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Ecophysiology of cognition: How do environmentally induced changes in physiology affect cognitive performance?

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ABSTRACT

Cognitive performance is based on brain functions, which have energetic demands and are modulated by physiological parameters such as metabolic hormones. As both environmental demands and environmental energy availability change seasonally, we propose that cognitive performance in free-living animals might also change seasonally due to phenotypic plasticity. This is part of an emerging research field, the 'ecophysiology of cognition': environmentally induced changes in physiological traits, such as blood glucose and hormone levels, are predicted to influence cognitive performance in free-living animals. Energy availability for the brain might change, and as such cognition, with changing energetic demands (e.g. reproduction) and changes of energy availability in the environment (e.g. winter, drought). Individuals spending more energy than they can currently obtain from their environment (allostatic overload type I) are expected to trade off energy investment between cognition and other life-sustaining processes or even reproduction. Environmental changes reducing energy availability might thus impair cognition. However, selection pressures such as predation risk, mate choice or social demands may act on the trade-off between energy saving and cognition. We assume that different environmental conditions can lead to three different trade-off outcomes: cognitive impairment, resilience or enhancement. Currently we cannot understand these trade-offs, because we lack information about changes in cognitive performance due to seasonal changes in energy availability and both the resulting changes in homeostasis (for example, blood glucose levels) and the associated changes in the mechanisms of allostasis (for example, hormone levels). Additionally, so far we know little about the fitness consequences of individual variation in cognitive performance. General cognitive abilities, such as attention and associative learning, might be more important in determining fitness than complex and specialized cognitive abilities, and easier to use for comparative study in a large number of species. We propose to study seasonal changes in cognitive performance depending on energy availability in populations facing different predation risks, and the resulting fitness consequences.

Key words: brain functions, phenotypic plasticity, glucose, steroids, food shortage, energy, fitness.

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I. INTRODUCTION: THE EMERGING RESEARCH FIELD OF ECOPHYSIOLOGY OF COGNITION

We predict that environmentally induced changes in physiology affect cognitive performance, which is thus expected to change seasonally. Animal cognition encompasses a range of mental abilities from simply perceiving and sensing to understanding and conceiving a notion (McLean, 2001). Although the term 'cognition' sometimes refers to complex manifestations of awareness beyond associative learning, including insightful abilities and subjective mental states (Call & Tomasello, 2008), we consider cognition more broadly as the neural processing of information from the external environment, including acquisition, integration, storage, retrieval of information and decision making (Shettleworth, 2001).

Cognition evolved such that animals can react appropriately in their natural environment, increasing their chances of survival and reproduction. While the evolution of cognition is driven by its benefits, it is constrained by its costs. The neuronal tissue which is the substrate of cognition is energetically highly demanding. Energy is the main limiting factor for most animal species, at least for some periods of the year. Energy is taken up in the form of fat, proteins and carbohydrates (Frayn, 2010), and the availability of these energy sources can differ seasonally. Animals spend energy on maintaining homeostasis, reproduction and survival, all of which are achieved by cognitive decisions regulating behaviour (Fig. 1). If energy availability in the environment decreases, many species terminate investment into reproduction, instead investing energy into survival. In periods when energy consumption is higher than energy intake, individuals enter allostatic overload type I (McEwen & Wingfield, 2003).

Animals have to expend energy to maintain life-sustaining processes such as glucose, pH, and O_2 levels of the blood in a narrow homeostatic range, avoiding homeostatic failure and death (Romero, Dickens & Cyr, 2009). When energy becomes restricted, they have to reduce energy expenditure of other traits, for example by being less active. We assume that energy trade-offs also influence how much energy is available and consumed by the brain, affecting cognitive performance. However, the conditions under which animals might directly reduce energy investment into cognitive processes (cognitive impairment) and the conditions under which they might keep this energetic investment unchanged (cognitive resilience) or improved (cognitive enhancement) remain unknown. In sum, the energy trade-offs between cognition and other energetically expensive processes in periods of low food availability are not well understood, nor are the constraints that physiological changes might impose on cognition. The ecophysiology of cognition investigates how environmentally induced physiological changes affect cognition, and the resulting fitness consequences. The ecophysiology of cognition aims to explain cognitive flexibility consisting of reversible within-individual variation in cognitive performance.

II. ENVIRONMENT SHAPES COGNITIVE TRAITS

Here, we discuss how cognitive traits are selected to match closely the cognitive demands posed by each species' environment. We review papers that demonstrate how cognitive performance can differ between species due to evolutionary adaptation or between populations and individuals due to phenotypic plasticity. Finally, we highlight the importance of differentiating specialized cognitive abilities that evolved as a response to specific environmental demands and general cognitive abilities that are present in most or all species.

(1) Definitions: evolutionary and physiological adaptations

Evolutionary biologists define adaptation as a trait increasing an individual's fitness that evolved *via* natural selection (Saccheri *et al.*, 2008). Physiologists define adaptation as reversible physiological processes that allow an individual

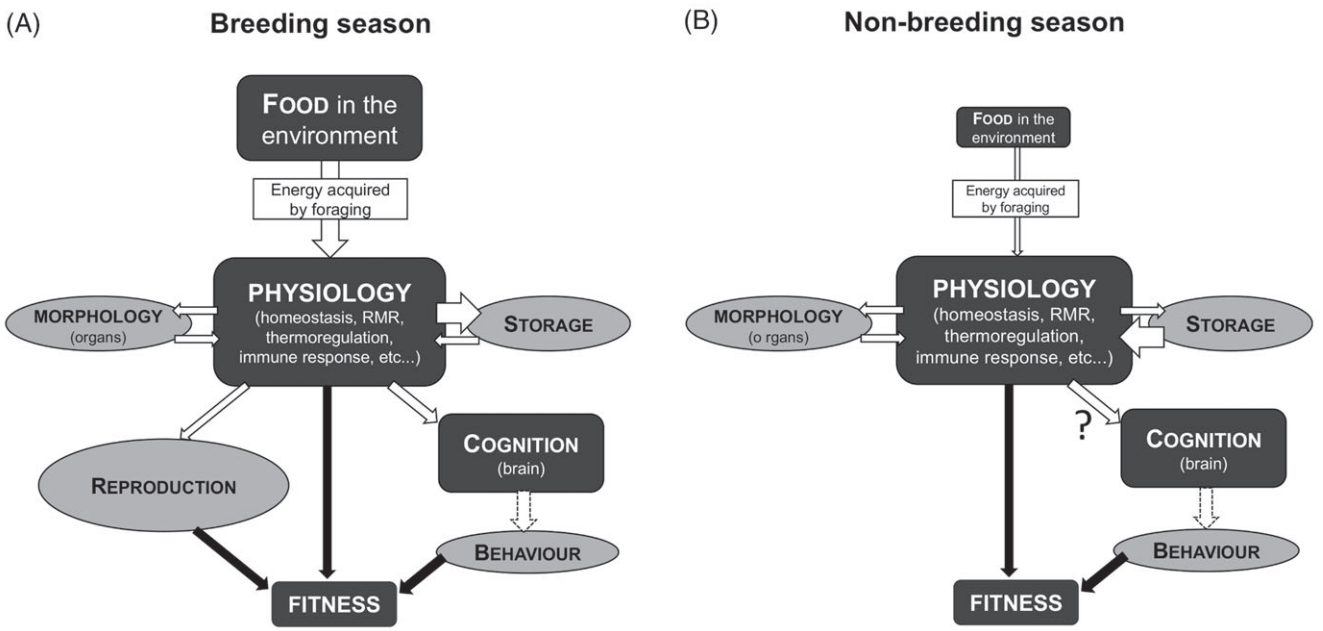

Fig. 1. Energy flow in the African striped mouse (*Rhabdomys pumilio*) during (A) the moist breeding season in spring (high food availability) and (B) the dry non-breeding season in summer (low food availability). This rodent does not reproduce when food is restricted. Black arrows indicate effects on fitness. White arrows represent energy invested in one process: arrow thickness represents amount of energy. Whether the amount of energy invested into cognition remains stable, decreases or increases during the dry non-breeding season is so far unknown (**?**; see Fig. 3). RMR, resting metabolic rate.

to cope with their current environment (Schulin, 2004). In both cases, adaptation refers to traits that increase fitness, physiological adaptation being an adaptive product of evolution. Thus, studying adaptation can help to bridge the gap between ultimate (evolutionary) and proximate (especially physiological) research.

Evolutionary biologists do not tend to use the term adaptation for physiological changes. Instead, evolutionary biologists often use the term phenotypic plasticity for all plastic phenotypic traits, including physiological adaptation (Ellers & Stuefer, 2010; Mery & Burns, 2010). When phenotypic plasticity is the product of evolution and thus increases individual fitness, it is called adaptive phenotypic plasticity, which can be divided into two forms (Piersma & Drent, 2003): (*i*) developmental plasticity often occurs early in development (pre- and postnatal stages) and leads to permanent/irreversible changes of the phenotype. Variation is due to organizational effects: different environmental factors activate alternative ontogenic pathways of one genotype. (*ii*) Phenotypic flexibility usually occurs in adults and leads to temporary/reversible changes of the phenotype enabling a rapid individual response to environmental changes. Variation is due to activational effects: environmental changes induce changes in phenotypic traits within a limited reaction norm.

(2) Evolutionary adaptation

Similarly to all phenotypic traits, cognitive traits (cognitive abilities and performance), are affected by both the genotype and the environment. As a product of natural selection, cognitive abilities are expected to be selected to match closely the cognitive demands posed by each species' environment (Healy & Jones, 2002). Evolutionary adaptation can explain cognitive differences between species (Healy *et al.*, 2009) and populations (Roth, LaDage & Pravosudov, 2010*b*).

Specialized cognitive abilities are represented in some but not all species because they evolve in response to specific environmental conditions (Healy *et al.*, 2009), such as complex foraging demands leading to food-storing in marsh tits *Parus palustris* (Clayton & Krebs, 1994) and tool use in chimpanzees *Pan troglodytes* (Emery & Clayton, 2009) or complex social systems linked with the use of intentional gestures in Old-World monkeys (Maille *et al.*, 2012; Bourjade *et al.*, 2014). For example, the ability to form coalitions is mainly found in some primate species (Borgeaud, van de Waal & Bshary, 2013; Bissonnette *et al.*, 2014). By contrast, general cognitive abilities such as attention and spatial memory are present in nearly all species as they are needed for most decision processes. It has recently been argued that one should follow a bottom-up approach and focus on general rather than specialized cognitive abilities to gain insight into both ultimate causes and proximate mechanisms of cognition (de Waal & Ferrari, 2010).

(3) Phenotypic plasticity

Phenotypic plasticity is the ability of an individual genotype to produce alternative phenotypes in response to prevailing environmental conditions. Developmental plasticity of

cognition can explain within-population variation, as it can lead to significant differences between individuals in the development of the nervous system, and thus ultimately cognitive performance, when the environment of a population changes consistently (Lupien *et al.*, 2009). Developmental plasticity of cognition has been demonstrated in studies inducing prenatal stress, which usually results in irreversible cognitive impairment [e.g. mammals (Castro, Tracy & Rudy, 1989; Bedi, 1992); birds (Fisher, Nager & Monaghan, 2006); for a recent review, see Buchanan, Grindstaff & Pravosudov (2013)].

This review focuses on cognitive flexibility consisting of reversible changes in cognition due to reversible changes in the structure or functioning of the nervous system, both influencing cognitive performance. Cognitive flexibility can occur either on a short-term or a long-term basis. For example, predator encounters cause shifts, lapses and narrowing of attention and faster decision-making, allowing animals adaptively to scrutinize the source of danger (Kavaliers & Choleris, 2001). Moreover, seasonal flexibility of spatial performance has been reported in food-storing birds (Sherry & Hoshooley, 2009) and some dispersing rodents (Galea, Kavaliers & Ossenkopp, 1996; Maille, Pillay & Schradin, 2015). Such seasonal changes in spatial memory are regulated proximately by structural modifications of the hippocampus, triggered by predictable environmental factors such as a decrease in food availability in food-storing birds (Pravosudov & Clayton, 2001) and photoperiod in dispersing rodents (Pyter, Reader & Nelson, 2005). Seasonal flexibility of cognition may have an adaptive value in species that disperse and breed seasonally by promoting range expansion and enhancing spatial learning and vigilance in new territories (Galea *et al.*, 1996). In sum, cognitive flexibility in response to seasonal environmental changes can be expected in numerous species.

III. PHYSIOLOGY INFLUENCES COGNITIVE PERFORMANCE

Here, we point out that physiological mechanisms of cognition have been well studied in the laboratory, but rarely under natural field conditions. For example, more research is needed on the influence of natural variation in blood glucose levels on cognitive performance. We also suggest that seasonal changes in hormone secretion might have pronounced effects on cognitive performance.

(1) Blood glucose levels

Glucose is the most important energy source for the brain, which is the organ where cognitive processes occur. Increased cognitive demands were shown to induce accelerated absorption of glucose from the blood in the brain of humans (Scholey, Harper & Kennedy, 2001) and rats (McNay, Fries & Gold, 2000). Under natural conditions, variation in blood glucose levels can be pronounced (e.g. African striped mouse *Rhabdomys pumilo*: Schradin *et al.*, 2015). Elevation in blood glucose levels after eating or drinking glucose-rich food was associated with improved cognitive performance (Gold, 1995). For example, in humans the number of words recalled in a memory task (Benton & Owens, 1993) or the number of errors measured in a Stroop task (reading of colour labels written in a similar or different colour: Fairclough & Houston, 2004) was positively related to blood glucose levels. However, not all studies found this positive relationship. For example, in both humans and rats the ingestion of a high-glycaemic-index meal, which significantly increases blood glucose levels, can lead to a decrease in cognitive performance (Benton *et al.*, 2003). Similarly, in rats chronic elevations in blood glucose levels resulting from an *ad libitum* consumption of a 10% sucrose solution for 28 days induced deficits in spatial learning (Kendig *et al.*, 2013).

By contrast, nothing is known about the influence of reduced blood glucose levels on cognitive performance. This may be related to the fact that the supply of glucose to the brain remains relatively constant even when blood glucose levels are decreasing. This is achieved *via* the glucose transporter GLUT3, which occurs only in the brain. GLUT3 allows a constant uptake of glucose from the blood relatively independent of blood glucose level (Simpson *et al.*, 2008). However, if blood glucose levels fall below 5 mM in humans, then glucose uptake in the brain by GLUT3 decreases (Frayn, 2010). As the GLUT3 transporter is important for brain metabolism in all mammals and is well studied in laboratory rodents (Simpson *et al.*, 2008), an analogous effect can be expected in other species. Blood glucose levels can commonly fall below 5 mM during periods of low food availability, as reported during droughts in African striped mice (Schradin *et al.*, 2015) and goats *Capra aegagrus hircus* (Pambu-Gollah, Cronje & Casey, 2000), and during cold winters in Norwegian reindeer *Rangifer tarandus* (Larsen *et al.*, 1985). Therefore, even though mechanisms exist to ensure a relatively constant supply of glucose to the brain, variation in blood glucose levels may influence cognitive performance. Studies are needed to clarify the conditions under which reduced blood glucose levels impair cognition.

(2) Corticosteroid hormones

The secretion of corticosteroids varies in response to environmental change (Wingfield *et al.*, 2000; Wikelski & Ricklefs, 2001; Reeder & Kramer, 2005). This can be either short-term change, such as acute stress or food uptake (McEwen & Wingfield, 2010), modifying the secretion of hormones to regulate blood glucose homeostasis (especially insulin, glucagon and leptin; Levin, Dunn-Meynell & Routh, 1999; Polakof, Mommsen & Soengas, 2011), or long-term change, such as seasonal changes in photoperiod (Pyter, Trainor & Nelson, 2006) or food availability (Schradin, 2008), demanding modifications in metabolism, osmoregulation, reproduction and social behaviour (Wingfield, 2009).

The effects of corticosteroids on cognition are centred in the hippocampus, a brain region containing large concentrations of both mineralocorticoid receptors (MRs)

and glucocorticoid receptors (GRs). MRs have a tenfold higher affinity for corticosterone than GRs (de Kloet, Oitzl & Joëls, 1999). Because of the differential activation of MRs and GRs (known as the Yerkes–Dodson law), corticosteroids have a dose-dependent biphasic effect on cognition, i.e. an inverted U-shaped relationship. At low doses, corticosteroids (mainly bound to MRs) stimulate synaptic plasticity and hippocampal excitability through long-term potentiation of neurons. Unsurprisingly, moderate increases in the basal level of corticosteroids have been shown to improve cognitive performance for attention in yellow-bellied marmots *Marmota flaviventris* (Blumstein, Patton & Saltzman, 2006), spatial learning in mountain chickadees *Poecile gambeli* (Pravosudov, 2003) and associative learning in ground squirrels *Spermophilus beldingi* (i.e. response to alarm calls: Mateo, 2008). By contrast, at high doses, corticosteroids (equally bound to MRs and GRs) have negative effects on cerebral functions, disrupting synaptic plasticity and blunting hippocampal excitability (Lupien & McEwen, 1997). Cognitive performance for spatial learning (Oitzl, Fluttert & de Kloet, 1994) and aversive learning (Roozendaal, 2002) was impaired in rats injected with high concentrations of corticosterone. This dose-dependent system is thought to enable the brain to distinguish between circadian rhythms (corticosteroid levels increase at the beginning of the activity period each day) and stress-dependent release of corticosteroids, enabling adaptive changes in information processing in unpredictable environments (de Kloet *et al.*, 1999).

The duration of increases in corticosteroid levels can modify their effects on cognition. A sustained exposure to elevated corticosteroid concentrations impairs spatial learning, for example in rats (McLay, Freeman & Zadina, 1998). This negative effect of long-term elevation of corticosterone levels is due to the translocation of glucose transporters from neuronal membranes to intracellular storage sites (Horner, Munck & Lienhard, 1987) and to decreased mRNA for the glucose transporter (Garvey *et al.*, 1989). As a consequence, chronic elevation of corticosteroid levels may cause atrophy of the dendrites of hippocampal neurons (Watanabe, Gould & McEwen, 1992) and even neuron loss (Bodnoff *et al.*, 1995), which does not occur following short-term increases in corticosteroid levels. Cognitive impairment under chronic stress is unlikely to have an adaptive value and rather reflects pathological consequences as predicted by the reactive scope model (Romero *et al.*, 2009). Whether seasonal changes in corticosteroid levels modulate cognition in free-living animals has not been investigated.

(3) Physiological response to acute stress

Exposure to acute stress induces release of metabolic hormones, which have a secondary effect on cognition *via* the regulation of blood glucose levels in three consecutive phases (Fig. 2).

Catecholamines such as adrenaline and glucagon act rapidly to raise blood glucose levels acutely whereas corticosteroids act slowly and extend this increase for hours

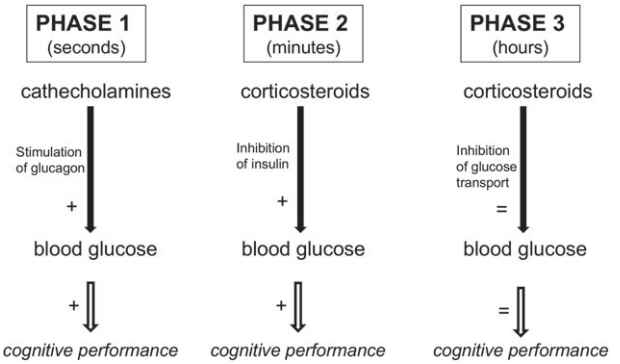

Fig. 2. Physiological responses to acute stress affect glucose metabolism in three successive phases (Sapolsky *et al.*, 2000). Phase 1 (sympathetic arousal, lasting seconds): catecholamines such as adrenaline stimulate glucagon secretion, which induces an increase in blood glucose levels. Phase 2 (beginning of the delayed stress response, lasting minutes): corticosteroids inhibit both the secretion and the transport of insulin, which induces an increase in blood glucose levels by decreased glucose uptake. Phase 3 (end of the delayed stress response, lasting hours): corticosteroids inhibit the transport and utilization of peripheral glucose, which induces stabilization of blood glucose levels at normal concentrations. Black arrows represent hormonal influences on blood glucose levels. White arrows represent effects of blood glucose levels on cognitive performance.

and finally prevent blood glucose levels from falling below the threshold for normal brain function (Sapolsky, Romero & Munck, 2000). Sympathetic action induces an increase in glucose supply to the brain because of accelerated cerebral blood flow (Joëls *et al.*, 2006), which plays an important role in cognitive enhancement under acute stress (Lupien *et al.*, 2007). Furthermore, the mobilization of existing glycogen stores following the stress response is often considered to be the mechanism underlying the cognitive enhancement reported in animals facing challenging events (Cahill & McGaugh, 1996; Lupien & McEwen, 1997).

(4) Other hormonal influences

Gonadal steroids affect cognition through the modulation of neurotransmitter production and release. Testosterone stimulates the cholinergic system in the hippocampus of male rats (Nakamura, Fujita & Kawata, 2002). Gonadal steroids have been shown to improve hippocampal synaptic plasticity by increasing dendritic density (Leranth, Petnehazy & MacLusky, 2003) and neuronal potentiation (Warren *et al.*, 1995). Physiological doses of testosterone and oestradiol improve cognition in mammals (Leonard & Winsauer, 2011). Cognitive performance for spatial learning (Sandstrom, Kim & Wasserman, 2006), aversive learning (Frye & Seliga, 2001) and object recognition (Aubele *et al.*, 2008) improved in gonadectomized male rats injected with testosterone. In human and non-human primates, a positive correlation was found between visuo-spatial attention and both testosterone levels (macaques *Macaca mulatta*: Lacreuse *et al.*, 2010; humans: Aleman *et al.*, 2004; Janowsky, 2006) and oestradiol

levels (macaques *Macaca fascicularis*: Voytko, 2002). In contrast to physiological doses, very high or chronic doses of testosterone can impair cognition in male mammals, for example spatial learning in rats (Neese & Schantz, 2012) or associative learning in macaques (Lacreuse *et al.*, 2009). Similarly, in females, high oestradiol levels impair spatial reference memory in rats (Chesler & Juraska, 2000) and deer mice *Peromyscus maniculatus* (Galea *et al.*, 1994), while at the same time enhancing spatial working memory (Daniel, 2006). Many experimental studies thus demonstrate that gonadal steroids can either have positive or negative effects on cognition under controlled laboratory conditions, with positive effects being more common when levels are within the natural range but negative effects more common when levels are unnaturally high. Gonadal steroid levels increase during the breeding season in animal species with seasonal reproduction. This leads us to predict that in free-living animals, cognitive performance will be increased during the breeding season when gonadal steroids are at naturally high levels.

Other hormones might affect cognition, including neuropeptides such as endorphin and vasopressin that are released both peripherally and centrally in response to stressors. Some studies suggest that endorphin (Kavaliers & Colwell, 1995) and vasopressin (Engelmann *et al.*, 1996) have an impairing effect on cognition. However, vasopressin has also been reported to have an enhancing effect on aversive learning (Kovács & de Wied, 1994) and spatial learning (Pan *et al.*, 2010). Vasopressin secretion changes seasonally, being higher during periods of low water availability, due to its important role in osmoregulation (Schoepf & Schradin, 2014).

IV. ENERGETIC COSTS OF COGNITION

Little is known about how individual variation in cognitive performance influences fitness. Cognitive traits that are important determinants of fitness might be affected by the supply of energy. Furthermore, the effect of food restriction on cognition might depend on the phase of starvation.

(1) Fitness consequences of cognitive variation

Whether inter-individual variation in cognitive traits affects survival and reproductive success has rarely been studied (Morand-Ferron & Quinn, 2015). Healy (2012) pointed out that the advantage of being smart seems to be so obvious that few researchers bother to demonstrate the fitness benefits of good cognitive performance. Studies using large sample sizes and conducted under varying ecological conditions could help us to understand the fitness consequences of cognition (Morand-Ferron, Cole & Quinn, 2015). Studies focusing on cognitive traits that are important determinants of fitness and present in many species, such as spatial learning for foraging or attention for avoiding predation, will enable us to compare a wide range of species living under different environmental constraints.

As expected, among the few studies that have correlated cognitive performance with fitness or fitness-related variables, some reported positive associations. For example, learning performance was positively correlated with growth rate in grasshoppers *Schistocerca americana* (Dukas & Bernays, 2000), with foraging success in bumble bees *Bombus terrestris* (Raine & Chittka, 2008) and with clutch size in great tits *Parus major* (Cole *et al.*, 2012). Similarly, performance in problem-solving tasks was positively correlated with hatching success and number of fledging chicks in great tits (Cauchard *et al.*, 2013). In addition, sexual selection appears to be a strong selection pressure on cognitive performance, with females choosing males with higher cognitive performance (Boogert, Fawcett & Lefebvre, 2011).

However, other studies reported negative associations between cognition and fitness-related variables. Learning performance of fruit flies *Drosophila melanogaster* was negatively correlated with longevity (Lagasse *et al.*, 2012) and with larval competitive ability (Mery & Kawecki, 2003). In addition, learning performance was negatively correlated with the number of eggs laid in butterflies *Pieris rapae* (Snell-Rood, Davidowitz & Papaj, 2011) or the number of offspring in guppies *Poecilia reticulata* (Kotrschal *et al.*, 2013). Improving cognitive performance thus seems to be constrained by increased costs, which must be taken into account to understand cognitive variation (Burns, Foucaud & Mery, 2011). The main costs of cognition are the energy and time invested to process and to retain information (Kawecki, 2010). Thus individuals might not show the maximal, but rather the optimal cognitive performance.

(2) Brain functions are energetically demanding

Cognition is a function of the central nervous system, which consumes a significant amount of energy. For example, in humans, 20% of the resting metabolic rate is due to the metabolic costs of the brain even though it represents only 2% of the body mass (Laughlin, 2001). The generation and propagation of neural signals increases energy consumption, because of the energetic costs of neurotransmitter synthesis and the activity of the Na^+/K^+ pumps, both of which use ATP (Gilsenan, de Bruin & Dye, 2009). Further, the storage of information requires additional neural tissue, either in numbers of neurons (Isler & van Schaik, 2006) or in numbers of connections between these neurons (Roth *et al.*, 2010*a*), which increases the energetic demands of the brain (Bauernfeind & Babbitt, 2015).

The supply of metabolic energy is thought to constrain the growth and function of the brain and consequently its cognitive performance. The capacity of the brain to store energy is very limited and the process of aerobic glucose degradation is completely dependent on a constant supply of glucose and oxygen from the blood (Fairclough & Houston, 2004). The importance of maintaining cognitive function is demonstrated by the fact that the blood supply to the brain remains relatively constant even during periods of intense physical activity, when other organs experience a significant reduction (Ide & Secher, 2000). As such, a strong decrease

Table 1. The three phases that characterize physiological responses to starvation (McCue, 2010)

Phase	Duration	Metabolic stage	Metabolic indicator (increase)
I	Few days	Mobilization of glycogen stores	Blood glucose
II	Weeks to months	Mobilization of lipid stores	Ketone bodies
III	Until death	Protein catabolism Inhibition of glucose utilization	Uric acid (birds) or urea (mammals)

in food intake, and consequently in brain extracellular levels of glucose, is likely to affect brain functions and cognition (Gilsenan *et al.*, 2009).

(3) Food restriction influences cognition

At the end of the Second World War, when severe famines were expected, A. Keys and colleagues studied how the physical and cognitive performance of human males changed as they underwent extended periods of starvation. Interestingly, starvation did not impair cognition qualitatively, as the tested men still could perform with the same reliability as before the onset of starvation (Keys *et al.*, 1950). However, the time needed to perform the cognitive tests significantly increased: starving men did not become stupid, but very slow (Keys *et al.*, 1950). For animals that have to make the correct cognitive decisions when facing life-threatening situations such as predation, making the correct decision more slowly could have significant consequences.

Numerous laboratory studies have assessed whether food restriction affects cognition in animals, with conflicting results. Some studies reported that food restriction induced impairment in cognitive performance for spatial learning in mice (Bellush *et al.*, 1996) and attention in humans (Benau *et al.*, 2014) and ground squirrels *Spermophilus beldingi* (Bachman, 1993). Other studies found that food restriction improved spatial learning, for example in mice (Means, Higgins & Fernandez, 1993; Steinman, Crean & Trainor, 2011), mouse lemurs *Microcebus murinus* (Dal-Pan *et al.*, 2011) and mountain chickadees (Pravosudov & Clayton, 2001), but also olfactory learning in rats (Aimé *et al.*, 2007), avoidance learning in mice (Dubey *et al.*, 1996) and verbal memory in humans (Witte *et al.*, 2009).

These discrepancies between studies may reflect differences in the duration and intensity of food restriction. Thus, the reason for the conflicting results might be that different phases of the physiological responses to starvation might have been induced by the different studies (Table 1). Cognitive impairments were mainly reported for prolonged (e.g. at least 5 months in rats: Yanai, Okaichi & Okaichi, 2004) and/or pronounced (e.g. 60% of *ad libitum* in mice: Bellush *et al.*, 1996) episodes of food restriction that cause excessive loss of body mass. Such episodes of food restriction would lead to cognitive impairment because of the brain glucose utilization decrease in phase III (McCue, 2010). By contrast, short episodes of food restriction might lead to cognitive enhancement because blood glucose levels increase during phase I of starvation (Robin *et al.*, 1988; Cherel *et al.*, 1991) and ketone bodies are produced from fatty acids during phase II, acting as an alternative energy source for the brain (Frayn, 2010).

In some studies, cognitive enhancement might have been induced because overweight captive individuals were used: food restriction would have improved general health by avoiding allostatic overload type II (pathologies due to prolonged stress without food restriction, leading to obesity: McEwen & Wingfield, 2003). For example, mouse lemurs, which tend to obesity in captivity, showed improvement in cognitive performance during food restriction. After food restriction, these mouse lemurs still had a body mass above that observed in nature (Dal-Pan *et al.*, 2011).

Therefore, to understand the influence of food restriction on cognition, it is essential to investigate which physiological mechanisms are being triggered. This will depend on (*i*) the intensity of food restriction; (*ii*) the duration of food restriction; and (*iii*) the body condition at which the individuals start the experiment (glycogen and fat stores).

V. POSSIBLE EFFECTS OF SEASONAL FOOD SHORTAGE ON COGNITIVE PERFORMANCE

Individuals spending more energy than they can currently obtain from their environment are expected to trade off energy investment between cognition and other life-sustaining processes. Thus, we predict (*i*) cognitive impairment when periods of food shortage are also periods of low cognitive demands; (*ii*) cognitive resilience when cognition helps to stabilize or improve the physiological state in challenging environments; and (*iii*) cognitive enhancement when cognition allows a net benefit in the energy budget.

(1) A trade-off between energy-saving and cognition

Both physiological adaptations and cognitive abilities are fitness-increasing traits that might be especially important in periods of reduced resource availability. Physiology indeed offers an important way to cope with energy restriction (Charmantier *et al.*, 2008) while many cognitive traits can help an individual to cope with dangerous events or to decrease allostatic load (Healy & Braithwaite, 2000). However, energy trade-offs exist between different energy-demanding processes. As cognition requires the development and maintenance of the underlying neuronal tissue, which is more energetically costly than other somatic tissue (Niven & Laughlin,

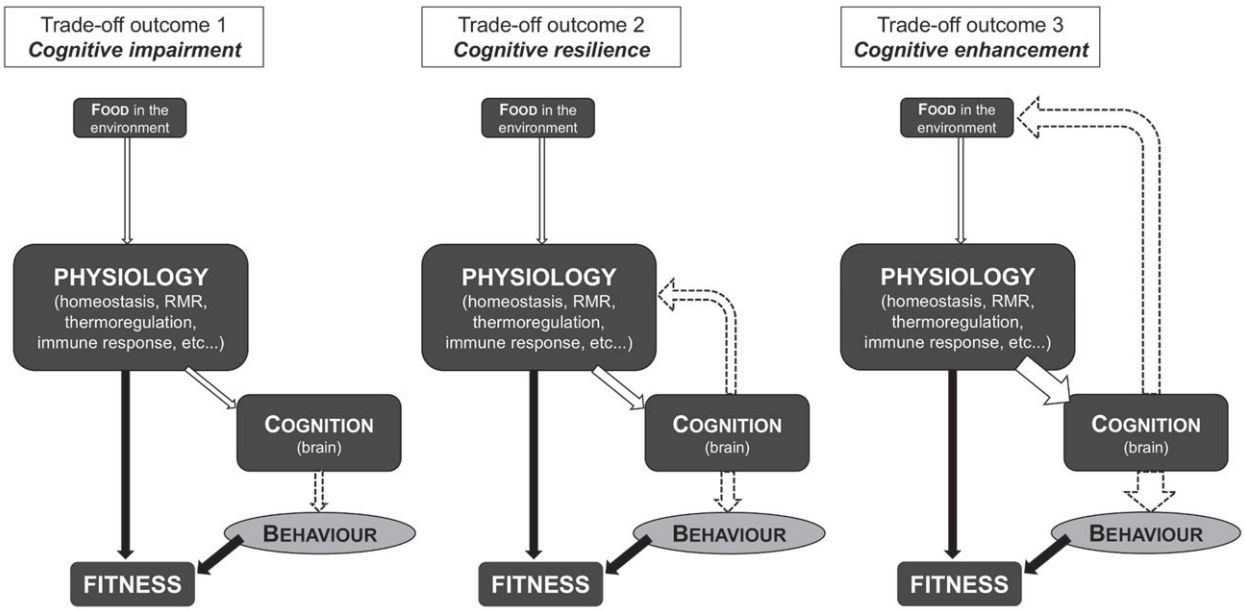

Fig. 3. Possible effects of seasonal food shortage on cognitive performance. Energy investment is traded-off between cognition and other life-sustaining traits or reproduction when food is restricted. Different trade-off outcomes can be expected depending on the fitness consequences of the trade-off in a specific environment. Cognitive impairment is predicted to occur when periods of food shortage are also periods of lower cognitive demands, and thus the fitness costs of reducing cognitive performance are lower than the fitness costs of reducing other important traits. Cognitive resilience, promoted by protective physiological mechanisms, is predicted to occur when cognition helps to stabilize or improve the physiological state. Cognitive enhancement, promoted by enhancing physiological mechanisms, is predicted to occur when increasing cognitive function leads to a net benefit in the energy budget. Black arrows indicate effects on fitness. Solid white arrows represent energy invested in a process: arrow thickness represents amount of energy. Dashed white arrows represent positive influences on other processes, such as foraging behaviour or physiology. RMR, resting metabolic rate.

2008), energy investment must be traded off between cognition and other life-sustaining processes during periods of food shortage. Different trade-off outcomes can be expected depending on the fitness consequences of the trade-off in a specific environment, such that cognitive impairment, cognitive resilience or cognitive enhancement might occur (Fig. 3). Among these trade-off outcomes, the optimal one could be selected for in species or populations that regularly experience periods of low food availability across many generations.

(2) Trade-off outcome 1: cognitive impairment

Cognitive performance might be impaired in periods of food shortage, such as drought or winter, either to save energy or because less energy can be allocated to cognition. Some physiological responses to starvation might affect cognition by reducing the physiological ability to process information (Laughlin, 2001). This assumption is supported by a study in fruit flies showing that improved physiological responses to poor nutrition were associated with reduced learning performance (Kolss & Kawecki, 2008). For example, reducing resting metabolic rate to allow a decrease in energy expenditure might impair cognition, as suggested by the positive correlation found between the metabolic rate of vertebrates and their perception of temporal information (Healy *et al.*, 2013). Cognitive impairment is predicted to occur when periods of food shortage are also periods of low cognitive demands, and thus the fitness costs of reducing cognitive performance are lower than the fitness costs of reducing other important traits. Lastly, cognitive impairment might arise as a non-adaptive consequence of energetic constraints impairing individual condition (Fig. 3).

(3) Trade-off outcome 2: cognitive resilience

Cognitive resilience describes the ability to maintain cognitive function despite external environmental challenges (Buchanan *et al.*, 2013), such as periods of food shortage. Cognitive resilience relies on specific physiological mechanisms protecting the brain against seasonal variation in energy availability and associated changes in hormone secretion. First, mechanisms allow the maintenance of high glucose levels within the brain despite a reduced energy intake. The brain-centered gluco-regulatory system, with the glucose transporter GLUT3, is able to modulate brain glucose levels *via* both insulin-dependent and -independent mechanisms (Schwartz *et al.*, 2013). Second, mechanisms protecting the brain may operate during short-term starvation. Food restriction has been shown to promote neuroprotection by preserving DNA repair enzymes (Ingram, Young & Mattison, 2007), reducing oxidative stress in the brain (Li, Wang & Zuo, 2013) and upregulating

antiapoptotic proteins such as brain-derived neurotrophic factor (BDNF) (Mattson, 2003) or glial cell line-derived neurotrophic factor (GDNF) (Maswood *et al.*, 2004). Mechanisms leading to cognitive resilience are predicted to evolve when cognition helps to stabilize or improve the physiological state in challenging environments (Fig. 3).

(4) Trade-off outcome 3: cognitive enhancement

Cognitive traits that promote resistance to food shortage by increasing food acquisition rates might be favoured during periods of low food availability when these lead to a net energy benefit (McLean, 2001; Roth *et al.*, 2010*a*). Mechanisms enhancing brain functions may operate during starvation to promote neuronal plasticity through mitochondrial activity (Fontán-Lozano *et al.*, 2008). Cognitive enhancement during periods of food shortage may thus have an adaptive value in enabling animals to detect both food and potential dangers more easily, increasing survival probability (Healy *et al.*, 2009). For example, food-caching birds increase their spatial memory performance in winter, which enables them to relocate their food caches more effectively (Sherry & Hoshooley, 2009). Cognitive enhancement is predicted to occur when increasing cognitive function leads to a net benefit in the energy budget (Fig. 3).

VI. PROPOSED RESEARCH FRAMEWORK FOR STUDYING THE ECOPHYSIOLOGY OF COGNITION

To understand whether cognition decreases, remains stable, or improves during energetically challenging periods, it is important to study its ecophysiology: how does the environment change, how does this influence basal physiological functions, and how do these changes affect cognition?

The ecophysiology of cognition studies how environmentally induced physiological changes influence cognition. This emerging field is of importance for understanding how cognition is affected by a wide range of events, such as social stress or seasonal changes in thermoregulation or levels of gonadal steroids. The example outlined herein (i.e. seasonal food shortage) highlights the conditions under which mechanisms underlying cognitive resilience or cognitive enhancement might be selected in populations living in energetically challenging environments, such as areas with cold winters or severe droughts. We predict cognitive impairment during periods of food shortage, except when environmental conditions affect energy trade-offs in a way that cognitive performance is maintained or improved at the cost of other physiological systems receiving less energy. Whether selection pressure for cognitive resilience or cognitive enhancement acts against cognitive impairment under periods of food shortage depends on a combination of environmental factors.

Predation risk is an important environmental factor to be taken into consideration when studying the ecophysiology of cognition. A mistake during a predator–prey interaction can dramatically increase the probability of an animal being killed. On the other hand, animals need to make compromises: to survive predatory events while managing energy intake, storage and expenditure. As a consequence, performance in cognitive traits important in predator avoidance, such as vigilance (attentional processes), risk assessment (the ability to discriminate predator cues according to their risk of threat) and escape strategies (choice of shorter and safer escape routes), is expected to be weaker during periods of low food availability (Abrams, 1994; Dukas, 2002).

We propose that the ecophysiology of cognition should be investigated in distinct populations facing periods of food shortage while living under different levels of predation risk. Cognitive impairment during periods of food shortage may increase the risk of death by predation. However, this would depend on predation risk: cognition should be impaired when predation risk remains constant or decreases, but cognition should be maintained or enhanced when predation risk is increased. For example, a study in woodfrog tadpoles *Lithobates sylvaticus* showed that cognitive performance of prey depends on predation risk: tadpoles briefly exposed to a high predation risk show an improvement in learning the accurate response to a predator stimulus (higher intensity and longer memory retention) in contrast to tadpoles maintained in a low-predation-risk environment (Ferrari, 2014). Finally, it is also possible that cognitive enhancement would only target specific cognitive traits that are involved in defence against predators, with performance in other traits remaining stable or being impaired.

VII. CONCLUSIONS

(1) Few field studies have addressed the relationship between metabolism, hormones and cognitive traits under natural conditions. One area of cognitive research has focused on variation in cognitive abilities of animals in an ecological context (Healy & Braithwaite, 2000), while another has focused on the influence of physiology on cognition under highly standardized laboratory conditions (e.g. Neese & Schantz, 2012).

(2) We must understand how the cognitive variation that we measure in the laboratory translates into fitness differences in the field. Cognitive research has long focused on cognitive abilities of species but has ignored individual variation. By studying cognitive performance at the individual level in the field, we will be able to translate cognitive variation into fitness differences. This will enable us to understand how natural selection has shaped cognitive processes in animals.

(3) To link individual traits to fitness, one needs to identify significant variation in the studied trait. Constraints imposed by the environment *via* physiological systems can

induce such variance in cognitive performance. Further, by experimentally altering or removing physiological constraints in some individuals, the physiological causes of differences in cognitive performance can be studied.

(4) The emerging field of the ecophysiology of cognition studies how physiological changes affect cognition in free-living animals exposed to natural environmental variation, such as seasonal variation in food availability and temperature. This will help us to reach a better understanding of the environmental conditions under which cognitive impairment, cognitive resilience or cognitive enhancement occurs.

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