Predictive Models Surrounding Stress

- 1860 Claude Bernard
- 1932 Cannon
  - Fight or Flight
- 1936 Selye
  - General Adaptation Syndrome
- 1977 Mazeaud et al.
  - Primary, Secondary, **Tertiary**

Predictive Models Surrounding Stress

- Useful definitions and models allow for wide ranging discussion. e.g ecology, deep space travel
- The latest iterations of these include the concepts of allostasis and reactive scope model
- "However, a definition of stress that fits into every disciplines conceptual framework is not on elusive, it may be impossible" Barton 1997

Physiology Models

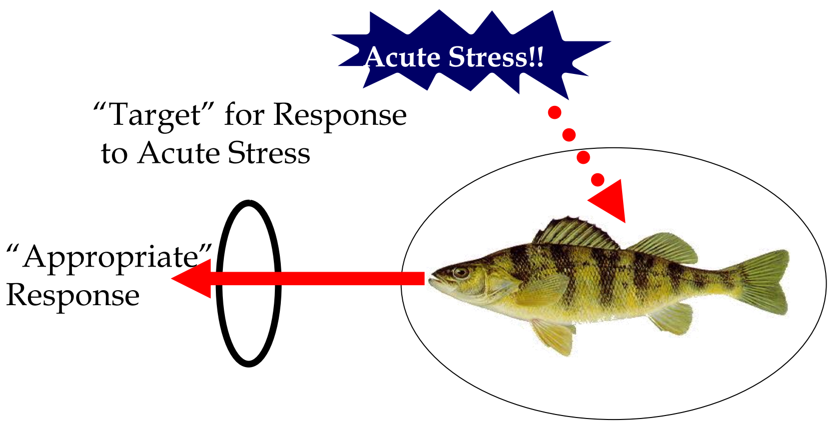
- **Homeostasis** implies that an organism remains within a certain range of physiological parameters to maintain stable function.
- **Allostasis** implies that an organism constantly varies and adjusts physiological parameters to maintain stable function.

Proposed Consequences -- Allostatic Load Model

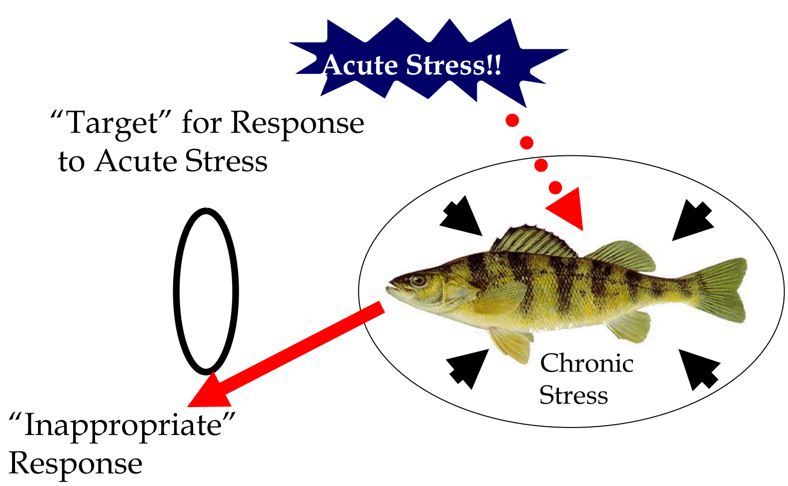
Allostasis: "Maintaining stability (or homeostasis) through change" Sterling and Eyer 1988

Allostatic Load: "Wear and tear that the body experiences due to repeated cycles of allostasis" McEwen 1998

Proposed Consequences – Alf's Allostatic Load Model



Proposed Consequences – Alf's Allostatic Load Model



Allostatic Load

- What do 'appropriate' and 'inappropriate' really mean?
- What is the stress response involved with?

What is stress response involved with?

Every Thing

Social Interactions	Predators
Agonistic Behaviors	Environmental Cues
Exposure to Pathogens	Energy Utilization
Etc.	

An "appropriate" stress response necessary

What Happens If….

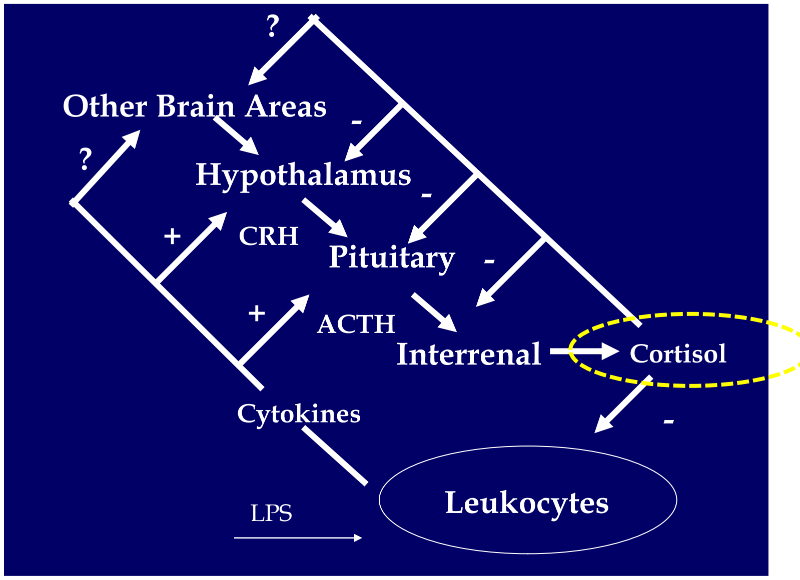
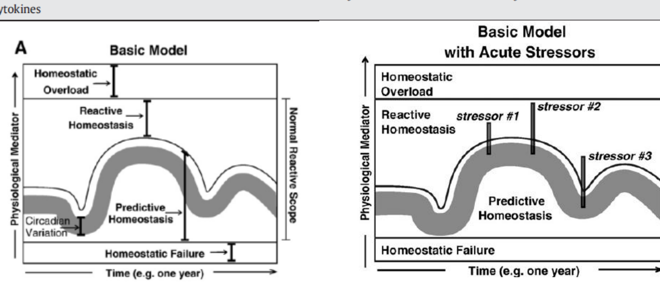


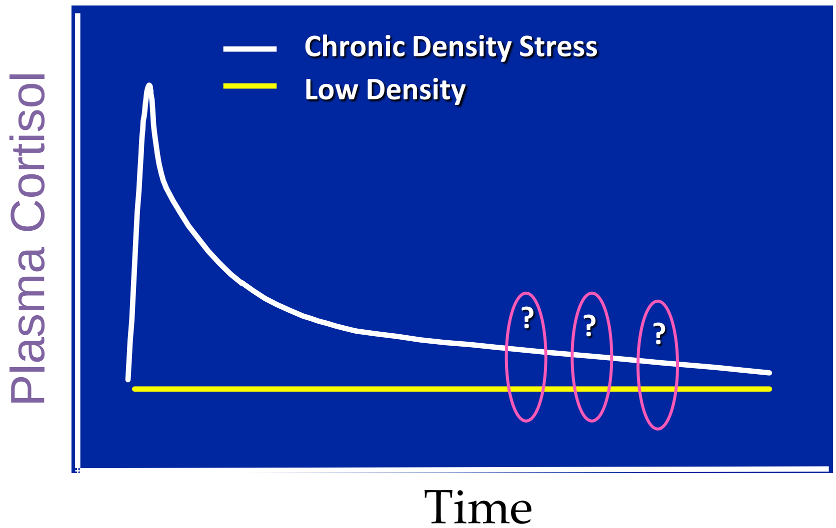
Table 1

Physiological system	Physiological mediator	Predictive homeostasis range	Reactive homeostasis range	Homeostatic overload range	Homeostatic failure range
Immune	Prostaglandin T-cell activation Antibody titers Cytokines	Seasonal ability to fight infection	Mobilization of immune system	Autoimmune Immunosuppression	Immune failure
HPA	Glucocorticoids ACTH	Seasonal life-history needs a. Energetic needs b. Behavioral needs c. Preparative needs	Inhibit immune system Energy mobilization Change behavior Inhibit reproduction Inhibit growth	Immunosuppression Diabetes Muscle breakdown Reproductive suppression Decreased survival	Energy dysregulation Water balance failure Catecholamine insufficiency Decreased survival
Cardiovascular (catecholamines)	Heart rate Heart rate variability Blood pressure	Life-history energy needs	Fight-or-flight Energy mobilization	Hypertension Myocardial infarction Muscle breakdown	Hypotension Lethargy Decreased survival
Behavior	Foraging/feeding Locomotion Migration Conspecific aggression	Life-history changes: a. Energy needs b. Energy availability c. Predator presence d. Mate access	Fleeing behavior Freezing behavior Increase/decrease foraging Increase food intake Increase vigilance Conspecific fighting	Tonic immobility Obesity Anxiety Fear Violence	
Central nervous system	Neurogenesis Dendritic arborization Neurotransmitter concentrations Cytokines	Life-history changes in neural networks Learning and memory	Increase neurotransmission (titers or receptors) Increase learning and memory	Neuronal atrophy/death Depression Decrease learning and memory	Post traumatic stress disorder

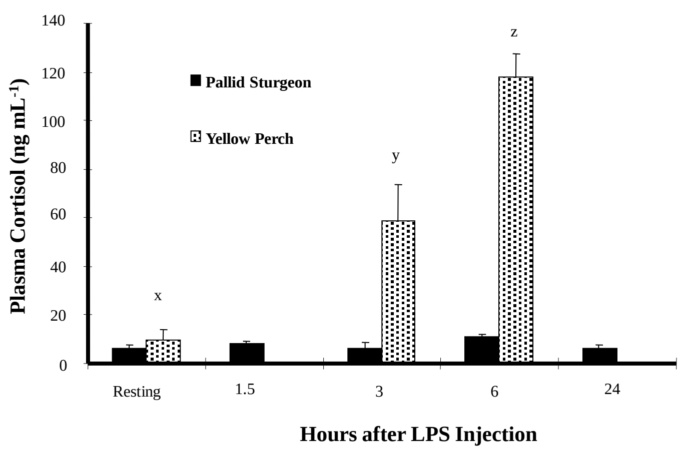


?? Allostatic Load Model ??

Pickering and Stewart (1984)

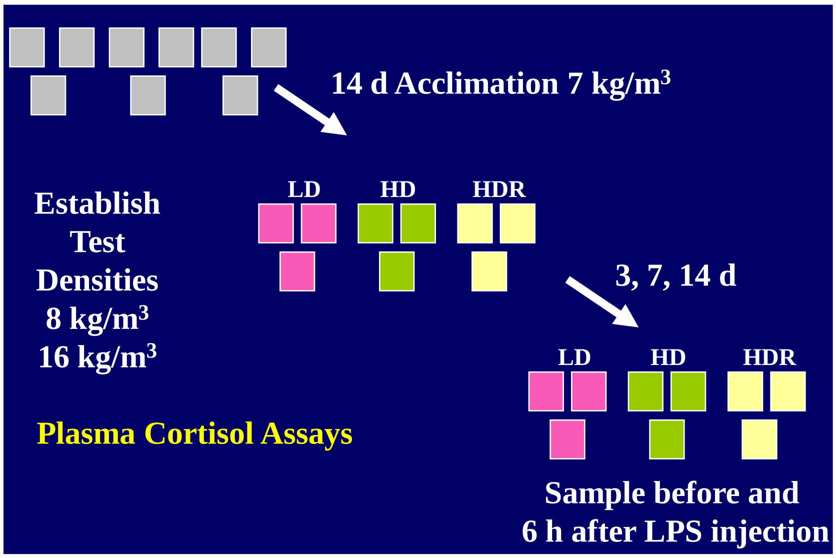


Species differences to an standardized inflammatory/immune (LPS) challenge



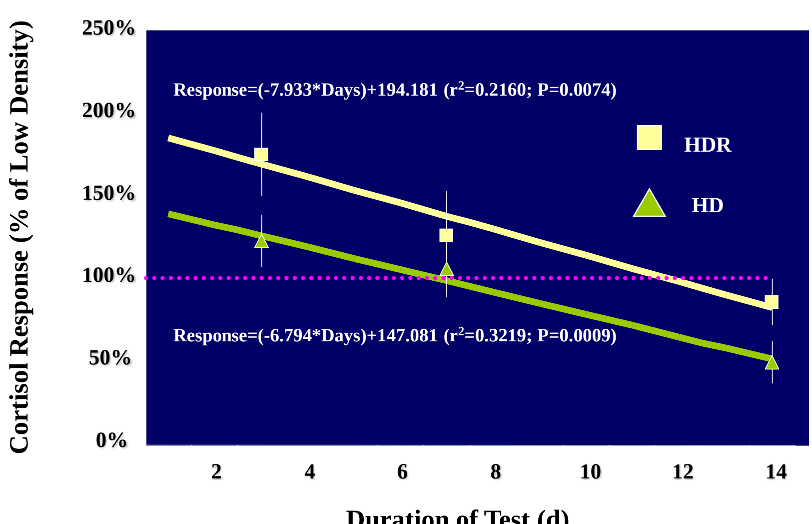
Haukenes et al. 2008

Rearing Density Leads to Differences in Response Following an Inflammatory Challenge

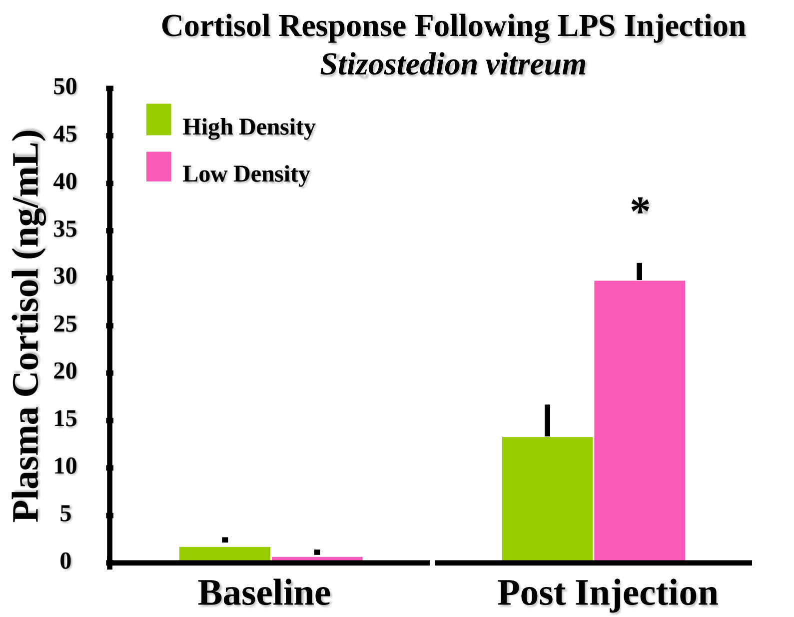


Haukenes and Barton 2004

High Density versus Low Density Cortisol Responses



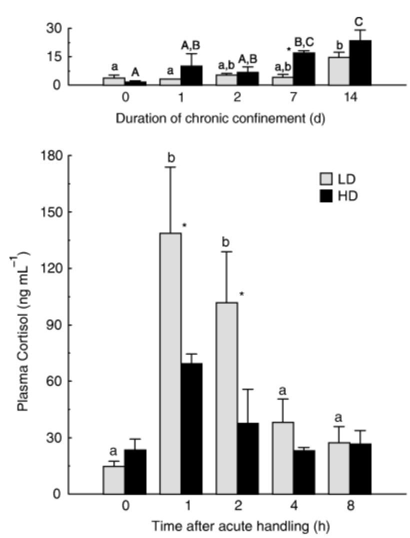
Haukenes and Barton 2004



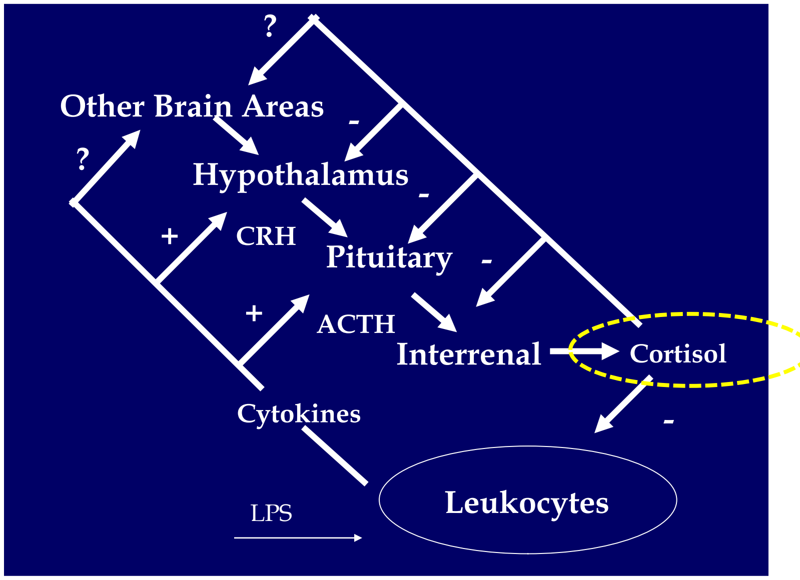
Haukenes, 2001

Follow Up Research

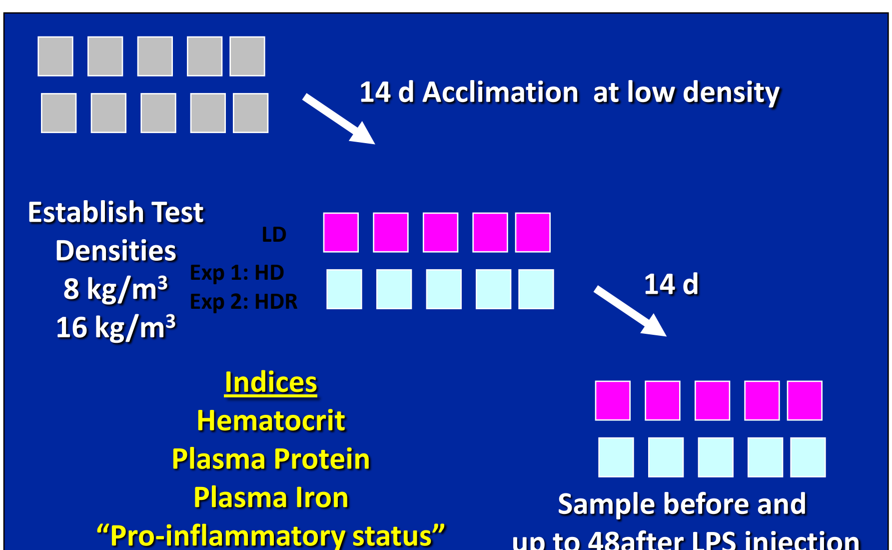
- Barton et al followed this up with handling stressor and found something similar
- **Effects of chronic confinement on physiological responses of juvenile gilthead sea bream, *Sparus aurata* L., to acute handling.** Bruce A Barton[1], Laia Ribas[2], Laura Acerete[2], Lluís Tort[2] 2005, 36:172-179



If this is correct, then what....



Density-Duration Trial 2



The universe is much easier now than it was in 1998-2000….Thank you Illumina and Qiagen

How do I test for pro-inflammatory status in the absence of whole bunch of 'sequence genies'

Cellular Responses – Bactericidal Properties

Macrophage and neutrophils respond to proinflammatory cytokines (Enhances their killing properties)

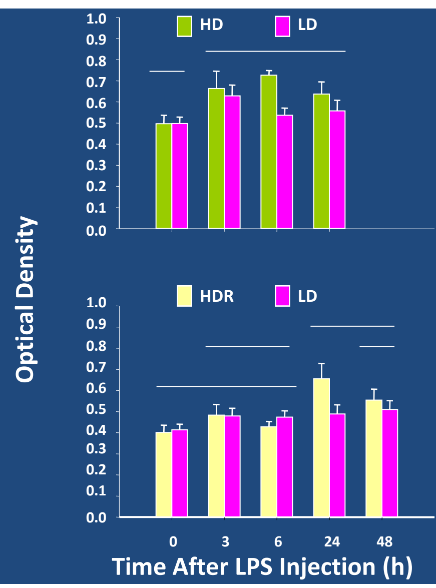
Reasonably easy to isolate (kidney). Glass adherent properties will allow them to stick to a microplate.

Plasma Pro-inflammatory Status Assay

Nitroblue Tetrazoleum Assay (Oxidative Burst)

→Plasma is collected from the different density groups
→Harvest kidneys from conspecifics for a uniform cell suspension
→Add equal volumes of cell suspension to microplate wells
→Allow cells to adhere and follow with rinse
→Incubate cell homogenate with NBT + Plasma samples
→Solubilize the NBT in KOH and read in a microplate reader.
→High Optical Density corresponds to a larger oxidative burst (Pro-inflammatory state)

Proinflammatory Status of Plasma Following LPS Injection



Density P = 0.0293
Time P = 0.0032
D x T P = 0.1990

Density P = 0.2578
Time P = 0.0027
D x T P = 0.1572

Let’s take stock in what we think we know

So do we believe there is variation in the cortisol response?

So do we believe there are both genetic and environmental influences?

Do we believe that this variation has impact outside of the cortisol response?

Another Awkward Segue

What happens if ‘Mom’ gets stressed and exhibits a appropriate/inapproapriate response? Important?

Forewarned is Fore-armed: Crickets Exposed to Predators Have More Cautious Offspring

Jonathan Storm and Steven Lima placed mated female fall field crickets in a container for 10 days with or without a wolf spider (*Hogna helluo*); the spider's fangs were covered with wax to prevent it from killing the cricket. The crickets were then removed and allowed to lay eggs; the researchers collected the offspring and put them into containers which had previously contained *H. helluo*. Juvenile crickets born of mothers who had been exposed to a spider behaved more cautiously; they froze for significantly longer than crickets whose mother had never met a spider. Their mother's experience with a spider forewarned the juveniles, changing the way they responded; somehow, information was being passed from one generation to the next even though the mothers didn't take care of their young.

Next, the team tested whether these behavioural differences affected the crickets' chance of surviving in the presence of a spider. Crickets and spiders were placed together in an enclosure with several hiding places and with cricket food out in the open, forcing the crickets to choose between food and safety. The team used an infrared camera to record what happened over the course of several days. They found that the "forewarned" offspring evaded capture better and survived significantly longer.

Female sticklebacks transfer information via eggs: effects of maternal experience with predators on offspring

Eric R. Giesing, Cory D. Suski, Richard E. Warner and Alison M. Bell

Proc. R. Soc. B 2011 **278**, doi: 10.1098/rspb.2010.1819 first published online 10 November 2010

Daily bouts of being chased with a northern pike model

Fish were stripped of eggs and artificially fertilized
- Paternal effects were also examined

Egg size, egg cortisol, egg oxygen consumption, behavior of the offspring

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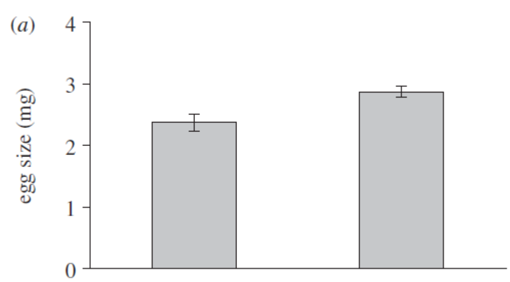

Females exposed to a predator during egg formation produced larger eggs ($F_{1,11} = 12.63$, $p = 0.005$; figure 1*a*), but there was no effect of treatment on the number of eggs ($F_{1,14} = 0.005$, $p > 0.05$). There was no effect of time spent in treatment or tank on egg size or number of eggs (all $p > 0.05$). Larger females produced more eggs ($F_{1,34} = 6.822$, $p = 0.013$).

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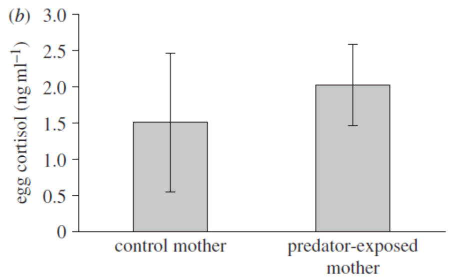

The eggs of mothers exposed to a predator had significantly higher concentrations of cortisol compared with the control group ($F_{1,9.6} = 5.18$, $p = 0.04$; figure 1*b*; experimental: 2.006 ng ml^{-1} ± 0.558, $n = 30$; control: 1.489 ± 0.951 ng ml^{-1}, $n = 13$). Egg cortisol content was not influenced by the mother's standard length, days spent in the treatment or tank (all $p > 0.05$).

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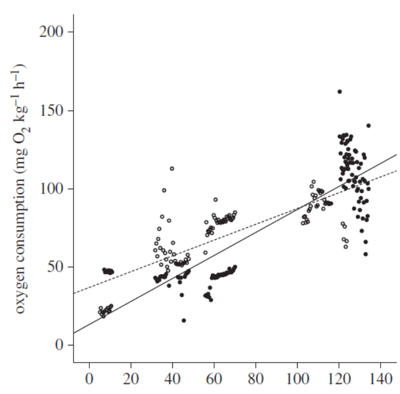

Figure 2. Oxygen consumption (mg O_2 kg^{-1} h^{-1}) per egg increased over time regardless of treatment. Eggs from mothers exposed to a stressor (experimental: $n = 6$ clutches, open circles, dashed line) consumed more oxygen than eggs from mothers not exposed to a predator stressor (control: $n = 6$ clutches, closed circles, solid line) soon after fertilization, but the difference attenuated close to hatching.

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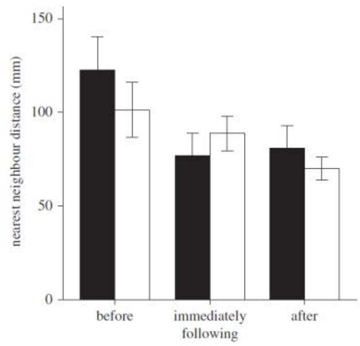

Figure 3. 'Before' a mild disturbance, the nearest-neighbour distance was significantly shorter between fry from mothers exposed to a predator than from mothers not exposed to a predator. There was no difference in nearest-neighbour distance between control and experimental fry 'immediately following' or 'after' a mild disturbance. Each bar represents the mean ± s.e. of $n = 9$ experimental and $n = 6$ control tanks across all six measurements (filled bar, offspring of control mothers; open bar, offspring of predator-exposed mothers). Statistical tests were carried out on square-root transformed values.

So let's begin to speculate

1. We can alter the stress response by varying environment.
2. We know there's a maternal contribution of hormones and other signals in the developing ova
3. Is it a leap to think that a maternal stress response might be important in sending signals to offspring
4. So if a stress response is varied by the environment we are holding the parents wouldn't this also have an impact on the offspring?
   - Adaptive
   - Maladaptive
5. How long might this impact last?
   - ??generations??
6. Is it just maternal input?
7. Are there species more or less susceptible to such impositions?
8. Is the response consistent across species?
9. What about the notion of supplementation hatcheries viewed through this lens?
10. Is this more, less, the same impact as is caused by domestication selection?