SUPPLEMENTARY INFORMATION

Supplementary information S2 (box) | Reward and stress effectors

Acute exposure to rewarding stimuli
When naive rats are first acutely administered rewarding drugs (that is, drugs of abuse), there is typically a robust activation of the hypothalamic-pituitary-adrenocortical (HPA) axis and an increase in sympathovagal activity (reflected by increased heart rate, blood pressure and/or levels of circulating catecholamines). This has been demonstrated for cocaine\(^1\)–\(^7\), amphetamine\(^4\)–\(^5\), nicotine\(^6\)–\(^7\), morphine\(^8\)–\(^9\) and ethanol\(^10\)–\(^14\). Many of these drugs can have direct actions, both in the periphery and at central sites (for example, activation of the reward system), that can contribute to altering the activity of the HPA axis and the autonomic nervous system (ANS)\(^15\)–\(^16\). By contrast, self-administration of drugs can reduce HPA and ANS responses\(^6\)–\(^13\),\(^17\)–\(^18\). Importantly, acute experiences with naturally rewarding stimuli do not always evoke stress-like responses\(^19\)–\(^24\).

Chronic exposure to rewarding stimuli
Chronic drug exposure generally induces a chronic-stress-like state in which the basal tone of the HPA axis and ANS and/or their responses to stress are increased\(^25\)–\(^33\). The effects of chronic exposure to natural rewards have undergone little investigation, with the exception of chronic intake of palatable foods: in no-choice paradigms (for example, when rats are given a sucrose drink instead of water, or lard mixed with chow), chronic intake of palatable food generally increases sympathetic and/or HPA axis tone\(^34\)–\(^40\). By contrast, in choice paradigms (for example, when rats are offered a sucrose drink and/or lard in addition to water and chow), chronic intake of palatable food reduces HPA and sympathetic activation after stress\(^41\)–\(^42\)–\(^44\). Moreover, the artificial non-caloric sweetener saccharin reproduces some of these effects\(^41\)–\(^44\), suggesting that palatability or reward, rather than the calories contained in the food, is sufficient to evoke these responses. Thus, the nature of the effect of repeated exposure to natural rewards on the HPA axis and the ANS seems to depend largely on whether the rats chose to engage in the natural reward.

Conditioned responses to rewarding stimuli
Cues that predict exposure to drugs of abuse elicit conditioned activation of the HPA axis and ANS\(^45\)–\(^46\). However, when the appetitive stimuli are natural rewards the conditioned response is more complex; cues generally evoke anticipatory HPA axis and ANS activation, with a rapid inactivation on receipt of the reward\(^47\)–\(^49\). Moreover, if the natural reward is not provided as expected, there is a further increase in HPA axis activation (‘frustration’)\(^47\)–\(^51\).


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An elegantly designed study showing that the effects of dietary lard on HPA axis responsivity depend on whether the individuals have a choice to consume the lard.


