# Dissociable cost and benefit encoding of future rewards by mesolimbic dopamine

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Reward-predicting cues evoke activity in midbrain dopamine neurons that encodes fundamental attributes of economic value, including reward magnitude, delay and uncertainty. We found that dopamine release in rat nucleus accumbens encodes anticipated benefits, but not effort-based response costs unless they are atypically low. This neural separation of costs and benefits indicates that mesolimbic dopamine scales with the value of pending rewards, but does not encode the net utility of the action to obtain them.

For individuals to prosper in diverse environments, they need to use predictive sensory information to optimize outcomes in a flexible manner. Decision-making processes weigh the benefits of a reward with the cost of obtaining it to determine the overall subjective value (utility) of the transaction<sup>1,2</sup>. Dopamine is a neural substrate that has been heavily implicated in this valuation process. Midbrain

dopamine neurons encode fundamental economic parameters pertaining to predicted rewards (magnitude, probability, delay and uncertainty) in their firing rate<sup>3–6</sup> and innervate areas that have been implicated in economic decision-making (prefrontal cortex, amygdala, dorsal striatum and nucleus accumbens)<sup>7–9</sup>. Moreover, dopamine in the nucleus accumbens core (NAcc) enables animals to respond to cues and overcome effortful response costs<sup>10,11</sup>. However, to fully understand decision-making computations encoded by the mesoaccumbens dopamine pathway, we need to deconstruct the nature of the valuation signal: specifically, how it accounts for changes in anticipated costs and benefits.

Rats were trained on decision-making tasks (**Supplementary Fig. 1**) that independently manipulated either benefits or cost. We employed fast-scan cyclic voltammetry (see **Supplementary Methods** and **Supplementary Fig. 2**) to record phasic dopamine transmission in NAcc (**Supplementary Fig. 3**) while rats performed these tasks. All of the procedures on animals were approved by the University of Washington Institutional Animal Care and Use Committee. Rats were trained to select between a reference option (16 lever presses for 1 food pellet) and an alternative that differed in either the reward magnitude (4 or 0 food pellets, benefit conditions) or response requirement (2 or 32 lever presses, cost conditions) (see **Supplementary Methods**). Cues signaling the availability of the reference and/or alternative options were presented either separately in forced trials or simultaneously in



**Figure 1** Decision making following manipulation of benefits or costs. (a) Example trials in the benefit condition. Center schematic represents cue lights (yellow star, active; gray circle, inactive) and levers (trapezoid, present; line, retracted) flanking the food magazine. Each frame represents response options on one trial (white background, forced; gray background, choice). The outside panels are representative examples of dopamine release evoked by presentation of cue (dashed line) predicting the availability of a response option resulting in four (left) or one (right) food pellets. The color plots provide electrochemical information for these examples with voltammetric scans plotted on the *y* axis, time of consecutive scans on the *x* axis and electrochemical current represented by color. (b) Post-criterion choice behavior (top) and cue-evoked dopamine release (bottom) across sessions in benefit and cost conditions. Data are mean  $\pm$  s.e.m. \* *P* < 0.05, \*\* *P* < 0.01 and \*\*\* *P* < 0.0001. DA, dopamine.

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**Figure 2** Effect of behavioral history on dopamine release. (a) Differences in cue-evoked dopamine release between the high- and low-utility options ( $[DA]_{HU} - [DA]_{LU}$ ) against behavioral history. (b) Post-criterion choice behavior (left) and cue-evoked dopamine release (right) for the high-benefit (4 food pellets for 16 lever presses, left) or low-cost (1 food pellet for 2 lever presses, right) option in rats given extended training (>9 sessions) with either contingency before testing. Data are mean ± s.e.m. \* P < 0.05, \*\* P < 0.01.

choice trials (**Fig. 1a** and **Supplementary Fig. 1**). Forced trials allowed the evaluation of cue-evoked dopamine for one option without the confound of another option being present and choice trials provided a measure of behavioral preference. Data were evaluated after the rats reached a behavioral criterion, choosing one option on  $\geq$ 75% of choice trials. To prevent side-bias, we always reversed the assignment of high-/low-utility options to the two levers from the previous session and included counterbalanced sessions for each contingency pair in the analysis.

Across all contingency pairs, the rats consistently chose the option with the highest benefit or lowest cost (**Fig. 1b**, see **Supplementary Fig. 4** for rate to criterion). Subjective preference was also evident on post-criterion forced trials where response latencies were significantly faster to higher-benefit or lower-cost options (all P < 0.001; **Supplementary Fig. 4**). Furthermore, when the highbenefit (4 pellets for 16 lever presses) and the low-cost (1 pellet for 2 lever presses) options were presented as concurrent choices in a decision-making session, the rats were indifferent, demonstrating equivalent utility (**Supplementary Fig. 5**). Thus, not only was the utility of reward options successfully modulated as expected by both benefit and cost conditions (that is, increased utility conferred to the option with greater benefit or lower cost), the additional utility conferred by increased benefits was equivalent to that conferred by decreased costs.

Despite predictable behavior, cue-evoked NAcc dopamine release did not track utility under all conditions. Manipulating reward

magnitude led to a corresponding increase (main effect of reward size,  $F_{1,5} = 15.61$ , P = 0.01) or decrease ( $F_{1,4} = 19.88, P = 0.01$ ) in cue-evoked dopamine compared with the reference option (Fig. 1b and Supplementary Fig. 6). Manipulations of response cost, on the other hand, did not always alter dopamine release. When the response cost of the alternative was increased, there was no difference in dopamine release between the reference and alternative option (main effect of response cost,  $F_{1.4} = 0.05$ , P = 0.84; Fig. 1b), despite the strong behavioral preference for the reference option. When the response cost was reduced, there was greater dopamine release to the low-cost cue than to the reference  $(F_{1,4} = 25.38, P = 0.007)$ , but this was only significant in the first of two counterbalanced sessions in each rat (session  $\times$  option interaction, P = 0.03,  $F_{1,4} = 10.92$ ; Supplementary Fig. 6). Post hoc tests indicated that this effect was driven by a reduction in dopamine release to the lowcost cue (P = 0.0006), but not the reference cue (P = 0.20), across sessions.

To further investigate across-session effects, we performed regression analysis between utility encoding and experience with any alternative contingency before recording. Experience-related changes in cue-evoked dopamine release were only observed in the reduced-cost condition, in which the preferential dopamine release for the low-cost cue diminished over time (Pearson's r = -0.830, P = 0.005, n = 9; Spearman's

rho = -0.817, P = 0.007; Fig. 2a). Additional experimentation with a cohort of rats that were given more experience (>9 sessions) with the high-benefit option before recording verified that both behavioral preference and preferential encoding of the higher benefits was maintained with extended training (P = 0.007, t = 4.08, degrees of freedom = 6, n = 7 session; Fig. 2b). Conversely, in a parallel experiment with the low-cost option, cue-evoked dopamine release did not preferentially encode the low-cost option after additional experience before recording (P = 0.16, t = 1.55, degrees of freedom = 8, n = 9 sessions), even though behavioral preference was preserved (Fig. 2b). These data are consistent with the notion that, although preferential encoding of high benefit by dopamine release is stable over training, low costs are only preferentially encoded early in training. Further analyses of the neurochemical data with respect to contextual framing, choice trials (Supplementary Fig. 7) and within-session learning (Supplementary Fig. 8) are included in the Supplementary Results.

When making sound economic choices, one must consider a reasonable cost to obtain an outcome on the basis of its perceived benefit. The data presented here indicate that phasic NAcc dopamine transmission reliably reflects the magnitude of the benefit, but only correlates with effort-discounted utility in situations in which the response cost is both novel and better than the reference. Incorporating these findings with those of previous studies showing that dopamine enables effortful responses, we reason that representation of reward magnitude by phasic dopamine provides

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a threshold to determine worthwhile cost expenditures in familiar situations<sup>10–12</sup>. Moreover, in novel situations, dopamine provides an additional opportunistic mechanism for exploitation of low-cost rewards that become available unexpectedly<sup>12,13</sup>. Thus, we found a dissociation between dopaminergic encoding of anticipated costs and benefits, indicating that, although dopamine release in the nucleus accumbens scales with the value of a pending reward, it is not sufficient to describe the net utility of the action to obtain it.

Note: Supplementary information is available on the Nature Neuroscience website.

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#### AUTHOR CONTRIBUTIONS

M.E.W. and P.E.M.P. conceived the study. J.O.G. and M.E.W. collected and analyzed the data. All authors contributed to experimental design and preparation of the manuscript.

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