**Brain wiring economics vary with population-level genomics**

Alicja Monaghan1,2\*, Danyal Akarca1 and Duncan E. Astle1,3

*Supplementary material*

**Footnote 1: Descriptive metrics across parcellations**

**Descriptive statistics for the distributions of local and global graph theory measures across 3 parcellations of varying granularity.** All are local measures, except density, and are defined in the Results. Note that the modularity statistic provided is a nodal measure of optimal community structure.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Parcellation | | | | | |
|  | Schaefer 100-Node | | Brainnetome 246-Node | | Schaefer 400-Node | |
| Metric | Mean (SD) | Range | Mean (SD) | Range | Mean (SD) | Range |
| Density | 6.55%  (.48) | 2.24 - 7.35 | 2.04% (.19) | .34 - 2.35 | .49% (.05) | .03 - .59 |
| Degree | 6.49 (3.17) | .65 - 15.57 | 4.99 (3.38) | 0 - 19.91 | 1.95 (2.08) | 0 - 11.30 |
| Clustering | .42 (.18) | 0 - .89 | .34 (.20) | 0 - .78 | .15 (.18) | 0 - .76 |
| Betweenness Centrality | 239.44 (290.42) | 0 - 1583.39 | 824.24 (996.12) | 0 - 6494.36 | 390.59 (812.89) | 0 -6910.37 |
| Eigenvector Centrality | .07 (.07) | 0 - .24 | .03 (.05) | 0 - .31 | .01 (.04) | 0 - .23 |
| Modularity | 3.47 (.33) | 2.89 - 4.01 | 5.76 (.53) | 3.80 - 6.88 | 10.28 (3.29) | 4.81 - 15.71 |
| Local Efficiency | .57 (.21) | 0 - .91 | .43 (.24) | 0 - .84 | .17 (.22) | 0 - .82 |
| Mean Total  Edge Length | 246.10 (177.23) | 11.42 - 1077.48 | 163.01 (140.50) | 0 - 736.61 | 44.84 (50.97) | 0 - 257.05 |

**Footnote 2: Genetic samples across donors and parcellations**

A picture containing graphical user interface

Description automatically generated**Distribution of mean number of samples per donor in the Allen Human Brain Atlas (AHBA) for 3 parcellations of increasing granularity.** (a) The Schaefer 100-node parcellation (Schaefer et al., 2018) has full AHBA spatial coverage, whilst this coverage decreases for the (b) Brainnetome 246-node (Fan et al., 2016) and (c) Schaefer 400-node parcellations (Schaefer et al., 2018), respectively. See Hawrylycz and colleagues (2012) for technical AHBA details.

**Footnote 3: Polygenic score model specification and performance at different thresholds Polygenic score model specification for European and Non-European subsets.** For each model, 6 principal components (PC) of ancestry were included as covariates.

*Note.* **\*** and \*\* represent significance at *p* < .01 and *p* < .001, respectively. Clumping thresholds of *p* = .1 and *p* = .2 were used for European and Non-European participants, respectively.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Ancestry | Parameter | Coefficient | Standard Error | t-value | Pr(>|t|) |
| European | Intercept | .456 | 2.924e-2 | 15.589 | 1.307e-53 **\*\*** |
|  | *g* Factor Loading | 26234.927 | 1824.743 | 14.377 | 5.196e-46 **\*\*** |
|  | Sex (Male) | -1.011e-1 | 4.029e-2 | -2.510 | .012 **\*** |
|  | PC1 | 3.008 | 1.526 | 1.971 | .049 |
|  | PC2 | -14.120 | 1.470 | -9.601 | 1.183e-21 **\*\*** |
|  | PC3 | 5.241 | 1.600 | 3.276 | .001 **\*\*** |
|  | PC4 | -1.685 | 1.469 | -1.146 | .252 |
|  | PC5 | -3.393 | 1.472 | -2.305 | .021 |
|  | PC6 | -6.737 | 1.476 | -4.564 | 5.130e-6 **\*\*** |
| Non-European | Intercept | -.372 | 6.167e-2 | -6.026 | 2.235e-9 **\*\*** |
|  | *g* Factor Loading | 18998.573 | 4164.188 | 4.564 | 5.578e-6 **\*\*** |
|  | Sex (Male) | -.121 | .008 | -1.432 | .152 |
|  | PC1 | .980 | 1.505 | .652 | .515 |
|  | PC2 | 4.892 | 1.494 | 3.274 | .001 **\*\*** |
|  | PC3 | -7.633 | 1.454 | -5.249 | 1.810e-7 **\*\*** |
|  | PC4 | -2.006 | 1.461 | -1.373 | .170 |
|  | PC5 | -2.519 | 1.475 | -1.708 | .088 |
|  | PC6 | -.539 | 1.454 | -.371 | .711 |

**Polygenic model performance for varying clumping thresholds for European and Non-European subsets.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Ancestry | Polygenic Clumping Threshold PT | Polygenic Model Fit *R2* | *p* | *β* | Standard Error |
| European | .001 | .025 | 3.359e-32 | 2225.124 | 187.124 |
|  | .05 | .038 | 1.969e-48 | 9579.576 | 648.438 |
|  | .1 | .040 | 5.070e-51 | 13024.307 | 857.635 |
|  | .2 | .039 | 7.729e-50 | 17479.276 | 1165.373 |
|  | .3 | .038 | 6.215e-48 | 20755.122 | 1412.636 |
|  | .4 | .037 | 2.958e-47 | 23757.929 | 1629.252 |
|  | .5 | .036 | 5.196e-46 | 26234.927 | 1824.743 |
| Non-European | .001 | .012 | 1.053e-4 | 1637.998 | 420.961 |
|  | .05 | .012 | 1.188e-4 | 5410.462 | 1401.212 |
|  | .1 | .014 | 3.557e-5 | 7804.361 | 1880.474 |
|  | .2 | .017 | 2.867e-6 | 12194.429 | 2593.133 |
|  | .3 | .017 | 4.226e-6 | 14646.042 | 3169.217 |
|  | .4 | .016 | 9.407e-6 | 16434.281 | 3693.490 |
|  | .5 | .016 | 5.578e-6 | 18998.574 | 4164.188 |

**Footnote 4: Generative model findings across parcellations**

**Lowest-energy group simulations with associated optimal η and γ parameters, across 3 parcellations.** Each generative rule was evaluated for 99,856 unique combinations of η [-7 ≤ η ≤ 7] and γ [-7 ≤ γ ≤ 7].

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Parcellation | | | | | | | | |
|  | Schaefer 100-Node | | | Brainnetome 246-Node | | | Schaefer 400-Node | | |
| Rule | Energy | η | γ | Energy | η | γ | Energy | η | γ |
| Clu-Avg | .120 | -6.422 | -4.822 | .228 | -4.200 | -2.289 | .173 | -5.089 | 1.000 |
| Deg-Avg | .148 | -5.578 | 1.667 | .240 | -4.556 | 1.978 | .138 | -3.533 | 1.444 |
| Matching | .100 | -3.800 | .333 | .106 | -2.467 | .333 | .110 | -2.956 | .467 |
| Neighbours | .090 | -2.911 | .244 | .110 | -2.200 | .289 | .107 | -2.911 | .378 |
| Spatial | .205 | -6.378 | 4.289 | .289 | -4.111 | .244 | .268 | -3.578 | 3.400 |

*Note.* “Clu-Avg” = Average Clustering Coefficient, “Deg-Avg” = Average Degree.

**Mean topological dissimilarity (TD) and correlations between simulated and observed degree for 1000 simulations of each generative model’s lowest energy η and γ combination, across 3 parcellations.** For the Brainnetome 246-node parcellation, the models differed significantly in their topological dissimilarity [*F*(4,4999) = 1654.00, *p* < .001] and ability to capture observed degree [*F*(4,4999) = 1643.50, *p* < .001], with all post-hoc comparisons highly significant (*p* < .001). For the Schaefer 400-node parcellation, the models also differed significantly in their topological dissimilarity [*F*(4,4999) = 4502.14, *p* < .001], with all post-hoc comparisons highly significant (*p* < .001). The models also differed in their correlation with observed degree [*F*(4,4999) = 2197.93, *p* < .001], with all post-hoc comparisons highly significant, apart from the two homophily models performing similarly to each other (*p* = .991).

|  |  |  |
| --- | --- | --- |
|  | Schaefer 100-Node | |
| GNM Rule | Topological Dissimilarity  (Mean ± SD) | Simulated – Observed Degree Pearson’s *r* (Mean ± SD) |
| Clu-Avg | 1.975 ± .156 | .165 ± .071 |
| Deg-Avg | .963 ± .236 | .343 ± .062 |
| Matching | 1.004 ± .280 | .394 ± .079 |
| Neighbours | .979 ± .265 | .412 ± .077 |
| Spatial | 1.058 ± .339 | .130 ± .062 |
|  | **Brainnetome 246-Node** | |
| Clu-Avg | 1.683 ± .132 | .050 ± .062 |
| Deg-Avg | 1.462 ± .264 | .076 ± .031 |
| Matching | 1.035 ± .239 | .119 ± .046 |
| Neighbours | 1.098 ± .252 | .129 ± .050 |
| Spatial | .973 ± .281 | -.018 ± .039 |
|  | **Schaefer 400-Node** | |
| Clu-Avg | 1.482 ± .188 | -.095 ± .120 |
| Deg-Avg | .998 ± .160 | .197 ± .044 |
| Matching | .618 ± .187 | .016 ± .070 |
| Neighbours | .577 ± .194 | .015 ± .073 |
| Spatial | .763 ± .138 | -.055 ± .044 |

*Note.* “Clu-Avg” = Average Clustering Coefficient, “Deg-Avg” = Average Degree.

**Footnote 5: Detailed gene enrichment analyses**

**Summary of Gene Ontologies for Parameterised Nodal Wiring Costs, Value, and Cognitive Ability.** Allen Human Brain Atlas (AHBA) genes predicted parameterised nodal wiring costs and values, separately, for each participant, through partial least squares regression. Following 10,000 permutations for each participant, AHBA genes with permuted *p*-values less than .05 across all participants were selected and then ranked by decreasing mean loading onto the first latent variable. 76,745 short-nucleotide polymorphisms were ranked by decreasing absolute β in the cognitive ability polygenic score. All gene lists were submitted separately to g:Profiler (Kolberg et al., 2020) for gene enrichment, with a cut-off of *p* < .05 corrected for multiple comparisons, and default parameters. Electronic annotations were excluded for robustness.

To examine the functional roles of these genes, we performed ordered pathway enrichment analysis for each list separately, using g:Profiler (Kolberg et al., 2020; Raudvere et al., 2019; Reimand et al., 2019). Pathway enrichment analysis tests whether inputted genes are significantly more likely to be grouped together compared to chance. In the case of ordered gene lists, the algorithm searches for the largest sub-list of genes significantly associated with an ontology, and adjusts for multiple comparisons of interdependent gene ontologies (Raudvere et al., 2019; Reimand et al., 2019).

Parameterised nodal wiring costs were significantly enriched for 19 pathways, most of which linked to molecular functions (73.68%). The strongest enrichments were for genes associated with transmembrane transporter activity of metal ions (*padj* = 2.116 x 10-4), cations (*padj* = 8.192 x 10-4), and inorganic molecules (*padj* = .004). Parameterised nodal wiring value were significantly enriched for 41 pathways, most of which linked to biological processes (43.90%). Rather than transporter activity, the strongest enrichments were for genes associated with different modes of signaling, including synaptic (*padj*= 1.130 x 10-5), cell-cell (*padj*= 1.949 x 10-5), and anterograde trans-synaptic (*padj*= 2.348 x 10-5).

Next, we submitted all 76,745 SNPs in the PGS, ranked by descending absolute β, to pathway enrichment analysis. SNPs predictive of cognitive ability were significantly enriched for 297 pathways, mostly encoding biological processes (49.50%). The strongest enrichments were for genes associated with synaptic (*padj*= 3.485 x 10-29) and post-synaptic (*padj*= 3.684 x 10-26) membranes, alongside synaptic (*padj*= 7.602 x 10-20) and trans-synaptic (*padj*= 3.821 x 10-20) signaling. Summaries for all pathway enrichment analyses and g:Profiler links are provided below.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Parameterised Nodal Wiring Costs | Parameterised Nodal Wiring Value | Cognitive Ability |
| Number of Genes | 951 | 561 | 15,234 |
| g:Profiler Link | https://biit.cs.ut.ee/gplink/l/m2E\_uLK0TG | https://biit.cs.ut.ee/gplink/l/T8OtQThDQ\_ | https://biit.cs.ut.ee/gplink/l/lGxCWYZpSo |
| % BP/CC/MF | 10.526% / 15.790% / 73.684% | 43.902% / 29.268% / 26.829% | 49.495% / 27.609% / 22.896% |
| Top 10 Enriched Categories | GO:0046873, Metal Ion Transmembrane Transporter Activity (*padj* = 2.116e-4) | GO:0099536, Synaptic Signaling (*padj*= 1.130e-5) | GO:0097060, Synaptic Membrane (*padj*= 3.485e-29) |
| GO:0005215, Transporter Activity (*padj* = 4.480e-4) | GO:0007267, Cell-Cell Signaling (*padj*= 1.949e-5) | GO:0045202, Synapse (*padj*= 2.586e-26) |
| GO:0008324, Cation Transmembrane Transporter Activity (*padj* = 8.192e-4) | GO:0098916, Anterograde Trans-Synaptic Signaling (*padj*= 2.348e-5) | GO:0098794, post-Synapse (*padj*= 3.684e-26) |
| GO:0022890, Inorganic Cation Transmembrane Transporter Activity (*padj* = 9.618e-4) | GO:0007268, Chemical Synaptic Transmission (*padj*= 2.348e-5) | GO:0045211, Post-Synapse Membrane (*padj*= 2.072e-24) |
| GO:0022857, Transmembrane Transporter Activity (*padj* = .002) | GO:0099537, Trans-Synaptic Signaling (*padj*= 3.284e-5) | GO:0043005, Neuron Projection (*padj* = 1.492e-20) |
| GO:0015075, Ion Transmembrane Transporter Activity (*padj* = .003) | GO:0071944, Cell Periphery (*padj*= 1.169e-4) | GO:0099537, Trans-Synaptic Signaling (*padj*= 3.821e-20) |
| GO:0015318, Inorganic Molecular Entity Transmembrane Transporter Activity (*padj* = .004) | GO:0005886, Plasma Membrane (*padj*= 4.230e-4) | GO:009536, Synaptic Signaling (*padj*= 7.602e-20) |
| GO:008514, Organic Anion Transmembrane Transporter Activity (*padj* = .005) | GO:0045202, Synapse (*padj*= 5.586e-4) | GO:0098916, Anterograde Trans-Synaptic Signaling (*padj*= 2.212e-19) |
| GO:0000149, SNARE Binding (*padj* = .005) | GO:0043005, Neuron Projection (*padj*= .002) | GO:0007268, Chemical Synaptic Transmission (*padj*= 2.212e-19) |
| GO:0015291, Secondary Active Transmembrane Transporter Activity (*padj*= .005) | GO:0022824, Transmitter-Gated Ion Channel Activity (*padj*= .004) | GO:0030054, Cell Junction (*padj*= 7.227e-19) |

*Note.* “MF” = Molecular function; “BP” = Biological processes; “CC” = Cellular Components.

**Gene ontologies for a comparative pathway enrichment analysis between parameterised nodal wiring costs, value, and cognitive ability PGS.** We created 3 ranked gene lists of genes predictive of parameterised nodal wiring costs, value, and SNPs predictive of the cognitive ability PGS (see Table S9). These gene lists were inputted into a multi-query comparative pathway analysis in g:Profiler with default parameters, and a cut-off of *p* < .01. Electronic annotations were excluded.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | | *p* values | | |
| GO ID | **Term Name** | Cost | Value | PGS |
| GO:0043005  CC | neuron projection | 1.000 | 0.002 | 1.573e-10 |
| GO:0030594  MF | neurotransmitter receptor activity | 1.000 | 0.013 | 1.846e-9 |
| GO:0034702  CC | ion channel complex | 1.000 | 0.173 | 5.946e-9 |
| GO:0099537  BP | trans-synaptic signaling | 1.000 | 3.284e-5 | 7.604e-9 |
| GO:0099536  BP | synaptic signaling | 1.000 | 1.130e-5 | 8.678e-9 |
| GO:0045202  CC | synapse | 0.324 | 0.001 | 1.301e-8 |
| GO:0034703  CC | cation channel complex | 1.000 | 0.168 | 1.330e-8 |
| GO:0098797  CC | plasma membrane protein complex | 1.000 | 0.456 | 1.735e-8 |
| GO:0007268  BP | chemical synaptic transmission | 1.000 | 2.348e-5 | 1.917e-8 |
| GO:0098916  BP | anterograde trans-synaptic signaling | 1.000 | 2.348e-5 | 1.917e-8 |
| GO:0007215  BP | glutamate receptor signaling pathway | 1.000 | 1.000 | 1.020e-7 |
| GO:0098794  CC | post synapse | 1.000 | 0.403 | 1.620e-7 |
| GO:0022836  MF | gated channel activity | 1.000 | 0.056 | 1.783e-7 |
| GO:0005230  MF | extracellular ligand-gated ion channel activity | 1.000 | 0.014 | 2.613e-7 |
| GO:0005272  MF | sodium channel activity | 1.000 | 1.000 | 5.191e-7 |
| GO:0022835  MF | transmitter-gated channel activity | 1.000 | 0.004 | 8.765e-7 |
| GO:0022824  MF | transmitter-gated ion channel activity | 1.000 | 0.004 | 8.765e-7 |
| GO:0035249  BP | synaptic transmission, glutamatergic | 1.000 | 1.000 | 1.466e-6 |
| GO:0045211  CC | postsynaptic membrane | 1.000 | 1.000 | 1.705e-6 |
| GO:0034706  CC | sodium channel complex | 1.000 | 0.271 | 1.851e-6 |
| GO:0098988  MF | G protein-coupled glutamate receptor activity | 1.000 | 1.000 | 4.098e-6 |
| GO:0001640  MF | adenylate cyclase inhibiting G protein-coupled glutamate receptor activity | 1.000 | 1.000 | 4.098e-6 |
| GO:0015081  MF | sodium ion transmembrane transporter activity | 0.315 | 1.000 | 4.676e-6 |
| GO:0005216  MF | ion channel activity | 1.000 | 0.032 | 4.712e-6 |
| GO:0005261  MF | cation channel activity | 1.000 | 1.000 | 9.966e-6 |
| GO:0097060  CC | synaptic membrane | 1.000 | 1.000 | 1.042e-5 |
| GO:0022834  MF | ligand-gated channel activity | 1.000 | 0.006 | 1.052e-5 |
| GO:0015276  MF | ligand-gated ion channel activity | 1.000 | 0.006 | 1.052e-5 |
| GO:0030424  CC | axon | 0.019 | 0.473 | 1.215e-5 |
| GO:0046873  MF | metal ion transmembrane transporter activity | 2.116e-4 | 1.000 | 1.234e-5 |
| GO:0001518  CC | voltage-gated sodium channel complex | 1.000 | 0.378 | 1.755e-5 |
| GO:0007267  BP | cell-cell signaling | 1.000 | 1.949e-5 | 0.270 |
| GO:0042995  CC | cell projection | 1.000 | 0.010 | 2.142e-5 |
| GO:0120025  CC | plasma membrane bounded cell projection | 1.000 | 0.006 | 2.563e-5 |
| GO:0042391  BP | regulation of membrane potential | 1.000 | 1.000 | 3.514e-5 |
| GO:0015267  MF | channel activity | 1.000 | 0.063 | 4.425e-5 |
| GO:0004970  MF | ionotropic glutamate receptor activity | 1.000 | 1.000 | 4.451e-5 |
| GO:0036477  CC | Somato-dendritic compartment | 1.000 | 0.138 | 4.665e-5 |
| GO:0022803  MF | passive transmembrane transporter activity | 1.000 | 0.064 | 4.815e-5 |
| GO:0051966  BP | regulation of synaptic transmission, glutamatergic | 1.000 | 1.000 | 4.958e-5 |
| GO:0086010  BP | membrane depolarization during action potential | 1.000 | 1.000 | 1.019e-4 |
| GO:0097447  CC | dendritic tree | 1.000 | 0.092 | 1.121e-4 |
| GO:0071944  CC | cell periphery | 1.000 | 1.169e-4 | 0.541 |
| GO:0098960  MF | postsynaptic neurotransmitter receptor activity | 1.000 | 0.907 | 1.448e-4 |
| GO:0035725  BP | sodium ion transmembrane transport | 1.000 | 1.000 | 1.534e-4 |
| GO:0005248  MF | voltage-gated sodium channel activity | 1.000 | 1.000 | 1.620e-4 |
| GO:0050804  BP | modulation of chemical synaptic transmission | 1.000 | 1.000 | 1.757e-4 |
| GO:0030425  CC | dendrite | 1.000 | 0.082 | 1.918e-4 |
| GO:0099177  BP | regulation of trans-synaptic signaling | 1.000 | 1.000 | 1.992e-4 |
| GO:1902495  CC | transmembrane transporter complex | 0.264 | 1.000 | 2.214e-4 |
| GO:0007216  BP | G protein-coupled glutamate receptor signaling pathway | 1.000 | 1.000 | 3.482e-4 |
| GO:0005886  CC | plasma membrane | 1.000 | 4.230e-4 | 1.000 |
| GO:0005215  MF | transporter activity | 0.001 | 1.000 | 1.000 |
| GO:0006814  BP | sodium ion transport | 1.000 | 0.844 | 0.001 |
| GO:0008328  CC | ionotropic glutamate receptor complex | 1.000 | 0.079 | 0.001 |
| GO:0015318  MF | inorganic molecular entity transmembrane transporter activity | 0.004 | 0.176 | 0.001 |
| GO:0022843  MF | voltage-gated cation channel activity | 1.000 | 1.000 | 0.001 |
| GO:0022890  MF | inorganic cation transmembrane transporter activity | 0.001 | 1.000 | 0.001 |
| GO:0098878  CC | neurotransmitter receptor complex | 1.000 | 0.180 | 0.001 |
| GO:0008324  MF | cation transmembrane transporter activity | 0.001 | 1.000 | 0.006 |
| GO:1990351  CC | transporter complex | 0.252 | 1.000 | 0.001 |
| GO:0001505  BP | regulation of neurotransmitter levels | 0.304 | 1.000 | 0.002 |
| GO:0019228  BP | neuronal action potential | 1.000 | 1.000 | 0.002 |
| GO:0008038  BP | neuron recognition | 1.000 | 1.000 | 0.002 |
| GO:0022857  MF | transmembrane transporter activity | 0.002 | 1.000 | 0.643 |
| GO:0015075  MF | ion transmembrane transporter activity | 0.003 | 0.513 | 0.027 |
| GO:0007156  BP | homophilic cell adhesion via plasma membrane adhesion molecules | 1.000 | 1.000 | 0.003 |
| GO:0005343  MF | organic acid: sodium symporter activity | 1.000 | 1.000 | 0.003 |
| GO:0030054  CC | cell junction | 1.000 | 0.005 | 0.004 |
| GO:0005244  MF | voltage-gated ion channel activity | 1.000 | 1.000 | 0.004 |
| GO:0022832  MF | voltage-gated channel activity | 1.000 | 1.000 | 0.004 |
| GO:0005283  MF | amino acid: sodium symporter activity | 1.000 | 1.000 | 0.004 |
| GO:0008514  MF | organic anion transmembrane transporter activity | 0.005 | 1.000 | 1.000 |
| GO:0015370  MF | solute: sodium symporter activity | 0.168 | 1.000 | 0.005 |
| GO:0000149  MF | SNARE binding | 0.005 | 1.000 | 1.000 |
| GO:0001504  BP | neurotransmitter uptake | 1.000 | 1.000 | 0.005 |
| GO:0031226  CC | intrinsic component of plasma membrane | 0.979 | 0.226 | 0.005 |
| GO:0008509  MF | anion transmembrane transporter activity | 0.005 | 1.000 | 1.000 |
| GO:0007196  BP | adenylate cyclase-inhibiting G protein-coupled glutamate receptor signaling pathway | 1.000 | 1.000 | 0.006 |
| GO:0004930  MF | G protein-coupled receptor activity | 1.000 | 1.000 | 0.006 |
| GO:0015291  MF | secondary active transmembrane transporter activity | 0.006 | 1.000 | 0.238 |
| GO:0005887  CC | integral component of plasma membrane | 0.699 | 0.429 | 0.006 |
| GO:0015277  MF | kainate selective glutamate receptor activity | 1.000 | 1.000 | 0.007 |
| GO:0098793  CC | Pre-synapse | 0.007 | 0.028 | 0.118 |
| GO:0044304  CC | main axon | 1.000 | 1.000 | 0.007 |
| GO:0003231  BP | cardiac ventricle development | 1.000 | 0.008 | 1.000 |
| GO:0099094  MF | ligand-gated cation channel activity | 1.000 | 1.000 | 0.008 |
| GO:0071870  BP | cellular response to catecholamine stimulus | 1.000 | 0.253 | 0.008 |
| GO:0071869  BP | response to catecholamine | 1.000 | 0.253 | 0.008 |
| GO:0071868  BP | cellular response to monoamine stimulus | 1.000 | 0.253 | 0.008 |
| GO:0071867  BP | response to monoamine | 1.000 | 0.253 | 0.008 |
| GO:0048699  BP | generation of neurons | 1.000 | 0.017 | 0.008 |
| GO:0099095  MF | ligand-gated anion channel activity | 1.000 | 0.009 | 0.086 |
| GO:1904315  MF | transmitter-gated ion channel activity involved in regulation of postsynaptic membrane potential | 1.000 | 1.000 | 0.009 |
| GO:0099529  MF | neurotransmitter receptor activity involved in regulation of postsynaptic membrane potential | 1.000 | 1.000 | 0.009 |

*Note.* “MF” = Molecular function; “BP” = Biological processes; “CC” = Cellular Components; “GO” =