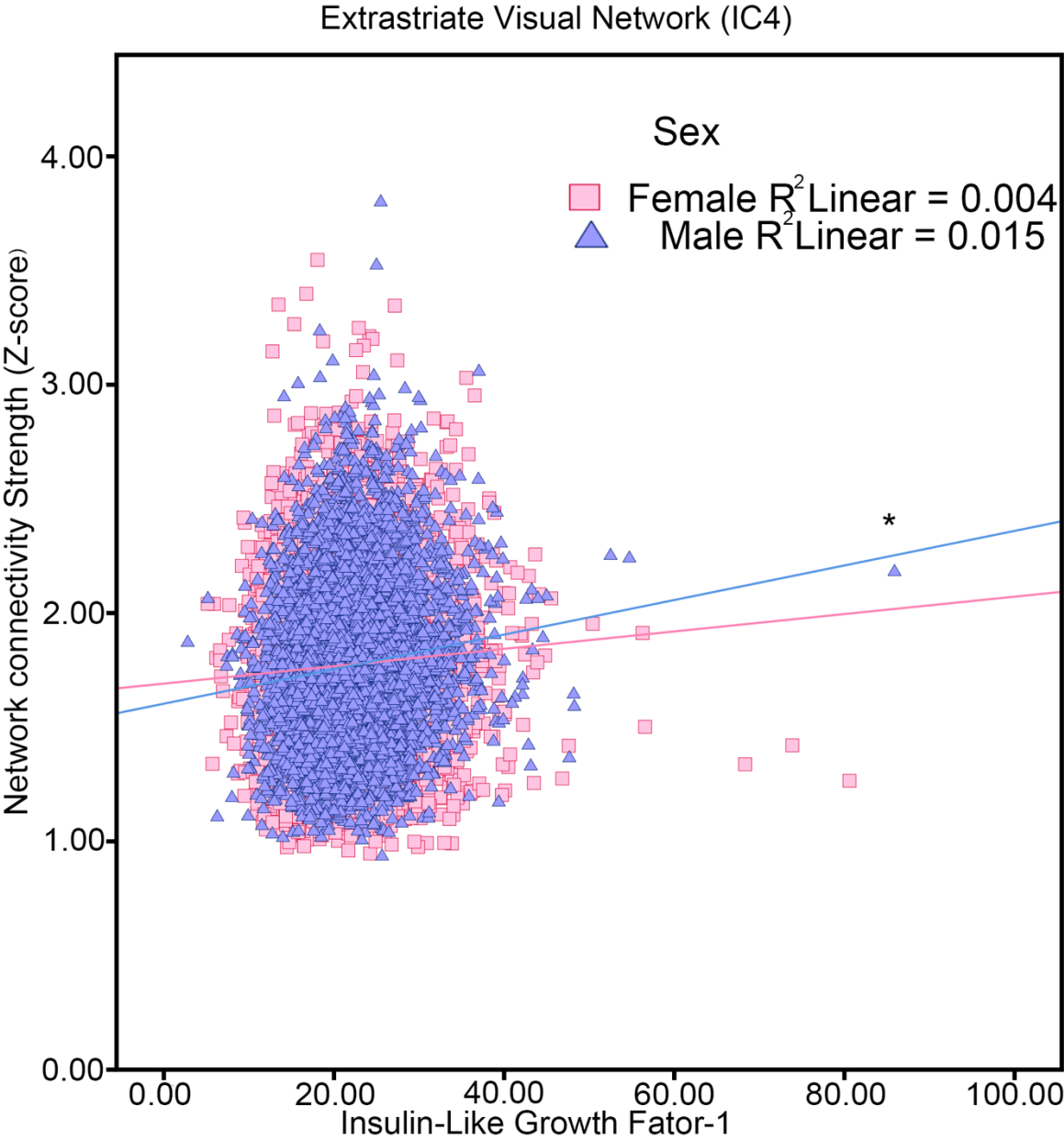
IC1 was “classic” Default Mode Network, with activation in medial prefrontal cortex and the posterior cingulate/precuneus region. IC2 showed lateral extrastriate activation in temporo-occipital junctions, moving down to inferior temporal gyrus and up to superior temporal gyrus, areas which are consistent with the ‘where’ and ‘what’ pathways respectively grading for spatial and object elements of visual stimuli. IC3 was predominantly composed of bilateral primary motor, pre-motor, and Supplementary Motor Area (SMA) cortices, cerebellum, medial cingulate cortex, and posterior insula, which may collectively grade for input and output relevant to motor function. IC4 was composed of extrastriate regions with some impingement on primary visual areas, suggesting a network focused on multi-modal visual processing. IC5 was “classic” executive network restricted to the left hemisphere, composed of inferior frontal and parietal gyri. IC6 had activation in bilateral inferior frontal gyri, pre-SMA, and cerebellum, suggesting a network focused on speech production and interpretation. IC7 was a memory consolidation network composed of activation in precuneus, posterior cingulate, and lateral parietal cortices that streamed down to medial temporal lobe including parahippocampal gyrus and entorhinal cortex, with little activity in hippocampus proper. IC8 showed activation exclusively in posteromedial occipital gyrus, suggesting primary visual processing in V1 rather than extrastriate areas seen in IC4. IC9 was “classic” central executive network and composed of bilateral inferior frontal and parietal gyri. IC10 had a contiguous region in either hemisphere comprising operculum, primary sensory and motor cortices, mid-frontal gyrus, and anterior insula, which

may represent synthesis of internal states to give rise to emotional processing and interpretation. IC11 was a motor execution network comprised almost exclusively of pre-central gyrus activity, thalamus, and both anterior and posterior medial cerebellum. IC12 was a sensorimotor network that almost exclusively included pre- and post-central gyri. IC13 was a right executive function network comprised of inferior and parietal gyri. IC14 was a fronto-cingular network composed of all segments of cingulate gyrus except for the rostrum, as well as medial frontal gyrus. IC15 was a cerebellar network that exclusively encompassed cerebellum. IC16 was comprised of dorsolateral prefrontal and anterior cingulate cortices, suggesting that this may be a frontopolar network involving in top-down control of cognitive and/or affect processes. IC17 comprised activation exclusively in superior temporal sulcus, suggesting a network revolving around Wernicke's area and therefore comprehension and production of coherent speech. IC18 touched on basal ganglia, motor, and pre-motor regions, suggesting a motor coordination loop. IC19 had activation almost exclusively in primary visual cortex with no impingement on extrastriate regions, which was highly posterior compared to IC8 which did not have the most posterior part of occipital cortex. IC20 comprised the posterior portion of Default Mode Network. IC21 was a complex neural network to interpret, with activation hot-spots predominantly in bilateral inferior frontal gyrus, as well as left superior mediofrontal and orbitofrontal gyri, precuneus, and left medial temporal cortex. This network may involve top-down cognitive processing of object stimuli in the 'what' pathway.

Supplementary Table 1. Interpretation of 21 Independent Components that Constitute Neural Networks in UK Biobank

Independent Component	Neural Network Description
1	Anterior and Posterior Default Mode Network
2	‘Where’ and ‘What’ Pathways
3	Motor Planning Network
4	Extrastriate Visual Network
5	Left Executive Function Network
6	Left Auditory Processing & Speech Production Network
7	Memory Consolidation Network
8	Primary Visual Network
9	Central Executive Function Network
10	Affect Processing Network
11	Motor Execution Network
12	Sensorimotor Network
13	Right Executive Function Network
14	Fronto-Cingular Network
15	Cerebellum Network
16	Frontopolar Network
17	Auditory/Language Comprehension Network
18	Substantia Nigra Cortico-Striatal Loop
19	Primary Visual Network
20	Posterior Default Mode Network
21	Prefrontal and ‘What’ Pathway Network

Supplementary Figure 1. The association between IGF-1 levels and Extrastriate Visual network (i.e., neural network activity) in adults in different sex (“Female”, “Male”). Pink squares and blue triangles respectively represent Female and Male participants. *p<0.05.



Supplementary Figure 2. The association between IGF-1 levels and Primary Visual network (i.e., neural network activity) in adults in different sex (“Female”, “Male”). Pink squares and blue triangles respectively represent Female and Male participants. *p<0.05.

