CHAPTER

Quantifying motivation with effort-based decision-making paradigms in health and disease

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Abstract

Motivation can be characterized as a series of cost–benefit valuations, in which we weigh the amount of effort we are willing to expend (the cost of an action) in return for particular rewards (its benefits). Human motivation has traditionally been measured with self-report and questionnaire-based tools, but an inherent limitation of these methods is that they are unable to provide a mechanistic explanation of the processes underlying motivated behavior. A major goal of current research is to quantify motivation objectively with effort-based decision-making paradigms, by drawing on a rich literature from nonhuman animals. Here, we review this approach by considering the development of these paradigms in the laboratory setting over the last three decades, and their more recent translation to understanding choice behavior in humans. A strength of this effort-based approach to motivation is that it is capable of capturing the wide range of individual differences, and offers the potential to dissect motivation into its component elements, thus providing the basis for more accurate taxonomic classifications. Clinically, modeling approaches might provide greater sensitivity and specificity to diagnosing disorders of motivation, for example, in being able to detect subclinical disorders of motivation, or distinguish a disorder of motivation from related but separate syndromes, such as depression. Despite the great potential in applying effort-based paradigms to index human motivation, we discuss several caveats to interpreting current and future studies, and the challenges in translating these approaches to the clinical setting.

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1 WHAT IS MOTIVATION?

Life is replete with instances in which we must weigh the potential benefits of a course of action against the associated amount of effort. Students must decide how intensively to study for an exam based on its importance. Employees decide how much effort to put into their jobs given their wage. Motivation is that process which facilitates *overcoming the cost of an effortful action to achieve the desired outcome*. It is a complex and multifaceted phenomenon, operating in several different domains: motivation to take a course of action, or to engage in cognitive effort, or to engage in emotional interaction. It is also influenced by many developmental, cultural, and environmental factors. A further challenge in studying motivation across individuals is that there is significant interindividual variability, ranging from healthy individuals who are highly motivated, to patients with disorders of motivation who suffer from debilitating disorders of diminished motivation, such as apathy.

Our current understanding of motivation has been shaped by the prescient observations of early philosophers and psychologists. In the 19th century, Jeremy Bentham cataloged a table of the "springs of action" that operate on the will to motivate one to act (Bentham, 1817). Shortly after this, William James, inspired by Darwin's recently published *Theory of Natural Selection* (Darwin, 1859), favored a more biological approach. He suggested that motivation comprised genetically programmed "instincts," which maintained or varied behavior in the face of changing circumstances to promote survival (James, 1890). Developing this idea, William McDougall outlined the instinct theory of motivation, in which he attributed all human behavior to 18 "instincts," or motivational dispositions (McDougall, 1908). He proposed that these instincts were important in driving goal-oriented behavior, which requires one to first attend to certain objects (the perceptual or cognitive component); experience an emotional excitement when perceiving that object (the emotional component); and initiate an act toward that object (the volitional component). This idea of fixed instincts later evolved to the concept of "needs" or "drives" giving rise to motivated behavior (Hull, 1943; Maslow, 1943).

More recently, motivation has been conceptualized as the behaviorally relevant processes that enable an organism to regulate its external and/or internal environments (Ryan and Deci, 2000; Salamone, 1992). These processes typically involve sensory, motor, cognitive, and emotional functions working together (Pezzulo and Castelfranchi, 2009; Salamone, 2010). However, only in the last few decades has attention turned to uncovering the precise mechanisms underlying motivated behavior in humans. Traditionally, studies on human motivation have been qualitative, or relied on subjective self-report or questionnaire-based measures (Table 1). The limitation of a questionnaire-based approach is that it is necessarily limited in its ability

Table 1 Questionnaires in Common Use to Measure Motivation in Healthy Individuals and Patients with Disorders of Diminished Motivation (eg, Apathy)

Healthy Individuals[a]	
Academic Amotivation Inventory	Legault et al. (2006)
Academic Motivation Scale	Vallerand et al. (1992)
Intrinsic Motivation Inventory	Choi et al. (2009) and Ryan (1982)
Sports Motivation Scale	Pelletier et al. (1995)
Patients[b]	
Apathy Evaluation Scale	Marin et al. (1991)
Apathy Inventory	Robert et al. (2002)
Apathy Scale	Starkstein et al. (1992) and Starkstein et al. (2001)
Behavioral Assessment of Dysexecutive Syndrome	Norris and Tate (2000)
Brief Psychiatric Rating Scale	Overall and Gorham (1962)
Dementia Apathy Interview and Rating	Strauss and Sperry (2002)
Dimensional Apathy Scale	Radakovic and Abrahams (2014)
Frontal Systems Behavior Scale	Grace and Malloy (2001)
Irritability Apathy Scale	Burns et al. (1990)
Key Behavior Change Inventory	Belanger et al. (2002)
Lille Apathy Rating Scale	Sockeel et al. (2006)
Neuropsychiatric Inventory	Cummings et al. (1994)
Positive and Negative Syndrome Scale	Kay et al. (1987)
Scale for the Assessment of Negative Symptoms	Andreasen (1984)

[a] *Questionnaires validated for healthy individuals do not contain defined cut-offs for lack of motivation (eg, Pelletier et al., 1995; Vallerand et al., 1992).*

[b] *Patient questionnaires either focus entirely on apathy, or include questions on apathy as one or more items within their inventory.*

to provide a mechanistic account of the processes underlying motivated behavior. Curiously, the questionnaires that are in use today have either been validated for use in the healthy population, or in patients (see Weiser and Garibaldi, 2015, for an extensive review), but few are in common use to measure motivation in both populations. This is likely to reflect historical trends, as current evidence suggests that motivation in health and disease is likely to be on a continuum (Chong and Husain, 2016).

The importance of being able to objectively characterize the cost–benefit processes that underlie motivated behavior is especially important in the clinical domain. Disorders of motivation, such as apathy, are common in several neurological and psychiatric disorders, such as Parkinson's disease (PD), stroke, depression, and schizophrenia. However, apathy is often under-recognized and undertreated, with one of the reasons being that we lack of a sensitive means to classify these disorders, and track their response to treatment. Questionnaires rely on patients having sufficient insight to respond to the questions that are posed, which is often not the case (de Medeiros et al., 2010; Njomboro and Deb, 2012; Starkstein et al., 2001). Although several questionnaires attempt to take this into account by providing alternative versions based on information provided by a caregiver, some other informant, or the clinician, responses to these multiple versions often only marginally concur (Chase, 2011).

Ultimately, therefore, there is a significant need to develop more objective methods to better characterize the mechanisms underlying human motivation, in both health and disease. Here, we discuss the utility of translating effort-based decision-making paradigms from the literature on nonhuman animals to index human motivation. For this reason, we do not consider emotional motivation, but focus on studies of effort operationalized in the physical and cognitive domains. This review primarily aims to summarize the potential and the limitations of the numerous methodologies that have been reported; a more detailed discussion of the underlying neurobiology of motivation is presented separately (Chong and Husain, 2016).

2 MOTIVATION AS EFFORT FOR REWARD

Recently, there has been a surge of interest in developing a mechanistic account of the neural and computational processes underlying motivated behavior in human health and disease. The vast majority of studies on the neurobiology of decision-making have inferred an animal's motivation by observing its response to rewarding outcomes. For example, a large corpus of studies has examined the effect of varying the delay—*temporal discounting*—or uncertainty of an outcome—*risk aversion* and *probability discounting* (Cardinal, 2006). In the language of more contemporary behavioral studies of motivation, animals must compute the perceived value (or "utility") of the motivational stimulus vs the costs (such as delay or uncertainty) involved in obtaining it (Salamone and Correa, 2012). Motivation has therefore been conceptualized in neuroeconomic terms as a cost–benefit trade-off, in which the animal seeks to maximize utility while minimizing the associated cost.

Effort Is Costly: In the last 5 years, particular interest has focused on another important component of motivation—namely, the amount of effort that an animal must be prepared to invest for a given reward. Effort, like delay and uncertainty, is usually perceived as a cost. It is particularly salient and aversive—so much so that a consistent finding across species is that animals will seek to minimize the amount of effort that they exert in pursuit of a given reward (Hull, 1943). Consequently, effort has the effect of *devaluing* the reward associated with it, such that the greater amount of effort that is required, the less the subjective value of the reward to the individual. This phenomenon is known as, "effort discounting."

This recent interest in human effort-related processes is grounded in a rich and substantial history of similar research in nonhuman animals, led predominantly by the pioneering work of John Salamone and his colleagues (Salamone and Correa, 2012; Salamone et al., 2006, 2007). These approaches have been extremely useful in capturing individual differences in animals, and providing an insight into the neural activity that underlies the trade-off between effort and reward. The many effort-based decision-making paradigms that have been developed in animals therefore offer a solid foundation on which to construct models of motivated behavior and motivational dysfunction in humans.

Effort-Based Decision-Making Is Useful to Capture Individual Differences: Motivation has been conceptualized as comprising two distinct phases. Both are usually driven by the presence of a target object that is typically a reward or highly valued reinforcer to the organism (eg, a preferred food). Usually, however, these rewards are not immediately available, and the organism must first overcome any distances or barriers between it and the target object (Pezzulo and Castelfranchi, 2009; Ryan and Deci, 2000; Salamone, 2010; Salamone and Correa, 2012). The first phase of motivated behavior therefore requires the organism to initiate behaviors that bring it in close proximity of the reward (the *approach phase*, also sometimes referred to as the preparatory/appetitive/seeking phase), before the reward can ultimately be consumed (the *consummatory phase*) (Craig, 1917; Markou et al., 2013).

The animal's behavior during the approach phase, therefore, represents the amount of effort that it is willing to exert in return for the reward on offer. It reflects behavior that is highly adaptive, as it enables the organism to exert effort to overcome the costs separating it from its rewards (Salamone and Correa, 2012). Importantly, however, although animals in general will seek to minimize effort, *individual animals* will differ in terms of the minimum amount of effort they are willing to invest for a given reward. Observing choice behavior during this approach phase of a decision-making task is therefore a particularly useful means to index the individual variability in motivation.

Effort Can Be Operationalized in Different Domains: One factor that influences the way in which effort interacts with reward to constrain choice behavior relates to the domain in which effort must be exerted (Fig. 1). Effort is often operationalized in terms of some form of physical requirement. In nonhuman animals, for example, it has been defined in terms of the height of a barrier to scale; the weight of a lever press; the number of handle turns; or the number of nose-pokes. Given that much of the research on effort-based decision-making has emerged from the animal literature, it is unsurprising that effort in human studies is also often defined physically—for example, as the number of button presses on a keyboard (Porat et al., 2014; Treadway et al., 2009), or the amount of force delivered to a hand-held dynamometer (Bonnelle et al., 2016; Chong, 2015; Chong et al., 2015; Cléry-Melin et al., 2011; Kurniawan et al., 2010; Prévost et al., 2010; Zénon et al., 2015).

However, effort can be perceived not only physically, but in the cognitive domain as well. Studies examining cognitive effort-based decisions in nonhuman animals are extremely rare, due to the associated challenges in training the animals to perform the task. One of the few attempts to do so was reported recently, and required rodents to identify in which one of five locations a target stimulus appeared, with cognitive effort being manipulated as the duration for which the target stimulus remained

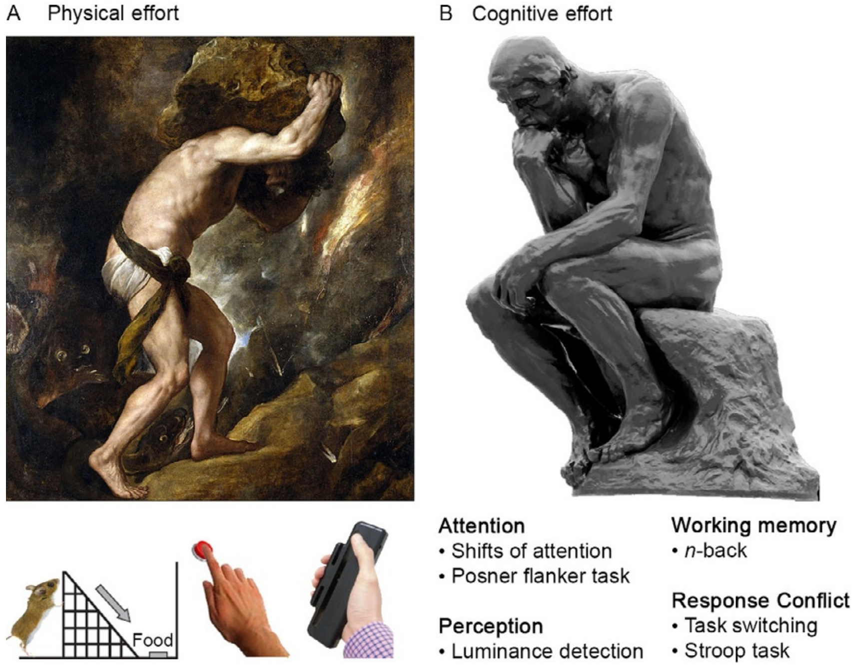

FIG. 1

Effort is typically operationalized in the physical and cognitive domains. (A) Physical effort has been manipulated in terms of the height or steepness of a barrier that an animal must overcome in pursuit of reward, or, in humans, as the number of button presses, or the amount of force applied to a hand-held dynamometer. (B) Cognitive effort in humans has been manipulated across several cognitive faculties. Note that many effortful tasks are aversive, not only because of the associated physical or cognitive demand, but also because of the greater amount of time it takes to complete the task, and the lower likelihood of completing it. For example, pushing a boulder up a mountain is aversive, not only because of the physical demand involved, but also because of the amount of time it would take, and the low probability of successfully accomplishing the task. In the case of Sisyphus, the effort involved in pushing the boulder up the mountain is considerable; the time it would take for him to do so and successfully maintain it at the peak is an eternity; and the probability of him completing the task is zero, thus infinitely reducing the subjective value of this course of action (and vindicating it as a suitable form of divine retribution). The distinction between effort, temporal, and probability discounting is discussed in Section 3.5.

Image credits: Left—*Titian, 1549,* Sisyphus*, Oil on canvas, 217 × 216 cm, Museo del Prado, Madrid.*
Right—*Rodin, c1904,* Le Penseur*, Bronze, Musée Rodin, Paris.*

on (Hosking et al., 2014, 2015). In humans, there has been growing interest in the neural mechanisms that underlie cognitive effort-based decisions. Typically in these studies, cognitive load is manipulated in paradigms involving spatial attention (Apps et al., 2015), task switching (Kool et al., 2010; McGuire and Botvinick, 2010), conflict (eg, the Stroop effect (Schmidt et al., 2012)), working memory (eg, as an *n*-back task (Westbrook et al., 2013)), and perceptual effort tasks similar to those described previously (Reddy et al., 2015). These studies confirm that, like physical effort, cognitive demands carry an intrinsic effort cost (Dixon and Christoff, 2012; Kool et al., 2010; McGuire and Botvinick, 2010; Westbrook et al., 2013).

In summary, organisms must be sensitive to effort-related response costs, and make decisions based upon cost/benefit analyses. Today, we have a great deal of knowledge on the neural circuits that process information about the value of motivational stimuli, the value and selection of actions, and the regulation of cost/benefit decision-making processes that integrate this information to guide behavior (Croxson et al., 2009; Guitart-Masip et al., 2014; Kable and Glimcher, 2009; Phillips et al., 2007; Roesch et al., 2009). Much of this knowledge on the neurobiological determinants of decision-making has been gleaned from paradigms in nonhuman animals, involving operant procedures requiring responses on ratio schedules for preferred rewards, or dual-alternative tasks in the form of T-maze barrier procedures. In the following section, we survey the development of these different paradigms in effort-based decision-making in nonhuman animals, prior to considering their utility in human studies of motivated decision-making (Fig. 2).

3 EXPERIMENTAL APPROACHES TO EFFORT DISCOUNTING

3.1 FIXED AND PROGRESSIVE RATIO PARADIGMS

Operant conditioning paradigms are a commonly used approach to determining the willingness of an animal to work for reward (Fig. 2A) (Randall et al., 2012; Salamone et al., 1991, 2002; Schweimer and Hauber, 2005). Typically, the animal is first trained to perform an action in return for a reward (Hodos, 1961). In a *fixed ratio* (FR) study, a predefined number of operant responses are required to receive one unit of reinforcer (eg, five lever-presses for one unit of reward) (Salamone et al., 1991). In a *progressive ratio* (PR) paradigm, the number of operant responses required to obtain one unit of reward gradually increases over sequential trials—for example, in an exponential design, the number of nose-pokes required for the delivery of successive rewards might be 2, 4, 8, 16, 32, etc. (Beeler et al., 2012; Randall et al., 2012).

Relative to FR paradigms, PR paradigms have been found to generate greater response variability, which has been useful to study individual differences in behavior (Randall et al., 2012, 2014). By requiring the animal to repeatedly make choices between effort and reward under conditions in which the ratio requirement gradually increases, PR paradigms use the *break-point* as the key metric of motivation. The break-point is the last ratio that the animal is willing to complete for the reward on offer, and therefore represents the maximum amount of effort that it is willing to execute for that reward (Richardson and Roberts, 1996).

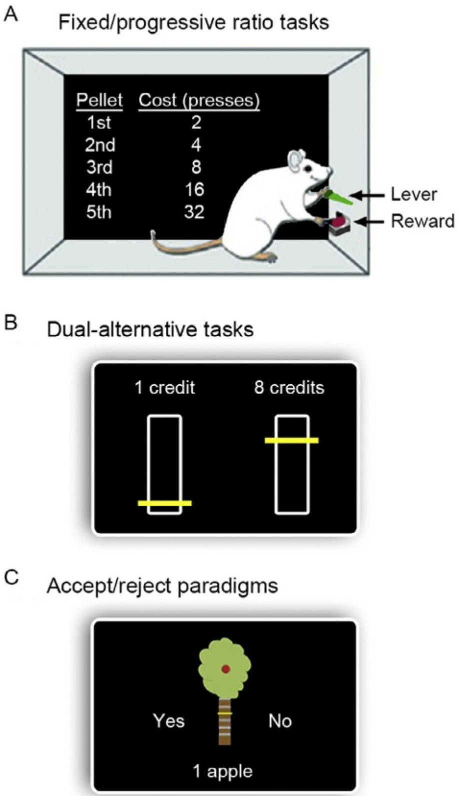

FIG. 2

Different approaches to effort-based decision-making. (A) In an operant paradigm, the subject decides how much effort to invest for a given reward. Illustrated is a progressive ratio paradigm. (B) In a dual-alternative paradigm, participants choose between two options—for example, a fixed baseline option vs a variable, more valuable, offer. In the example, participants choose whether they prefer to exert the lowest level of effort for 1 credit, or a higher level of effort for 8 credits. (C) In an accept/reject paradigm, participants are offered a single combination of effort and reward, and they decide to accept or reject the given offer. Here, participants choose whether they are willing to exert a high level of effort (indicated by the *yellow* bar) for the given reward (1 apple).

Panel B: After Apps, M., Grima, L., Manohar, S., Husain, M., 2015. The role of cognitive effort in subjective reward devaluation and risky decision-making. Sci. Rep. 5, 16880. Panel C: Adapted from Chong, T.T.-J., Bonnelle, V., Manohar, S., Veromann, K.-R., Muhammed, K., Tofaris, G., Hu, M., Husain, M., 2015. Dopamine enhances willingness to exert effort for reward in Parkinson's disease. Cortex 69, 40–46.

PR paradigms have been used for decades, primarily to study the reinforcing effects of psychostimulants and drug-seeking behavior in rodents (Richardson and Roberts, 1996; Stoops, 2008). More recently, several groups have used these tasks in humans to index motivation. For example, studies in children have used lever-press responses in return for monetary rewards, and found that break-points vary as a function of age and gender (Chelonis et al., 2011a). Similar investigations have shown that break-points can be increased following administration of psychostimulants such as methylphenidate, which increase levels of monoamines including dopamine (Chelonis et al., 2011b). In contrast, acute phenylalanine/tyrosine depletion, which reduces dopamine levels, has the effect of lowering break-points (Venugopalan et al., 2011). Such reports link parsimoniously with the literature in animals, by showing the importance of dopamine in increasing the motivation to work for reward (Chong and Husain, 2016).

In attempting to understand the mechanisms of motivated decision-making, it is particularly important to disentangle *choices* from the associated instrumental responses. A limitation of PR paradigms is that they are unable to do so unambiguously. Specifically, the break-points determined in a PR paradigm represent both the amount of effort that an animal is willing to invest for a particular reward, as well as the amount of effort that it is physically capable of performing for that reward. Thus, they are a function, not only of the animal's preferences, but also motor parameters that may be secondarily and nonspecifically affected by the experimental manipulation. This may be particularly important in the case of dopaminergic manipulations, as dopamine is known to augment the vigor with which physical responses are made (Niv et al., 2007), and the task would therefore be unable to disentangle the effect of dopamine on motivation vs its motor effects. In sum, a potential difficulty with operant conditioning paradigms in motivation research is that a lower break-point can be viewed as either a reduced willingness to expend effort, or due to a reduction in motor activity.

3.2 DUAL-ALTERNATIVE DESIGNS IN NONHUMAN ANIMALS

One paradigm that has been used to examine effort-based choices involves providing animals with a choice between a highly valued reinforcer (eg, a greater amount of food or a preferred food such as Bioserve pellets) and a less-valued reinforcer (eg, a smaller amount of food or lab chow) that is concurrently available. The key manipulation is that the rodent is required to exert a particular amount of effort (eg, climbing a barrier) to obtain the more valued reward. At baseline, most rodents will be willing to exert a greater amount of effort in exchange for the more valuable reward (Salamone et al., 1991).

The classic design in rodents involves the animal having to make a choice between the two offers in a T-maze procedure (Cousins et al., 1996; Salamone et al., 1994; Walton et al., 2002). It is first trained to learn the locations of the less- and more highly valued reinforcer, which are placed in opposite arms of the T-maze. Then, after an experimental intervention (a lesion or pharmacological manipulation), a physical barrier is added to the high-reward arm, which the animal must now overcome to obtain the more lucrative offer. The rate at which the high-effort/high-reward offer is chosen can be taken as a proxy of the animal's motivation, and one can then compare differences in these rates as a function of the experimental manipulation.

An advantage of this paradigm over the PR paradigm is that here it is possible to separate choice (the progression of a rodent down one arm of the T-maze) from motor execution (climbing the barrier). However, it remains important to ensure that the animal's choices are not influenced by the probability that they will succeed in overcoming that barrier to reach the reward. In addition, one potential limitation of this design is that the reinforcement magnitude for each arm typically remains the same on each trial. Thus, as the rodents become satiated after repeated visits to the large-reward arm, choice behavior may be more variable during later trials, which may in turn reduce the sensitivity of the task to different manipulations (Denk et al., 2005).

To overcome this reservation, the paradigm subsequently evolved to vary the amount of reward on offer in what has been termed an *effort-discounting* paradigm (Bardgett et al., 2009; Floresco et al., 2008). In this version, after a rodent chooses a high-reward option, the total reward available on that arm is reduced by one unit prior to the subsequent trial. By repeating this procedure until the rodent chooses the small-reward arm, it is possible to derive the *indifference points* between two choices to calculate sensitivities to different costs and reward amounts (Richards et al., 1997). This may be a more sensitive approach to determining the neurobiological substrates of effort-based decision-making (Green et al., 2004; Richards et al., 1997).

Over the last 35 years, these dual-alternative tasks have been of great utility in identifying the distributed circuit that regulates motivated decision-making in rodents. By systematically inactivating or lesioning specific components of the putative reward network, T-maze procedures have revealed that dopamine depletion in the nucleus accumbens biases rats toward the low-effort/low-reward option (Cousins et al., 1996; Salamone et al., 1994). Using similar procedures, lesions of the rodent medial prefrontal cortex, including the anterior cingulate cortex, led to fewer effortful choices, in contrast to lesions of the prelimbic/infralimbic and orbitofrontal cortices, which did not (Rudebeck et al., 2006; Walton et al., 2002, 2003). A final important example of the utility of the T-maze procedure is that bilateral inactivation of the basolateral amygdala, or unilateral inactivation of the basolateral amygdala concurrent with inactivation of the contralateral anterior cingulate cortex, decreases effortful behavior driven by food reward (Floresco and Ghods-Sharifi, 2007).

In summary, much of the knowledge that we have now of the neural regions responsible for effort-based decision-making has been based on applying these simple effort-discounting paradigms (Font et al., 2008; Ghods-Sharifi and Floresco, 2010; Hauber and Sommer, 2009; Mingote et al., 2008; Nunes et al., 2013a,b; Salamone and Correa, 2012; Salamone et al., 2007).

3.3 DUAL-ALTERNATIVE DESIGNS IN HUMANS

Given the utility of dual-alternative paradigms in animals, several tasks have been designed to translate these effort-discounting paradigms to humans (Fig. 2B). One example of a task that was inspired by the T-maze procedures in rodents is the effort expenditure for rewards task (Treadway et al., 2009; Wardle et al., 2011). In this task, effort is operationalized as the number of button presses delivered in a fixed period of time. The high-effort condition typically requires 100 button presses using the nondominant fifth digit within 21 s, whereas the low-effort condition requires 30 button presses using the dominant index finger within 7 s. The reward for successfully completing the low-effort task was fixed at \$1.00, but that for the high-effort task was varied between \$1.24 and \$4.30. This experiment also included a probabilistic component to the reward outcome, such that successful completion of each trial was rewarded with either high (88%), medium (50%), or low (12%) probability, and participants were informed of this prior to the beginning of the trial.

The most straightforward approach to analysing such data is to define motivation as the proportion of trials in which participants opt for the high-effort/high-reward option relative to the low-effort/low-reward option. This simple *ratio measure* has been used to characterize effort-based decision-making in several patient populations, including depression (Treadway et al., 2012a), schizophrenia (Barch et al., 2014), and autism (Damiano et al., 2012). For example, patients with major depressive disorder are typically less willing to choose the high-effort/high-reward option than healthy controls (Treadway et al., 2012a), as are patients with schizophrenia with a high degree of negative symptoms (Gold et al., 2013). In contrast, patients with autism spectrum disorder were more willing to expend effort than controls, regardless of the reward contingencies (Damiano et al., 2012).

In addition to ratio analyses, data from dual-alternative paradigms can also be subject to *computational modeling approaches*, to quantify effort discounting within individual subjects. For example, a recent study aimed to model effort discounting in a physical effort task (Klein-Flügge et al., 2015). Participants were required to exert sustained contractions on a hand-held dynamometer for a fixed duration of time, and at varying levels of force. The levels of force for each subject were independently calibrated to their maximal voluntary contraction (MVC). They were then required to choose between a low-effort/low-reward option and a high-effort/high-reward offer, with the magnitude of the effort and reward varied from trial to trial.

The authors then fitted several models of effort discounting—including linear, quadratic, hyperbolic, and sigmoidal functions—which differ in their predictions of how effort should subjectively devalue the reward on offer (Fig. 3). For example, linear models would predict constant discounting of value with increasing effort, such that an additional fixed cost devalues reward by the same amount. These linear models have been suggested in the context of effort-based choice behavior when persistent effort has to be made over time (eg, repeated lever presses). In contrast, concave models (eg, parabolic) would predict that changes in effort at higher levels would have greater impact on subjective value than changes at lower levels, and

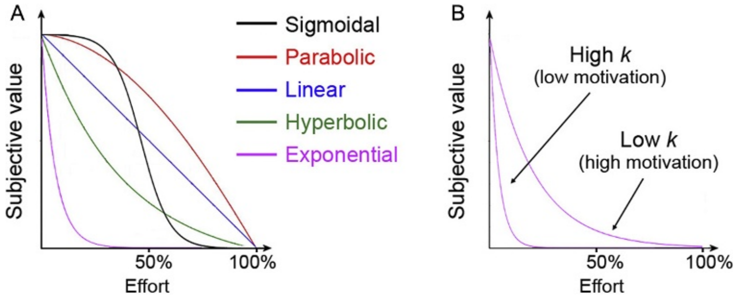

FIG. 3

Effort-discounting functions are useful to quantify individual differences in motivated decision-making. (A) Classes of function that have been used to computationally model effort-discounting behavior. These functions differ in their predictions of how effort should subjectively devalue the reward on offer. (B) An example of the utility of modeling effort discounting to capture individual differences. Two hypothetical participants are illustrated here in the context of a task in which effort discounting is exponential. The less motivated individual has a steeper discounting function, as indexed by a higher discounting parameter (k). These parameters can then be used to compare individual differences in motivation.

convex models (eg, hyperbolic) would predict the opposite. With Bayesian model comparisons, the authors found that a sigmoidal model, incorporating characteristics of both the concave and convex functions, appeared to best describe effort-discounting behavior.

By fitting sigmoidal functions to individual participants, it was possible to derive unique, subject-specific parameters that describe each individual's effort discounting. In this specific instance, the parameters fitted included the steepness of the curve and the turning point of the sigmoid. Although deriving these parameters was not the principal aim of this study (which was to compare effort and temporal discounting), the approach demonstrates the potential utility of deriving specific parameters which may then be used to index individuals' motivation, and to follow it over the course of a disease or of treatment.

A third approach to quantify effort-based decisions in individuals is to use *staircase paradigms* in order to derive subject-specific effort indifference points (Klein-Flügge et al., 2015; Westbrook et al., 2013). This approach typically involves holding the value of the low-effort/low-reward option constant, while titrating the high-effort/high-reward option incrementally as a function of participants' responses. Thus, if the high-effort/high-reward offer is rejected, then participants on a subsequent trial will be presented with an offer that has an incrementally lower effort requirement or higher reward value. Repeating this procedure then leads to a point at which participants are indifferent between the baseline option and each of the higher effort levels. These indifferent point values can thus be used as an objective metric to characterize how costly individuals perceive increasing amounts of effort, in an identical manner to that described for the apple-gathering task described next (Chong et al., 2015).

3.4 ACCEPT/REJECT TASKS IN HUMANS

Another approach inspired by effort-discounting paradigms in animals has been to present participants with a single combination of effort and reward on individual trials and have them decide whether to accept or reject each of the combinations on offer (Fig. 2C) (Bonnelle et al., 2015, 2016; Chong et al., 2015). A potential advantage of this approach, relative to the dual-alternative designs predominantly used in animals, is that it involves simpler displays, which may be more suitable to testing patient populations who might have impaired information processing (Bonnelle et al., 2015).

Here, we provide an illustrative example of an effort-based decision-making task we recently developed, which demonstrates the utility of such paradigms to index human motivation (Bonnelle et al., 2015, 2016; Chong et al., 2015). In this task, participants were presented with cartoons of apple trees and were instructed to accumulate as many apples as possible based on the combinations of stake and effort that were presented (Fig. 4A). Effort was operationalized as the amount of force delivered to a pair of hand-held dynamometers and was indexed to each participant's MVC, as determined at the beginning of each experiment. By referencing the effort levels to each individual's maximum force, we were able to normalize the difficulty of each level across individuals.

Potential rewards were indicated by the number of apples on the tree, while the associated effort was indicated by the height of a yellow bar positioned on the tree trunk, and ranged over six levels as a function of each participant's MVC. On each trial, participants decided whether they were willing to exert the specified level of effort for the specified stake. If they judged the particular combination of stake and effort to be "not worth it," they selected the "No" response and the next trial would commence. If, however, they decided to engage in that trial, they selected the "Yes" option and began squeezing the dynamometer in order to receive the apples on offer.

Dissecting the Components of Motivation: One of the advantages of this paradigm is that it is possible to separate different components of motivated behavior. Specifically, by parametrically manipulating effort and reward in an accept/reject context, this task was able to differentially examine the effect of effort and reward on individuals' choices (Bonnelle et al., 2015). In one set of analyses, we applied logistic regression techniques to derive the effort indifference points for each participant—that is, the effort level at which each reward was accepted and rejected on 50% of occasions (Bonnelle et al., 2015; Chong et al., 2015). The converse analysis was undertaken to determine reward indifference points as a function of effort level.

The power of this approach is that it achieves a quantifiable point of equivalence between increasing amounts of effort and reward. This allowed us then to examine reward and effort indifference points separately, and use these points to define a preference function for each subject, characterized by a subject-specific slope and intercept. We found that apathy ratings were correlated with the intercept of individuals'

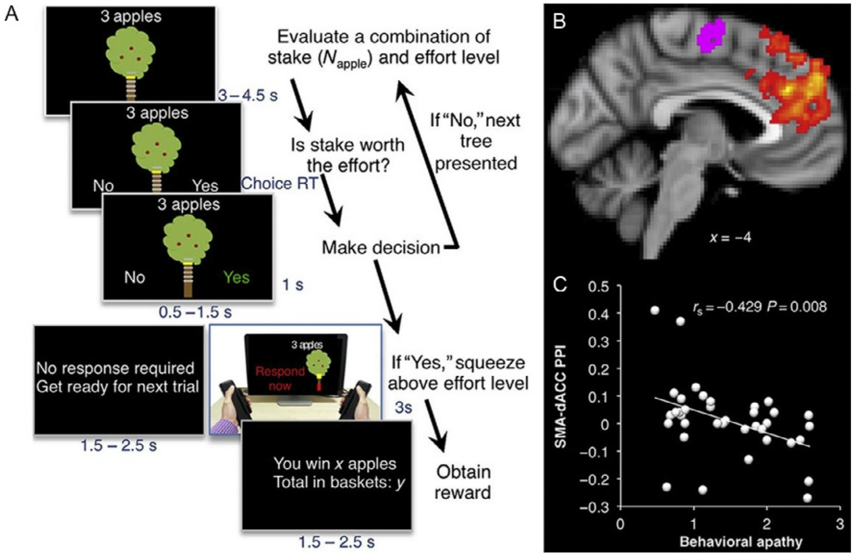

FIG. 4

(A) In the apple-gathering task, each trial started with an apple tree showing the stake (number of apples) and effort level required to win a fraction of this stake (trunk height) (Bonnelle et al., 2016). Rewards were indicated by the number of apples in the tree and effort was indicated by the height of a *yellow* bar on the tree trunk. Effort was operationalized as the amount of force to be delivered to hand-held dynamometers as a function of each individual's maximum voluntary contraction (MVC). Participants made an accept/reject decision as to whether to engage in an effortful response for the apples on offer. To control for fatigue, the accept option was followed by a screen indicating that no response was required on 50% of trials. (B) Relation between the supplementary motor area (SMA) functional connectivity and apathy traits. *Yellow–orange* voxels depict regions in which activity during the decision period on "accept" trials was more strongly correlated with activity in the SMA (*purple*) in more motivated individuals. (C) Correlation between behavioral apathy scores and the strength of the correlation (or functional connectivity) between the SMA and the dorsal anterior cingulate cortex.

Adapted from Bonnelle, V., Manohar, S., Behrens, T., Husain M., 2016. Individual differences in premotor brain systems underlie behavioral apathy. Cereb. Cortex 26 (2), 2016, 807–819.

effort indifference lines, which was a measure of the spontaneous level of effort that individuals were willing to engage for the smallest possible reward. In contrast, there was no relationship between apathy scores and the slope of the effort indifference line, which represented how much reward influenced the subjective cost associated with effort. These results demonstrate how a task can explain apathetic traits more sensitively than questionnaire-based measures and may be utilized to examine impairments in motivation in patient populations (Bonnelle et al., 2015).

Characterizing the Neural Substrates of Motivation: This paradigm has also been applied to determine the neural correlates of lowered motivation (apathy) in healthy individuals (Bonnelle et al., 2016). Using functional magnetic resonance imaging (fMRI), individuals who had higher subjective apathy ratings were found to be more sensitive to physical effort and had greater activity in areas associated with effort discounting, such as the nucleus accumbens. Interestingly, however, lower motivation was associated with increased activity in areas involved in action anticipation, such as the supplementary motor area (SMA) and cingulate motor zones. Furthermore, these less motivated individuals had decreased structural and functional connectivity between the SMA and anterior cingulate cortex (Fig. 4B). This led to the hypothesis that decreased structural integrity of the anterior cingulum might be associated with suboptimal communication between key nodes involved in action energization and preparation, leading to increased physiological cost, and increased effort sensitivity, to initiate action. This speculation remains to be confirmed, but serves to illustrate the utility of applying effort-based paradigms to capture the range of interindividual differences in motivation, even within healthy individuals, and to reveal their functional and structural markers.

Detecting Subclinical Deficits in Motivation: In addition to characterizing motivation in healthy individuals, a further useful role for effort-based paradigms is in detecting subclinical deficits in motivation within patient populations. Disorders of diminished motivation are currently diagnosed based on questionnaire-based measures of motivation, which may be insufficiently sensitive to detect more subtle motivational deficits. Using the apple-gathering task, we were able to show that patients with PD, regardless of their medication status, were willing to invest less effort for low rewards, as revealed by their lower effort indifference points (Fig. 5) (Chong et al., 2015). Importantly, none of these patients were clinically apathetic as assessed with the Lille Apathy Rating Scale (LARS), suggesting that deficits in motivation may nevertheless be present in individuals who are not clinically apathetic, but that these deficits are detectable with a sufficiently sensitive measure. Thus, the utility of these paradigms is being able to quantify components of effort-based decisions that may lead to earlier diagnosis and institution of therapy than would be otherwise possible with conventional self-report-based questionnaires. Furthermore, given the potential sensitivity of these techniques, they may offer us a more objective means of diagnosis and monitoring responses to treatment (Chong and Husain, 2016).

Distinguishing Apathy from Related Symptoms: Although it is conventionally established that apathy is separate from depression (Kirsch-Darrow et al., 2006; Levy et al., 1998; Starkstein et al., 2009), it is clear that these two disorders share several overlapping features, which may sometimes be difficult to distinguish. The utility of effort-based decision-making paradigms is in their potential to dissociate the two. For example, in the apple-gathering task, there was no relationship between effort indifference point measures and responses on a depression scale (the depression, anxiety, and stress scale, DASS) (Chong et al., 2015). This is similar to other studies that have shown that effort discounting is strongly correlated with apathy, but not with related symptoms such as diminished expression in

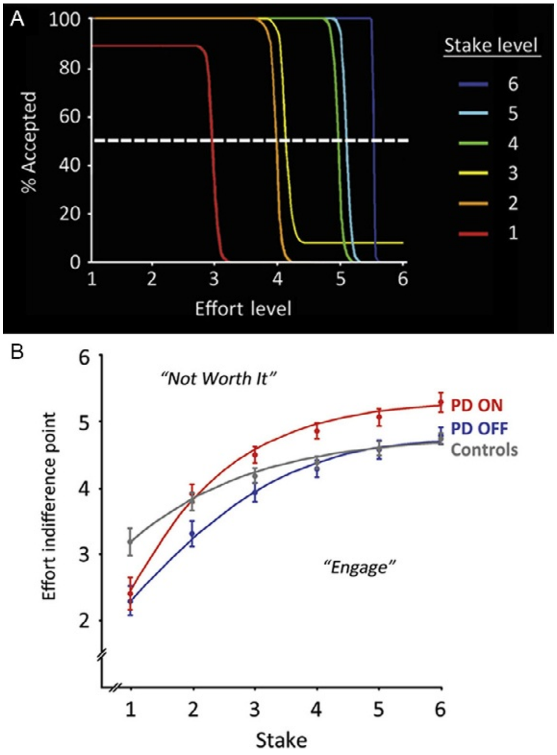

FIG. 5

We recently applied the apple-gathering task to patients with Parkinson's disease (Chong et al., 2015). (A) An example of the fitted probability functions for a representative participant. Logistic functions were used to plot the probability of engaging in a trial as a function of the effort level for each of the six stakes. Each participant's effort indifference points—the effort level at which the probability of engaging in a trial for a given stake is 50% (indicated by the *dashed line*)—were then computed. (B) Effort indifference points were then plotted as a function of stake for patients and controls. Regardless of medication status, patients had significantly lower effort indifference points than controls for the lowest reward. However, for high rewards, effort indifference points were significantly higher for patients when they were ON medication, relative not only to when they were OFF medication, but even compared to healthy controls. *Error bars* indicate ±1 SEM.

Adapted from Chong, T.T.-J., Bonnelle, V., Manohar, S., Veromann, K.-R., Muhammed, K., Tofaris, G., Hu, M., Husain, M., 2015. Dopamine enhances willingness to exert effort for reward in Parkinson's disease. Cortex 69, 40–46.

schizophrenia (Hartmann et al., 2015). Effort-based tasks may therefore offer an objective means to quantifiably distinguish apathy from other symptoms of neurologic and psychiatric disease, which bear some surface resemblance to apathy, but which may have potentially different underlying mechanisms.

3.5 THE CHALLENGES OF EFFORT-DISCOUNTING TASKS

The preceding discussion highlights the range of effort-discounting paradigms that have been applied, using different methodologies and different methods of analysis. A challenge in isolating effort as a unique cost is that it is often associated with other costs, such as risk or temporal delay. In designing and applying effort-based paradigms, it is critical to consider and account for other factors that might impact on individuals' decision-making. To illustrate the measures that we have taken to control for these other costs, here we consider a cognitive effort task that we recently applied to measure motivation in healthy individuals (Apps et al., 2015).

In this cognitive effort study (Fig. 6), we manipulated effort as the number of switches of attention from one spatial location to another. We used an rapid serial visual presentation (RSVP) paradigm, in which participants had to attend to one of two peripheral target streams, to the left and right of fixation, for a target number "7." Each of these peripheral target streams was surrounded by three, task-irrelevant, distractor streams. Simultaneously, they had to fixate on a central stream of characters for a number "3," which was a cue to switch their attention to the opposite stream. We operationalized effort as the number of times attention had to be switched from one stream to the other (1–6), and verified that this corresponded to subjective increases in perceived cognitive effort.

Each experimental session commenced with an extensive training session, in which participants became practiced at each of the six different effort levels. After the training phase, participants undertook the critical choice phase, which required them to choose between a fixed, low-effort/low-reward baseline option, and a variable, high-effort/high-reward offer. The baseline option involved performing the lowest level of effort (one attentional switch) for 1 credit, and the offer varied from 2 to 6 attentional switches for 2 to 10 credits. Participants were instructed that each credit would be converted to monetary reward at the conclusion of the experiment.

Controlling for Probability Discounting: Choice data showed that, as predicted, participants chose the higher effort option less frequently with increasing effort levels, which would be consistent with the considerable literature on effort discounting summarized previously. However, this raises a challenging issue in the effort-discounting literature, which is how to control for probability costs. A well-established finding in economics is that humans are risk-averse and prefer a certain outcome over one that is associated with a degree of risk (probability discounting). In the context of an effort-based decision-making paradigm, it is therefore important to ensure that individuals' aversion to the higher effort levels is not due to the relatively lower likelihood that they will be able to successfully perform them (see Fig. 1).

Indeed, on this cognitive effort task, we found that individuals' performance did decline as a function of effort. Critically, however, we took a methodological approach to minimize the effect of probability discounting as a potential factor in our results. During the preliminary training phase, participants were rewarded a credit for every trial performed adequately. We set the requirements for a successful (rewarded) trial at a level that every participant was *able to achieve* on almost every trial. Thus,

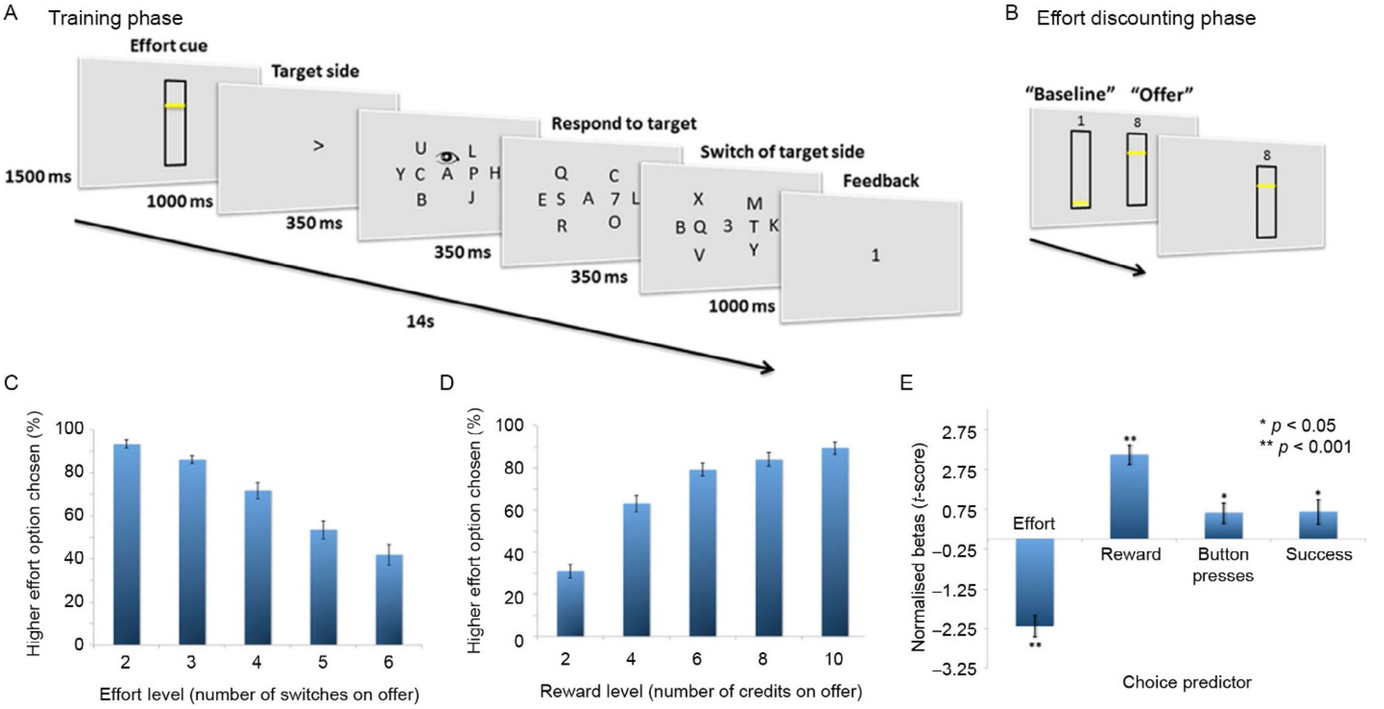

FIG. 6

See figure legend on opposite page.

even though performance declined with increasing effort, the rates at which participants were reinforced were very similar across effort levels. In a subsequent logistic regression analysis, we found that, even though the ability to complete a given effort level did influence individuals' preferences, effort was a significantly better predictor of choice behavior than success rates. These procedures therefore allowed us to minimize and account for the effect of probability discounting in a cognitive effort-discounting task.

Controlling for Temporal Discounting: Most effortful tasks take longer to complete than those that are less effortful (see Fig. 1). For example, a commonly employed procedure involves manipulating effort as the number of presses of a button or a lever (Treadway et al., 2009). An advantage of this procedure is that it draws from a rich tradition in research on nonhuman animals, and is simple to implement in the laboratory. However, although it is intuitive that a higher number of presses is more effortful, such a manipulation is also associated with a greater time cost. A very well-established finding in humans is that temporal delays are discounted hyperbolically, such that we tend to prefer smaller amounts sooner, rather than larger amounts later. Thus, another challenge in designing effort-based tasks is therefore to be able to ensure that any apparent effort discounting is not being driven by an element of temporal discounting.

FIG. 6

In a recent cognitive effort task, we manipulated cognitive effort as the number of shifts of attention in a rapid serial visual presentation task (Apps et al., 2015). (A) In a preliminary training phase, participants maintained central fixation as an array of letters changed rapidly and attend to a target stream presented horizontally to the left or right of a central stream, in order to detect targets (the number "7"). The initial target side was indicated at the beginning of the trial by an *arrow*. During each trial, a cue in the center of the screen (anumber "3") indicated that the target side was switching, requiring participants to make a peripheral shift of attention. Effort was manipulated as the number of attentional shifts, which varied from one to six. In the training session feedback was provided in the form of credits (1 credit or 0) at the end of each trial if participants successfully detected a sufficient number of targets. (B) Effort-discounting task. Choices were made between a fixed "baseline" and a variable "offer." The baseline was fixed at the lowest effort and reward (1 credit, 1 shift). The offer varied in terms of reward and effort (2, 4, 6, 8, 10 credits and 2, 3, 4, 5, 6 shifts). Choices on this task indexed the extent to which rewards were devalued by shifts of attention. (C) Results showed that shifts of attention were effortful and devalued rewards. As the number of attentional shifts increased, the less likely it was that the offer was chosen. (D) Similarly, as the amount of reward offered increased, the more likely it was that the offer was chosen. (E) Results of a logistic regression analysis, showing that effort was a significantly better predictor of choice than task success and the number of button presses for each effort level. The *y*-axis shows mean normalized betas for predictors of choosing the higher effort/higher reward offer.

Adapted from Apps, M., Grima, L., Manohar, S., Husain, M., 2015. The role of cognitive effort in subjective reward devaluation and risky decision-making. Sci. Rep. 5, 16880.

In the case of the cognitive effort task described earlier, controlling the temporal profile of each effort level was relatively straightforward. We set each trial to last a fixed duration of 14 s, and participants had to sustain their attention on the task for that entire period, with effort being manipulated simply as the number of spatial shifts of attention (Apps et al., 2015). This ensured that the temporal parameters of every trial at every effort level were identical. In the physical effort tasks that we have employed, we have attempted to overcome the issue of temporal discounting through the use of hand-held dynamometers (Bonnelle et al., 2015, 2016; Chong et al., 2015), which are an effective means to minimize the temporal difference between low- (eg, 40% MVC) and high-effort trials (eg, 80% MVC). This difference is further minimized by holding the actual duration of each trial constant.

The Effect of Fatigue on Effort Discounting: An important feature of effort as a cost is that it accumulates over time. Thus, with increasing time-on-task, individuals are likely to fatigue, which will have an obvious effect on their choice preferences later in the experiment. In all of the traditional tasks described in animals, the animal must actually execute their chosen course of action. Thus, it is possible that decisions in the later parts of the experiment might be affected by the accumulation of effort in the form of fatigue.

In humans, several approaches have been adopted to eliminate the effect of fatigue on participants' responses. The main approach has been to require participants to perform only a random subset of their revealed preferences. In the case of our cognitive effort task, these random trials were deferred until the conclusion of the experiment (Apps et al., 2015), whereas other tasks have required the choices to be executed immediately after the response is provided (Bonnelle et al., 2015, 2016; Klein-Flügge et al., 2015). In studies that have required participants to execute choices on every trial, it is important to verify that increasing failures to complete the high-effort trials cannot account for any preference shifts (eg, with regression techniques) (Treadway et al., 2012a).

Few studies have explicitly attempted to model the effect of fatigue on choice decision-making (Meyniel et al., 2012, 2014). More recently, however, fatigue has become the subject of increasing neuroscientific interest (Kurzban et al., 2013). For example, there have been recent attempts to computationally model a labor/leisure trade-off in describing when the brain decides to rest (Kool and Botvinick, 2014). A closer integration between the effects of fatigue on effort discounting should be an important focus of future studies.

4 FUTURE CHALLENGES AND APPLICATIONS

The preceding sections surveyed the different techniques that have been applied to quantify effort-based decision-making in human and nonhuman animals. Applying these techniques in humans has given us great insight into the mechanisms of effort-based motivation in healthy individuals and has provided us with an understanding of the neural circuitry involved in reward valuation and effort discounting.

Given the volume of research that will surely follow in the next few years, a challenge will be to parse the wealth of data from disparate paradigms across, and within, species. For example, the decision-making process in a dual-alternative design is necessarily different from that of an accept/reject design, which differs again from decision-making in a foraging context. Tasks also differ according to the degree to which they account for such factors as probability discounting, temporal discounting and fatigue, and reinforcement can occur with varying magnitudes and schedules. Furthermore, various domains of effort have been examined across the species—including perceptual, cognitive, and physical effort. Given this heterogeneity, perhaps it is all the more impressive that, despite the wide range of methodologies employed, most findings in studies of effort-based decisions have been relatively consistent—pointing, for example, to the importance of dopamine within the mesocorticolimbic system as being critical in overcoming effort for reward (Chong and Husain, 2016; Salamone and Correa, 2012).

However, future research will need to clarify the precise effect of varying task parameters on choice. For example, one distinction that is yet to be clarified is the difference in the way the brain processes costs associated with different types of effort (eg, cognitive vs physical). Phenomenologically, cognitive and physical effort are perceived as distinct entities. Furthermore, physical effort has the advantage of being relatively straightforward to manipulate in animals; being easily characterized objectively (eg, as force); and having demonstrable physiological and metabolic correlates. In contrast, cognitive effort is more difficult to conceptualize; cannot be defined in metabolic terms; and may be experienced differently depending on the cognitive faculty that is being loaded (attention, working memory, etc.).

This distinction between cognitive and physical effort processing is an example of a question that is not only relevant to understanding the basic neuroscience of motivation—of how the brain processes different effort costs—but also one that is clinically relevant. For example, at present there is a somewhat arbitrary distinction between constructs such as “mental” or “physical” apathy, which is intuitive, and based primarily on questionnaire data. This distinction suggests that the domains are separate, but the extent to which they rely on shared vs independent mechanisms has not been thoroughly investigated. Studies in animals suggest potentially dissociable neural substrates (Cocker et al., 2012; Hosking et al., 2014, 2015), but the neural correlates underlying the subjective valuation of cognitive and physical effort in humans remains to be defined (but see Schmidt et al., 2012).

The natural extension of the literature on effort-based decisions is its applications to diagnosing and monitoring disorders of diminished motivation in patients (Chong and Husain, 2016). Several authors have suggested that effort-based decision-making paradigms could be useful for modeling the motivational dysfunction seen in multiple neurological and psychiatric conditions (Salamone and Correa, 2012; Salamone et al., 2006, 2007; Yohn et al., 2015). Effort is a particularly salient variable in individuals with apathy who lack the ability to initiate simple day-to-day activities (Levy and Dubois, 2006; van Reekum et al., 2005). This lack of internally generated actions may stem from impaired incentive motivation: the ability to convert basic valuation of reward into action execution (Schmidt et al., 2008). Only relatively recently, however, have researchers started to apply effort-based decision-making paradigms to assess patients with clinical disorders of motivation.

Despite studies of effort-based decisions in patients being a relatively recent undertaking, several populations have already been tested. The broad conclusion from many of these studies is similar, with apathetic individuals being inclined to exert less effort for reward: patients with PD are willing to apply less force to a dynamometer for low rewards than age-matched controls (Chong et al., 2015; Porat et al., 2014); patients with major depression fail to modulate the amount of effort they exert in return for primary or secondary rewards (Cléry-Melin et al., 2011; Sherdell et al., 2012; Treadway et al., 2012a); patients with schizophrenia are less inclined to perform a perceptually, cognitively, or physically demanding task for monetary reward than controls (Reddy et al., 2015). Collectively, these studies show that deficits in effort-based decision-making are not unique to any one disease entity (Barch et al., 2014; Dantzer et al., 2012; Fervaha et al., 2013a,b; Gold et al., 2013; Treadway et al., 2012b).

On the one hand, this may be taken as evidence that apathy, as a common thread between these conditions, is associated with damage to a mesocorticolimbic system that generates internal association between action and its consequences. This would be consistent with preclinical studies, suggesting a key involvement of medial prefrontal areas and the pallido–striatal complex in the anticipation and execution of effortful actions. However, the question arises as to why different pathologies leading to different brain disorders give rise to the identical phenotype of reduced motivation to exert effort. Do the behavioral manifestations of higher effort indifference points or higher break-points in apathetic patients simply represent the same surface phenotype of some common underlying neural dysfunction? Or are there distinguishing features to the impairments of effort-based decisions within these populations that may be dissociable with sufficiently sensitive measures? A focus of future research will be to identify the specific components of effort-based decision-making that are affected in these populations (eg, the evaluation of the effort costs vs the costs of having to act).

Although the translation of effort-based tasks from animals to patients holds great promise, a practical challenge will be to precisely identify the parameters and paradigms which maximize the sensitivity and specificity of detecting any potential decision-making impairments in a population of interest. In deciding on an approach, it is worth acknowledging the advantages and limitations of the aforementioned paradigms, and their ability to capture the putative motivational deficit in the population of interest. For example, patients whose motivational deficits are more likely to be physical rather than cognitive would be more apt to be tested with a task involving effort in the former domain. However, due to the nascency of this field, extant data do now allow us to unequivocally advocate one approach over another in exploring specific motivational deficits in a given patient population. The difficulty of choosing an appropriate paradigm is exemplified by a recent study in patients with schizophrenia, who were administered several effort-based decision-making tasks in order to measure motivated behavior (Reddy et al., 2015). The tests were all essentially dual-alternative paradigms, but involved different forms of effort—namely, perceptual effort, task switching, grip force, and button presses. Although these tasks were useful in capturing some of the differences in motivation in patients with schizophrenia, they were each found to have different psychometric properties. Thus, prior to translating such effort-based paradigms for wide-spread clinical use, it remains for us to determine and standardize the parameters and constraints of these tasks to maximize the probability of detecting any motivational deficits.

In conclusion, the rich history of effort-based decision-making tasks in animals provides us with a large corpus of basic neuroscience data on which to draw. Through these paradigms, we have gained a deep understanding of the neural networks that are involved in encoding cost–benefit trade-offs. Extending these studies to humans therefore holds great potential in allowing us to understand the process of healthy motivation, and develop parsimonious models of motivation across species. A key advantage of these paradigms is their ability to sensitively capture individual differences. Furthermore, these tasks offer multiple metrics that may be more objective, sensitive, and specific to the identification of disorders of motivation than traditional self-report and questionnaire-based measures. The availability of such metrics should act as an incentive to develop new treatments, and to determine the efficacy of existing drugs. Ultimately, it is hoped that we may be able to combine different metrics of decision-making to devise a useful index of motivational impairments in disease, which will allow us to more accurately diagnose, monitor, and treat disorders of motivation.

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