

Flashback: The neurobiology of operant conditioning

Björn Brembs 

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*During my [flyfishing vacation last year](#), pretty much nothing was happening on this blog. Now that I've migrated the blog to WordPress, I can actually schedule posts to appear when in fact I'm not even at the computer. I'm using this functionality to re-blog a few posts from the [archives](#) during the month of august while I'm away. This post is from [April 28, 2011](#):

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It turns out, [operant conditioning](#) is very different from other forms of learning, all the way from the genes up. When I started my research on [operant conditioning](#) in 1995, I did so with the opposite hypothesis, namely that the underlying mechanism of all learning processes was always [synaptic plasticity](#) with the well-known molecular pathway: Ca⁺⁺, cAMP, PKA, CamK, CREB and so on. After all, wasn't that pathway conserved all the way from flies, snails and mice to humans? By the time I finished by PhD in 2000, [Eric Kandel](#) had received the Nobel prize for exactly these learning mechanisms – he wouldn't have gotten the prize if the pathways had not been so conserved. In principle, changing the weight of the synapses is all you need to do to store whatever information you want. There is no a priori need to have several different mechanisms by which neural networks are modified.

A few years ago, I started getting data from fruit flies (*[Drosophila](#)*) that were exactly the opposite of what my initial hypotheis was: the genes required for standard synaptic plasticity (such as the *[rutabaga](#)* adenylyl cyclase) were not required in our form of [operant conditioning](#). In contrast, a gene which had previously been shown not to be involved in [classical conditioning](#), protein kinase C (PKC) turned out to be crucial for [operant conditioning](#). What made the whole story even more intriguing was that the same evidence started to show up in the lab where I did my postdoc, using the marine snail *[Aplysia](#)* as a model system: PKC was required, but the *rut*-cyclase was not.

Why had nobody discovered this dichotomy between the learning mechanisms before us? It turned out that the crucial experimental advance was to prevent the animals from learning about anything else besides their behavior. As soon as we let the animals learn about any external cues in addition to their behavior, the results go back to the expected canonical pathways being required and PKC not. Obviously, nobody had been able to completely isolate [operant conditioning](#) to the extent that was required. Because all our experiments were operant in nature, but only differed in whether or not the animals were able to learn about environmental cues or not, we called the PKC-dependent learning mechanism operant self-learning and the other, well-described form, operant world-learning.

How far is this new form of plasticity (in *[Aplysia](#)* it is a form of 'intrinsic plasticity' modifying the entire neuron and not just the synapse; in *[Drosophila](#)* we don't know) conserved? We are currently in the process of writing up our experiments on the 'language gene' *[FoxP2](#)*. *[Drosophila](#)* has an orthologue of this gene and if we mutate it (or knock it down with RNAi), we find that it is required for operant self-learning, but not for operant world-learning, paralleling the results we had for PKC. This means we now have a new learning mechanism at hand that is clearly distinct from the well-known synaptic plasticity pathway, but is equally conserved among invertebrates and vertebrates. These results suggest an ancient evolutionary origin for operant

self-learning, possibly at the root of the bilaterian branch, and a complementary role to world-learning.

I have summarized these results in an [invited review](#) on occasion of the 2010 conference of [SQAB](#) in the journal “Behavioural Processes”. Unfortunately, there are a few mistakes in the copy available from the publisher. Some spaces are missing between words and the references Brembs 2009a and Brembs 2009b are mixed up. I’ve notified the publisher, but they said it was too late to fix. I’ve now fixed the [HTML version of my local copy](#), but I can’t fix [my PDF copy](#) as they use a font that is not freely available. So if anybody knows how I can fix my own PDF copy, please let me know!

Brembs, B. (2011). Spontaneous decisions and [operant conditioning](#) in fruit flies Behavioural Processes DOI: [10.1016/j.beproc.2011.02.005](https://doi.org/10.1016/j.beproc.2011.02.005)