benefits and risks of an increasing flood of genetic knowledge.

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Dopamine's Role

Ingrid Wickelgren's Special News Report "Getting the brain's attention" (3 Oct., p. 35) presents the views of those who question the current orthodoxy that dopamine acts in the nucleus accumbens as a key neurotransmitter underlying the behavioral effects of positive reinforcement or the feeling of pleasure, or both. However, the most important evidence against this hypothesis receives little attention.

"One line of research that could settle the debate," Wickelgren writes, "is directed at dopamine's role, if any, in unpleasant events." She goes on to say that evidence on this score is "controversial." We are not sure to what controversy she refers. The considerable evidence that dopamine release in the nucleus accumbens is reliably observed under conditions of stress has recently been summarized by Salamone *et al.* (*1*). This evidence shows that unpleasant events such as footshock increase extracellular levels of dopamine in the nucleus accumbens, as measured, for example, by in vivo intracerebral microdialysis. The only controversy relating to such reports, as far as we are aware, is whether they reflect the unpleasantness or the novelty of the footshock (*2*). Our own work, also applying microdialysis to the nucleus accumbens, circumvents this problem. We have shown that a simple sensory stimulus, such as a light or a tone, which before Pavlovian conditioning does not affect extracellular dopamine levels in the nucleus accumbens, elicits such dopamine release after conditioning with a footshock unconditioned stimulus (*3*). This effect, which controls for the novelty of the conditioned stimulus, has been essentially replicated in somewhat different paradigms (*4*).

We believe, in the light of findings such as these, that there is no special relationship between dopamine release in the nucleus accumbens and positive reinforcement. Indeed, our more recent findings go farther. In these experiments (*5*), we exposed groups of rats either to five Pavlovian pairings of light (as conditioned stimulus) and tone (as unconditioned stimulus), or to an equal number of presentations of light and tone over an equivalent period of time, but in an unpaired manner. For both groups the tone was then paired twice with footshock, followed by a test to determine the response to the light (not itself paired with footshock). In the light-tone conditioning group, but not in the random light-tone group, the light on the test trial elicited dopamine release in the nucleus accumbens. Thus, Pavlovian conditioning, even when it pairs stimuli that are not normally considered biological reinforcers and which before conditioning do not elicit accumbens dopamine release, is sufficient to confer upon such stimuli the capacity to do so.

Wickelgren considers the hypothesis that "the dopamine signal serves to draw attention to salient events of all sorts." We believe that this is probably along the right lines. Strong support comes from research showing that the phenomenon of latent inhibition (in which a stimulus loses salience, as measured by its ability subsequently to enter into a Pavlovian conditioned association, as a result of repeated unreinforced presentation) depends on changes in stimulus-elicited dopamine release in the nucleus accumbens. Thus, latent inhibition may be increased by experimental reduction, or overcome by augmentation, of accumbens dopaminergic transmission (*6*). The neural route by which such effects are achieved seems likely, in our opinion, to require pathways other than the connections from the accumbens to the frontal cortex. The latter are probably related more to motor than to sensory processing. A plausible alternative is the projection, recently demonstrated by Lavin and Grace (*7*), from the nucleus accumbens, by way of the ventral pallidum, to the nucleus reticularis thalami and onward to thalamocortical sensory projections. Increased activity in this pathway, consequent upon augmented accumbens dopamine release, might well provide a basis for the enhanced sensory awareness that is characteristic of both schizophrenia (*8*) and drug abusers (*9*).

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Wickelgren's article effectively reveals two major hurdles in the conceptual and experimental progress toward the determination of neuronal mechanisms mediating drug addiction. First, attempts to determine the neuronal substrate of "pleasure" or "reward" ignore the fact that the brain is not processing such psychological constructs. Just as the optic nerve does not function as a television cable, mesolimbic dopamine does not act as a "pleasure juice." Constructs such as "reinforcement" need to be unlocked and possibly replaced by cognitive models that describe the biased attention to, and the enhanced processing of, stimuli and contexts associated with repeated addictive drug use [(*1*); see also (*2*)]. Second, the well-substantiated focus on mesolimbic dopamine appears to obfuscate the fact that the cognitive significance of increased dopaminergic transmission in the nucleus accumbens requires an understanding of the effects on efferent networks. As suggested by Grant *et al.* (*3*), enhanced cortical processing represents a functional component of such networks. Stimulation of dopaminergic receptors in the nucleus accumbens, via a GABAergic projection to the basal forebrain, results in increases in cortical acetylcholine (ACh) efflux (*4*). Psychostimulants, including cocaine, increase cortical ACh efflux (*5*), presumably by means of this trans-synaptic mechanism. As it has been suggested (*6*) that increases in cortical ACh mediate abnormal attenional biases, increases in cortical ACh may represent the critical step in the attribution of "incentive salience" (*1*) to drug-related stimuli and thus in compulsive drug-seeking. Such a conceptual extension of the consequences of increased activity of mesolimbic dopaminergic afferents to cortical information processing may also assist in reconciling the role of mesolimbic dopamine in schizophrenia (*7*).

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Olfactory "Consciousness"?

The explosion of molecular biological research in the main olfactory and vomeronasal systems, as described in the Nota Bene "Unconscious odors" by Pamela J. Hines (3 Oct., p. 79) has contributed insight into how these systems may function. However, the setting up of a strict dichotomy between pheromones that are detected through the vomeronasal organ (VNO) and other odorants that are detected by way of the main olfactory system (*1*, *2*) has led to the assumption that gene families expressed in the VNO encode pheromone receptors. The accessory olfactory system plays an important role in social communication, but both systems are responsive to pheromones and to other odorants. Garter snakes use the VNO to detect both aggregation pheromones and prey odors (nonpheromones) (*3*). Hamsters can use the main olfactory system to detect pheromones (*4*) and the VNO to recognize the odors of other individuals (*5*). Labeling gene products "pheromone receptors" on the basis of presence in the VNO is therefore premature. Their function remains to be tested.

The suggestion that animals are conscious of "garden-variety" odorants, while pheromones are detected unconsciously remains to be verified (*1*). There is not, to my knowledge, any experimental finding that indicates these animals are "conscious" of some stimuli and unconscious of others, even though they may elicit a behavioral response. Do garter snakes consciously perceive the chemical they use to trail prey, but not those they use to find and aggregate with conspecifics? How do we measure consciousness in any animal? If an animal can use an odorant in an operant task to obtain an unrelated reward, is it conscious of that stimulus? If so, then domestic pigs are conscious of the odor of androstenone, which is a pheromone in that species (*6*).

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Sexual Selection in Asian Elephants

In an article by Pallava Bagla (Research News, 27 June, p. 1972), a negative correlation between tusk length and parasite numbers in Asian elephant males (*1*) is reported, potentially another example of William Hamilton's theory that secondary sexual characteristics may be indicative of parasite levels (*2*). However, it remains an "unanswered question . . . whether longer tusks really do attract females." We (*3*) investigated the occurrence of tusk-bearing males (tuskers) and males without any tusks (maknas) in Asian elephant populations in a stochastic population simulation based on available data for the last 2000 years in Sri Lanka (with a decrease in tusker frequency from about 90% to about 10%) and in South India (stable tusker frequency of about 90%). The model predicts that, in the framework of preferential human impact on tuskers, the tusk character could only survive if sexual selection were to occur in favor of tuskers. The best fit to census data was achieved if tuskers were 1.4 to 1.5 times more likely than maknas to be chosen by a female. Among tuskers, which differ from one another only by tusk length, the differences in attraction to females might be even smaller. Thus, determining whether sexual selection is based on an elephant's tusk character may not be possible in field

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