

Supplementary Material

Investigating common molecular signatures and network motifs within a group of neurodegenerative diseases

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Table 1: Common genes between NDs

| #Disease1 | #Disease2 | Common genes | Number of common genes |
|-----------------------------|---------------------------------|--|------------------------|
| Alzheimer'sDisease | AmyotrophicLateralSclerosis | APP, PSEN1, MAPT, SNCA, CASP3, MT3, CHAT, CDK5, PRNP, NOS1, GDNF, BDNF, NGF, SQSTM1, EIF2AK2, SYP, RTN4, GFAP, TARDBP, CYCS, GRN, MAP2, NGFR, MAOB, NTRK1, CST3, SOD1, NTRK2, SLC18A3, SLC1A2, SLC1A3, GAP43 | 32 |
| Alzheimer'sDisease | FrontotemporalDementia | RELN, APP, SORL1, PSEN2, PSEN1, APOE, MAPT, SNCA, BCHE, PRNP, ACHE, PIN1, SQSTM1, PCSK1N, TARDBP, GRN, STH, SOD1 | 18 |
| Alzheimer'sDisease | Huntington'sDisease | BDNF, PRNP, CASP8, GRIN2B, CASP3, SOD1, GAPDH, GRIN2A, GRIN1, CYCS, SQSTM1, CASP2, CHAT, DLG4, ITPR1 | 15 |
| Alzheimer'sDisease | LewyBodyDisease | APP, PSEN1, APOE, MAPT, SNCA, SNCB, BCHE, CDK5, PRNP, ACHE, TARDBP, GRN, MAOB, SNCG | 14 |
| Alzheimer'sDisease | Parkinson'sDisease | MAPT, MT-ND1, SNCA, MAOB, GDNF, SNCB, UCHL1, SNCG, BDNF, CASP3, SOD1, APOE, CDK5, NGF, APP, HMOX1, MAPK8, CHAT, CYCS, ACHE, CAT, SLC6A4, STH, CASP9, NOS1, MAP2, NQO1, BCHE, GRIN2B, SQSTM1, NTRK2, GAPDH, MAPK3 | 33 |
| Alzheimer'sDisease | PeroxisomeBiogenesisDisorder 1b | CAT | 1 |
| Alzheimer'sDisease | PrionDisease | APP, MAPT, ADAM10, IL1B, PRNP, MAP2 | 6 |
| Alzheimer'sDisease | RefsumDisease | CAT | 1 |
| Alzheimer'sDisease | SpinalCordInjury | GDNF, GFAP, BDNF, TNF, CASP3, NGFR, NOS1, GRIN1 | 8 |
| Alzheimer'sDisease | ToxicEncephalopathy | HMOX1, BACE1, CASP3, BDNF, MAOB, PRNP, APP, NGF, GRIN2B, ACHE, GRIN2A, CYCS, SNCA, SLC1A2, MAPK8, IL1B, GFAP | 17 |
| AmyotrophicLateralSclerosis | Friedreich'sataxia | ATXN2, SETX, TERC | 3 |
| AmyotrophicLateralSclerosis | FrontotemporalDementia | SOD1, TARDBP, NEFH, C9orf72, VCP, UBQLN2, SQSTM1, FUS, CHCHD10, HNRNPA1, PFN1, CHMP2B, CCNF, UNC13A, TBK1, TREM2, MAPT, TMEM106B, GRN, SNCA, APP, RPS27A, PSEN1, HNRNPA2B1, TUBA4A, PRNP, INA | 27 |
| AmyotrophicLateralSclerosis | Huntington'sDisease | HTT, BDNF, PRNP, TGM2, CASP3, CREBBP, CALB1, SOD1, CYCS, SQSTM1, PPARGC1A, CHAT, CASP1, CNTF | 14 |
| AmyotrophicLateralSclerosis | LewyBodyDisease | TARDBP, MAPT, GRN, CDK5, SNCA, APP, RPS27A, MAOB, PSEN1, PRNP, TH | 11 |
| AmyotrophicLateralSclerosis | Parkinson'sDisease | SOD1, SQSTM1, ATXN2, CNTF, RNF19A, MAPT, GDNF, CDK5, CHAT, BDNF, SNCA, CASP3, NGF, HTT, PVALB, NOS1, APP, SOD2, CNR1, RPS27A, MAOB, HSPA8, CYCS, NTRK2, TH, CALB1, TGM2, MAP2, TSPO | 29 |
| AmyotrophicLateralSclerosis | PrionDisease | MAPT, APP, MAP2, PRNP | 4 |
| AmyotrophicLateralSclerosis | SpinalCordInjury | GDNF, BDNF, GFAP, CASP3, NOS1, NGFR | 6 |
| AmyotrophicLateralSclerosis | Spinocerebellarataxia | ATXN2 | 1 |
| AmyotrophicLateralSclerosis | ToxicEncephalopathy | CASP3, TH, BDNF, MAOB, PRNP, APP, NGF, CYCS, SNCA, SLC1A2, GFAP | 11 |
| Ataxia-telangiectasia | Friedreich'sataxia | APTX | 1 |
| Ataxia-telangiectasia | Huntington'sDisease | TP53 | 1 |
| Friedreich'sataxia | Huntington'sDisease | ATXN3, ATXN1 | 2 |
| Friedreich'sataxia | Parkinson'sDisease | ATXN3, ACO1, ATXN2 | 3 |
| Friedreich'sataxia | RefsumDisease | TTPA | 1 |
| Friedreich'sataxia | Spinocerebellarataxia | ATXN3, CACNA1A, ATXN2 | 3 |
| FrontotemporalDementia | Huntington'sDisease | PRNP, SOD1, SQSTM1 | 3 |
| FrontotemporalDementia | LewyBodyDisease | PSEN1, MAPT, GRN, TARDBP, SNCA, APOE, APP, RPS27A, ACHE, PRNP, LRRK2, BCHE | 12 |
| FrontotemporalDementia | Parkinson'sDisease | MAPT, LRRK2, SNCA, SOD1, APOE, APP, ACHE, STH, BCHE, RPS27A, SQSTM1 | 11 |

| | | | |
|---------------------------------|---------------------------------|---|----|
| FrontotemporalDementia | PrionDisease | PRNP, MAPT, APP | 3 |
| FrontotemporalDementia | ToxicEncephalopathy | SNCA, APP, ACHE, ACHE, PRNP | 4 |
| Huntington'sDisease | LewyBodyDisease | | 1 |
| Huntington'sDisease | Parkinson'sDisease | HTT, BDNF, GRIN2B, TGM2, CASP3, TBP, CALB1, SOD1, GAPDH, CYCS, AKT1, ATXN3, SQSTM1, CHAT, GRM5, ADORA2A, CNTF | 17 |
| Huntington'sDisease | PrionDisease | PRNP | 1 |
| Huntington'sDisease | SpinalCordInjury | BDNF,CASP3, GRIN1 | 3 |
| Huntington'sDisease | Spinocerebellarataxia | ATXN3 | 1 |
| Huntington'sDisease | ToxicEncephalopathy | BDNF, PRNP, GRIN2B, CASP3, GRIN2A, CYCS, AKT1 | 7 |
| LewyBodyDisease | Parkinson'sDisease | MAPT, GBA, LRRK2, PRKN, SNCAIP, SNCA, TH, PARK7, SLC6A3, MAOB, SNCB, SLC18A2, SNCG, CYP2D6, APOE, CDK5, APP, ACHE, BCHE, RPS27A | 20 |
| LewyBodyDisease | PrionDisease | MAPT, PRNP, APP | 3 |
| LewyBodyDisease | ToxicEncephalopathy | SNCA, SLC6A3, SLC18A2, ACHE, MAOB, PRNP, TH, APP | 8 |
| Parkinson'sDisease | PeroxisomeBiogenesisDisorder 1b | CAT | 1 |
| Parkinson'sDisease | PrionDisease | MAPT, MAP2, APP | 3 |
| Parkinson'sDisease | RefsumDisease | CAT | 1 |
| Parkinson'sDisease | SpinalCordInjury | GDNF, NOS1, BDNF, CASP3, PDYN | 5 |
| Parkinson'sDisease | Spinocerebellarataxia | ATXN2, ATXN3 | 2 |
| Parkinson'sDisease | ToxicEncephalopathy | HMOX1, TRPV1, CASP3, TH, BDNF, SLC6A3, MAOB, APP, NGF, GRIN2B, ACHE, SLC18A2, CYCS, SNCA, MAPK8, AKT1 | 16 |
| PeroxisomeBiogenesisDisorder 1b | RefsumDisease | PHYH, PEX7, CAT, PEX5, PEX16, HSD17B4, PEX14, GNPAT | 8 |
| PrionDisease | ToxicEncephalopathy | PRNP, IL1B, APP | 3 |
| SpinalCordInjury | ToxicEncephalopathy | GFAP, BDNF, CASP3 | 3 |

Table 2: Common genes between PPI networks

| #Disease1 | #Disease2 | Common genes | Number of common genes |
|-----------------------------|---------------------------------|---|------------------------|
| Alzheimer'sDisease | AmyotrophicLateralSclerosis | APBB1, APP, XIAP, CASP3, CDK5, CDK5R1, NOS1, CYCS, NTRK1, NGF, SNCA, PSEN1, MAPT, TARDBP, SOD1, SQSTM1, RTN4, BDNF, NTRK2, NGFR | 20 |
| Alzheimer'sDisease | Friedreich'sataxia | CALM2, NDUFAB1, CACNA1A | 3 |
| Alzheimer'sDisease | FrontotemporalDementia | APP, PIN1, SNCA, PSEN2, PSEN1, TARDBP, SOD1, SQSTM1 | 8 |
| Alzheimer'sDisease | Huntington'sDisease | XIAP, CASP3, GRIN1, GRIN2A, DLG4, GRIN2B, CASP8, CASP2, SOD1, GAPDH, SQSTM1 | 11 |
| Alzheimer'sDisease | LewyBodyDisease | APP, SNCA, PSEN1 | 3 |
| Alzheimer'sDisease | Parkinson'sDisease | MT-ND1, NDUFAB1, VPS29, VPS35, VPS26A, APP, CASP3, CDK5, CASP9, NOS1, GRIN2B, MAPK3, CYCS, SNCA, MAPT, SOD1, GAPDH, CAT, SQSTM1, HMOX1, BDNF, NTRK2, SLC6A4 | 23 |
| Alzheimer'sDisease | PeroxisomeBiogenesisDisorder 1b | CAT | 1 |
| Alzheimer'sDisease | RefsumDisease | CAT | 1 |
| Alzheimer'sDisease | SpinalCordInjury | CALM2, NOS2, CALM1, XIAP, CASP3, CALM3, NOS1, GRIN1 | 8 |
| Alzheimer'sDisease | Spinocerebellarataxia | CALM2, CACNA1A | 2 |
| Alzheimer'sDisease | ToxicEncephalopathy | APBB1, APP, XIAP, CASP3, GRIN1, GRIN2A, GRIN2B, CYCS, SNCA, BDNF | 10 |
| AmyotrophicLateralSclerosis | FrontotemporalDementia | FAU, RPS16, RPS12, RPS24, RPS27A, NPLOC4, UFD1L, VCP, FAF1, UBUN7, RPS10, DERL1, CHMP2B, UBA52, APP, FUS, UBQLN2, TUBA4A, SOD1, SNCA, TARDBP, SQSTM1, PSEN1, PRNP, HNRNPA2B1, HNRNPA1 | 26 |

| | | | |
|---------------------------------|---------------------------------|---|----|
| AmyotrophicLateralSclerosis | Huntington'sDisease | CREBBP, CITED2, XIAP, CASP3, SOD1, SQSTM1, HTT | 7 |
| AmyotrophicLateralSclerosis | LewyBodyDisease | FAU, RPS16, RPS12, RPS24, RPS27A, RPS10, UBA52, APP, SNCA, PSEN1, TH | 11 |
| AmyotrophicLateralSclerosis | Parkinson'sDisease | RPS27A, CASP3, APP, CDK5, NOS1, CALB1, PVALB, HSPA8, SOD2, SOD1, SNCA, SQSTM1, CYCS, MAPT, BDNF, NTRK2, HTT, RNF19A, TH | 19 |
| AmyotrophicLateralSclerosis | SpinalCordInjury | XIAP, CASP3, NOS1 | 3 |
| AmyotrophicLateralSclerosis | ToxicEncephalopathy | XIAP, CASP3, APBB1, APP, SNCA, CYCS, BDNF, TH | 8 |
| Ataxia-telangiectasia | Huntington'sDisease | TP53 | 1 |
| Friedreich'sataxia | Parkinson'sDisease | NDUFAB1 | 1 |
| Friedreich'sataxia | SpinalCordInjury | CALM2 | 1 |
| Friedreich'sataxia | Spinocerebellarataxia | CACNA1A, CALM2 | 2 |
| FrontotemporalDementia | Huntington'sDisease | SQSTM1, SOD1 | 2 |
| FrontotemporalDementia | LewyBodyDisease | FAU, RPS16, RPS12, RPS24, RPS27A, SNCA, APP, LRRK2, PSEN1, RPS10, UBA52 | 11 |
| FrontotemporalDementia | Parkinson'sDisease | RPS27A, SNCA, APP, LRRK2, SQSTM1, SOD1 | 6 |
| FrontotemporalDementia | ToxicEncephalopathy | SNCA, APP | 2 |
| Huntington'sDisease | Parkinson'sDisease | TBP, GRIN2B, AKT1, SOD1, GAPDH, HTT, SQSTM1, CASP3 | 8 |
| Huntington'sDisease | SpinalCordInjury | GRIN1, XIAP, CASP3 | 3 |
| Huntington'sDisease | Spinocerebellarataxia | TAF10 | 1 |
| Huntington'sDisease | ToxicEncephalopathy | GRIN2B, AKT1, GRIN2A, GRIN1, XIAP, CASP3 | 6 |
| LewyBodyDisease | Parkinson'sDisease | SLC6A3, SNCA, APP, TH, LRRK2, SNCAIP, PARK2, RPS27A | 8 |
| LewyBodyDisease | ToxicEncephalopathy | SLC6A3, SNCA, APP, TH | 4 |
| Parkinson'sDisease | PeroxisomeBiogenesisDisorder 1b | CAT | 1 |
| Parkinson'sDisease | RefsumDisease | CAT | 1 |
| Parkinson'sDisease | SpinalCordInjury | CASP3, NOS1 | 2 |
| Parkinson'sDisease | ToxicEncephalopathy | SNCA, CYCS, AKT1, CASP3, GRIN2B, SLC6A3, TH, APP, BDNF, NTF3 | 10 |
| PeroxisomeBiogenesisDisorder 1b | RefsumDisease | PEX5, PEX14, ACAA1, PEX7, PEX19, HSD17B4, CAT | 7 |
| SpinalCordInjury | Spinocerebellarataxia | CALM2 | 1 |
| SpinalCordInjury | ToxicEncephalopathy | XIAP, CASP3, GRIN1 | 3 |

Table 3: Common pathways between PPI networks

| PAIR OF DISEASES | NUMBER OF COMMON PATHWAYS | KEGG PATHWAY NAME |
|------------------------------|---------------------------|-------------------------------------|
| AD, ALS | 3 | Alzheimer's disease |
| | | Apoptosis |
| | | Amyotrophic lateral sclerosis (ALS) |
| AD, FRIEDREICH ATAXIA | 3 | Alzheimer's disease |
| | | Dopaminergic synapse |
| | | Calcium signaling pathway |
| AD, FD | 2 | Alzheimer's disease |
| | | Amyotrophic lateral sclerosis (ALS) |
| AD, HD | 4 | Alzheimer's disease |

| | | |
|---------------------------------|---|-------------------------------------|
| | | Amyotrophic lateral sclerosis (ALS) |
| | | Apoptosis |
| | | Long-term potentiation |
| AD, LBD | 3 | Alzheimer's disease |
| | | Dopaminergic synapse |
| | | Amphetamine addiction |
| AD, PD | 3 | Alzheimer's disease |
| | | Amyotrophic lateral sclerosis (ALS) |
| | | Neurotrophin signaling pathway |
| AD, SPINAL CORD INJURY | 6 | Alzheimer's disease-Homo sapiens |
| | | Amyotrophic lateral sclerosis (ALS) |
| | | Long-term potentiation-Homo sapiens |
| | | Amphetamine addiction |
| | | Circadian entrainment |
| | | Calcium signaling pathway |
| AD, SPINOCEREBELLAR | 4 | Long-term potentiation |
| | | Dopaminergic synapse |
| | | Amphetamine addiction |
| | | Calcium signaling pathway |
| AD, TOXIC ENCEPHALOPATHY | 4 | Alzheimer's disease |
| | | Dopaminergic synapse |
| | | Amphetamine addiction |
| | | Amyotrophic lateral sclerosis (ALS) |
| ALS, FRIEDREICH ATAXIA | 1 | Alzheimer's disease-Homo sapiens |
| ALS, FD | 3 | Amyotrophic lateral sclerosis (ALS) |
| | | Alzheimer's disease |
| | | Ribosome |
| ALS, HD | 6 | Amyotrophic lateral sclerosis (ALS) |
| | | Alzheimer's disease |
| | | Huntington's disease |
| | | Apoptosis |
| | | Mitophagy |

| | | |
|---|---|-------------------------------------|
| | | Cocaine addiction-Homo sapiens |
| ALS, LBD | 3 | Alzheimer's disease |
| | | Ribosome |
| | | Cocaine addiction |
| ALS, PD | 4 | Amyotrophic lateral sclerosis (ALS) |
| | | Alzheimer's disease |
| | | Huntington's disease |
| | | Cocaine addiction |
| ALS, PRION | 1 | Ribosome |
| ALS, SPINAL CORD INJURY | 2 | Alzheimer's disease |
| | | Amyotrophic lateral sclerosis (ALS) |
| ALS, TOXIC ENCEPHALOPATHY | 4 | Amyotrophic lateral sclerosis (ALS) |
| | | Alzheimer's disease |
| | | Huntington's disease |
| | | Cocaine addiction |
| FRIEDREICH, FD | 1 | Alzheimer's disease |
| FRIEDREICH, HD | 2 | Alzheimer's disease-Homo sapiens |
| | | Nicotine addiction |
| FRIEDREICH, LBD | 2 | Dopaminergic synapse |
| | | Alzheimer's disease |
| FRIEDREICH, PD | 1 | Alzheimer's disease |
| FRIEDREICH, SPINAL CORD INJURY | 3 | Calcium signaling pathway |
| | | Phototransduction |
| | | Alzheimer's disease-Homo sapiens |
| FRIEDREICH, SPINOCEREBELLAR | 5 | Dopaminergic synapse |
| | | Calcium signaling pathway |
| | | Nicotine addiction |
| | | Phototransduction |
| | | Type II diabetes mellitus |
| FRIEDREICH, TOXIC ENCEPHALOPATHY | 3 | Dopaminergic synapse |
| | | Alzheimer's disease |
| | | Nicotine addiction |
| FD, HD | 2 | Alzheimer's disease |
| | | Amyotrophic lateral sclerosis (ALS) |
| FD, LBD | 3 | Ribosome |

| | | |
|---------------------------------|---|--|
| | | Alzheimer's disease |
| | | Notch signaling pathway |
| FD, PD | 2 | Amyotrophic lateral sclerosis (ALS) |
| | | Alzheimer's disease |
| FD, PRION | 1 | Ribosome |
| FD, SPINAL CORD INJURY | 2 | Alzheimer's disease |
| | | Amyotrophic lateral sclerosis (ALS) |
| FD, TOXIC ENCEPHALOPATHY | 2 | Alzheimer's disease |
| | | Amyotrophic lateral sclerosis (ALS) |
| HD, LBD | 2 | Alzheimer's disease |
| | | Cocaine addiction |
| HD, PD | 4 | Huntington's disease |
| | | Amyotrophic lateral sclerosis (ALS) |
| | | Alzheimer's disease |
| | | Cocaine addiction |
| HD, SPINAL CORD INJURY | 3 | Alzheimer's disease |
| | | Long-term potentiation |
| | | Amyotrophic lateral sclerosis (ALS) |
| HD, SPINOCEREBELLAR | 3 | Basal transcription factors-Homo sapiens |
| | | Nicotine addiction |
| | | Long-term potentiation |
| HD, TOXIC ENCEPHALOPATHY | 5 | Huntington's disease |
| | | Amyotrophic lateral sclerosis (ALS) |
| | | Alzheimer's disease |
| | | Cocaine addiction |
| | | Nicotine addiction |
| LBD, PD | 3 | Parkinson's disease |
| | | Alzheimer's disease |
| | | Cocaine addiction |
| LBD, PRION | 1 | Ribosome |
| LBD, SPINAL CORD INJURY | 2 | Alzheimer's disease |
| | | Amphetamine addiction |

| | | |
|---|---|---|
| LBD, SPINOCEREBELLAR | 2 | Amphetamine addiction |
| | | Dopaminergic synapse |
| LBD, TOXIC ENCEPHALOPATHY | 6 | Parkinson's disease |
| | | Alzheimer's disease |
| | | Cocaine addiction |
| | | Amphetamine addiction |
| | | Dopaminergic synapse |
| | | Alcoholism |
| PD, SPINAL CORD INJURY | 2 | Alzheimer's disease |
| | | Amyotrophic lateral sclerosis (ALS) |
| PD, TOXIC ENCEPHALOPATHY | 5 | Parkinson's disease |
| | | Alzheimer's disease |
| | | Huntington's disease |
| | | Amyotrophic lateral sclerosis (ALS) |
| | | Cocaine addiction |
| PEROXISOME, REFSUM | 7 | Peroxisome |
| | | Biosynthesis of unsaturated fatty acids |
| | | Glyoxylate and dicarboxylate metabolism |
| | | Primary bile acid biosynthesis |
| | | alpha-Linolenic acid metabolism |
| | | Tryptophan metabolism |
| | | Fatty acid degradation |
| SPINAL CORD INJURY, SPINOCEREBELLAR | 4 | Calcium signaling pathway |
| | | Amphetamine addiction |
| | | Long-term potentiation |
| | | Phototransduction |
| SPINAL CORD INJURY, TOXIC ENCEPHALOPATHY | 3 | Alzheimer's disease |
| | | Amphetamine addiction |
| | | Amyotrophic lateral sclerosis (ALS) |
| SPINOCEREBELLAR, TOXIC ENCEPHALOPATHY | 3 | Dopaminergic synapse |
| | | Amphetamine addiction |
| | | Nicotine addiction |

Table 4: Top 10 significantly enriched pathways for each ND

| AD | ALS | Ataxia-telangiectasia | Friedreich Ataxia | FD | HD | LB | PD | Peroxisome | Refsum | Spinal Cord | Spinocerebellar ataxia | Toxic Encephalopathy |
|-------------------------------------|-------------------------------------|----------------------------|--------------------------------------|---|-------------------------------------|-----------------------|-------------------------------------|---|---|---------------------------------|-----------------------------|-------------------------------------|
| Alzheimer's disease | Amyotrophic lateral sclerosis (ALS) | Non-homologous end-joining | Sulfur metabolism | Ribosome | Basal transcription factors | Ribosome | Proteasome | Biosynthesis of unsaturated fatty acids | Peroxisome | Arginine biosynthesis | Phototransduction | Cocaine addiction |
| Amyotrophic lateral sclerosis (ALS) | Apoptosis | Homologous recombination | Thiamine metabolism | Spliceosome | Huntington's disease | Parkinson's disease | Amyotrophic lateral sclerosis (ALS) | Glyoxylate and dicarboxylate metabolism | Biosynthesis of unsaturated fatty acids | Phototransduction | Dopamine synthesis | Alzheimer's disease |
| Long-term potentiation | Alzheimer's disease | p53 signaling pathway | Phototransduction | Prion diseases | Amyotrophic lateral sclerosis (ALS) | Cocaine addiction | Parkinson's disease | Primary bile acid biosynthesis | Primary bile acid biosynthesis | Pertussis | Nicotine addiction | Amyotrophic lateral sclerosis (ALS) |
| Amphetamine addiction | Cocaine addiction | DNA replication | Nicotine addiction | Protein processing in endoplasmic reticulum | Viral carcinogenesis | Amphetamine addiction | Epstein-Barr virus infection | alpha-Linolenic acid metabolism | PPAR signaling pathway | Circadian entrainment | Basal transcription factors | Amphetamine addiction |
| Apoptosis | Legionellosis | Cell cycle | Dopamine synthesis | Ferroptosis | Cocaine addiction | Folate biosynthesis | Alzheimer's disease | Alanine, aspartate and glutamate metabolism | alpha-Linolenic acid metabolism | Long-term potentiation | Type II diabetes mellitus | Parkinson's disease |
| Dopamine synthesis | Huntington's disease | Mismatch repair | Porphyria and chlorophyll metabolism | Notch signaling pathway | Mitophagy | Alzheimer's disease | Cocaine addiction | Glycine, serine and threonine metabolism | Glyoxylate and dicarboxylate metabolism | Amphetamine addiction | Calcium signaling pathway | Nicotine addiction |
| Tuberculosis | MAPK signaling pathway | Cellular senescence | Type II diabetes mellitus | Amyotrophic lateral sclerosis (ALS) | Nicotine addiction | Tyrosine metabolism | Huntington's disease | Tryptophan metabolism | Lysosome | Alzheimer's disease | Long-term depression | Huntington's disease |
| Circadian entrainment | Mitophagy | Fanconi anemia pathway | Retrograde endocannabinoid signaling | Alzheimer's disease | Long-term potentiation | Dopamine synthesis | Colorectal cancer | Fatty acid degradation | Tryptophan metabolism | Arginine and proline metabolism | Long-term potentiation | Alcoholism |

| | | | | | | | | | | | | |
|-------------------------------|---------------|--------------------------|-------------------------|---|------------------|-----------------------|------------------------------|---|--|-----------------------------------|----------------------|----------------------|
| Neurotrophinsignaling pathway | Ribosome | Nucleotideexcisionrepair | Alzheimerdisease | Necrotosis | Apoptosis | Notchsignalingpathway | Toxoplasmosis | ABC transporters | Fattyaciddegradation | Amyotrophiclateralsclerosis (ALS) | Amphetamineaddiction | Dopaminergicsynapse |
| Calciumsignalingpathway | RNA transport | Baseexcisionrepair | Calciumsignalingpathway | SNARE interactions in vesicular transport | Alzheimerdisease | Ribosome | Neurotrophinsignalingpathway | Biosynthesis of unsaturated fatty acids | Valine, leucine and isoleucine degradation | Calciumsignalingpathway | Reninsecretion | Smallcelllung cancer |

Table 5: Metrics of Diseases part 1

| DISEASES\METRICS | NODES | EDGES | MAX DEGREE | MEAN DEGREE | MAX STRENGTH | MEAN STRENGTH | MAX EIGENVECTOR | MEAN EIGENVECTOR |
|-----------------------------------|-------|-------|------------|-------------|--------------|---------------|-----------------|------------------|
| ALZHEIMER'S DISEASE | 146 | 363 | 35 | 4.972 | 31.687 | 3.611 | 1 | 0.099 |
| AMYOTROPHIC LATERAL SCLEROSIS | 113 | 180 | 10 | 3.185 | 9.111 | 2.203 | 1 | 0.079 |
| ATAXIA TELANGIACTASIA | 20 | 53 | 13 | 5.3 | 8.995 | 3.424 | 1 | 0.424 |
| FRIEDREICH'S ATAXIA | 10 | 10 | 4 | 2 | 2.719 | 1.630 | 1 | 0.4505 |
| FRONTOTEMPORAL DEMENTIA | 38 | 66 | 8 | 3.47 | 7.171 | 2.443 | 1 | 0.184831 |
| HUNTINGTON'S DISEASE | 36 | 66 | 12 | 3.666 | 10.242 | 2.472 | 1 | 0.203 |
| LEWY BODY DISEASE | 15 | 28 | 7 | 3.733 | 5.902 | 2.864 | 1 | 0.424 |
| PARKINSON'S DISEASE | 91 | 394 | 27 | 8.659 | 25.942 | 7.725 | 1 | 0.275 |
| PEROXISOME BIOGENESIS DISORDER 1B | 21 | 46 | 11 | 4.380 | 7.818 | 2.853 | 1 | 0.3787143 |
| PRION DISEASE | 5 | 9 | 4 | 3.6 | 3.992 | 3.592 | 1 | 0.9292 |
| REFSUM DISEASE | 10 | 12 | 5 | 2.4 | 3.297 | 1.684 | 1 | 0.4745 |
| SPINAL CORD INJURY | 9 | 12 | 5 | 2.666 | 3.968 | 2.174 | 1 | 0.5384444 |
| SPINOCEREBELLAR ATAXIA | 6 | 3 | 1 | 1 | 0.953 | 0.927 | 1 | 0.3333333 |
| TOXIC ENCEPHALOPATHY | 16 | 12 | 3 | 1.5 | 2.143 | 1.133 | 1 | 0.2658125 |

Table 6: Metrics of Diseases part 2

| DISEASES\METRICS | MAX WEIGHTED EIGENVECTOR | MEAN WEIGHTED EIGENVECTOR | MAX CLOSENESS | MEAN CLOSENESS | MAX BETWEENNESS | MEAN BETWEENNESS | TRANSITIVITY | CLUSTER COEFFICIENT |
|-------------------------------|--------------------------|---------------------------|---------------|----------------|-----------------|------------------|--------------|---------------------|
| ALZHEIMER'S DISEASE | 1 | 0.099 | 0.000318 | 0.00027 | 2173000 | 205.280 | 0.3579 | 0.3507 |
| AMYOTROPHIC LATERAL SCLEROSIS | 1 | 0.0795 | 0.000313 | 0.00025 | 1400 | 129.380 | 0.5181477 | 0.2260079 |
| ATAXIA TELANGIACTASIA | 1 | 0.4243 | 0.019216 | 0.015927 | 46.5 | 6.2 | 0.4098 | 0.4087 |
| FRIEDREICH'S ATAXIA | 1 | 0.4505 | 0.022701 | 0.018002 | 7 | 1.1 | 0.5625 | 0.3166667 |
| FRONTOTEMPORAL | 1 | 0.184831 | 0.001495 | 0.001172474 | 131 | 13.526 | 0.7386364 | 0.4632832 |

| <i>DEMENTIA</i> | | | | | | | | |
|-----------------------|--|-------------------|-----------------|----------------|--|--|---|--|
| DISEASES\MET RICES | WEIGHT ED CLUSTE R COEFFI CIENT | ASSORTA TIVITY | COMMU NITIES | MODUL ARITY | AVG SHOR TEST PATH LENG TH NETW ORK | AVG SHOR TEST PATH LENG TH ER RAND OM NETW ORK | CLUSTE R COEFFI CIENT ER RANDO M NETWO RK | SMAL L WORL D PROPE RTY |

| | | | | | | | | |
|--|---|-----------|--------------|-----------------|------|---------|-----------|---------------|
| <i>HUNTINGTON'S DISEASE</i> | 1 | 0.2036667 | 0.00400 9 | 0.00330 5167 | 144 | 28.833 | 0.46 | 0.361249 4 |
| <i>LEWY BODY DISEASE</i> | 1 | 0.424 | 0.06456 6 | 0.04739 447 | 48 | 13 | 0.7894737 | 0.426666 7 |
| <i>PARKINSON'S DISEASE</i> | 1 | 0.275 | 0.00133 6 | 0.00114 8769 | 1479 | 106.065 | 0.943473 | 0.440214 8 |
| <i>PEROXISOME BIOGENESIS DISORDER 1B</i> | 1 | 0.3787143 | 0.01719 4 | 0.01408 262 | 15.0 | 9.380 | 0.4854772 | 0.542644 1 |
| <i>PRION DISEASE</i> | 1 | 0.9289824 | 0.25062 7 | 0.23052 28 | 1 | 0.2 | 0.875 | 0.9 |
| <i>REFSUM DISEASE</i> | 1 | 0.4745 | 0.03581 3 | 0.02860 57 | 10 | 2.8 | 0.5 | 0.373333 3 |
| <i>SPINAL CORD INJURY</i> | 1 | 0.5384444 | 0.04303 3 | 0.03464 667 | 5 | 1.333 | 0.6 | 0.481481 5 |
| <i>SPINOCEREBE LLAR ATAXIA</i> | 1 | 0.3333333 | 0.04016 7 | 0.04011 7 | 0 | 0 | 0 | 0 |
| <i>TOXIC ENCEPHALOPA THY</i> | 1 | 0.2658125 | 0.00736 3 | 0.01948 875 | 15 | 2.75 | 0 | 0 |

Table 7: Metrics of Diseases part 3

| | | | | | | | | |
|--|-----------|-------------|----|----------|-------|-------|-----------|--------|
| ALZHEIMER'S DISEASE | 0.3599 | 0.0732 | 15 | 0.61 | 4.632 | 3.218 | 0.0276 | 8.828 |
| AMYOTROPHIC LATERAL SCLEROSIS | 0.2302392 | 0.579202 | 20 | 0.84 | 4.899 | 3.972 | 0.0147 | 12.461 |
| ATAXIA TELANGIACTASIA | 0.4131 | -0.2810043 | 5 | 0.18 | 1.792 | 1.836 | 0.2257 | 1.856 |
| FRIEDREICH'S ATAXIA | 0.3072447 | 0.4736842 | 4 | 0.38 | 1.529 | 1.681 | 0.15 | 2.321 |
| FRONTOTEMPORAL DEMENTIA | 0.4685162 | 0.6611111 | 7 | 0.68 | 3.052 | 2.803 | 0.4632832 | 4.973 |
| HUNTINGTON'S DISEASE | 0.366754 | 0.2767374 | 6 | 0.47 | 3.153 | 2.755 | 0.086 | 3.642 |
| LEWY BODY DISEASE | 0.4274835 | 0.3754209 | 2 | 0.32 | 2.761 | 1.952 | 0.2549206 | 1.183 |
| PARKINSON'S DISEASE | 0.4434868 | 0.9065337 | 9 | 0.33 | 3.718 | 2.307 | 0.08847 | 3.087 |
| PEROXISOME BIOGENESIS DISORDER 1B | 0.5399686 | -0.06901233 | 3 | 0.31 | 2.122 | 2.128 | 0.2890401 | 1.883 |
| PRION DISEASE | 0.8999916 | -0.5 | 1 | -2.8e-17 | 1.1 | 1.1 | 0.9 | 1 |
| REFSUM DISEASE | 0.367791 | 0.2222222 | 3 | 0.32 | 1.965 | 1.714 | 0.2166667 | 1.502 |
| SPINAL CORD INJURY | 0.4881417 | 0.0952381 | 3 | 0.2 | 1.545 | 1.833 | 0.3851852 | 1.482 |
| SPINOCEREBELLAR ATAXIA | 0 | Nan | 3 | 0.67 | 1 | 1.25 | 0 | Nan |
| TOXIC ENCEPHALOPATHY | 0 | -0.173913 | 5 | 0.67 | 2.257 | 2.818 | 0.3851852 | 0 |

Table 8: Common Hubs

| PAIR OF DISEASES | UNIPROT ID | GENE SYMBOL | GENE NAME |
|--------------------------|------------|-------------|---|
| AD, ALS | P04629 | NTRK1 | Neurotrophic tyrosine kinase |
| | P01138 | NGF | Beta-Nerve Growth Factor |
| | P00441 | SOD1 | Superoxide Dismutase 1 |
| | Q13501 | SQSTM1 | Sequestosome 1 |
| AD, FRIEDREICH'S ATAXIA | P0DP24 | CALM2 | Calmodulin 2 |
| | O00555 | CACNA1A | Voltage-dependent P/Q-type calcium channel subunit alpha-1A |
| AD, FD | Q13501 | SQSTM1 | Sequestosome 1 |
| AD, LBD | P37840 | SNCA | Synuclein Alpha |
| AD, PD | P37840 | SNCA | Synuclein Alpha |
| | Q13501 | SQSTM1 | Sequestosome 1 |
| AD - SPINAL CORD INJURY | P0DP23 | CALM1 | Calmodulin 1 |
| | P0DP24 | CALM2 | Calmodulin 2 |
| | P0DP25 | CALM3 | Calmodulin 3 |
| AD, SPINOCEREBELLAR | P0DP24 | CALM2 | Calmodulin 2 |
| AD, TOXIC_ENCEPHALOPATHY | P05067 | APP | Amyloid-beta A4 protein |
| | P37840 | SNCA | Synuclein Alpha |
| ALS, FD | Q9UHD9 | UBQLN2 | Ubiquilin 2 |
| | P46783 | RPS10 | Ribosomal Protein S10 |

| | | | |
|---|--------|-----------|--|
| | Q92890 | UFD1L | Ubiquitin Recognition Factor In ER Associated Degradation 1 |
| | P62249 | RPS16 | Ribosomal Protein S16 |
| | P62847 | RPS24 | Ribosomal Protein S24 |
| | P62979 | RPS27A | Ribosomal Protein S27a |
| | Q3MIH3 | UBA52 | Ubiquitin A-52 Residue Ribosomal Protein Fusion Product 1 |
| | P62861 | FAU | FAU, Ubiquitin Like And Ribosomal Protein S30 Fusion |
| | Q13501 | SQSTM1 | Sequestosome 1 |
| | Q8TAT6 | NPLOC4 | Nuclear protein localization protein 4 homolog |
| | P25398 | RPS12 | Ribosomal Protein S12 |
| | P04156 | PRNP | Prion Protein |
| | P22626 | HNRNPA2B1 | Heterogeneous nuclear ribonucleoproteins A2/B1 |
| ALS, LBD | P46783 | RPS10 | Ribosomal Protein S10 |
| | P62847 | RPS24 | Ribosomal Protein S24 |
| | P62979 | RPS27A | Ribosomal Protein S27a |
| | Q3MIH3 | UBA52 | Ubiquitin A-52 Residue Ribosomal Protein Fusion Product 1 |
| | Q3MIH3 | UBA52 | Ubiquitin A-52 Residue Ribosomal Protein Fusion Product 1 |
| ALS, PD | Q13501 | SQSTM1 | Sequestosome 1 |
| | P10636 | MAPT | Microtubule-associated protein tau |
| ALS, PRION | P39019 | RPS19 | Ribosomal Protein S19 |
| ALS, TOXIC ENCEPHALOPATHY | P99999 | CYCS | Cytochrome C |
| FREIDREICH'S ATAXIA,SPINAL CORD INJURY | P0DP24 | CALM2 | Calmodulin 2 |
| FREIDREICH'S ATAXIA,SPINOCEREBELLAR | P0DP24 | CALM2 | Calmodulin 2 |
| FD, LBD | Q3MIH3 | UBA52 | Ubiquitin A-52 Residue Ribosomal Protein Fusion Product 1 |
| | P62847 | RPS24 | Ribosomal Protein S24 |
| | P46783 | RPS10 | Ribosomal Protein S10 |
| | P25398 | RPS12 | Ribosomal Protein S12 |
| | P62979 | RPS27A | Ribosomal Protein S27a |
| FD, PD | Q13501 | SQSTM1 | Sequestosome 1 |
| HD, PD | P20226 | TBP | TATA-Box Binding Protein |
| HD, SPINOCEREBELLAR | Q12962 | TAF10 | TAF10 RNA polymerase II, TATA-Box Binding Protein Associated Factor 10 |
| HD,TOXIC ENCEPHALOPATHY | Q05586 | GRIN1 | Glutamate Ionotropic Receptor NMDA Type Subunit 1 |
| LBD, PD | P37840 | SNCA | Synuclein Alpha |
| LBD, TOXIC ENCEPHALOPATHY | P37840 | SNCA | Synuclein Alpha |
| PD, TOXIC ENCEPHALOPATHY | P37840 | SNCA | Synuclein Alpha |
| PBD1B-REFSUM | O00628 | PEX7 | peroxisomal biogenesis factor 7 |
| | P50542 | PEX5 | peroxisomal biogenesis factor 7 |
| SPINAL CORD INJURY-SPINOCEREBELLAR | P0DP24 | CALM2 | Calmodulin 2 |
| SPINAL CORD INJURY-TOXIC ENCEPHALOPATHY | P42574 | CASP3 | Caspase 3 |

Table 9: Common bridges

| PAIR OF DISEASES | UNIPROT ID | GENE SYMBOL | GENE NAME |
|------------------|------------|-------------|---------------------------------|
| AD,ALS | Q13501 | SQSTM1 | Sequestosome 1 |
| PBD1B-REFSUM | O00628 | PEX7 | peroxisomal biogenesis factor 7 |

Table 10: Common Articulation Points

| PAIR OF DISEASES | UNIPROT ID | GENE SYMBOL | GENE NAME |
|--------------------------|------------|-------------|--|
| AD,ALS | P29475 | NOS1 | Nitric oxide synthase 1 |
| | P05067 | APP | Amyloid-beta A4 protein |
| | Q16620 | NTRK2 | Neurotrophic tyrosine kinase |
| | Q13501 | SQSTM1 | Sequestosome 1 |
| AD, FD | Q00535 | CDK5 | Cyclin Dependent Kinase 5 |
| | Q13526 | PIN1 | Peptidylprolyl Cis/Trans Isomerase, NIMA-Interacting 1 |
| | P37840 | SNCA | Synuclein Alpha |
| | P05067 | APP | Amyloid-beta A4 protein |
| AD, HD | P00441 | SOD1 | Superoxide Dismutase 1 |
| | Q13501 | SQSTM1 | Sequestosome 1 |
| | P00441 | SOD1 | Superoxide Dismutase 1 |
| | Q13501 | SQSTM1 | Sequestosome 1 |
| AD, LBD | P05067 | APP | Amyloid-beta A4 protein |
| | P37840 | SNCA | Synuclein Alpha |
| AD, PD | P37840 | SNCA | Synuclein Alpha |
| | P29475 | NOS1 | Nitric Oxide Synthase, brain |
| | P00441 | SOD1 | Superoxide Dismutase 1 |
| | Q16620 | NTRK2 | Neurotrophic tyrosine kinase |
| AD, SPINAL CORD INJURY | Q13501 | SQSTM1 | Sequestosome 1 |
| | P29475 | NOS1 | Nitric Oxide Synthase, brain |
| AD, TOXIC_ENCEPHALOPATHY | P05067 | APP | Amyloid-beta A4 protein |
| | P37840 | SNCA | Synuclein Alpha |
| | P99999 | CYCS | Cytochrome C |
| ALS, FD | Q13501 | SQSTM1 | Sequestosome 1 |
| | P05067 | APP | Amyloid-beta A4 protein |
| ALS, HD | Q13501 | SQSTM1 | Sequestosome 1 |
| ALS, LBD | P05067 | APP | Amyloid-beta A4 protein |
| ALS, PD | Q13501 | SQSTM1 | Sequestosome 1 |
| | Q16620 | NTRK2 | Neurotrophic tyrosine kinase |
| | P29475 | NOS1 | Nitric Oxide Synthase, brain |

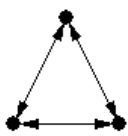
| | | | |
|---------------------------|--------|--------|---------------------------------|
| | P11142 | HSPA8 | Heat shock 70kDa protein 8 |
| ALS, SPINAL CORD INJURY | P29475 | NOS1 | Nitric Oxide Synthase, brain |
| ALS, TOXIC ENCEPHALOPATHY | P99999 | CYCS | Cytochrome C |
| | P98170 | XIAP | X-Linked Inhibitor Of Apoptosis |
| | P42574 | CASP3 | Caspase 3 |
| FD, HD | P00441 | SOD1 | Superoxide Dismutase 1 |
| | Q13501 | SQSTM1 | Sequestosome 1 |
| FD, PD | P00441 | SOD1 | Superoxide Dismutase 1 |
| | Q13501 | SQSTM1 | Sequestosome 1 |
| | P37840 | SNCA | Synuclein Alpha |
| | Q5S007 | LRRK2 | Leucine Rich Repeat Kinase 2 |
| FD, TOXIC ENCEPHALOPATHY | P05067 | APP | Amyloid-beta A4 protein |
| | P37840 | SNCA | Synuclein Alpha |
| HD, PD | P00441 | SOD1 | Superoxide Dismutase 1 |
| | Q13501 | SQSTM1 | Sequestosome 1 |
| LBD, PD | P37840 | SNCA | Synuclein Alpha |
| LBD, TOXIC ENCEPHALOPATHY | P37840 | SNCA | Synuclein Alpha |
| | P05067 | APP | Amyloid-beta A4 protein |
| PD, SPINAL CORD INJURY | P29475 | NOS1 | Nitric Oxide Synthase, brain |
| PD, TOXIC ENCEPHALOPATHY | P37840 | SNCA | Synuclein Alpha |

Table 11: Common genes that are hubs and articulation points or bridges simultaneously

| PAIR OF DISEASES | UNIPROT ID | GENE SYMBOL | GENE NAME | COMMENTS |
|------------------|------------|-------------|-----------|----------|
|------------------|------------|-------------|-----------|----------|

| | | | | |
|---------------------------|--------|--------|---------------------------------|--------------------------|
| AD,ALS | Q13501 | SQSTM1 | Sequestosome 1 | hub,bridge, articulation |
| AD, FD | Q13501 | SQSTM1 | Sequestosome 1 | hub, articulation |
| AD, LBD | P37840 | SNCA | Synuclein Alpha | hub, articulation |
| AD, PD | P37840 | SNCA | Synuclein Alpha | hub, articulation |
| | Q13501 | SQSTM1 | Sequestosome 1 | hub, articulation |
| AD, TOXIC_ENCEPHALOPATHY | P05067 | APP | Amyloid-beta A4 protein | hub, articulation |
| | P37840 | SNCA | Synuclein Alpha | hub, articulation |
| ALS, FD | Q13501 | SQSTM1 | Sequestosome 1 | hub, articulation |
| ALS, PD | Q13501 | SQSTM1 | Sequestosome 1 | hub, articulation |
| ALS, TOXIC ENCEPHALOPATHY | P99999 | CYCS | Cytochrome C | hub, articulation |
| FD, PD | Q13501 | SQSTM1 | Sequestosome 1 | hub, articulation |
| LBD, PD | P37840 | SNCA | Synuclein Alpha | hub, articulation |
| LBD, TOXIC ENCEPHALOPATHY | P37840 | SNCA | Synuclein Alpha | hub, articulation |
| PD, TOXIC ENCEPHALOPATHY | P37840 | SNCA | Synuclein Alpha | hub, articulation |
| PBD1B-REFSUM | O00628 | PEX7 | peroxisomal biogenesis factor 7 | hub, bridge |

Table 12: 3 node network motifs - experiments

| Characteristics /Diseases | ID | Adj | Frequency [Original] | Mean-Freq [Random] | Standard-Dev [Random] | Z-score | p- Value |
|---------------------------|-----|---|-------------------------|-----------------------|--------------------------|---------|----------|
| AD | 238 |  | 15.669% | 0.57931% | 0.0020854 | 72.358 | 0 |

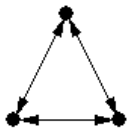
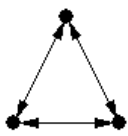
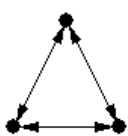

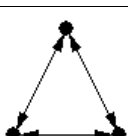
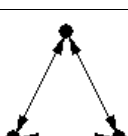
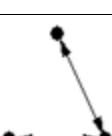
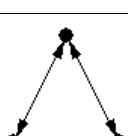
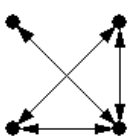
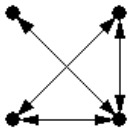
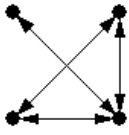
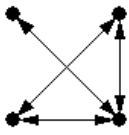
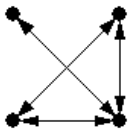
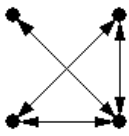
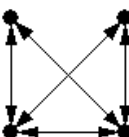
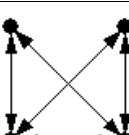
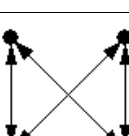
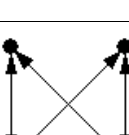
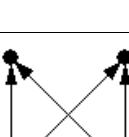
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|---------------------------------------|-----|---|---------|-----------|------------|-----------|---|
| ALS | 238 |  | 26.386% | 0.600093% | 0.00099348 | 264.99 | 0 |
| FD | 238 |  | 48.507% | 1.0288% | 0.0057228 | 82.964 | 0 |
| HD | 238 |  | 22.115% | 0.37726% | 0.0033201 | 65.475 | 0 |
| LBD | 238 |  | 55.556% | 15.285% | 0.021516 | 18.716 | 0 |
| PD | 238 |  | 94.356% | 88.249% | 0.00086776 | 70.373 | 0 |
| Spinal cord injury | 238 |  | 33.333% | 12.5% | 0 | Undefined | 0 |
| Toxic Encephalopathy | 78 |  | 100% | 100% | 0 | Undefined | 0 |
| Peroxisome biogenesis disorder | 238 |  | 23.926% | 4.3532% | 0.0055487 | 35.275 | 0 |

Table 13: 4 node network motifs – experiments

| Characteristics /Diseases | ID | Adj | Frequency [Original] | Mean-Freq [Random] | Standard-Dev [Random] | Z-score | p- Value |
|---------------------------|------|---|-------------------------|-----------------------|--------------------------|---------|----------|
| AD | 4958 |  | 18.855% | 1.7625% | 0.0061489 | 27.798 | 0 |

| | | | | | | | |
|---------------------------------------|-------|---|---------|------------|------------|--------|-------|
| ALS | 4958 |  | 22.166% | 0.14295% | 0.0026185 | 84.106 | 0 |
| Ataxia-telangiectasia | 4958 |  | 25.846% | 18.758% | 0.0063396 | 11.181 | 0.002 |
| FD | 4958 |  | 25.103% | 2.6258% | 0.013031 | 17.25 | 0 |
| HD | 4958 |  | 31.287% | 0.088046% | 0.0075141 | 40.465 | 0 |
| Peroxisome biogenesis disorder | 4958 |  | 30.072% | 5.4878% | 0.011132 | 22.084 | 0 |
| AD | 13278 |  | 5.8847% | 0.15461% | 0.001092 | 52.472 | 0 |
| ALS | 13278 |  | 8.9787% | 0.0028797% | 0.00011526 | 778.74 | 0 |
| Ataxia-telangiectasia | 13278 |  | 13.641% | 6.8306% | 0.0017722 | 38.428 | 0 |
| FD | 13278 |  | 14.403% | 0.15165% | 0.0017892 | 79.654 | 0 |
| HD | 13278 |  | 10.673% | 0.025022% | 0.00059427 | 179.17 | 0 |

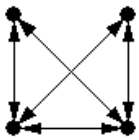


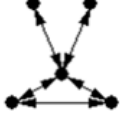
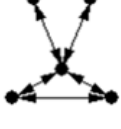


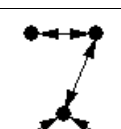
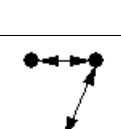
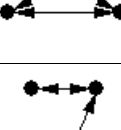
| | | | | | | | |
|---------------------------------------|-------|---|---------|----------|-----------|--------|---|
| LBD | 13278 |  | 12.821% | 8.5144% | 0.016245 | 2.6507 | 0 |
| Peroxisome biogenesis disorder | 13278 |  | 11.957% | 0.41345% | 0.0031345 | 36.826 | 0 |

Table 14: 5 node network motifs - experiments

| Characteristics /Diseases | ID | Adj | Frequency [Original] | Mean-Freq [Random] | Standard-Dev [Random] | Z-score | p- Value |
|--------------------------------|---------|---|-------------------------|-----------------------|--------------------------|---------|----------|
| AD | 1084606 |  | 15.507% | 1.2451% | 0.0035057 | 40.682 | 0 |
| ALS | 1084606 |  | 2.7552% | 0.059241% | 0.0010796 | 24.973 | 0 |
| HD | 1084606 |  | 10.46% | 0.51646% | 0.0048208 | 20.627 | 0 |
| Peroxisome biogenesis disorder | 1084606 |  | 8.7307% | 4.2351% | 0.0055944 | 8.0358 | 0 |
| AD | 1082430 |  | 23.723% | 22.141% | 0.0053065 | 2.9812 | 0.009 |
| LBD | 1082430 |  | 4.717% | 2.5487% | 0.0074041 | 2.9285 | 0.001 |
| AD | 8948910 |  | 4.4262% | 0.49889% | 0.0015215 | 25.812 | 0 |
| ALS | 8948910 |  | 13.868% | 0.087719% | 0.0014661 | 93.992 | 0 |
| FD | 8948910 |  | 20.39% | 1.1426% | 0.0052964 | 36.342 | 0 |

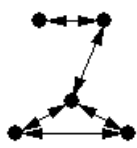
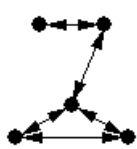

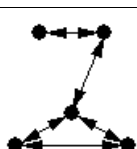

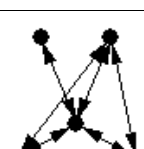
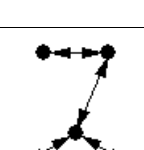
| | | | | | | | |
|---------------------------------------|---------|---|----------|------------|------------|--------|-------|
| HD | 8948910 |  | 8.6086% | 0.41093% | 0.0030057 | 27.274 | 0 |
| LBD | 8948910 |  | 13.208% | 5.3531% | 0.014872 | 5.2814 | 0 |
| PD | 8948910 |  | 0.30076% | 0.0201863% | 0.00033042 | 8.4405 | 0.001 |
| Peroxisome biogenesis disorder | 8948910 |  | 12.074% | 0.80886% | 0.0041524 | 27.13 | 0 |

Table 15: 5 node network motifs– LBD

| Characteristics /Diseases | ID | Adj | Frequency [Original] | Mean-Freq [Random] | Standard-Dev [Random] | Z-score | p- Value |
|---------------------------|---------|---|-------------------------|-----------------------|--------------------------|---------|----------|
| LBD | 7598014 |  | 9.434% | 0.35984% | 0.0023799 | 38.129 | 0 |
| LBD | 1289662 |  | 15.094% | 1.4764% | 0.0055939 | 24.344 | 0 |
| LBD | 8948910 |  | 13.208% | 5.3531% | 0.014872 | 5.2814 | 0 |


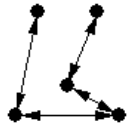





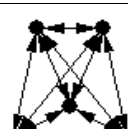
| | | | | | | | |
|------------|----------|---|---------|---------|-----------|-----------|-------|
| LBD | 1082430 |  | 4.717% | 2.5487% | 0.0074041 | 2.9285 | 0.001 |
| LBD | 2133644 |  | 25.472% | 16.754% | 0.030254 | 2.8814 | 0 |
| LBD | 16510910 |  | 10.377% | 0% | 0 | Undefined | 0 |

Table16: 5 node network motifs

| Characteristics /Diseases | ID | Adj | Frequency | Mean-Freq | Standard-Dev | Z-score | p- Value |
|---------------------------------------|----------|---|------------|-----------|--------------|-----------|----------|
| | | | [Original] | [Random] | [Random] | | |
| HD | 1150398 |  | 9.5596% | 0.042987% | 0.0011152 | 85.335 | 0 |
| HD | 2133678 |  | 8.1582% | 0.56604% | 0.0091283 | 8.4122 | 0 |
| Peroxisome biogenesis disorder | 2133644 |  | 13.437% | 5.7576% | 0.0015215 | 25.812 | 0 |
| Peroxisome biogenesis disorder | 1150398 |  | 9.5975% | 0.7698% | 0.0053311 | 16.559 | 0 |
| FD | 16510910 |  | 7.8091% | 0% | 0 | Undefined | 0 |









| | | | | | | | |
|------------------------------|----------|---|---------|---------|------------|-----------|-------|
| FD | 1289662 |  | 13.449% | 0% | 0 | Undefined | 0 |
| Ataxia-telangiectasia | 1150398 |  | 9.7058% | 7.11% | 0.0063702 | 4.0749 | 0.002 |
| ALS | 1289662 |  | 6.6585% | 0% | 0 | Undefined | 0 |
| PD | 16510910 |  | 82.223% | 65.416% | 0.00073545 | 228.52 | 0 |

Table 17: 6 node network motifs - experiments

| Characteristics /Diseases | ID | Adj | Frequency | Mean-Freq | Standard-Dev | Z-score | p- Value |
|---------------------------|------------|---|------------|-----------|--------------|---------|----------|
| | | | [Original] | [Random] | [Random] | | |
| FD | 2199165980 |  | 17.05% | 0.52725% | 0.0028013 | 58.983 | 0 |
| HD | 2199165980 |  | 4.3023% | 0.13759% | 0.001358 | 30.669 | 0 |
| LBD | 2199165980 |  | 32.558% | 0.20021% | 0.0029245 | 110.64 | 0 |
| Peroxisome | 2199165980 |  | 2.9921% | 0.010945% | 0.00023051 | 129.33 | 0 |

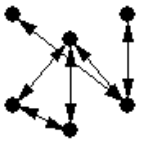

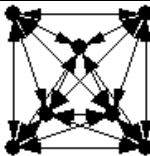
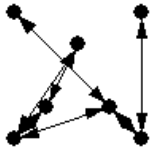

| | | | | | | | |
|-----------|-----------------|---|---------|-----------|-------------|-------|---|
| FD | 2182388 814 |  | 9.1004% | 0.30933% | 0.0017443 | 50.4 | 0 |
| PD | 3408918 9246 |  | 46.638% | 0.053176% | 3.5563e-005 | 13099 | 0 |

Table 18: 7 node network motifs – experiments

| Characteristics /Diseases | ID | Adj | Frequency | Mean-Freq | Standard-Dev | Z-score | p- Value |
|------------------------------|-------------------------|---|------------|------------|--------------|---------|----------|
| | | | [Original] | [Random] | [Random] | | |
| PD | 2803711 5327257 4 |  | 27.784% | 0.0042747% | 4.025e-006 | 69019 | 0 |
| FD | 4538208 111814 |  | 12.487% | 0.20892% | 0.0012093 | 101.53 | 0 |
| LBD | 4433224 306288 |  | 28.475% | 0.50436% | 0.0010393 | 273.49 | 0 |

