Fly dreams and the boundaries of evolutionary science

January 2 2014, by John Hewitt

Jean-Baptiste Lamarck
Credit: Wikipedia

In 2002, Secretary of state Donald Rumsfeld made a statement regarding weapons of mass destruction that today is still well known. He famously parsed the evidence (or lack thereof) into "known knowns, known unknowns, and unknown unknowns." In squeezing virtually all that it can from the ideas of Darwin, evolutionary biology has produced a mountain of facts and ideas that fall squarely in the realm of Rumsfeld's first two categories.

However those mechanisms that first generated life, and by implication continue to refashion it as fast as we try to comprehend, are still unknowns of a nature we have scarcely imagined. Strict adherence to the concepts of random genetic mutation followed by *natural* selection thrusts up a steep barrier to a full understanding of variation in the natural world. In order to push beyond this cusp, scientists have now turned to the ideas of Lamarck. The latest installment in the genetic saga of individual experience has just been published on the *arxiv* preprint server by Harvard neurosurgeon Ziv Williams.

Ziv's new results were obtained with flies, and they shadow the recent provocative data on murine (mouse) inheritance of ancestral fears. The latter study raised the roof on what is now possible in a scientific experiment. In demonstrating not only a mechanism for sperm-specific transmission of acquired traits from the father, but also precision modification of neural circuitry, that report set the bar extremely high for what might be proved in a study—and also for what might be swallowed by the larger community.

With mice, it is possible to isolate the mechanism of transmission of a particular experience to the father's sperm by doing in vitro insemination. While that is not so simple in flies, there is one big advantage to working with them—experiments can be more easily done at high n factor (number of flies). This is critical for discerning complex, but often weak, effects. The principle that information of a hereditary nature ratchets only in the direction from germ cells to somatic (body) cells is known as Weismann's barrier. It is expected that any breakdown of this evolutionary diode (such as feedback from somatic to germ cells) would be a weak effect because the bandwidth for transmission of experience to germ cells would, at first glance, appear to be severely limited.

It should be pointed out that many genetic therapies now on the table are based on treatment of somatic cells. If heritable changes to the genome can be introduced via predictable breaches in Weismann's barrier, as many now presume exist, that is something we probably want to know more about. We need look no further than plants to see that genetic changes in germ lines can be produced as a result of genetic changes in somatic lines. Here somatic cell lineages (vegetative meristems) may be old enough to have accumulated many mutations subject to natural selection since seed germination.

Neurobiologists are more interested in those heritable skills or experiences that can be packaged quickly into the germ line, almost perhaps, instantaneously. In many species, sperm are produced at a tremendous rate and practically speaking, they turn over daily. For his fly experiments, Ziv paired different odors with either an aversive or an appetitive stimulus, and trained them over the course of a few days to make the proper associations.

The aversive stimulus was an electrified copper grid which presumably was distasteful enough to be seen as a non-lethal assault, but not so powerful as to prevent any formative interactions. Electrical shock may not be the cleanest stimulus (after all we know from the experiments of Miller and Urey that electricity of sufficient voltage can spawn amino-acids from gases), it seems to have what it takes to make a good impression. The appetitive stimulus in this case was of an appetitive nature—corn meal and sugar. While the opposite of shock may not be a sugar snack, the pair do provide a clear choice between good and evil.

If precise mechanisms of inheritance are to be attributed to specific details of a stimulus, then the particulars of the odors themselves (3-octanol (OCT) or 4-Methylcyclohexanol (MCH)) are important in these studies. Other experiments, like those in mice, used acetophenone because a fair bit is already known about the receptors and circuitry involved in detecting it. Using a T-maze setup, Ziv was able to show that after the parents had mastered associations of odors with good and evil, the offspring of those flies later showed heightened sensitivity to them as well. However, for whatever reason, the effect was only strong with the MCH stimulus, and in the aversive pairing. Not only that, but the response to MCH was the opposite from the response that the parents had learned: the offspring preferred to move toward MCH instead of avoiding it.

Ziv suggests that since the sensitivity to MCH was inherited, but the seemingly useful response (avoidance) was not, there is no inheritance of change at the neural circuit level going on. While that may be a fair enough conclusion, we really can't make any sweeping conclusions at this point as to what is really going on. Ziv, like other explorers of Lamarckian inheritance, merely offers his controlled study with error margins in the same spirit as nearly every other scientific study put on the charts. If we take any of them at face value, we take all of them.

Scientists look for inheritance of specific experiences because they can be quickly inserted into animal, and then later measured to clear effect. To further probe these behavioral phenomena, Ziv suggests that olfactory processes could be blocked at various stages in the adults. Reversibly altering specific pathways using dominant temperature-sensitive transgenes like UAS-Shi for example, would perhaps be one way to do this.

Ultimately scientists want to look beyond transient effects and explore the inheritance of actual physical characteristics, like longer necks in giraffes or bigger hands in farmer's sons. Opponents may argue that any significant results that one might obtain would merely uncover previous genetic pathways already built into the organism. In a way we have the same bottleneck that sensory neurobiogists decry when they try to account for the massive compression of information in a visual stimulus through the retina, and unto the digital output of the optic nerve spike train. However if we figure the entire retina, or the entire body, as a molecular computing volume down to the samllest scale, rather than just considering a few membrane-constrained channels, we hint at the source of power.

More information: arxiv.org/ftp/arxiv/papers/1312/1312.7331.pdf

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