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Genes associated with basolateral amygdala morphology are involved in neuronal development.

Although not terribly romantic, the amygdala is much more important than the heart to emotion. Morphology of the amygdala is altered in people with diseases that affect emotions, including schizophrenia, autism, depression and William syndrome. Now Mozhui *et al*. report the association of genes involved in neuronal development with the size and cellular composition of the basolateral amygdala in a recent article in *Behavior Genetics*.

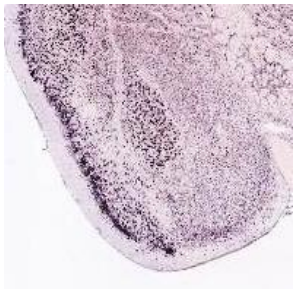

Image from the Allen Brain Atlas shows *Large* expression in the basolateral amygdala complex.

Together, the DNA sequences of C57BL/6J and DBA/2J inbred mouse strains contain nearly two million single nucleotide polymorphisms. Researchers bred these two mouse strains and inbred their progeny to generate nearly 100 independent BXD (Bl6 X Dba) mouse strains. GeneNetwork contains phenotype and genetic sequence information for many of the BXD strains.

The authors measured the volume and cellular composition of the basolateral amygdala complex (BLAc), which contains both lateral and basolateral nuclei, in 35 BXD strains as well as parental C57BL/6J and DBA/2J mouse strains. BLAc volume and the number and density of BLAc neurons did not differ between parental strains, but spread over a two-fold range in BXD strains. Non-neural cells showed more variation than did neurons. Among BXD strains, the number of glia and endothelial cells varied over eight- and five-fold ranges, respectively.

Quantitative trait loci (QTL) analysis identified a region on chromosome 8 that linked to BLAc volume. This QTL, which the authors named *Vol8a*, localized roughly 10 Mb from *Cbs8a*, which associates with cerebellar size. The authors also found a suggestive link between glial cell density and a region on chromosome 11.

Vol8a may regulate the size of several brain regions. BLAc volume correlated with hippocampal volumes reported in GeneNetwork. QTL analysis of GeneNetwork phenotypes showed that *Vol8a* associated with cerebellar and hippocampal volume as well as behavior in an open field.

Candidate genes within *Vol8a* compose or modify the extracellular matrix. The Allen Brain Atlas showed expression in the BLAc of *Vol8a* genes like-glycosyltransferase (*Large*), which glycosylates proteins in the extracellular matrix, and chondroitan sulfate proteoglycan 3 (*Cspg3* or *neuroglycan*) and *Spock3*, which are extracellular matrix proteoglycans.

Several candidate genes important in neural development

localized to the QTL on chromosome 11. Neurogenic differentiation 2 (*NeuroD2*) is important in the differentiation of neurons and glia. Expression of *NeuroD2* correlated with BLAc volume and the density of neurons and glia in the BLAc. Similarly, *NeuroD2* knockout mice have smaller BLAc and show increased aggressive and decreased anxiety behaviors relative to wild-type mice. The Allen Brain Atlas showed high levels of thyroid horomone alpha (*Thra*) expression in BLAc. *Thra* mutant mice have deficits in anxiety, memory and locomotion, consistent with damage to the amygdala.

Together, these data suggest that genes associated with BLAc morphology control the development of multiple brain structures, and that diseases with adult onset that alter the morphology of the amygdala, such as schizophrenia and depression, may be developmental in nature.

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1. Mozhui, K. , Hamre, K. M. , Holmes, A. , Lu, L. and Williams, R. W. Genetic and structural analysis of the basolateral amygdala complex in BXD recombinant inbred mice. *Behavior Genetics* **37**, 223–243 (2007). | Article |