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Title: Hippocampal expression profiling of rats bred for high and low activity in the forced swim test

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Using selective breeding, we have generated two rat lines that exhibit either active (i.e. struggling, referred to as SwHi) or passive responses (i.e. floating, SwLo) upon their initial exposure to a forced swim test. Chronic, but not acute administration of a number of antidepressant drugs including imipramine, desipramine, venlafaxine, phenelzine and buproprion increased swim-test activity, particularly struggling behavior, in SwLo animals, while having little effect on swim-test behavior in SwHi rats.
To further characterize these two divergent Sprague Dawley rat lines, which are now in their 35th+ generation, we used Affymetrix microarrays to identify genes differentially expressed in the hippocampus of SwHi and SwLo rats. Hippocampal tissue was prepared for microarray analysis according to the manufacturer's recommended protocol. From the 4500+ genes screened, we generated PCR primer sets against 11 of the genes that showed the most robust and consistent changes via the microarray. In addition, we generated primers to the CRF1, CRF2 and the glucocorticoid receptor, as well as the urocortin and CRF genes. Hippocampal cDNA samples from each of the 8 animals included in the initial gene chip, as well as 9 additional animals from the same breeding generation, were then individually analyzed via reverse transcriptase-PCR. Of the 11 transcripts successfully amplified via RT-PCR, 8 revealed differential expression patterns consistent with the initial high throughput microarray analysis.
We subsequently obtained hippocampal cDNA from a second independent group of SwHi (n=6) and SwLo (n=6) from a different breeding generation from those initially analyzed. We further evaluated 6 of the primers that had shown consistent changes in the previous generation. Of those 6 genes, we were able to detect significant and consistent differences in gene expression between SwHi and SwLo rats for 4 of the genes.
A total of four genes remained significant at a $p<0.05$ throughout all three analyses (i.e. gene chip, RT-PCR in the first set of animals, and via RT-PCR in a second independent group of animals) which included BDNF, Apolipoprotein CI and the ESTs AA891054 and AA893172. Additional testing addressing the functional role, if any, of these transcripts in the behavioral and pharmacological phenotypes of these animals is ongoing.

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