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REVIEW

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Amines and motivated behaviors: a simpler systems approach to complex behavioral phenomena

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Abstract Recent investigations in invertebrate neurobiology have opened up new lines of research into the basic roles of behavioral, neurochemical, and physiological effects in complex behavioral phenomena, such as aggression and drug-sensitive reward. This review summarizes a body of quantitative work, which identifies biogenic amines as a pharmacological substrate for motivated behaviors in the crayfish, *Orconectes rusticus*. Specifically, this paper details progress that has (1) explored links between serotonin and an individual's aggressive state, and (2) demonstrated the existence of crayfish reward systems that are sensitive to human drugs of abuse, such as psychostimulants. First, we summarize a set of experimental approaches that explore aggression in crayfish and the significance of aminergic systems in its control. Agonistic behavior in crustaceans can be characterized within a quantitative framework; different *types* of behavioral plasticity in aggressive behavior are in need of physiological explanation, and pharmacological intervention involving serotonergic systems bring about characteristic changes in behavior. A second set of experiments demonstrates that psychostimulants (cocaine and D-amphetamine) serve as rewards when an intra-circulatory infusion is coupled to a distinct visual environment. Work in novel model systems such as crayfish constitutes a useful comparative approach to the study of aggression and drug addiction.

Keywords Biogenic amine · Aggression · Agonistic behavior · Motivation · Addiction

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Introduction

"Under carefully controlled experimental circumstances, an animal will behave as it damned well pleases"—E. O. Wilson's *Basic Law of Animal Behavior* effectively sums up our combined sense of wonder and frustration as multiple presentations of a specific stimulus rarely evoke identical responses, even under rigorously specified environmental conditions. Thus, altered responses must be attributed to changes in the internal state of an individual. Terms such as "specific arousal", "motivation", or "behavioral state" collectively refer to the subset of reversible, short-term alterations in behavior that are not associated with fatigue or learning (Immelmann and Beer 1989). Used purely as an intervening concept and without regard to its neural underpinnings, the predictive value of a "motivation" depends on whether it provides a simpler representation of relationships within the given system (Hinde 1982). It is of little use when we are forced to postulate a separate motivation for each pattern we wish to explain. Indeed, with a full understanding of a particular behavior's causes, we would have no need for such a term at all (Dawkins 1995).

Traditionally, motivations were viewed as individual, unitary properties corresponding to broad behavioral categories such as eating, parental care, or fighting (Tinbergen 1951). These forces were thought to interact, and thereby guide behavior, in a "great parliament of instincts" (Lorenz 1966). This classical ethological view of the term "motivation" has not been without its critics, and such models have now largely been superseded by a more complex, multidimensional view, where each particular behavioral response arises from the close interaction of several independent physiological or stimulus axes. In the present paper, we view behavior as a set of individual decisions—each with a particular probability of occurrence, a motivational context, and controlled by the interplay of distinct underlying causative mechanisms. Motivational states thus simply refer to intrinsic

forces that promote the occurrence of defined sets of behaviors within an adaptive context, without implying a specific underlying framework (e.g., psycho-hydraulic model—Lorenz 1966, neuro-evolutionary constructs—MacLean 1990; Panksepp 1998). It is important to note that without knowledge of their underlying substrates, action tendencies cannot be measured directly but can only be assessed a posteriori through observations of behavior under defined circumstances of stimulus (Seitz 1940). In some instances, however, estimates of behavioral states may be gained via known correlates, such as color patterns (Summers and Greenberg 1994; Belthoff and Gowaty 1996; O'Connor et al. 1999), social status (Raab et al. 1986; Saltzman et al. 1996; Yang et al. 2001), territoriality (Wazlavek and Figler 1989; Bolyard and Rowland 2000; Ratti 2000), or neurochemical measures (Yodyingyuad et al. 1985; Dillon et al. 1992; Lopez et al. 2002).

A comprehensive understanding of the causation of behavior, beyond the intervening level of motivations, requires that behavioral variability is ultimately mapped onto its underlying proximate mechanisms. Monoamine systems are attractive candidates for the control of such motivational axes as they modify neural function at multiple levels and may thereby bring about coordinated responses to environmental perturbations (Libersat and Pflüger 2004). Neuromodulators and neurohormones are generally considered to selectively sensitize or depress sensory elements, organize neuronal activity in central circuits, or bias motor systems towards contextually appropriate states (e.g., Harris-Warrick and Kravitz 1984; Beltz and Kravitz 1986; Beyer and Feder 1987; Bicker and Menzel 1989). In this manner, amines are thought to alter the activity of specific neural decision-making centers (Nader et al. 1997). Rather than produce behavior per se, these substances appear to tune ongoing activity and, in a given context, promote the occurrence of adaptive behaviors (e.g. feeding, flight, fight, or mating) over contraadaptive ones (Kravitz 1988; Libersat and Pflüger 2004). Considerations about their specificity reflect shifts in our expectations from a view of neural mechanisms "for" a particular behavior, to one that modifies neural environments "fostering" the occurrence of specific behaviors (Heinrich et al. 2001; van Staaden and Huber 2001). Such systems are particularly difficult to study in behavioral contexts since aminergic neurons send extensive projections across large areas of nervous tissue (Azmitia and Segal 1978; Lidov and Molliver 1982; Beltz and Kravitz 1987) to respective targets that possess a full complement of receptors, each with a unique coupling mechanism and binding profile (Hen 1992, 1993; Kroeze and Roth 1998; Tierney 2001). Moreover, depending on the precise context and species, amines such as serotonin serve as a trophic factor during development, a classical neurotransmitter, a neuromodulator, or a neurohormone. Thus, the very properties that make neuromodulators attractive for hypotheses relating to the coordination of behavior also make them inherently difficult to study. It has become increasingly clear that neither the classical ethological nor a traditional neuropharmacological approach will suffice alone. For an integrated analysis of neuromodulators in complex behavior, it is essential that we combine studies of physiology, biochemistry, pharmacology, and molecular genetics with quantitative behavioral analyses (Lederhendler and Shulkin 2000; Chen et al. 2002; van Staaden and Huber 2001).

Aminergic mechanisms that generalize across broad taxonomic boundaries reflect an ancient evolutionary emergence of amine-signaling mechanisms predating that of the chordate lineage. Specifically, such systems share significant commonalities in their neurobiological substrates: sequence homologies of key receptor elements (Hen 1992, 1993), pharmacological properties (Tierney 2001), methods of inactivation (Porzgen et al. 2001), general modes of action (Vernier et al. 1995, 1997), and association with similar behavioral contexts (Kravitz 1988, 2000). G protein-coupled, metabotropic monoamine receptors appear to have arisen during the evolutionary transition to multicellular life (Vernier et al. 1995). Presumably, early metazoans adopted monoamine systems to represent global motivational states, which coordinate functions of individual cells in different parts of the body for adaptive responses towards environmental perturbations. Due to phylogenetic conservation, vertebrates and invertebrates offer significant homologies within functional sets of receptor families (Peroutka and Howell 1994; Walker et al. 1996; Chan and Jan 1999). Since the Precambrian, however, independent evolutionary paths have given rise to the present-day diversity of (ortho as well as paralogous) subtypes, their respective pharmacological profiles, and individual links with specific behaviors.

Crayfish have continued to play a unique role among invertebrate models for studies of mechanisms due to a nervous system that is uniquely accessible to a wide range of behavioral, neural, and neurochemical approaches. Behaviors contain stereotyped elements and its CNS consists of relatively few, large, recognizable neurons embedded within a well-characterized functional neuroanatomy for modulatory substances (Kravitz 1988, 2000; Libersat and Pflüger 2004). Offering greatly reduced complexity compared to any other vertebrate, its main strength lies in experimental opportunities to first identify and then obtain a detailed understanding of the inner workings at key neuronal sites for the behavioral plasticity in question. However, a comprehensive framework linking neuromodulator function with motivated behavior has remained elusive.

Recent work has helped to extend basic neuroethological generalities towards an ethopharmacological exploration of increasingly complex behavioral phenomena. The present paper addresses such fundamental issues by reviewing recent findings from (1) studies exploring the role and specificity of serotonin in crayfish aggression, and (2) work characterizing natural reward mechanisms in crayfish that are sensitive to human drugs of abuse.

Serotonergic modulation of crayfish aggression

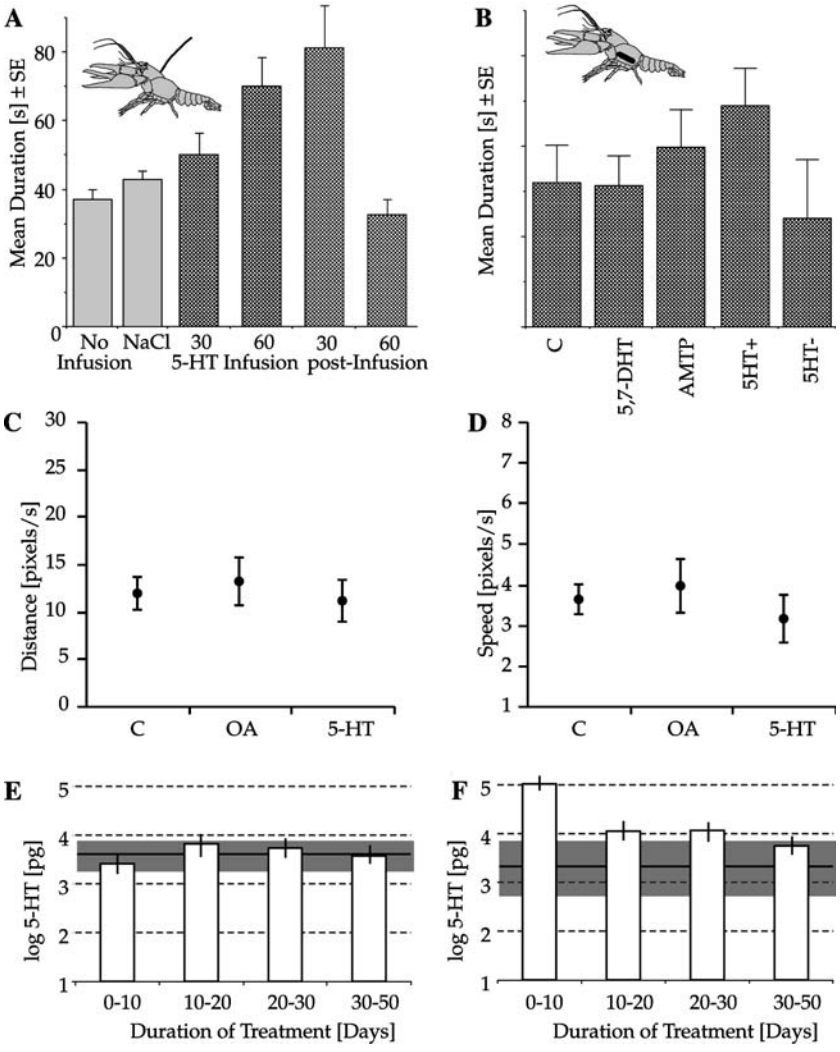
Views on the behavioral importance of the indoleamine serotonin have converged on its importance in orchestrating social behaviors such as aggression and affiliation in a wide range of taxa (Insel and Winslow 1998; Nelson and Chiavegatto 2001). Precisely where, how, and under what conditions these substances exert their effects, however, remains unclear. Increased serotonin function is often considered to lower aggression in vertebrates, while the opposite scenario appears to hold true for invertebrate taxa (Edwards and Kravitz 1997; Weiger 1997). Although it is possible that serotonin systems underlying aggression simply underwent a sign change during early vertebrate evolution, a more complex picture is emerging. In both vertebrates and invertebrates, either enhanced or reduced aggression may result from elevating or lowering levels of serotonin depending on the particular taxa studied (Eichelman 1990; Ison et al. 1996; Doernberg et al. 2001), the brain region involved (Romaniuk et al. 1987; Wieczorek and Romaniuk 1994; Koprowska and Romaniuk 1997), the individual's social status (Ison et al. 1996), the method used to manipulate serotonin levels (Cases et al. 1995; Panksepp and Huber 2002), or the precise behavioral paradigm examined (Raleigh et al. 1991; Harrison et al. 1997). Disagreement also arises from the use of disparate, incompatible, and often poorly defined, perspectives of "aggression" (e.g., aggressive state, risk taking, lack of control for impulsiveness, violence, negative effects of stress, an ability to win single agonistic encounters, or achieving and maintaining social dominance).

Crayfish offer a system in which to characterize serotonergic effects in the causation of aggression using a simplified scenario. Our initial work examined fighting behavior in crayfish pairs with large size asymmetries ($>30\%$), where the smaller (subordinate) individual received acute serotonin infusions via a fine-bore, fused silica cannula (Huber et al. 1997a, b; Huber and Delago 1998). During such treatment, infused individuals again reengaged their larger opponents, resulting in longer fights that reached higher levels of intensity compared to controls (Fig. 1a). Multivariate techniques (e.g., discriminant function analysis) revealed that serotonin treatment had specifically altered the decision to retreat from an opponent, without affecting how likely the animal was to initiate fights, how individual fights progressed to higher intensities, or in the case of large size asymmetries, the eventual social rank that was achieved. Serotonin appears to act upon key sites for agonistic "decision making" in the crayfish's central nervous system. Although arriving at similar empirical outcomes, alternative interpretations have been advanced (e.g., Peeke et al. 2000) holding rather that an inhibition of retreat occurs through global downregulation of activity or motor coordination.

It is likely that serotonin reuptake mechanisms play a crucial role in this behavioral change as the behavioral effects associated with acute serotonin infusion were blocked in the presence of fluoxetine (Huber et al. 1997a, b; Huber and Delago 1998). This finding suggests that a functional high-affinity serotonin reuptake mechanism (Livingstone et al. 1980) is a prerequisite, that serotonin-associated behavioral plasticity required the preloading of synaptic terminals (which can be blocked by fluoxetine), and that they were possibly mediated through the activity of slow acting, metabotropic receptors. However, this work serves as a reminder not to view aminergic neuromodulatory systems as too simplistic. For instance, fluoxetine, which by itself would be expected to result in similar short-term effects as serotonin infusion, did not produce an increase in fighting. We should keep in mind that the control of amine levels and release constitutes only one component of a highly dynamic system in action. Although intriguing, the particulars of such associations are not yet clear and await further clarification perhaps using pharmacological manipulation of specific 5HT-receptor subtypes.

To further distinguish between specific aggression-enhancing effects of serotonin and more global effects on motor activity/coordination, the present study has explored levels of activity, movement patterns, and space utilization in individuals receiving serotonin in ways that corresponded in dose, mode, site, and time course of infusion to our earlier fighting studies. Under these conditions the present studies failed to detect significant differences in locomotion and movement patterns compared with controls. For instance, neither mean speed nor mean distance traveled differed significantly (Fig. 1c, d) for individuals who received saline at 3 µl/min for 60 min (control, C), containing 3 µg/min of octopamine (OA), or serotonin (5-HT).

Subsequent work using chronic augmentation or disruption of serotonin function explored to what degree considerations of time scales and dynamic properties enhance our understanding of the links between amines and behavior. Pharmacological intervention of the amine system function appears to be accompanied by a rapid induction of compensatory mechanisms that counteract any such treatment. Differences in fighting behavior resulting from chronic infusions of serotonin were initially accompanied by predicted effects for behavior and pharmacology, followed by a steady decrease in serotonin's effectiveness (Panksepp and Huber 2002; Panksepp et al. 2004). Infusions from silastic tube implants containing serotonin (Panksepp and Huber 2002) and lasting up to several weeks initially boosted absolute amine levels (Fig. 1e, f). Within a week, however, the system acquired an ability to counteract the effects of constant infusion and absolute levels of serotonin returned to pretreatment levels. Moreover, with continued serotonin infusion, some individuals even showed evidence of serotonin depletion as compensatory mechanisms evidently brought about a decrease in serotonin. Such neuronal compensation may involve changes at a variety of levels, including synthesis (Stachowiak et al.



1986; Sivam 1995), amine release (Lent 1984; Hall et al. 1999), metabolic activity (Ase et al. 2000; Fickbohm et al. 2000), or receptor turnover (Patel et al. 1996; Woo et al. 1996). Behavior in studies using chronic treatments did not track the aggression-enhancing effects of serotonin that have emerged from acute infusions (Fig. 1b). Although this advises caution when discussing the presence of links between amines and behavior in general, it more likely reflects the essential constraints and properties of a dynamic system where the relative size of a signal relative to a given setpoint as well as its timing are critical.

Psychostimulants activate crayfish reward

The usefulness of this model system for studies of addiction was not previously recognized because a drug-reward phenomenon had not been documented. However, the demonstration that crayfish are indeed fully capable of exhibiting conditioned place preference for environments in which they received cocaine or D-amphetamine (Panksepp et al. 2004; Panksepp and Huber 2004) has remedied this deficit.

Success of the present exploratory venture will result in a formal characterization of drug-sensitive reward and develop our initial observations into a validated, well-characterized research model. With highly accessible, modularly organized, and neural/neuromodulatory systems of relatively low complexity, crayfish may provide a comparably efficient, simplified model for cross-species insights complementing investigations into mammalian systems. Neuronal "simplicity" combined with the potential for elegant behavioral analyses suggest that this model is highly suited for comprehensive, experimental analyses of specific mechanisms underlying drug reward and addictive properties at the level of single neurons and identified synaptic sites. Clearly, this work is motivated by the promise of enhanced understanding at increasingly reductionistic levels of analysis, such as the identification of drug-induced plasticity in cellular properties of identified neurons, circuits, and modulatory systems. Success in this endeavor will

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Fig. 1 Composite figure illustrates differences in fight duration resulting from pharmacological manipulations of crayfish serotonin systems. **a** Fine-bore fused silica capillaries were used to infuse serotonin into freely moving, subordinate animals at 3 μg/min. Serotonin infusion resulted in longer fighting that persisted well after the infusion pump was turned off. **b** Duration of fighting in individuals, which received chronic silastic implants containing either 5-HT synthesis inhibitors (5,7-dihydroxytryptamine or alpha-methyltryptamine) or serotonin at one of two different rates. No significant differences in fight duration existed among these groups ($F_{(4,314)} = 1.06$, $P = 0.374$). **c, d** Measures of locomotion were obtained for crayfish (*Orconectes rusticus*) during infusion of 3 μl vehicle/min (control, C) or with an equal volume containing 3 μg/min OA or 5-HT. Movements of treated individuals (masses: 8.1–17.0 g) were videotaped from above for 60 min. Locations (x and y coordinates) were obtained every 5 s from a series of digitized frames using video-tracking software (freely available at http://caspar.bgsu.edu/~software/java/ based on Quicktime for Java libraries). The average straight-line distance in screen pixels between consecutive captures was used to obtain measures for **c** mean distance and **d** speed of locomotion for each individual. ANOVA revealed no significant main effects for treatment (distance: $F_{(2,18)} = 0.229$, $P = 0.797$; speed: $F_{(2,18)} = 0.487$, $P = 0.623$). **e, f** 5-HT content [log of 5-HT(pg) ± standard deviation (SD)] for **e** brain and **f** the remainder of the CNS tissues in experimental groups, which had received serotonin chronically for 1–50 days. Levels of serotonin in untreated controls are indicated by the *horizontal gray region* (mean ± SD). Brain levels have remained unchanged throughout this study. Levels in the remainder of the nervous systems were initially higher than controls but over time returned to control levels

depend critically on the more immediate characterization and validation of this general study system with respect to its behavioral phenomena in addiction.

Except for some recent initiatives (e.g., Hill and Newlin 2002), evolutionary factors in addiction research have received scant attention compared with cultural, environmental, biological, or pathological concerns (Nesse and Berridge 1997). As with humans, it has become clear that a wide range of animals will work long and hard to obtain psychostimulant drugs through compulsive self-administration (Johanson et al. 1976; Wise 1998). Such addictive properties likely involve the action of specific reward pathways. As a result of selective pressures, activation of natural reward systems is usually aligned with an individual's adaptive purpose, enticing it to satisfy inherent motivations for nourishment, sex, or "contact comfort" (Panksepp et al. 2002). Addictive compounds are thus likely to act on evolutionarily conserved brain substrates for reward beyond those unique to humans. During the addictive process, natural reward systems are being commandeered by highly purified chemical compounds, which promote compulsive behavior, even as they result in negative outcomes, such as starvation (Wise 1998).

Behavioral stereotypes following exposure to addictive drugs have recently been reported for several invertebrates (Palladini et al. 1996; Mcclung and Hirsch 1999; Torres and Horowitz 1998). Fruit flies exposed to high doses of cocaine derivatives exhibit conspicuous behaviors such as grooming, stereotypical locomotion, and akinesia. These behavioral changes are subject to sensitization upon repeated application (Mcclung and Hirsch 1999), which is thought to reflect an intensification of drug craving in mammals (Robinson and Berridge 1993). Consistent with work on both mammals and flies, presynaptic catecholaminergic mechanisms appear to modulate the formation of behavioral sensitization, while postsynaptic elements act in its maintenance.

Besides underscoring the neurochemical similarities of vertebrate and invertebrate lineages, work with psychostimulants in *Drosophila* has also contributed new hypotheses and insights concerning the roles of trace amines and circadian mechanisms in drug addictions. Tyramine, the monohydroxyphenol analog of dopamine, is essential for behavioral sensitization of *Drosophila*. Mutants with reduced levels of this trace amine exhibit a normal initial response to cocaine exposure, but do not sensitize, while an increase in tyramine mirrors behavioral sensitization of wild-type flies (Mcclung and Hirsch 1999). Moreover, behavioral sensitization in flies depends on tyramine interactions with members of the circadian gene family. In contrast to wild-type flies, those lacking the *per* gene do not exhibit a normal sensitization response when challenged with postsynaptic stimulation of a vertebrate D_2 agonist (Andretic et al. 1999; Andretic and Hirsh 2000). With attention focused on these processes in mammals, recent work has suggested that the validity of such findings could well span wide, taxonomic borders. Tyramine occurs at trace levels in the mammalian brain (Durden and Davis 1993), mostly supplied through food intake. Its pharmacological profile in vertebrates is "amphetamine-like", as it augments synaptic catecholamines through inhibition of membrane transporter uptake (Sitte et al. 1998). Moreover, some of the 15 trace amine receptors that have since been cloned in both rats and humans are located in the ventral tegmental area (Borowsky et al. 2001). Finally, upregulated transcription of *per*, a circadian gene required for sensitization in flies, has been demonstrated in mammalian dorsal striatal regions receiving input from midbrain dopamine neurons (Nikaido et al. 2001). Such work highlights how an exploration of basic processes in simpler systems can advance unanticipated hypotheses for a study of related phenomena in mammals. Few studies, however, have addressed an association between reward and drugs of abuse in invertebrates using behavioral criteria. A study of natural substrate preference in planarians demonstrated a switch to the nonpreferred environment when it was paired with methamphetamine, an effect that was blocked by pretreatment with selective vertebrate D_1 and D_2 antagonists (Kusayama and Watanabe 2000). Crayfish, where a complex behavioral repertoire combines with detailed knowledge of neurochemical systems and a body size that supports in vivo handling, offered distinct advantages for an ethopharmacological dissection of invertebrate reward.

We have demonstrated that both cocaine and amphetamine are able to serve as reinforcers when crayfish are subjected to a place-conditioning schedule (Panksepp and Huber 2004; Panksepp et al. 2004). For

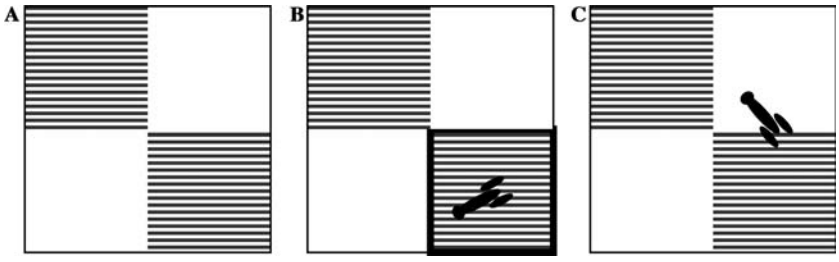
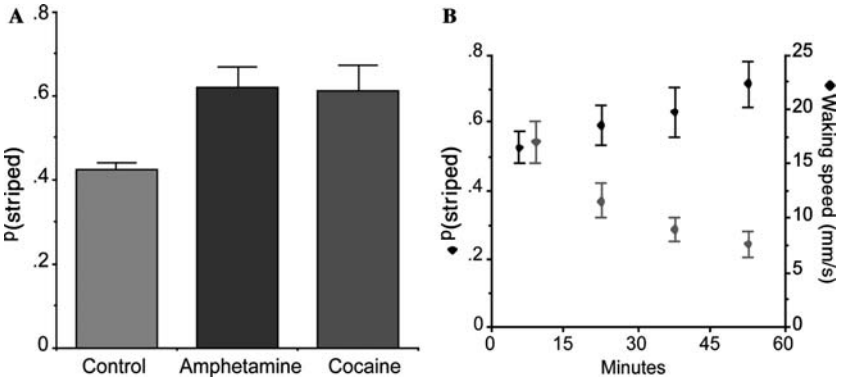


Fig. 2 **a** An arena with two distinct visual environments (*white* or *striped*). **b** On each of five consecutive days, crayfish with a cannula implanted into the pericardial sinus, received two conditioning trials a day in random order and separated by 8–12 h. Individuals were confined to one environment for 30 min where they received a 5-min infusion followed by 25 min without treatment. In control individuals ($n = 13$), both environments were paired with saline (i.e., vehicle). One experimental group ($n = 12$) received infusion of D-amphetamine (5 μg/g body mass) in the striped environment, with its strong visual cues and naturally aversive properties, whereas the white environment was associated with the infusion of vehicle. Cocaine (2.5 μg/g body mass) was applied to a second experimental group ($n = 5$) in the striped environment instead. **c** After 5 days of conditioning, crayfish were allowed unrestricted access to the entire arena for 60 min in a "drug-free" state with locations monitored continuously using a video-tracking system

these initial experiments, we used a particular combination of conditions (Fig. 2), i.e., we used drug doses that were large but did not impair motor systems. We paired drug with distinct visual cues, and we applied repeated training trials over 5 days. Results for the control group following a 5-day conditioning schedule indicated the presence of a small, natural aversion to the striped visual environment, with a mean of 42% of the time spent there. This result was replicated in two additional experiments. The slight bias against the striped environment is expressed as an average preference for individuals across days rather than being the result of variability in environmental preference due to individual differences. Treatment effects were thus analyzed as a biased design (viz., "Can the negative preference for the striped environment be reversed by pairing it with drugs of abuse?"). Individuals exhibited a robust shift to the striped environment (Panksepp et al. 2004) when it was paired with amphetamine or cocaine (Fig. 3a). Even a single conditioning trial for control ($n = 8$) and amphetamine ($n = 10$) produced a noticeable, although nonsignificant, shift (ANOVA $F_{[1,16]} = 3.46$; $P = 0.08$; power = 0.42) to the conditioned environment (not shown), suggesting that effect strength increases with repeated application. A temporal analysis (Fig. 3b) illustrated that crayfish first explored the experimental field, irrespective of treatment. As exploration slowed, both amphetamine- and cocaine-conditioned animals progressively settled into the conditioned quadrant, while controls settled on white. We anticipate that larger treatment effects will result from further optimization of experimental conditions. Five-day conditioning experiments, nonetheless, were associated with a high degree of power (value = 0.97) indicating a robust and replicable phenomenon (i.e., where all individuals showed some drug-rewarded place conditioning) even in individuals caught in the wild (Panksepp and Huber 2004). Power analysis also allowed us to suggest minimum sample sizes needed for experiments using independent groups of individuals.

The development of robust behavioral paradigms for measures of reward strength associated with drugs of abuse will offer a powerful model for subsequent behavioral, physiological, biochemical, pharmacological, or molecular dissections of reward systems in crayfish. Neuro-pharmacological systems of crayfish, which are comparatively less complex, and more accessible than those in mammals, will allow us to direct our attention towards a subsequent comprehensive phar-

Fig. 3 **a** Mean proportion of time (out of 60 min) spent in the striped environment (±SE) after 5 days of conditioning with vehicle ($n = 13$), amphetamine ($n = 12$), or cocaine ($n = 5$). Pairing with drugs of abuse produced a significant shift towards the conditioned environment (ANOVA $F_{[2,27]} = 10.08$; $P < 0.001$; power = 0.97). **b** Amphetamine-conditioned crayfish initially explored the tank, but slowed down (i.e., walking speed decreases) and progressively settled into the drug-conditioned environment (*partially striped*)



macological deconstruction of reward mechanisms in crayfish. With the success of the experiments described above, a large number of studies become feasible. We may (1) block or interfere with the strength of reward measures using pharmacological disruptors of dopamine systems, (2) identify the precise brain drug levels at which crayfish return for another bolus during different stages of the self-administration cycle, (3) examine the existence of interactions during coinfusions with amines or pharmacological agents, (4) compare effects from multiple reward schedules, (5) distinguish the effects across multiple addictive substances, or pharmacological agents, (6) address natural reward mechanisms in crayfish through the development of operant, self-administration paradigms, (7) search for genetic determinants underlying behavioral heterogeneity (e.g., 5HT receptor polymorphism), or (8) explore differences in expression profiles using conserved sequences. Despite marked differences in neuroanatomy between vertebrates and invertebrates, these data support the notion that similarities in neurochemistry are sufficient to support motivational changes associated with addictive substances. Although we do not yet suggest what type of motivational construct might explain such a process in crayfish, the respectively paired environment may have been perceived with a heightened level of ''attraction''. It will be of interest to now extend the exploration of drug effects to more natural contexts, such as those that involve foraging or aggression.

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