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Title: Error management theory and the adaptive significance of transgenerational maternal-stress effects on offspring phenotype

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Running Head: Error management of maternal stress

Abstract

It is well established that circulating maternal stress hormones (glucocorticoids, GCs) can alter offspring phenotype. There is also a growing body of empirical work, within ecology and evolution, indicating that maternal GCs link the environment experienced by the mother during gestation with changes in offspring phenotype. These changes are considered to be adaptive if the maternal environment matches the offspring's environment, and maladaptive if it does not. While these ideas are conceptually sound, we lack a testable framework that can be used to investigate the fitness costs and benefits of altered offspring phenotypes across relevant future environments. We present Error Management Theory as the foundation for a framework that can be used to assess the adaptive potential of maternal stress hormones on offspring phenotype across relevant post-natal scenarios. To encourage rigorous testing of our framework, we provide field-testable hypotheses regarding the potential adaptive role of maternal stress across a diverse array of taxa and life histories, as well as suggestions regarding how our framework might provide insight into past, present, and future research. This perspective provides an informed lens through which to design and interpret experiments on the effects of maternal stress, provides a framework for predicting and testing variation in maternal stress across- and within taxa, and also highlights how rapid environmental change that induces maternal stress may lead to evolutionary traps.

Keywords. Maternal stress effects, maternal programming, maternal effects, developmental plasticity, signal detection theory, predictive adaptive responses

Introduction

Changes in the parental phenotype can act as a signal to offspring about the future environment that they will encounter and these parental cues can induce adaptive plasticity in offspring characteristics (adaptive transgenerational phenotypic plasticity or adaptive parental effects). Recently, this phenomenon has been increasingly studied in vertebrates in the context of maternal-stress effects, largely because the maternal phenotype or cue that may induce plasticity in offspring traits (maternal stress hormone levels) is both measureable and amenable to experimental manipulations. In vertebrates, exposure to maternally-derived stress hormones (glucocorticoids; i.e., 'maternal stress') is increasingly recognized as a significant factor mediating transgenerational phenotypic plasticity in offspring (Barbazanges et al. 1996; Gluckman et al. 2005; Meaney et al. 2007; Love et al. 2013). The consequences of maternal stress have long been considered to be maladaptive in biomedical fields because offspring phenotypes that can occur in response to maternal stress (e.g., smaller size, slower growth, lower energetic demand, higher anxiety-like behaviour) are assumed to confer reduced fitness (Sheriff and Love 2013). However, researchers have recently proposed that maternal stress can play adaptive roles across a wide variety of animal taxa if stress-induced phenotypes better prepare offspring for a stressful post-natal environment in mammals (Sheriff et al. 2010; Dantzer et al. 2013; Bian et al. 2015; Sheriff 2015), birds (Love et al. 2005; Love & Williams 2008; Chin et al. 2009; Coslovsky & Richner 2011), reptiles (de Fraipont et al. 2000; Meylan & Clobert 2005; Bestion et al. 2015), and fish (Giesing et al. 2011). Despite this recent progress, a unified framework that both explains the selective mechanisms and allows field-testing of the adaptive role of maternal stress has yet to be proposed.

Recent theoretical models and meta-analysis have been generated to examine the evolution of parental and maternal effects generally (e.g., Uller et al. 2013; Kuijper & Hoyle 2015; Leimar & McNamara 2015). Using insights from these theoretical models in addition to those from Error Management Theory (EMT; Haselton & Buss 2000), we provide a framework for generating field-testable hypotheses regarding the adaptive potential of maternal stress under different scenarios. By providing a mechanistic basis for examining the adaptive potential of maternal-stress effects (defined as the influence of maternal stress on offspring phenotype), our framework aims to i) describe how selection pressures can shape these adaptive responses, ii) provide a basis for testing new hypotheses, and overall iii) catalyze the study of maternal-stress

effects across a diversity of species, life histories, and environments. A strength of our approach is that it provides a means for examining the general maternal stress – offspring phenotype relationship, regardless of whether this relationship is primarily controlled by mothers, offspring, or both. Further, it allows testing of the adaptive potential of maternal stress from the mother's perspective, the offspring's perspective, or both (i.e., does maternal stress increase maternal or offspring fitness or both). We begin by summarizing critical considerations to be appreciated when examining the maternal stress – offspring phenotype relationship. We then outline how applying EMT to transgenerational maternal-stress effects generates several novel hypotheses and predictions that inform discussions pertaining to the evolution and variation in strength of this relationship across taxa. We finish by using EMT-generated hypotheses to predict the consequence of this relationship as animals face novel stressors from anthropogenic sources. Although we focus on the maternal stress – offspring phenotype relationship in vertebrates, as this is the area where we feel current paradigms could use productive assessment, our work also has implications for understanding the adaptive value of maternal effects more broadly; we develop this component of our work in our concluding section.

Evaluating the potential adaptive value of maternal stress in vertebrates

Although the ecology of maternal stress has been an active area of research, the traditional biomedical view that maternal stress generates negative outcomes for both mothers and offspring (i.e., is maladaptive) often still prevails (Sheriff & Love 2013). Indeed, stress-induced offspring phenotypes are commonly perceived to have a lower phenotypic quality (i.e., smaller size, slower growth, altered behaviour/physiology, etc.), generating assumptions that performance in nature will likewise be impaired, and often leaving potential context-specific benefits untested and therefore underappreciated. This perspective has recently been challenged by ecological hypotheses (e.g., the Environmental Matching Hypothesis; Love & Williams 2008) and supporting evidence that stress-induced phenotypes can improve offspring performance in *stressful* (but not benign) post-natal or adult environments (e.g., Dantzer et al. 2013; reviewed in Sheriff & Love 2013).

To move this field ahead in a productive manner, we suggest that three critical points must be considered prior to assigning any hypothetical adaptive or maladaptive value to maternal-stress effects (*sensu* Love et al. 2013; Sheriff & Love 2013; Uller et al. 2013; Sheriff et al., 2017). First, we must appreciate that the value of any phenotype, whether stress-induced or

not, can only be understood by examining performance or fitness in an ecologically-relevant context (and not simply assuming the outcome based on the phenotype alone). Second, we must consider the evolutionary and life-history context of the organism before experiments can be designed to test phenotype-performance relationships. For example, if predation risk is the most salient selection pressure in the evolution of a species' stress response, testing phenotypic performance in a food-restricted environment is unlikely to yield useful inference regarding the fitness value of stress-mediated offspring plasticity. Finally, we must appreciate that testing phenotypic performance in a singular post-natal environment, particularly if the relative quality of the post-natal environment does not match that of the pre-natal environment, is invalid for determining the adaptive potential of maternal stress. For instance, testing the performance of stress-induced phenotypes relative to control phenotypes in a stressful post-natal environment (and not simply in a control environment) is an absolute requirement for correct inference regarding the adaptive value of stress-induced plasticity. Stated another way, the fitness outcomes of phenotypes induced by elevated maternal glucocorticoids need to be examined across more biologically and ecologically appropriate environments.

The general under-appreciation for this latter phenotype-matching aspect, in particular, is what makes the development of a testable framework to assess the general adaptive potential of maternal stress so valuable. In nature, animals interact with their environments over dynamic spatio-temporal scales. As such, the quality of the maternal and offspring environment may be temporally or spatially matched, such as may occur in species where there are overlapping generations (temporal matching) or where offspring disperse to areas that are similar to parental environments. Alternatively, past cues may not reliably predict the future (such as in long-lived animals or those with long-distance natal dispersal); increasing or decreasing the likelihood that the maternal and offspring environments match (Sheriff & Love 2013; Sheriff et al. 2017). Thus, to correctly assess the potential adaptive role (if any) of maternal stress, the *relative* offspring-phenotype fitness value across biologically relevant environmental scenarios must be examined (Figure 1; Love & Williams 2008; Uller et al. 2013). Importantly, there are likely very different costs/benefits associated with offspring phenotypic performance depending upon the match or mismatch to future environments (Box 1), and the costs of mismatches, not matches, are expected to play a significant role in the origin and maintenance of transgenerational maternal-stress effects.

Error management theory and a cost-benefit perspective of vertebrate maternal stress

Error management theory, an evolutionary perspective based on signal detection theory (Box 1), provides a formal theoretical framework for evaluating how organisms (including humans) should make decisions amidst uncertainty (Swets 1992; Haselton & Buss 2000; Johnson et al. 2013). EMT has been successfully used to examine many biological phenomena, such as plant defense mechanisms against herbivores (Orrock et al. 2015), mate-selection behaviour (Haselton and Buss 2000), deception in animal communication (Wiley 1994), optimal anti-predator behaviour (Bouskila & Blumstein 1992), and defense mechanisms in human health and disease (Nesse 2005). The broad applicability of EMT is possible because it comprises the basic components common to most decisions made by microbes, plants, and animals: based on some amount of information regarding the likelihood of an event, an organism chooses to respond (or not to respond), and that response (or lack of response) has some probability of being incorrect in two distinct ways (analogous to type I and type II errors in standard hypothesis testing). Importantly, EMT posits that, when the two different types of error have different fitness costs (or benefits), selection will favor individuals that err towards making the least costly error to avoid making a costlier one.

Since the quality of the maternal environment can often be indicative of the conditions experienced by her offspring, EMT may be a particularly tractable framework for considering the adaptive significance of maternal-stress effects given the framework's ability to compare the relative fitness costs and benefits of phenotypic changes within relevant future environments. Specifically, EMT can be used to assess whether the effects of maternal glucocorticoids on offspring phenotype generate relatively better (benefits) or worse (costs) fitness outcomes for mothers or offspring depending on the relative match of that adjusted phenotype to the future environment (Figure 1). Because future conditions cannot be predicted with complete accuracy, maternal-stress effects can be incorrect in two ways. First, exposure to elevated maternal stress may induce a phenotypic response in offspring but the future environment that they encounter is not stressful, a false-positive error expected to reduce offspring fitness compared to an unaltered offspring in that benign environment. Second, elevated maternal stress does not induce a phenotypic response in offspring and the future environment encountered by the offspring is stressful, a false-negative error expected to reduce offspring fitness compared to an altered

offspring in that stressful environment. Effects of maternal stress on offspring can in turn also be correct (i.e., with no associated error) in two distinct ways, collectively generating four possible offspring phenotype-postnatal environment scenarios (Table 1, Figure 1): i) unaltered offspring phenotype in a benign postnatal environment (no error), ii) altered offspring phenotype in a benign environment (error of unnecessary offspring modification), iii) unaltered offspring phenotype in a stressful environment (error of failing to modify offspring when necessary), and iv) altered offspring phenotype in a stressful environment (no error). Although EMT typically focuses on the costs and benefits of errors in affecting optimal decision making, within our framework, it is the costs and benefits of the actual decisions that are ultimately important and which influence the evolution of maternal-stress effects (Box 1). Our framework is also cast in terms of offspring that may inhabit a future environment that is either benign or stressful. Although this dichotomous classification may suffice to capture relevant differences in many species (especially over the relatively short window early in life when environmental stressors are likely the biggest agents of offspring mortality), we note that the main conclusions of our work also apply in cases where offspring may inhabit environments that vary greatly in their stressfulness (Nesse 2005). As such, our framework shows how the influence of maternal stress can be adaptive even when the stress-induced phenotype of the offspring is not a perfect match to the environment (i.e., it demonstrates how seemingly maladaptive offspring phenotypes are actually adaptive when we incorporate the reality of an uncertain future and the likelihood of different error costs over time; Box 2).

[Note to Editor: Consider inserting Box 1 here]

Predicting the relative strength of vertebrate maternal-stress effects

Our framework provides further predictive power enabling researchers to forecast variation in the influence of maternal stress on offspring phenotype across taxa and life histories (Box 3). First, EMT provides a means for predicting the threshold at which a developmental decision will be made within a given species (Box 1), where the decision is the phenotypic response of offspring (more akin to a mechanistic reaction than a typical decision) and the threshold is the level of maternal stress (i.e., glucocorticoid hormones) at which this response occurs in offspring. For example, our framework predicts that species that experience much greater costs

to producing an unaltered offspring in the face of a stressful environment (i.e., a false-negative error) should have a much lower maternal stress threshold at which offspring phenotypic response occurs compared to a species where the costs of false-negative errors are lower (or the costs of false-positive errors are higher). Highly vulnerable prey, such as species with type III survivorship curves (i.e., very low offspring survivorship), should respond at a much lower maternal-stress threshold compared to prey species that are not as vulnerable to predation, such as those with type I or II survivorship curves (i.e., very high or moderately higher offspring survivorship, respectively). This relationship may also be influenced by where species fall along the precocial-altricial axis of life-history variation (precocial and altricial offspring differ in the duration of postnatal parental care). We would expect species producing more precocial offspring (requiring shorter periods of postnatal care) to respond at a lower maternal-stress threshold than species producing more altricial offspring (requiring longer periods of postnatal care). This is because the greater duration of parental care in the more altricial species may offer an opportunity to reduce the costs of a mismatch of offspring phenotype and post-natal environment (i.e., an error that can somewhat be corrected). For example, in both laboratory studies of rats and field studies of birds, maternal stress can alter offspring phenotype; however, post-natal maternal/parental care can reverse or enhance these effects or can modify an unmodified neonate's phenotype (Meaney et al. 2007; Love & Williams 2008). All of which has the potential to reduce the costs of mismatch errors (i.e., false negative/positive errors) in species that exhibit high degrees of parental care (e.g., primates or passerine bird species).

Our framework also predicts that maternal-stress effects should be strongest in species where there is generally high spatial and/or temporal variation in stressors among generations but relative consistency in stressor magnitude and from the time of gestation through to offspring experience (early-life); as these are situations where errors are most likely to occur over evolutionary time. As such, in species that experience periodic and/or unpredictable extremes in predator populations, food availability, or conspecific density among generations, but inhabit a relatively consistent environment from the time of gestation through to the early life of offspring (e.g., Sheriff et al. 2010; Dantzer et al. 2013; Kuijper et al. 2014), we would expect a lower maternal-stress threshold at which offspring phenotypic response occurs than in species with either high or low, but chronic, inter-annual exposure to such stressors. Examples of such species include snowshoe hares (*Lepus americanus*) or North American red squirrels (*Tamiasciurus*

hudsonicus) in the Yukon, Canada that can experience extreme inter-annual fluctuations in the abundance of predators, food, or conspecifics. These fluctuations in predation risk for snowshoe hares occur in a regular 10 year cycle (Krebs et al., 1995) whereas the fluctuations in food and density in red squirrels (Boutin et al., 2006; Dantzer et al., 2012, 2013) are episodic, occurring every 3-4 years. For both species, the environments faced by offspring are qualitatively different (i.e., either benign or very stressful), and remain so for the course of offspring development (i.e., for the purposes of offspring survival, the environments remain either benign or stressful).

Our perspective may also provide insights into determining the origin of sex-specific sensitivity to maternal or developmental stress (Box 3; Love et al. 2005; Brunton & Russel 2010; Bale & Epperson 2015). In species where there is disparity in the proximate or ultimate costs of raising a given sex, our framework predicts that the more expensive sex would have a lower threshold to respond to maternal stress given that the costs of errors would be higher compared to the less expensive sex (Love et al. 2005; Love & Williams 2008). Likewise, in species with sex-biased natal dispersal, our framework would predict that the dispersing sex should have a higher threshold to respond to maternal stress compared to the philopatric sex, given the reliability of the information about the future environment is lower in the dispersing sex (de Fraipont et al. 2000; Meylan & Clobert 2005). This idea can be expanded to species with natal dispersal in general, and interestingly, to natal habitat preference induction, where dispersing individuals will select habitats that are most similar to their natal habitat (Davis & Stamps 2004). This phenomenon would increase the match between the maternal and offspring environment and potentially reduce the cost of errors in offspring phenotype response.

Maladaptive errors in response to novel stressors

As outlined above, species-specific responses of offspring to maternal stress are likely to have been optimized by natural selection based on species life history and environmental variation experienced (Gluckman et al. 2005; Sheriff & Love 2013). Thus, as with any adaptive phenotypic response that has been shaped by predictable variability in intrinsic or extrinsic environmental quality, there are potential negative implications with regards to human-induced rapid environmental change (i.e., HIREC; Sih 2013) many animals now face. Two likely scenarios have the potential to emerge as animals increasingly face novel stressors in their environments. First, these stressors will result in offspring phenotypes that may be maladapted to

the novel stressor due to the presence of false-positive errors. This circumstance is analogous to a situation where cues that once induced adaptive phenotypic plasticity now become unreliable (Trimmer et al. 2017). For example, consider animals such as common lizards (*Zootoca vivipara*) in which maternal stress increases offspring propensity to disperse as an adaptive response to increasing predation risk (Meylan & Clobert 2005; Bestion et al. 2015). If such animals now face a novel anthropogenic stimulus (e.g., traffic noise) that also induces maternal stress, the resultant offspring phenotype may exhibit a false-positive error (since the stressor was not predation risk), and the cost of this error may now decrease (rather than increase) offspring fitness. Second, animals may not respond to a novel stressor if mothers do not perceive it as stressful (i.e., a false-negative error). For example, mothers may be faced with novel introduced predators, but fail to perceive them as threatening (Sih et al. 2010), resulting in unaltered offspring phenotypes and likely lowered fitness in the new high predation environment. EMT predicts that animals will likely make maladaptive errors, in both direction and relative strength, to novel stressors since their decision bias (in our case maternal-stress effects) was shaped over evolutionary time. This bias could then result in evolutionary traps (Schlaepfer et al. 2002) given present-day environmental changes that may increase the degree of mismatch between the maternal and offspring environments or decrease the reliability of cues that mothers generate that offspring in turn may use to forecast the environments they will encounter at independence.

Future directions: extending model predictions and applications to other systems

While we focus on maternal-stress effects in vertebrates, maternal effects via other mechanisms have been documented in a variety of systems, including plants (e.g., Schuler & Orrock 2012) and arthropods (Mousseau & Dingle, 1991) as well as reptiles, amphibians, birds, and mammals (Mousseau & Fox, 1998; Uller, 2008). Several of the key predictions from our framework may extend to these groups as well, where they can be useful in generating both species-specific predictions and testing environmentally specific hypotheses in the field. For example, it is well established that plants exhibit a multitude of transgenerational effects in response to a diverse array of environmental stressors, including herbivory, temperature, and resource-related stress (Agrawal, 2001; Crisp et al., 2016; Walter et al., 2016). EMT could be used to broadly examine the environmental and life-history conditions under which these transgenerational effects are adaptive. More specifically, EMT would predict that for plants that produce small seeds (e.g.,

often annual plants), transgenerational maternal-stress effects might be triggered at relatively modest levels of environmental stress, since the costs of false-negative errors may be very high for small-seeded species whose seedlings do not have large energy or resource reserves for tolerating stress. On the other hand, plant species producing larger seeds should pay lower costs for false-negative errors (because seedlings have greater reserves to help ameliorate the cost of a false-negative error), and EMT would predict a reduced response of seed phenotype to maternal stress.

In many plant species, as well as aquatic or terrestrial invertebrates and vertebrate species, that produce numerous, low cost propagules in their lifetime, offspring may experience very high mortality during development. As such, these species may adopt a bet-hedging, rather than preparative, strategy with regards to future stressors (Herman et al., 2014), where current stress signals are ignored even if they are predictive of future stress. An important future direction (Box 4) will be examining predictions generated with EMT in these species.

Overall, we have chosen to outline the EMT framework focused primarily on vertebrate taxa that experience fluctuating environments in which we expect parental/maternal effects to have a large influence on offspring phenotype relative to other sources of variation (Leimar & McNamara, 2015) and compared to other mechanisms of dealing with fluctuating environments such as bet-hedging (Proulx & Teotónio, 2017). Although we have focused on maternal-stress effects in vertebrates, we expect that future studies in any organism could use the same framework, substituting their own taxa- or species-specific mechanism or signal of environmental quality that a parent can pass to their offspring. Studies expanding this framework to other organisms are both greatly needed and have the power to more robustly test EMT within this maternal-effect framework.

Concluding remarks

When viewed from an EMT perspective, the adaptive nature of seemingly maladaptive maternal stress effects becomes more readily apparent (Box 1). The EMT framework outlined here provides a means to reconcile the persistence of the sometimes seemingly maladaptive role of maternal stress (Box 2), an array of hypotheses (Box 3), and generates additional functional questions (Box 4) to help us further characterize and appreciate the tremendous variation in phenotypes and fitness outcomes that are often observed. It further allows us to better predict

how animals may (or may not) respond to novel stressors. An important pragmatic benefit of our EMT approach is that, unlike some theoretical models, it can provide qualitative predictions that can be readily tested by experimental manipulation of components known to alter vertebrate maternal stress and quantifying how this alters offspring phenotype, and the relative performance and fitness outcomes. We expect that new studies adopting experimental manipulations of maternal stress across related species that exhibit a diversity of life histories and across a continuum of environmental fluctuations will be particularly useful in testing the predictions of EMT to explain the adaptive role of maternal stress. Expanding the EMT framework to other taxa is especially needed to test both the generality and the robustness of EMT for predicting transgenerational maternal-stress effects in a variety of ecological and life-history contexts.

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Box 1. Error management theory and the adaptive role of maternal stress

Selection should favor individuals where maternal stress (e.g., levels of glucocorticoid hormones in vertebrate models) alters offspring phenotype when the benefit of doing so outweighs the costs of not doing so. Because environmental conditions often covary in time and space, current conditions experienced by the mother (i.e., the degree to which the current environment is stressful, represented by the level of maternal stress) may be indicative of conditions that will be experienced by a mother's offspring. If the maternal environment can be used to gauge the future environment, offspring phenotype should be altered at some threshold level (called the decision threshold) where the level of current environmental stressors experienced by the mother has sufficient reliability for predicting likely future environmental stressors for the offspring. The reliability of the current environment to predict the future environment may be indicated by the level of maternal stress hormones. In the figure below, the frequency distributions of the two possible future environments (unstressful or stressful) are plotted against the level of current maternal stress. The level of maternal stress at which offspring phenotype becomes modified

determines the relative likelihood of a successful match between offspring phenotype and the type of environment the offspring will experience (i.e., a true positive, TP, or true negative, TN), as well as influences the likelihood of an error, i.e., the false positive, FP, (unnecessary modification of offspring phenotype) or a false-negative error (FN, failing to modify offspring phenotype when the future is stressful). Given that the fitness costs of each of these types of error differ (likely such that $F_{TN}>F_{TP}>F_{FP}>F_{FN}$; Table 1), and the background probability that the future environment will be stressful (P(s)) or unstressful (P(ns)), offspring phenotype should be modified whenever the value of maternal stress is greater than $\frac{P(ns)}{P(s)} \times \frac{(F_{TN}-F_{FP})}{(F_{TP}-F_{FN})}$; an example threshold is indicated in the figure below (the vertical line in the middle of the two distributions). The red area to the right of the threshold represents the probabilities of true positives and false positives that would be realized at that particular decision threshold.

[NOTE TO EDITOR: Suggest inserting Fig. for Box 1 here]

Within the EMT perspective, the costs of TN and TP are often assumed to be identical, as the focus is typically on the evolutionary implications of errors. However, within our framework, and as our matrix shows (Table I), each of the four outcomes is likely to have a different fitness value (indicated by F_{TN}, F_{TP}, F_{FN}, F_{FP}), because each outcome has a different combination of the two possible error costs. False positive errors of producing altered offspring that experience benign environments are expected to be much less costly (in terms of reduced offspring fitness in the benign environment) than false negative errors of producing unaltered offspring that experience very stressful environments. However, quantitative assessments of those predictions are rare as few studies perform full factorial experiments in wild animals and assessment of the fitness consequences of false positive errors is rare.

In our framework, fitness values can be measured as offspring performance or fitness (e.g., survival) and thus, the relative fitness value of that phenotype can be measured within a given environment. Importantly, our framework can also be expanded to measure relative maternal performance or fitness (e.g., Love et al. 2008) to better understand the adaptive potential of maternal stress for a mother's fitness. This may also allow a comparison of the relative fitness values to the mother and offspring, and expand our understanding of potential

mother-offspring conflict.

Table I. Fitness outcomes of maternal-stress effects should be compared across all scenarios within a 2 x 2 framework, representing the four possible outcomes when offspring phenotype may (or may not) be modified in a way that does (or does not) match the future environment. For simplicity, we label the environment experienced by the mother or her offspring as "Stressful" (high levels of glucocorticoids relative to the species-typical levels) or "Unstressful". In general, we anticipate fitness rankings of $F_{TN} > F_{TP} > F_{FP} > F_{FN}$ or $F_{TN} > F_{FP} > F_{TP} > F_{FN}$; which of these is accurate depends upon the relative costs of false positive (FP) errors and true positive (TN) outcomes. Importantly, regardless of the relative fitness values of F_{TP} and F_{FP}, we always expect F_{FN} to have the least fitness (and often by a substantial margin), such that error management would predict that mothers would produce offspring that are least likely to experience this error (i.e., mothers should err towards producing altered offspring to reduce the likelihood of failing to produce altered offspring that later experience a highly stressful environment). In general, we expect that many situations exist where offspring experience environments that are well-approximated by a simple dichotomy of stressful vs. benign environments (especially over the relatively brief window early in life where offspring survival is typically most constrained). However, we note that the general predictions of the model still follows in cases where offspring may experience a range of stresses in the natal environment (so that the natal environment is not well described by a simple stressful/unstressful classification). As long as the fitness costs of the two types of error are asymmetrical and current information has some predictive utility for future conditions, we expect selection to favor maternal-stress effects that lead to modified offspring when the costs of making unnecessarily altered offspring are much lower than the costs of failing to modify offspring then future stress is imminent (Nesse 2005).

		Environment Experienced by Offspring	
		Unstressful	Stressful
Maternal-stress Alteration of Offspring	Unstressful	Unaltered offspring in benign environment, no error *True Negative (TN)*	Error of failing to modify offspring when necessary *False Negative (FN)*

Phenotype		
Stressful	Error of unnecessary offspring alteration *False Positive (FP)*	Altered offspring in stressful environment, no error *True Positive (TP)*

490

491

492 **Box 2. Error management helps resolve the value of maternal stress**

493 Empirical evidence from ecological studies support the idea that maternal-stress effects can be
494 adaptive if the quality of the mother's environment predicts (i.e., matches) that of its offspring
495 (i.e., a true-negative or true-positive), but maladaptive if it does not (i.e., false-negative or false-
496 positive; Love and Williams 2008; Sheriff and Love 2013; Uller et al. 2013). The overall
497 outcome is a dichotomous value of maternal stress. For example, snowshoe hares exhibit a 10-
498 year population cycle with their main predator, Canada lynx (Krebs et al., 1995). During the
499 decline phase of their population cycle (when their population size is declining from its peak),
500 hares experience extreme predation risk from lynx and exhibit increases in maternal
501 glucocorticoids (Sheriff et al. 2011). These elevations in maternal glucocorticoids result in
502 smaller, lighter offspring that have elevated hormonal responsiveness to a stressor, but which are
503 assumed to be adapted to the high predation environments the offspring encounter (Sheriff et al.
504 2009, 2010). Although these modified offspring born during the decline phase encounter extreme
505 predation risk from lynx, this is not the case for offspring that are born at the end of the decline
506 phase or during the low phase of their population cycle (when population size is at its nadir;
507 Sheriff et al. 2011). Thus, exposure to maternal stress may cause adaptive changes in offspring
508 during the decline phase and yet seemingly maladaptive effects in offspring during the low phase
509 because it seems to poorly match the environmental conditions the offspring will experience at
510 independence (a low predation environment). However, when considered in our EMT-based
511 framework the costs of the potential errors must be compared, (i.e., the fitness value of a false-
512 positive vs. a false-negative). Given this perspective, it is likely that maternal stress is adaptive
513 throughout the hare cycle; living in a benign (low predation) environment as an altered offspring
514 is likely far less costly than living in a predator-rich environment as an unaltered offspring; i.e.,
515 lower reproduction vs. quick death. In other words, the fitness costs of being an altered hare
516 during the low phase when predation risk is low are likely outweighed by the fitness benefits of

being an altered hare during the decline phase when predation risk is high. Thus, through the lens of EMT, the correct assessment of the relative adaptive function of maternal-stress effects can be made since the EMT framework provides the relative fitness outcomes across various future environments.

Box 3. Predictions for variation in offspring response to maternal stress across life histories.

[NOTE TO EDITOR: Suggest inserting Fig. for Box 3 here]

Error management theory can help inform qualitative predictions about the variation in the strength of influence of maternal stress on offspring phenotype (maternal-stress effects) both among and within species and populations. (A) Focusing on situations where successful matches (i.e., true positive and true negative outcomes) have the same benefit, the relative cost of failing to modify offspring phenotype when necessary (false-negative errors) compared to the cost of unnecessary modification in a benign environment (false-positive errors) may drive the threshold at which an offspring's phenotype responds to maternal stress. (1) When costs of false-negative errors are small relative to costs of false-positive errors, we expect that offspring phenotype will only be modified at relatively high levels of maternal stress. Alternatively, (2) when costs of false-negative errors are very large relative to costs of false-positive errors (e.g., when highly lethal stressors are common in the offspring environment), we expect that offspring phenotype will be modified at relatively low levels of maternal stress. (B) We expect that particular life-history traits, as well as particular ecological situations, will influence the amount (or threshold) of maternal stress required to initiate a change in offspring phenotype. (1) We expect relatively weak maternal-stress effects for those organisms where there is i) a low risk of offspring mortality (type I) or an equal risk of mortality across lifestages (type II), ii) parental care to buffer offspring's exposure to the post-natal environment (altricial species), iii) a relatively constant environment, and iv) a significant disconnect between maternal and offspring environment (high-dispersal or long-lived species), (2) while we expect a lower threshold of response and relatively strong maternal-stress effects in organisms which display opposing traits.

Box 4. Outstanding questions in integrating EMT into maternal-stress effects

548
549 1) Are the fitness benefits of maternal stress dependent upon the environment offspring
550 experience at independence? It is important to quantify effects of stress-induced phenotypes in
551 offspring in both stressful and non-stressful environments to fully characterize the costs and
552 benefits of offspring phenotypes modified by maternal stress.
553
554 2) Are the effects of maternal stress on offspring characteristics dependent upon the ecological
555 trigger inducing maternal stress? Environmental stressors such as reduced food availability or
556 high predation risk can both increase maternal glucocorticoids, but it is unclear whether the
557 effects of elevated maternal glucocorticoids on offspring phenotype are the same for these
558 different ecological triggers of maternal stress.
559
560 3) Do offspring or mothers control the point at which elevated maternal glucocorticoids alter
561 offspring traits? Offspring and mothers can be in conflict with how maternal stress alters
562 offspring traits, can offspring resist the effects of maternal glucocorticoids and, if so, how?
563
564 4) What role do fathers play in this EMT view of maternal-stress effects? In species with
565 biparental care, fathers could buffer the effects of maternal stress on offspring by modifying the
566 cost of false-negative or false-positive errors. Fathers may also buffer the environment
567 experienced by the mother, reducing her level of stress.
568
569 5) How does anthropogenic environmental change modify the occurrence of false-negatives and
570 false-positives relative to environments over a species' evolutionary past? For example, the
571 mismatch between maternal and offspring environments is likely elevated due to human-induced
572 rapid environmental change, which should increase the frequency of errors. Moreover, different
573 kinds of human-induced rapid environmental change (i.e., HIREC, see Sih et al. 2013) could
574 generate mismatches that vary in type and magnitude. For instance, introduced predators may
575 increase false-negative errors because they are not recognized as dangerous and do not cause
576 maternal stress. Resource subsidies from ephemeral anthropogenic habitats (e.g., agricultural
577 fields) might lead to increased false-positive errors because food is plentiful for mothers, but
578 may not be for their offspring.

579

580 6) How effectively does the EMT framework capture transgenerational maternal-stress effects
581 for organisms (e.g., many plants, invertebrates, and vertebrates) that produce very large numbers
582 of propagules/offspring? Are transgenerational EMT effects, which would lead to directional
583 shifts in offspring phenotype (i.e., deterministic maternal effects, sensu Proulx & Teotónio) more
584 commonly observed for such species than strategies based upon randomly increasing the range
585 of phenotypes exhibited by offspring (diversifying bet-hedging via random maternal effects;
586 Proulx & Teotónio 2017)?

587

588 7) If mothers bear substantial costs for unnecessary modifications of offspring phenotype (false-
589 positives), how does this alter the predictions of our EMT framework? We focus on offspring
590 fitness, but mothers may suffer substantial fitness costs for true- or false-positives and this could
591 affect the predicted fitness rankings of each scenario shown in Table 1.

592 **Figure Captions.**

593

594 **Figure 1.** (A) The environment experience by mothers during reproduction can either be
595 unstressful (leading to the dashed arrow pathway) or stressful values (leading to the pathway
596 represented by solid arrows), with the latter occurring when her stress hormone levels are
597 increased beyond some threshold of normal baseline (i). This dichotomy leads to 'unaltered'
598 offspring phenotypes or 'altered' offspring phenotypes in response to elevated maternal stress
599 (ii). These offspring then have the potential to also encounter two different environments; an
600 'unstressful' environment, or, alternatively, a 'stressful' environment (iii), and their fitness value
601 will depend upon the interaction between their phenotype and the environment they experience
602 (iv). We suggest the adaptive potential of maternal stress thus needs to be considered as the
603 *relative* offspring fitness across these scenarios, in a 2x2 comparative framework ((F_{TN} –
604 F_{FP})/(F_{TP} – F_{FN}); Box 1). Additionally, the adaptive potential of maternal stress to maternal
605 (inclusive) fitness can also be evaluated within our framework if the end fitness outcomes (iv)
606 are that of the mother (i.e., do mothers survive better and have greater future reproduction if they
607 raise altered offspring in a stressful environment as opposed to attempting to raise unaltered
608 offspring?).

Figure 1.