**Supplementary file S1:** The file contains all supplementary figures and supplementary table S1, S2, S3, S, S10, and S13.

**Data file S1**: Raw phenotypic measurements of DGRP lines exposed to sucrose (treatment = 0), and to methylphenidate (treatment = 1). The table contains experimental information on the different days a particular measurement was obtained (day), plate identification number (plate\_id), information on if a particular fly had neighboring circular arena on all sides or not (coded as 1 or 2 for no and yes, respectively), and finally which individual circular arena the fly was located within (arena\_id). The raw phenotype is within the column distance (unit is in cm). The final column contains the average amount of solution ingested within each capillary tube (unit is uL/fly).

**Data file S2**: Phenotypic measurements of wild type flies exposed to sucrose (treatment = 0), and to methylphenidate (treatment = 1). The table contains information on which generation the measurements are obtained from (generation); the treated parental flies (p) or the unexposed F1 individuals (F1), indicators on day and plate id (run\_id and plate\_id), and finally the obtained phenotype (distance\_cm).

**Data file S3**: Phenotypic measurements of gene expression knockdown lines exposed to sucrose (treatment = 0), and to methylphenidate (treatment = 1). The table contains information which id/gene (or control line) the phenotype is obtained from (line id and gene id) and an identifier of activity plate (plate id), and finally the obtained phenotype (distance\_cm).

**Table S5**: Gene expression analysis of assayed probes of wild type males. Contains information on FlyBase ID (and gene symbol) of the corresponding gene probes, the logarithm of fold change in gene expression between control and MPH treatment (*logFC*), the average expression across replicates and treatments (*AveExp*), the test statistic for being differentially expressed (*t statistic*) with corresponding unadjusted (*P\_value*) and Benjamini-Hochberg adjusted P values (*adjusted\_P\_value*), the log-odds that the gene is differentially expressed (*B\_statistic*), and the probability that the gene is differentially expressed (Pr\_diffExp), which is computed as exp(B)/(1+exp(B)).

**Table S6**: KEGG pathway enrichment analysis of differentially expressed transcripts from WT males and WT F1 males from the wild type mass population. The *summary statistic* is the within KEGG pathway sum of the absolute t-values of all the genes within that particular KEGG pathway (*No\_Genes*) with corresponding unadusted (*P\_value*) and FDR P adjusted values (*Adjusted\_P\_value*).

**Table S7:** Raw and adjusted line mean, standard error (SE) and number of replicates (*n*) for DGRP lines treated with sucrose (suc) and methylphenidate (mph). The response to treatment was computed as the difference in adjusted phenotype between sucrose and MPH treatment.

**Table S8**: Complete table containing prediction results based on gene networks. Each gene network is created using the STRING database of known protein-protein interactions, and each network has one bait gene (*FlyBase\_protein\_ID & protein\_symbol*), i.e., the gene that all other genes within that particular network interact directly with. The table contains the mean predictive ability (*PA*), standard error of the mean (*SE*), unadjusted (*P*) and false-discovery adjusted P values (FDR *P* value) for increased predictive performance compared to the NULL model weighting all SNP markers equally, the proportion of variance explained (*PoEV*), the number of proteins the network contains (*nProteins*) and the number of segregating SNPs within the network in the DGRP (*nSNPs*). In the columm "*FlyBase protein symbol*" the "-" indicate unknown conversions of protein ID to symbol by FlyBase.org.

**Table S9**: Ranking of the genes within the complete predictive gene network based upon the CVAT summary statistic. The P values indicates if that particular gene capture significantly more of the total variance than a random, equally sized, set of SNPs.

**Table S11**: Gene expression analysis of assayed probes of wild type F1 flies. Contains information on FlyBase ID of the corresponding gene probes, the logarithm of fold change in gene expression between control and MPH treatment (*logFC*), the average expression across replicates and treatments (*AveExp*), the test statistic for being differentially expressed (*t\_statistic*) with corresponding unadjusted (*P value*) and Benjamini-Hochberg adjusted P values (*adjusted\_P\_value*), the log-odds that the gene is differentially expressed (*B\_statistic*), and the probability that the gene is differentially expressed (Pr\_diffExp), which is computed as exp(B)/(1+exp(B)).

**Table S12**: Gene network enrichment analysis of differentially expressed transcripts from WT males and WT F1 males. The bait protein is the gene that particular network is based upon, i.e. that all other genes interact with that particular gene. The summary *statistic* is the within PPI network sum of the absolute t-values of all the genes within that particular PPI network (*No. Genes*) with corresponding unadusted (*P\_value*) and FDR P adjusted values (*adjusted\_P\_value*).