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Using a Connectome and Virtual Brain to Identify Neurons for Motivation and Conflict Resolution

Animal life is full of daily decision making. These are easy when rewards are available at no cost or peril. However, many situations require a weighing of the cost vs. benefits of specific decisions. To model decisions that require a cost/benefit analysis, we have established a novel assay where Drosophila choose between a small reward (eg. 10mM sucrose) at little cost (liquid solution) and a larger reward (30mM sucrose) at a higher cost (food embedded in agarose, which requires work to get the sucrose out). We find that the internal state of a fly (eg. food deprivation) will motivate them to prefer the high reward/high cost option over the low/low one. Silencing ~half of the flies' brain dopamine neurons causes them to show the same motivation for sucrose, but reduced motivation to "work for" amino acids when amino acid-deprived. In lieu of a classical anatomical screen, we have simulated this situation in the connectome-derived virtual brain and screened for dopaminergic neurons, which affect this cost/benefit calculation. We focus on 2 sets of in silico-identified DA neurons and predicted that one set will be involved in signaling satiety but will not alter the hi reward+cost vs. low reward+cost calculation. For the other set of DA neurons, we predicted the opposite result. Manipulating these two sets of DA neurons in vivo confirmed our prediction. We thus identify: 1] a set of DA neurons mediating satiety (anti-motivation). 2] a second set that is specifically involved in motivating flies to consume amino acids at the cost of work (hard food), but not of bitterness (aversive due to the potential cost of toxicity). 3] the value of using a virtual brain simulation to find motivation-relevant neurons in vivo. We next seek to understand how these distinct motivation neurons react to chronic psychostimulant exposure.

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