GENES AND BEHAVIOR

When we think of behavior, we generally tend to think of some complex human traits such as criminality, extovertedness, and similar traits that are likely to be affected by many genes interacting with the environment. Lets look at some simple examples in several organisms where it is possible to show that behavioral differences can be simply inherited, including some cases in man.

Several traits that we are all familiar with seem to be controlled by a single gene, at least in some studies.

Natural trotting gait versus pacing in horses is said to be simply inherited, with trotting (left front and right rear legs go forward together) versus pacing where both legs on the same side advance together) being dominant. Though this is no proof at all of dominance, trotters are much more prevalent than pacers.

Pointing versus setting in bird dogs is also reported to show simple inheritance, and I think pointing is supposed to be dominant.

The simple act of hand clasping in humans may also have a genetic factor. Clasp your hands, and note whether your left or right thumb is on top. Now try it the other way, and you will see how "unnatural" it feels. Again there are reports that this behavior is determined by a single gene, but I have not seen the kinds of pedigrees that would confirm it.

The same goes for tongue rolling versus 'squashing' Some can roll the tongue and other people simply cannot. I don't know which is dominant if it is a single gene trait.

One place that progress is being made on genetic analysis of behavior is in work with *Drosophila*. These flies have courtship rituals that are similar to what we see in birds, ie displays, of ducking turning etc. where the action of one sex leads to an "appropriate response in the other. When a mutant is detected, say a male doesn't turn around three times after the female brushes him with her antennae, she will not allow him to mate. In natural populations this would be a dead end, but in the lab where no other males are around, he may eventually be accepted, and the inheritance of the trait can be analyzed. Many individual steps in the courtship ritual have been shown to be regulated by single genes.

A lot of folks have thought of neat tricks to identify unusual behavior patterns, capture the fly, and make crosses.

Examples include mazes where a series of decisions must be made. For example, deciding to go toward or away from light, or, up versus down (gravitropism). In these cases crosses between the flies that always choose the up by up tend to give up progeny etc. and up X down crosses give a normal distribution indicating that many genes are involved, ie it is a quantitative trait. However a neat trick can be done with flies; chimeric flies can be made where, for example, 1/2 the body is yellow/up and the other half is gray/down. I saw a short movie of one of these flies and it was walking around the bottle halfway up the side, with the up side up and the down side down. It seemed to have an impossible decision, but showed that the two halves of the brain were independent as far as the go up or go down decision was concerned. It must have decided to eat somewhere and somehow!

Others have noticed that normal flies always land on the bottom of a glass-bottomed cage facing the figures that are coming up on a revolving drum below the cage. Abnormal flies that land other ways can be sucked up with a piece of tubing (put in a piece of cotton) and used in crosses. Seymour Benzer has isolated hundreds of mutants this way and most of them turn out to be blind. Instead of being disappointed, Benzer has used these flies to show the function of many of the genes that are involved in eye formation, optic nerve development, etc.

Other flies have been identified that have temperature sensitive behavior traits. One of these isolated by David Suzuki (TV"star") is called TKO, since as the temperature raises, the flies become totally immobile, and then if it is lowered soon enough, away they go. These flies have a missense mutation that prevents restoration of the nerve synapse when the needed protein is inactivated at a high temperature.

A really classic case of a simply inherited behavior is referred to as "**hygenic bees**" Bees that are uu,rr, will uncap cells in the comb that contain an infected larva and remove it. Those that are uuR_ will uncap only, while U_, rr will remove the larva only if someone else uncaps it. If all the bees are U_R_, the infection will spread though the hive, and often kill it out. Thus we see in this case that only double homozygous bees have both characters needed to preserve the hive.

A mouse has been produced that completely looses the normal "maternal instinct" when homozygous for knockout versions of the *fosB*- gene, a gene that was being tested for abnormal development or cancer. At first when all the babies died the researchers assumed the defect led to an early lethal effect, but it turned out the mothers never bothered to nurse the pups.

Lets look at some single gene traits in humans that affect behavior.

One of these is **PKU**, the disease we talked about that can be treated by a special diet and leads to very low IQ unless it is treated. Untreated younger patients

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show a kind of "hypertonic" behavior, where they seem to give a startle response at the slightest incident. As they age however, they tend to develop repetitive movement patterns. In many instance they assume a "tailors" position, where they seem to be hunched over and sewing all day long,

Another example of a well known single gene defect that affects behavior in humans is **Lesch Nyhan Syndrome.** This is a sex linked gene and is a genetic lethal, so it is seen only in boys.

Affected boys excrete large amounts of uric acid in their urine, which provided the clue as to what pathway and enzyme might be defective. Drs. Lesch and Nyhan at Johns Hopkins in 1964 identified the missing enzyme as HGPRTase. This is an enzyme that lets all of us recycle purines. That is, when mRNA is degraded, or DNA is digested from our food we can reuse many of the bases (by converting them back to nucleotides) instead of making them from scratch. When the enzyme is totally defective, the excess purines are broken down to uric acid which can crystallize in joints and organs, (Partial inactivity is the basis for gout). The affected child starts out normal, but progressively becomes more and more spastic, has cerebral palsy, seems mentally retarded, and can't walk alone.

But the reason we are discussing it is a bizarre from of behavior that it causes. These boys have a real tendency to mutilate themselves, Even though they know it will painful, they will chew away their fingers, lips or anything else they can reach. If they have a chance, they may bash their head against a doorframe (or someone elses head!). The episodes seem to be linked to anxiety, so the disease has been compared to finger-nail biting with the volume turned on high. Tom Caskey at Baylor Med told me one of his patients would bash his head against any sharp object he could reach. Eventually the accumulation of uric acid causes kidney failure, vomiting, and eventually death. Allopurinol, which is used for gout can alleviate the kidney problem, but not the self mutilation. It will increase the life expectancy from 5 years to 20 years.

For a different perspective than you may have obtained from this clinical description, details from a case history showed that the compulsion of the little boy under study to mutilate himself "turned on" when his mother was ill and he was worried about her.

See: http://www3.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?300322

Recently, alarge Dutch amily pedigree where14 males in 3 generations had committed violent acts, often involving arson and almost always after some acute family stress was examined. It was shown that the individuals involved shared a specific nonsense allele of monoamine oxidase A that is less than normal in activity. Since the normal function is to help break down neurotransmitters such as serotonin that are involved in fight versus flight responses, and the gene is on the X chromosome, it was hypothesized that the defective allele had a role in the males behavior.

See: http://www3.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?309850

Twin and other studies implicate a genetic role in autism, schizophrenia, Tourettes syndrome (tics and sometimes coprolalia), dyslexia, attention deficit hyperactivity disorder etc. but often the diagnosis can be difficult. There may be