

Opinion

Agency and the Calibration of Motivated Behavior

Justin M. Moscarello¹ and Catherine A. Hartley^{2,*}

The controllability of positive or negative environmental events has long been recognized as a critical factor determining their impact on an organism. In studies across species, controllable and uncontrollable reinforcement have been found to yield divergent effects on subsequent behavior. Here we present a model of the organizing influence of control, or a lack thereof, on the behavioral repertoire. We propose that individuals derive a generalizable estimate of agency from controllable and uncontrollable outcomes, which serves to calibrate their behavioral strategies in a manner that is most likely to be adaptive given their prior experience.

The Organizing Influence of Control

Humans, and other animals, are remarkably attuned to their ability to effect change in the world around them. By taking action and observing the consequences, individuals can assess what outcomes they are – or are not – able to influence. When voluntary behavior can be used to bring about desired or beneficial outcomes, an individual has control. As the phenomenon of learned helplessness famously established [1–3], controllability of biologically relevant outcomes can radically alter subsequent behavior. Here we present a cognitive and neurobiological model of the profound influence control exerts on the behavioral repertoire of the organism. We argue that both humans and animals draw on past experiences to estimate whether opportunities for control are likely in a novel environment. Such estimates of agency serve to calibrate ongoing behavioral strategies, promoting proactive goal-directed and exploratory behaviors when opportunities for adaptive instrumental action are likely and innate reactive behaviors when the environment is assumed to afford little control. We illustrate the principles of this model using the example of defensive behavior and propose that the same principles also govern reward-guided behavior. This conceptual framework may provide insight into the divergent cognitive and psychological effects of high- and low-control environments. The goal of this review is to synthesize the disparate literature relevant to this topic, thus generating new insight into the psychological and neurobiological processes that contribute to the effects of control on behavior.

Using Estimates of Agency to Calibrate Subsequent Behavior

We define agency as the perceived breadth of an organism's influence over its environment. By ascertaining the relationship between actions and motivationally significant outcomes, humans and animals can infer which aspects of a particular context are under their control (Box 1). Repeated experiences in which important outcomes are controllable suggest a wide sphere of influence, whereas repeated experiences with uncontrollable outcomes suggest a sphere of influence that is relatively narrow. Thus, agency reflects an estimate, inferred over some aggregate of past experiences, of whether important environmental events and stimuli are predominantly controllable (i.e., high agency) or are consistently outside one's control (i.e., low agency).

Trends

Across species, the ability to control important outcomes has a powerful effect on subsequent behavioral responses to environmental challenges.

Recent convergent research in rodents and humans has provided a provisional model of the brain systems involved in the assessment of control and its alteration of ongoing behavior.

This work suggests a plausible neural implementation of proposed psychological theories in which estimates of agency, derived from past experiences of control, are used to bias the organism toward proactive or reactive behavioral responses.

¹Department of Psychology, Texas A&M University, College Station, TX, USA

²Department of Psychology and Center for Neural Science, New York University, New York, NY, USA

*Correspondence: cate@nyu.edu (C.A. Hartley).

Box 1. Action–Outcome Learning as the Basic Unit of Inference for Agency Estimation

We propose that estimates of agency are drawn from learned relationships between actions and contingent outcomes that either directly enhance adaptive fitness or carry some indirect fitness benefit. Neutral outcomes, even if fully under the control of an action, are less relevant to agency estimation.

To infer a contingent action–outcome relationship, the outcome must follow the action more frequently than it occurs randomly. While covariance between action and outcome is a necessary minimal requirement for instrumental learning, it is not entirely known how humans and animals learn precisely which action yields a particular outcome, particularly when actions and outcomes are separated in time. This ‘credit assignment’ problem, which is the subject of a broader literature on reinforcement learning [69], highlights the complexity of determining controllability, even when actions and outcomes are correlated.

Specific features of action–outcome relationships can either promote or undermine inferences of controllability [9] and thus contribute to agency estimation. For instance, a single action can yield multiple outcomes. If one of those outcomes is more likely, or if cues in the environment provide information about which contingency to expect, this circumstance may contribute to an inference of control. However, outcomes can also be highly entropic, occurring at relatively low probabilities with no means to determine which outcome will follow the action. As controllability requires that an action be a reliable means to achieve a particular outcome, entropic action–outcome relationships undermine the inference of control, even if a weak but discernible relationship exists between the action and each outcome.

Conversely, when multiple actions lead to a single outcome this bottleneck reduces the perception of controllability. While it can be useful to have multiple means by which to attain an important goal, when many actions yield only one or a few outcomes a sense of those outcomes’ inevitability reduces a sense of control. Moreover, other important outcomes may be perceived as unachievable.

Thus, an inference of control is likely when low-entropy relationships exist between one or a small number of actions and a specific desired outcome and when an increasing repertoire of such relationships facilitates the achievability of multiple possible goal states in a particular context [9].

We propose that humans and animals generalize estimates of agency to uncertain novel situations. Akin to a Bayesian prior (i.e., an *a priori* belief about an uncertain property of the environment), agency estimates provide a best guess of the probability that a novel situation will be controllable and thus can inform how best to respond to environmental challenges. While the specific inferential principles governing this generalization process are not well understood (Box 2), here we argue that estimates of agency calibrate an individual’s response along a behavioral continuum ranging from proactive (‘What can I do in this environment?’) to reactive (‘What can this environment do to me?’). Thus, agency estimates orchestrate a behavioral strategy that, according to historical experience, is most likely to be adaptive (Figure 1).

Fundamentally, a reactive profile of behavior comprises responses drawn from an innate repertoire selected over an evolutionary timescale [4]. These responses can be directly elicited by environmental threats [5,6] or rewards. This can be highly adaptive, as many environmental challenges require a response that can be deployed rapidly without an intervening volitional process. Moreover, reactive behavior requires no explicit consideration of the causal consequences of the elicited reaction (i.e., no action–outcome learning). Thus, in situations affording little opportunity for control (i.e., few beneficial outcomes that are contingent on one’s actions), an individual can rely on these reactive strategies to cope with behavioral challenges.

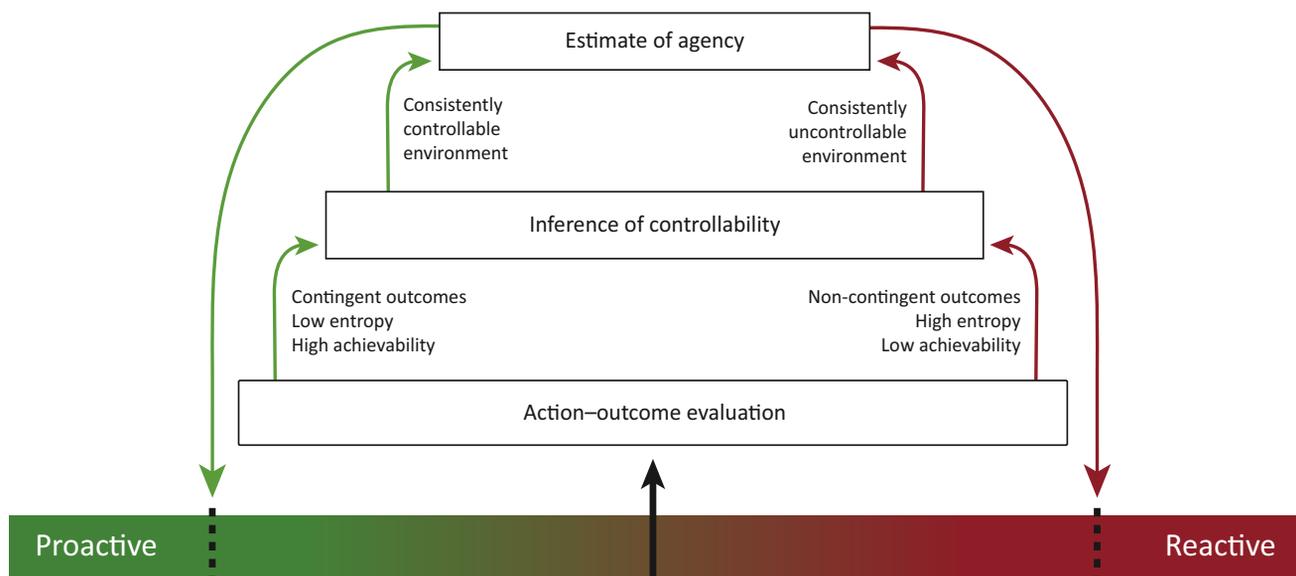
By contrast, a proactive profile of behavior takes advantage of the ability to bring about important outcomes through action. Proactive behavior is characterized by the tendency to explore and discover the structure of available reinforcement opportunities in the environment and to exploit learned action–outcome relationships to achieve one’s current goals. Proactive responding depends on diverse cognitive processes that support the discovery and representation of relevant action–outcome contingencies (i.e., a cognitive model of the current context) and the evaluation and selection of appropriate goal-directed actions [7]. When such

Box 2. Generalization of Agency Beliefs

When an individual infers control across diverse scenarios and contexts, this gives rise to the higher-order inference of agency, or the likelihood of the ability to exert control, within a novel context. We contend that humans and animals use this generalizable inference of agency to calibrate how threat evaluation systems respond to ambiguous stimuli, thus striking the necessary balance between appetitive and defensive behavior. The value of generalizing beliefs about agency is predicated on the assumption that what is learned in one context can be applied to another. However, contexts (which may incorporate temporal and spatial features [70]) may differ substantially in the degree to which they afford control. For example, control may be lower in another person's home than in one's own, in the presence of a more socially dominant conspecific versus in their absence, or when danger is imminent versus distant. When novel contexts are encountered, beliefs about agency may be modulated by the similarity of the current context to those in which controllability has been evaluated in the past.

Cues associated with the environmental conditions in which control is inferred may facilitate its generalization. For example, a vending machine that is lit up suggests the presence of electricity, which is a necessary but not sufficient condition for food delivery. Neither the light nor the electricity it indicates directly causes the food to be delivered. Instead, they signal the opportunity to successfully implement a learned action–outcome relationship. Such stimuli, sometimes referred to as ‘occasion setters’, are analogous to discriminative stimuli used in animal learning tasks, which may, for instance, signal that a lever press will be reinforced with food [71,72]. One important feature of these cues is that their absence does not alter learned action–outcome relationships. A vending machine without electricity does not support the conclusion that food can no longer be obtained from similar lit-up machines but instead signals a likely absence of control that is specific to the current scenario. Thus, the presence of such contextual cues may promote the transfer of specific learned action–outcome relationships, and control expectancies, from context to context, while their absence may signal contextual exceptions. Thus, individuals can use contextual cues to disambiguate circumstances of high and low agency, allowing them to deploy proactive or reactive strategies in a manner that is appropriate for a given situation.

Truly novel contexts that bear little similarity to past environments may draw on a more global agency estimate that aggregates over the individual's cumulative prior experiences of control in a context-independent manner (akin to Rotter's concept of a trait-like ‘internal locus of control’ [50]).



Trends in Cognitive Sciences

Figure 1. Estimates of Agency Stem from a Series of Nested Inferences. In a given situation, individuals evaluate action–outcome contingencies. Low entropy (i.e., predictability) and high achievability of contingent action–outcome relationships support an inference of control, whereas the converse suggests a lack of control. An estimate of agency is drawn from multiple assessments of the controllability of important outcomes. We argue that this estimate, indicating the perceived breadth of an individual's influence, determines whether novel challenges are met with a proactive or reactive behavioral strategy. This, in turn, alters the manner in which the action–outcome contingencies in novel situations are explored and evaluated, creating a positive feedforward loop when the environment is consistently controllable. If action–outcome evaluation repeatedly supports inferences of minimal controllability, low agency estimates promote the kind of reactive responses best suited to an environment in which threats and challenges are not well managed through learned behavior.

deliberative action selection can yield a better outcome than the reactive 'default' behavior, the cognitive costs of proactive responding are warranted [8]. However, in uncontrollable contexts the cognitive and physical effort involved in exploration, contingency assessment, and action selection is wasted.

To the extent that individuals can correctly predict the level of control afforded by a new environment based on their past experience, they stand to benefit by calibrating their behavior accordingly. Conversely, mismatches between an individual's estimate of agency and the true degree of environmental controllability can be costly [9]. In the next section, we use defensive behavior as a means to examine how estimates of agency guide adaptive defensive responses by calibrating an individual's tendency to rely on proactive versus reactive behavioral strategies.

'Error Management' and Reactive Defensive Behavior

There are circumstances in which it can be adaptive to assume the worst. A shadow passing overhead or the sound of footsteps approaching from behind can signify the presence of a predator or an assailant. Yet in many situations, these cues may not signal threat at all. While such stimuli are ambiguous and interpretation of their significance is prone to error, not all errors are equally costly. Because undetected threats can have potentially lethal consequences, the mistaken assumption of safety in the presence of danger has a disproportionately high cost. By contrast, there is a much lower cost to incorrectly assuming danger when one is safe. According to error management theory, this asymmetry has fostered the evolution of threat detection systems that are innately biased toward false positives [10,11]. The tendency to assume danger in ambiguous situations is thus an adaptive default setting for defense circuits in the mammalian brain [2,5,6].

Threat evaluation circuits can protect the organism by evoking a reactive profile of defensive responses in response to the prediction of potential danger. These ingrained response strategies, as well as the physiological changes that promote them, are drawn from an innate behavioral repertoire. In rodents, for example, innate defensive reactions fall along a continuum determined by the proximity of danger [6]. Exploratory risk assessment occurs when a far-off danger is detected, transitioning to freezing when the source of danger is directly encountered and culminating with fleeing at the point of maximum peril. For instance, looming shadows, regardless of their source, tend to produce rapid immobility in rodents, probably because they signify a potential encounter with an avian predator [12]. Humans show an analogous continuum of defensive reactions, such as anxious checking, immobility, and flight [13,14]. As suggested above, these innate reactions offer the advantage of speed [5], which is crucial in moments of existential threat. Moreover, because of their relationship to consistent aspects of a species' behavioral ecology, they also represent a kind of evolutionarily hard-wired 'best guess' for how a given animal should respond to the potential worst-case scenario. In this manner, a threat evaluation system biased toward false positives can yield substantial adaptive benefits.

Opportunity Costs of Reactive Defensive Biases

While there are benefits to possessing a threat evaluation system that tends to produce false positives, there are also costs. Because defensive reactions typically divert attentional focus, arrest motion, and promote behavioral withdrawal from aversive stimuli, they have a highly disruptive effect on other adaptive behaviors. A classic example is conditioned suppression, a form of Pavlovian-to-instrumental transfer in which an aversive cue halts food-seeking behavior, even in animals highly motivated by hunger [15]. Defensive reactions across diverse species produce similar opportunity costs by interfering with foraging, various forms of social behavior, and other reward-motivated behaviors [16].

This fundamental tension between defense and other essential activities is at the heart of mammalian behavior, as described in optimal foraging theory [17]. A behavioral repertoire dominated by reactive defensive responses to ambiguous stimuli will fail to take advantage of the potential rewards afforded by the environment, while an under-reactive threat detection system can prove lethal. How does the organism strike a balance between appetitive action and defense that is appropriate for its environment?

We argue that estimations of agency are used to solve this problem by calibrating the brain circuits of defense. Given our conceptualizations of proactive and reactive behavior, an individual's position on the continuum between these opposing response profiles informs how threatening stimuli are evaluated and dealt with. If past experience dictates that danger tends to defy control, it is beneficial to produce a reactive defense even when stimuli are ambiguous. The resulting reaction, which can be elicited with minimal information, confers adaptive benefits by reducing the possibility of injurious false negatives (i.e., the mistaken assumption that one is safe when one is actually in danger). Conversely, when the environment tends to be controllable, threats can probably be addressed using an acquired behavioral strategy. False positives, by disrupting ongoing forms of adaptive behavior, will carry substantial opportunity costs.

Thus, estimations of agency can inform whether reactive or proactive behavioral strategies are likely to be most adaptive depending on what one's past experience suggests about the controllability of the environment. In the next section, we review empirical data that provide support for our account of how agency orchestrates defensive behavior.

Controllability Alters Defensive Behavior

Empirical research demonstrates the profound influence of controllability on defensive behavior. Corroborating early demonstrations of learned helplessness [1,3], exposure to uncontrollable electric shock in rodents increases defensive reactions (e.g., freezing) to threat-associated cues and contexts [18], induces endogenous opioid-mediated analgesia [19], attenuates social exploration [20], and impairs instrumental learning in later controllable contexts [21]. Strikingly, controllable shock exposure produces an opposing behavioral profile, decreasing freezing, increasing social exploration, and improving instrumental learning, often to levels exceeding those of unstressed control animals (see [22] for a review). Further evidence comes from the signaled active avoidance paradigm, in which animals learn that a shuttling action performed during a cue prevents shock delivery. Initially, animals freeze to the shock predictive cue, but as the proactive behavior is acquired, reactive behavior becomes suppressed [23]. Intriguingly, active avoidance training robs the aversive stimulus of its ability to disrupt ongoing forms of appetitive behavior (i.e., conditioned suppression). Presentation of the shock-predictive cue while animals are lever-pressing for food causes less behavioral interference in animals with previous avoidance training [24–26]. Similar to control over a shock itself, the ability to terminate the presentation of shock-predictive cues also attenuates subsequent reactive freezing [27].

There has been little direct examination directly comparing the effects of prior controllability on the response to certain versus ambiguous predictors of danger (e.g., the actual presence of a predator versus a looming shadow). Consistent with evidence that control does not diminish freezing to a predator odor [18], estimates of agency might specifically inform the response to ambiguous stimuli without altering the reactive response to aversive stimuli that are highly dangerous and definitively uncontrollable.

Bidirectional effects of controllability are also evident in humans, with uncontrollable shock potentiating and controllable shock diminishing subsequent physiological conditioned

responses to stimuli signaling potential threat [28] and control attenuating conditioned responses to novel learned threats [29]. Collectively these findings are consistent with our proposal that increases in agency engendered by control over shock yield a more proactive behavioral setting, attenuating the reactive response to threatening stimuli.

Strikingly, both the inference of controllability and its behavioral consequences appear to generalize across valence, suggesting that experiences of control over rewarding outcomes may be equally important as control over stressors in shaping an individual's reliance on proactive versus reactive behavioral strategies (Box 3).

The Amygdala and Pavlovian Defensive Reactions

In both humans and animals, the amygdala is a central node in the brain's threat-processing network (Figure 2). This cluster of nuclei in the medial temporal lobe can detect relationships between environmental stimuli and dangerous outcomes (i.e., aversive Pavlovian learning) and use this information to coordinate defensive reactions when those stimuli are encountered in the future. In a typical Pavlovian conditioning experiment, a rodent learns that a tone predicts an aversive shock. Subsequent presentation of the tone evokes a host of defensive reactions, including changes in cardiac output, altered hormonal levels in the blood, and immobility or freezing [30,31]. Information about the tone and shock is integrated in the lateral nucleus of the amygdala [32,33] before being routed to the central nucleus [34], which is a key output structure. The projection targets of the central amygdala, such as the periaqueductal gray of the midbrain (a key driver of freezing [35]), mediate distinct aspects of the response to the tone [36]. Via this circuitry, a tone associated with even a relatively mild shock can elicit an innate behavior designed to deter predation [6].

In humans, damage to the amygdala prevents the production of defensive reactions in response to a stimulus that predicts an aversive shock, although the declarative memory of learning remains intact [37,38]. Brain imaging data further support the role of the amygdala in threat processing and defense [39] while also suggesting the contribution of brainstem regions (e.g., the periaqueductal gray) to the expression of reactive defensive behavior [40]. These results lend support to the idea of a subcortical threat-processing system that is highly homologous in mammals.

Box 3. Inferences and Effects of Agency Generalize across Valence

Both the inference of agency and its modulation of subsequent behavior appear to generalize across aversive and appetitive valence domains. Providing animals with non-contingent 'free' food and water leads to later impairment in learning to obtain controllable contingent food rewards [73]. Furthermore, non-contingent reward impairs subsequent shock avoidance learning [74], indicating that lack of control over rewarding outcomes disrupts proactive learning in the aversive domain. Experience with operant control over various types of appetitive reinforcement has been reported to improve subsequent avoidance learning [74], increase exploratory behavior [75], and reduce neophobia [76]. Similarly, control over an aversive foot shock improves subsequent instrumental reward learning [77].

In a classic experiment [75], rats were reared from birth in a contingent environment in which they were able to control the delivery of food and water as well as lighting conditions. Compared with animals reared without control over these salient environmental elements, these rats showed a strong reduction in wall-clinging behavior in an open field, a defensive reaction to environments that lack cover but do not present any particular danger (an ambiguous potential threat). This reduction in reactive defensive responses facilitated their exploration of the novel test environment, an important aspect of the rat's basic foraging behavior.

Collectively, this evidence suggests that consistent experience with control over reinforcement, regardless of whether it is in the appetitive or the aversive domain, yields broad attenuation of reactive behaviors and promotes exploration and proactive goal-directed learning.

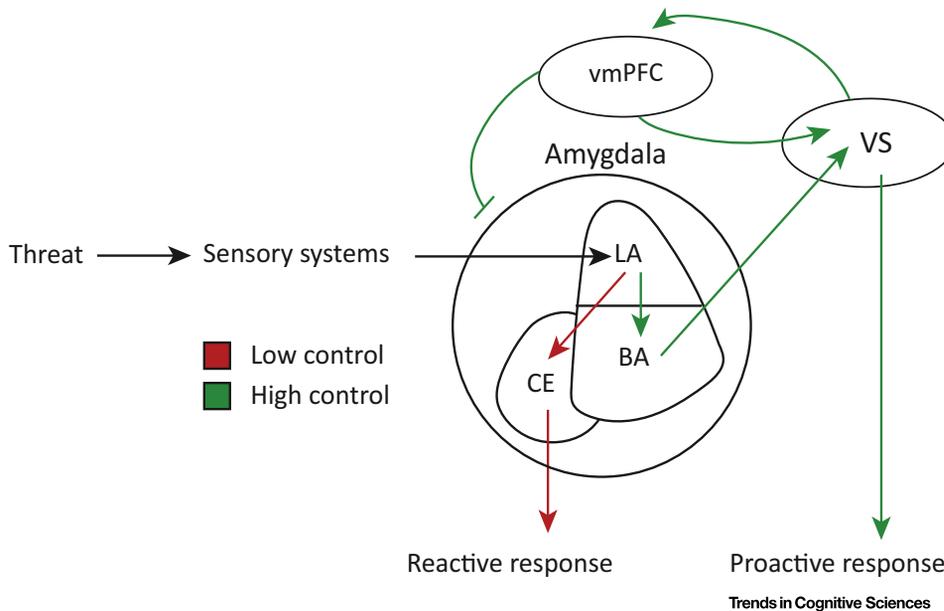


Figure 2. Proactive and Reactive Responses to Threatening Cues Are Mediated by Distinct Pathways Emanating from the Lateral Amygdala (LA). Arrows represent information flow across neural pathways that may be multisynaptic. Reactive behaviors require the flow of information from the LA to the central nucleus (CE), which projects to brainstem regions that underpin innate responses such as freezing. By contrast, proactive behaviors require the flow of information from the LA to the basal amygdala (BA), which projects to the ventral striatum (VS), an important substrate of active avoidance and other goal-directed behaviors. Connections between the striatum and prefrontal cortex implicated in action–outcome learning are proposed to play a central role in the detection of instrumental control. Resulting increases in activity in the ventromedial prefrontal cortex (vmPFC) reduce the expression of reactive behaviors via projections to the amygdala as well as other midbrain and brainstem nuclei.

The Neurocircuitry of Proactive Defensive Behavior

Proactive and reactive responses to threatening cues are mediated by distinct amygdalar output pathways. In a signaled avoidance paradigm in which an action performed during a tone can prevent the delivery of a shock, behavior is initially dominated by central amygdala-mediated Pavlovian reactions like freezing [41,42]. However, the proactive responses that influence aversive stimuli engage basal amygdalar outputs to the ventral striatum [43]. Thus, information about threat-predictive cues is integrated in the lateral amygdala [41], as in a purely Pavlovian paradigm, but are routed to distinct output projections depending on the animal's ability to exert control.

Convergent cross-species evidence suggests that the ventromedial prefrontal cortex (vmPFC) plays a central role in the calibration of defensive systems through estimates of agency. A circuit including the vmPFC and striatum is crucial for the detection of control over both aversive and appetitive outcomes [7,44], while vmPFC projections to serotonergic nuclei in the midbrain facilitate a desensitized response to stressors as a result of learned control [22]. Work on signaled avoidance suggests a similar role for the vmPFC, which suppresses defensive reactions and facilitates proactive responses as the animal learns to gain control over its circumstances [23]. In this context the vmPFC may act as a toggle between different amygdalar pathways encoding mutually exclusive responses to conditioned cues. We argue that the transition between distinct functional output circuits of the amygdala instantiates a shift along a continuum between reactive and proactive responses to conditioned threats, which is calibrated by the vmPFC on the basis of agency estimates.

Human neuroimaging studies largely corroborate this neural model. Individuals who learn an active response to avoid a predicted shock exhibit greater neural synchrony between the amygdala, the medial PFC, and the striatum than those who do not learn [45]. A similar recent study found that subjects who are able to actively avoid shock receipt show greater activity in the striatum and vmPFC than those who experience passive omission of shock [29]. Moreover, active avoiders exhibited greater vmPFC activation and reduced levels of Pavlovian responses during uncontrollable presentations of a threat-predictive cue the following day. Control over an anticipated fear-relevant stimulus increases vmPFC activation and amygdalar–vmPFC connectivity in patients with specific phobia [46], and individuals who report greater reliance on proactive coping strategies in their everyday lives exhibit increased vmPFC activation in response to an uncontrollable stressor [47]. Ethologically inspired fMRI studies have demonstrated that distal threats tend to engage the vmPFC, which is associated with the effective evasion of danger [40]. Controllability may produce a similar effect on the brain networks engaged by environmental threats, allowing recruitment of the vmPFC and other regions necessary to plan and implement complex threat prevention strategies [14]. Collectively these findings suggest that engagement of the amygdalar–striatal–vmPFC circuitry appears to play a critical role in the assessment and lasting behavioral consequences of control across a variety of mammalian species.

Real-World Controllability and Its Behavioral Consequences

Here we have proposed that individuals' life experiences of control give rise to an estimate of agency that informs their action tendencies. This notion closely resembles earlier psychological formulations of 'self-efficacy' beliefs [48], or a 'locus of control' [49,50], indexing whether environmental events are construed to be predominantly under their own 'internal' control or determined by 'external' factors. While these frameworks conceptualize control beliefs as stable trait-like characteristics, our account focuses on the dynamics of their construction as well as their potential for experience-dependent change.

How estimates of agency are inferred during development and how they shape behavioral trajectories has been a topic of little study. In infants, contingent positive outcomes facilitate and non-contingent outcomes impair subsequent instrumental learning and exploratory behavior, suggesting that controllability is assessed and generalizes to later behavior from early in development [51–53]. Control over aversive outcomes (e.g., hunger, threat) in infancy is achieved primarily through contingent caregiver responding. Accordingly, maternal responsiveness has been proposed to provide a foundation for control expectancies in infancy [54]. Recent work in rodents suggests that experiencing control over a stressor in adolescence promotes a proactive behavioral profile in adulthood [55]. This long-lasting effect depends on the same vmPFC region that is critical for the effects of control in adulthood, suggesting that early control experiences may promote a lasting bias toward proactive coping strategies. An important question for future research is whether there are specific 'sensitive periods' during development in which controllability, or a lack thereof, exerts particularly pronounced and persistent effects on an individual's behavioral repertoire.

Insight into the effects of high- and low-control rearing environments on affective and cognitive development may also be gleaned from studies examining the differential consequences of high and low socioeconomic status [56]. Low socioeconomic status (SES) is defined by a reduction in the ability to secure and control positive reinforcement and is associated with increased exposure to uncontrollable adversity (e.g., illness, eviction, violence). Low childhood SES is associated with deficits in working memory and cognitive control [57] and in the executive functions needed to support goal-directed behavior, as well as heightened risk for anxiety and depression [58]. Consistent with our suggestion that such effects may reflect a

low degree of environmental control, a key mediator of these behavioral outcomes is a high reported level of chaos in the home [59].

More generally, uncontrollable adverse life experiences are a primary risk factor for anxiety, mood, and stress-related disorders as well as substance abuse [60,61]. This increased vulnerability to multiple forms of psychopathology may stem in part from a common underlying shift toward a reactive behavioral profile due to estimates of low agency [62]. Such an etiological account suggests potential treatment approaches for these disorders that incorporate training in proactive coping behaviors [63].

Concluding Remarks and Future Perspectives

In the conceptual framework presented here, discovering contingent action–outcome associations yields an inference of control and repeated experiences of control over positive or negative reinforcers are aggregated into an estimate of agency. Agency, or the perceived breadth of one’s influence, is then used to calibrate behavioral responses in novel scenarios on a continuum ranging from proactive to reactive. This process of inference and generalization allows both humans and animals to draw on past experiences with control (or the lack thereof) to determine how best to respond to new environmental challenges. Future work is needed to clarify the principles that govern this generalization process [9,64] (see Outstanding Questions). We emphasize that, depending on an individual’s experience, both proactive and reactive responses can be adaptive. Goal-directed and exploratory behaviors can be advantageous in situations that are likely to be manageable through action, while relatively invariant behaviors drawn from an innate repertoire are advantageous in situations presumed to be unmanageable. The acquisition of agency estimates and their resulting influence on behavior depend on a complex brain circuitry including prefrontal, striatal, and amygdalar components. Controllability also modulates the functioning of multiple neuromodulatory systems (e.g., serotonin, dopamine, endocannabinoids) that are centrally implicated in the control of motivated behavior [65–68], although their detailed mechanistic roles within this functional architecture are not presently well understood. We propose that experience-dependent changes within these circuits exert an organizing role in cognitive and emotional functioning, giving rise to individual differences in the behavioral strategies used to cope with environmental challenges. Greater clarity on how controllability of life experiences differentially influences behavior across the lifespan may inform our understanding of the developmental origins of such differences. Importantly, while extensive research has focused on stressful life experiences as a risk factor for psychopathology, the perspective we have presented, supported by a large theoretical and empirical literature [1–3], suggests that the behavioral effects of negative (or positive) life experiences depend critically on the individual’s degree of control over those outcomes.

Acknowledgments

This work was supported by the Brain and Behavior Research Foundation (Young Investigator Grant to C.A.H.) and the National Science Foundation (CAREER grant 1654393 to C.A.H.).

References

1. Maier, S.F. and Seligman, M.E. (1976) Learned helplessness: theory and evidence. *J. Exp. Psychol. Gen.* 105, 3
2. Maier, S.F. and Seligman, M.E. (2016) Learned helplessness at fifty: insights from neuroscience. *Psychol. Rev.* 123, 349
3. Seligman, M.E. and Maier, S.F. (1967) Failure to escape traumatic shock. *J. Exp. Psychol.* 74, 1
4. Breland, K. and Breland, M. (1961) The misbehavior of organisms. *Am. Psychol.* 16, 681
5. Bolles, R.C. (1970) Species-specific defense reactions and avoidance learning. *Psychol. Rev.* 77, 32–48
6. Fanselow, M.S. and Lester, L.S. (1988) A functional behavioristic approach to aversively motivated behavior: predatory imminence as a determinant of the topography of defensive behavior. In *Evolution and Learning* (Bolles, R.C., ed.), pp. 185–212, Lawrence Erlbaum Associates
7. Balleine, B.W. and O’Doherty, J.P. (2009) Human and rodent homologies in action control: corticostriatal determinants of goal-directed and habitual action. *Neuropsychopharmacology* 35, 48–69
8. Boureau, Y.-L. et al. (2015) Deciding how to decide: self-control and meta-decision making. *Trends Cogn. Sci.* 19, 700–710
9. Huys, Q.J. and Dayan, P. (2009) A Bayesian formulation of behavioral control. *Cognition* 113, 314–328

Outstanding Questions

What are the inferential principles governing the generalization of controllable or uncontrollable experiences?

Are there sensitive periods during development in which controllability of reinforcement exerts particularly persistent effects?

Multiple neuromodulatory systems are sensitive to the controllability of experience. What roles do these systems play in the inference and behavioral consequences of control?

10. Haselton, M.G. *et al.* (2015) The evolution of cognitive bias. *Handb. Evol. Psychol.* Published online November 18, 2015. <http://dx.doi.org/10.1002/9780470939376.ch25>
11. McKay, R.T. and Dennett, D.C. (2009) The evolution of misbelief. *Behav. Brain Sci.* 32, 493–510
12. Yilmaz, M. and Meister, M. (2013) Rapid innate defensive responses of mice to looming visual stimuli. *Curr. Biol.* 23, 2011–2015
13. Blanchard, D.C. *et al.* (2001) Human defensive behaviors to threat scenarios show parallels to fear- and anxiety-related defense patterns of non-human mammals. *Neurosci. Biobehav. Rev.* 25, 761–770
14. Mobbs, D. and Kim, J.J. (2015) Neuroethological studies of fear, anxiety, and risky decision-making in rodents and humans. *Curr. Opin. Behav. Sci.* 5, 8–15
15. Bouton, M.E. and Bolles, R.C. (1980) Conditioned fear assessed by freezing and by the suppression of three different baselines. *Anim. Learn. Behav.* 8, 429–434
16. Kavaliers, M. and Choleris, E. (2001) Antipredator responses and defensive behavior: ecological and ethological approaches for the neurosciences. *Neurosci. Biobehav. Rev.* 25, 577–586
17. Stephens, D.W. and Krebs, J.R. (1986) *Foraging Theory*, Princeton University Press
18. Baratta, M. *et al.* (2007) Controllable versus uncontrollable stressors bi-directionally modulate conditioned but not innate fear. *Neuroscience* 146, 1495–1503
19. Grau, J.W. *et al.* (1981) Long-term stress-induced analgesia and activation of the opiate system. *Science* 213, 1409–1411
20. Christianson, J.P. *et al.* (2008) The role of prior stressor controllability and the dorsal raphe nucleus in sucrose preference and social exploration. *Behav. Brain Res.* 193, 87–93
21. Amat, J. *et al.* (2005) Medial prefrontal cortex determines how stressor controllability affects behavior and dorsal raphe nucleus. *Nat. Neurosci.* 8, 365–371
22. Maier, S.F. (2015) Behavioral control blunts reactions to contemporaneous and future adverse events: medial prefrontal cortex plasticity and a corticostriatal network. *Neurobiol. Stress* 1, 12–22
23. Moscarello, J.M. and LeDoux, J.E. (2013) Active avoidance learning requires prefrontal suppression of amygdala-mediated defensive reactions. *J. Neurosci.* 33, 3815–3823
24. Kamin, L. *et al.* (1963) Conditioned suppression as a monitor of fear of the CS in the course of avoidance training. *J. Comp. Physiol. Psychol.* 56, 497
25. Mineka, S. and Gino, A. (1980) Dissociation between conditioned emotional response and extended avoidance performance. *Learn. Motiv.* 11, 476–502
26. Bravo-Rivera, C. *et al.* (2014) Neural structures mediating expression and extinction of platform-mediated avoidance. *J. Neurosci.* 34, 9736–9742
27. Cain, C.K. and LeDoux, J.E. (2007) Escape from fear: a detailed behavioral analysis of two atypical responses reinforced by CS termination. *J. Exp. Psychol. Anim. Behav. Process.* 33, 451
28. Hartley, C.A. *et al.* (2014) Stressor controllability modulates fear extinction in humans. *Neurobiol. Learn. Mem.* 113, 149–156
29. Boeke, E.A. *et al.* (2017) Active avoidance: neural mechanisms and attenuation of Pavlovian conditioned responding. *J. Neurosci.* 37, 4808–4818
30. LeDoux, J.E. (2000) Emotion circuits in the brain. *Annu. Rev. Neurosci.* 23, 155–184
31. Moscarello, J.M. and LeDoux, J. (2014) Diverse effects of conditioned threat stimuli on behavior. *Cold Spring Harb. Symp. Quant. Biol.* 79, 11–19
32. Johansen, J.P. *et al.* (2011) Molecular mechanisms of fear learning and memory. *Cell* 147, 509–524
33. Maren, S. and Quirk, G.J. (2004) Neuronal signalling of fear memory. *Nat. Rev. Neurosci.* 5, 844–852
34. Jimenez, S.A. and Maren, S. (2009) Nuclear disconnection within the amygdala reveals a direct pathway to fear. *Learn. Mem.* 16, 766–768
35. Tovote, P. *et al.* (2016) Midbrain circuits for defensive behaviour. *Nature* 534, 206–212
36. LeDoux, J.E. *et al.* (1988) Different projections of the central amygdaloid nucleus mediate autonomic and behavioral correlates of conditioned fear. *J. Neurosci.* 8, 2517–2529
37. Bechara, A. *et al.* (1995) Double dissociation of conditioning and declarative knowledge relative to the amygdala and hippocampus in humans. *Science* 269, 1115–1118
38. LaBar, K.S. *et al.* (1995) Impaired fear conditioning following unilateral temporal lobectomy in humans. *J. Neurosci.* 15, 6846–6855
39. LaBar, K. *et al.* (1998) Human amygdala activation during conditioned fear acquisition and extinction: a mixed-trial fMRI study. *Neuron* 20, 937–945
40. Mobbs, D. *et al.* (2007) When fear is near: threat imminence elicits prefrontal-periaqueductal gray shifts in humans. *Science* 317, 1079–1083
41. Choi, J.-S. *et al.* (2010) The role of amygdala nuclei in the expression of auditory signaled two-way active avoidance in rats. *Learn. Mem.* 17, 139–147
42. Lázaro-Muñoz, G. *et al.* (2010) Sidman instrumental avoidance initially depends on lateral and basal amygdala and is constrained by central amygdala-mediated Pavlovian processes. *Biol. Psychiatry* 67, 1120–1127
43. Ramirez, F. *et al.* (2015) Active avoidance requires a serial basal amygdala to nucleus accumbens shell circuit. *J. Neurosci.* 35, 3470–3477
44. Amat, J. *et al.* (2014) Control over a stressor involves the posterior dorsal striatum and the act/outcome circuit. *Eur. J. Neurosci.* 40, 2352–2358
45. Collins, K.A. *et al.* (2014) Taking action in the face of threat: neural synchronization predicts adaptive coping. *J. Neurosci.* 34, 14733–14738
46. Kerr, D.L. *et al.* (2012) Controllability modulates the anticipatory response in the human ventromedial prefrontal cortex. *Front. Psychol.* 3, 557
47. Sinha, R. *et al.* (2016) Dynamic neural activity during stress signals resilient coping. *Proc. Natl. Acad. Sci. U. S. A.* 113, 8837–8842
48. Bandura, A. (1977) Self-efficacy: toward a unifying theory of behavioral change. *Psychol. Rev.* 84, 191
49. Lefcourt, H.M. (1982) *Locus of Control: Current Trends in Theory and Research*, Lawrence Erlbaum Associates
50. Rotter, J.B. (1966) Generalized expectancies for internal versus external control of reinforcement. *Psychol. Monogr. Gen. Appl.* 80, 1
51. Finkelstein, N.W. and Ramey, C.T. (1977) Learning to control the environment in infancy. *Child Dev.* 48, 806819
52. Gunnar, M.R. (1980) Contingent stimulation: a review of its role in early development. In *Coping and Health* (Levine, S. and Ursin, H., eds), pp. 101–119, Springer
53. Tarabulsky, G.M. *et al.* (1996) Contingency detection and the contingent organization of behavior in interactions: implications for socioemotional development in infancy. *Psychol. Bull.* 120, 25
54. Lewis, M. and Goldberg, S. (1969) Perceptual-cognitive development in infancy: a generalized expectancy model as a function of the mother-infant interaction. *Merrill Palmer Q. Behav. Dev.* 15, 81–100
55. Kubala, K.H. *et al.* (2012) Short- and long-term consequences of stressor controllability in adolescent rats. *Behav. Brain Res.* 234, 278–284
56. Hackman, D.A. *et al.* (2010) Socioeconomic status and the brain: mechanistic insights from human and animal research. *Nat. Rev. Neurosci.* 11, 651–659
57. Noble, K.G. *et al.* (2007) Socioeconomic gradients predict individual differences in neurocognitive abilities. *Dev. Sci.* 10, 464–480
58. Shanahan, L. *et al.* (2008) Specificity of putative psychosocial risk factors for psychiatric disorders in children and adolescents. *J. Child Psychol. Psychiatry* 49, 34–42
59. Evans, G.W. *et al.* (2005) The role of chaos in poverty and children's socioemotional adjustment. *Psychol. Sci.* 16, 560–565
60. Koob, G.F. (2008) A role for brain stress systems in addiction. *Neuron* 59, 11–34

61. Lupien, S.J. *et al.* (2009) Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nat. Rev. Neurosci.* 10, 434–445
62. Nees, F. *et al.* (2015) A mechanism-oriented approach to psychopathology: the role of Pavlovian conditioning. *Int. J. Psychophysiol.* 98, 351–364
63. LeDoux, J.E. and Gorman, J.M. (2001) A call to action: overcoming anxiety through active coping. *Am. J. Psychiatry* 158, 1953–1955
64. Lieder, F. *et al.* (2013) Learned helplessness and generalization. *Proceedings of the 35th Annual Conference of the Cognitive Science Society, Cognitive Science Society*
65. Fiore, V.G. *et al.* (2015) Corticolimbic catecholamines in stress: a computational model of the appraisal of controllability. *Brain Struct. Funct.* 220, 1339–1353
66. Lloyd, K. and Dayan, P. (2016) Safety out of control: dopamine and defence. *Behav. Brain Funct.* 12, 15
67. Maier, S.F. and Watkins, L.R. (2005) Stressor controllability and learned helplessness: the roles of the dorsal raphe nucleus, serotonin, and corticotropin-releasing factor. *Neurosci. Biobehav. Rev.* 29, 829–841
68. Worley, N.B. *et al.* (2017) Prefrontal endocannabinoids, stress controllability and resilience: a hypothesis. *Prog. Neuropsychopharmacol. Biol. Psychiatry* Published online April 7, 2017. <http://dx.doi.org/10.1016/j.pnpbp.2017.04.004>
69. Sutton, R.S. and Barto, A.G. (1998) *Reinforcement Learning: An Introduction*, MIT Press
70. Maren, S. *et al.* (2013) The contextual brain: implications for fear conditioning, extinction and psychopathology. *Nat. Rev. Neurosci.* 14, 417–428
71. Bouton, M.E. and Swartzentruber, D. (1986) Analysis of the associative and occasion-setting properties of contexts participating in a Pavlovian discrimination. *J. Exp. Psychol. Anim. Behav. Process.* 12, 333
72. Holland, P.C. (1992) Occasion setting in Pavlovian conditioning. *Psychol. Learn. Motiv* 28, 69–125
73. Overmier, J.B. *et al.* (1980) Environmental contingencies as sources of stress in animals. In *Coping and Health* (Levine, S. and Ursin, H., eds), pp. 1–38, Springer
74. Goodkin, F. (1976) Rats learn the relationship between responding and environmental events: an expansion of the learned helplessness hypothesis. *Learn. Motiv.* 7, 382–393
75. Joffe, J. *et al.* (1973) Control of their environment reduces emotionality in rats. *Science* 180, 1383–1384
76. Mineka, S. *et al.* (1986) Control and early socioemotional development: infant rhesus monkeys reared in controllable versus uncontrollable environments. *Child Dev.* 57, 1241–1256
77. Lucas, M. *et al.* (2014) Long-term effects of controllability or the lack of it on coping abilities and stress resilience in the rat. *Stress* 17, 423–430