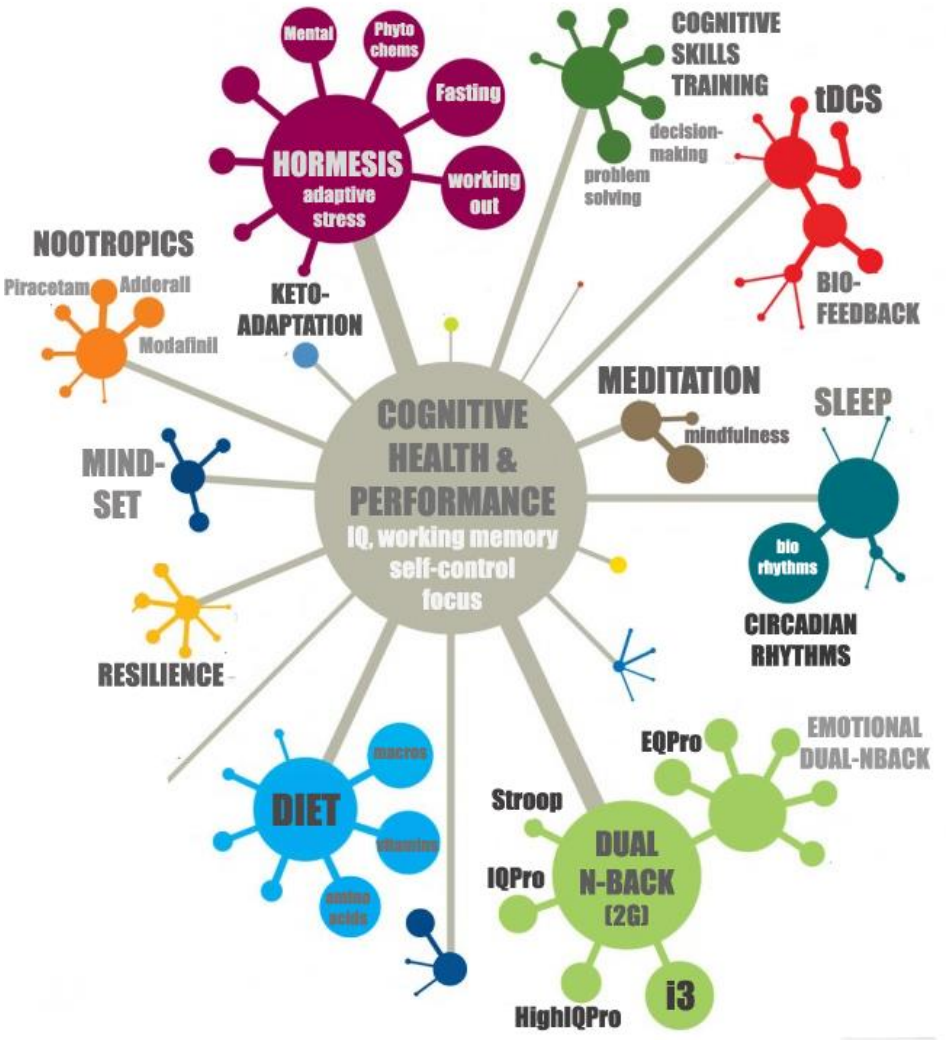
IQMINDWARE
health, resilience, performance



Brain Cross Training

Hormesis

The Principle of Good Stress

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Foreword

My training is in cognitive neuroscience. I earned my doctorate from Carnegie Mellon and the University of Pittsburgh's flagship Center for the Neural Basis of Cognition program. I have since worked as a Lecturer/Assistant Professor at the University of Cambridge's Experimental Psychology Department – the top ranking Psychology Department in the top ranking University in the UK - where the basis of IQ Mindware's training program was devised.

In this series of eBooks I present you with the most effective, evidence-based cognitive interventions within a brain 'cross training' paradigm that combines computerized brain training with other strategies to improve brain health, resilience, performance and creativity.

Enjoy your training!

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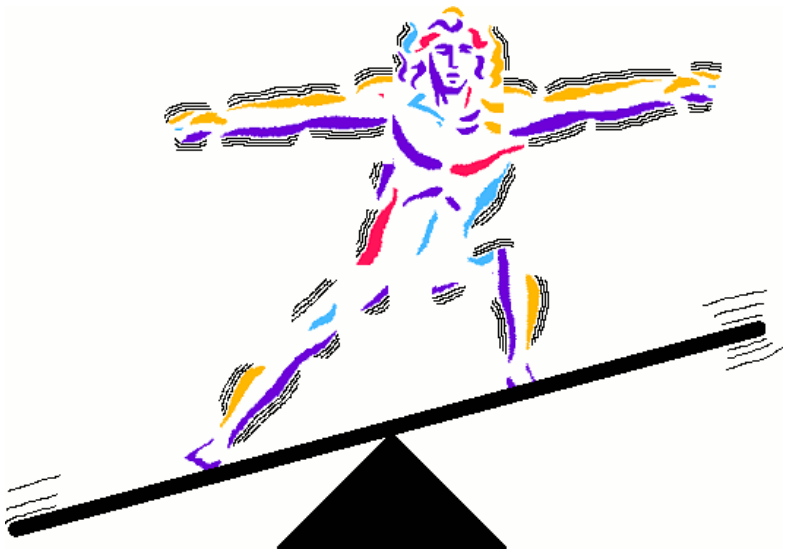
This chapter is an introduction to a very powerful brain training principle: that *stress* – physical and psychological – is a 'magic bullet' for improving the brain's resilience, health and performance.

Stress and Homeostasis

Before explaining why, we needs some key definitions.

What is *stress*? Stress can be understood in terms of biological homeostasis.

Homeostasis is a biologically evolved self-regulation mechanism that works to keep internal conditions (such as body temperature) stable in the face of internal or external effects ('stressors') that tip the system off balance (such as a fever or severe cold). The more 'dynamic homeostasis' a system has the more it can 'bounce back' and the more *resilient* it is.



Stress – which can be physical or emotional - is a state in which homeostasis is threatened, when our internal systems that keep us in good health and able to perform are made more unstable.

Stress in Evolution

"Daka Homo erectus" by Henry Gilbert and Kathy Schick - Own work. Licensed under CC BY-SA 3.0 via Wikimedia Commons

In the drier environments of our distant ancestors, food was often scarce, and energy expenditure high. Life was stressful, and this stress shaped the evolution of our brains. Three stressors in particular - relating to energy demands (called 'energetic stressors') - put strong pressures on the evolution of human brains and biochemistry:

- **Physical work** in times of intense or prolonged physical challenges such as hunting or long-distance travel. This was when we had to burn up a precious metabolic energy.

- **Caloric (energy) restriction** (CR) in times of food scarcity. This is when energy sources for powering our bodies and brains was lacking.

- **Cognitive challenges** when we were faced with complex situations needing learning or problem solving, or when we needed to plan and strategize to accomplish complex goals. The brain has evolved to be highly energy-consuming due to the work it does.

In addition to these energy-related stressors, there have been another type of stressor that have recurred for millions of years, shaping the evolution of our brain biochemistry:

- **Plant food chemicals** called **phytochemicals** that evolved to protect plant health and deter plant consumption. This kind of plant chemical defence mechanism is behind the intense taste of peppers and spices.

As our species evolved, those individuals who could cope with and thrive on these common stressors had an ***adaptive advantage*** in the struggle for survival and reproduction, and their genes flourished. Over long periods of time, the human body and brain has become biochemically adapted to these stressors, and has developed biochemical mechanisms – called adaptive cellular stress responses - to actually benefit from them in profound ways.

Vitagenes

Over time we have evolved genes controlling a biochemical package of **adaptive cellular stress responses** to the stressors our ancestors faced. These amazing biochemical mechanisms repair and build resilience, promoting our physical and mental performance. These genes are known as **vitagenes** – genes for cellular protection, repair and successful adaptation in the face of stress.

The specific biochemical pathways switched on by the vitagenes in response to **caloric restriction**, **exercise** and **cognitive challenges** – are shown in scientific detail in *Appendix 1*.

Adaptive cellular responses are also triggered by phytochemicals, **temperature stress** and – the research suggests - brief periods of **sleep deprivation**.

As meta-reviewed here and here, the health benefits of stress-triggered cellular stress responses include:

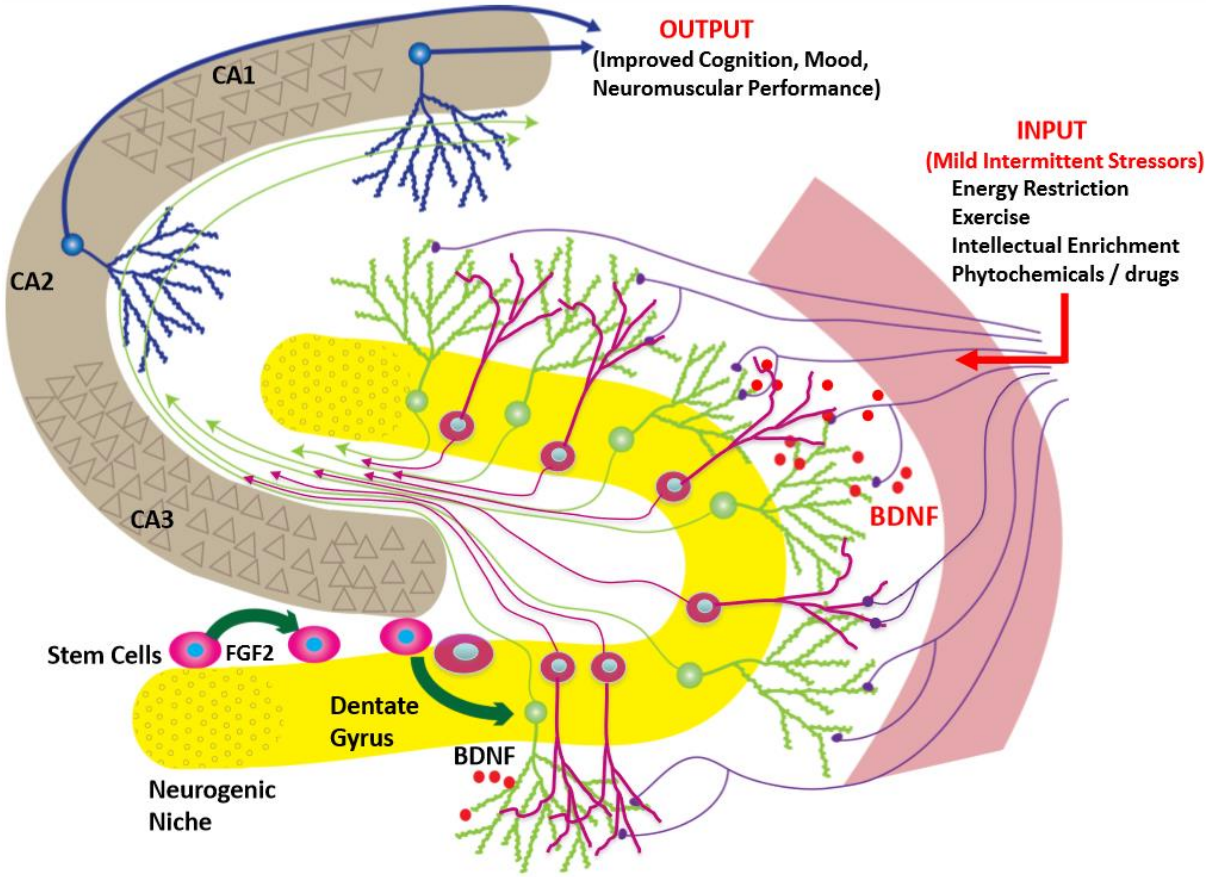
- Increased brain cell growth (neurogenesis) and neuroplasticity for learning and memory by producing nerve growth factors such as Brain Derived Neurotrophic Factor (BDNF) and insulin-like growth factor (IGF-1)
- Improved mitochondrial function and energy metabolism
- Removal of damaged organelles and cells
- Activation of DNA repair systems for DNA stability

- Production of fatty acids/ketone bodies. Ketones protect brain cells (neurons) against exposure to toxins associated with Alzheimer's or Parkinson's. They also provide a more efficient fuel source for the brain.
- Reduced cancer causing anabolic hormones
- Improved insulin sensitivity & reduced diabetes risk
- Reduced inflammation
- Possible increased life-expectancy due to the protective stress response gene SIRT3.

Brain Benefits of Adaptive Cellular Stress Responses

Via the same adaptive cellular stress response that improves immune function, health and longevity reviewed above, **caloric restriction, exercise, cognitive effort and phytochemicals can all promote optimal brain function and resistance to age-related brain diseases**, and does so via overlapping and complementary mechanisms.

The diagram below illustrates at a neuron (brain cell) circuit level the four types of brain training strategy that result in brain health and performance benefits from adaptive cellular stress responses.

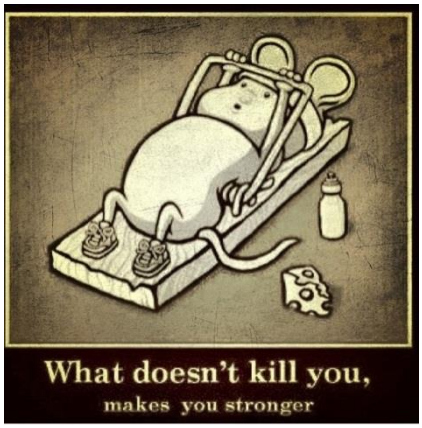


A **hormesis** response results in the **strengthening of neural circuits** via **protein enzymes (neuroplasticity)** and **neuron stress resistance via DNA repair enzymes** and **antioxidant enzymes**. This results in improved cognition, mood and muscle activation.

Hormesis: How to Switch On the Vitagenes

So how do we switch on (upregulate) our vitagenes that control the cellular stress responses, to unlock the remarkable benefits to health and brain function?

We do some biohacking to harness the **hormesis response**.

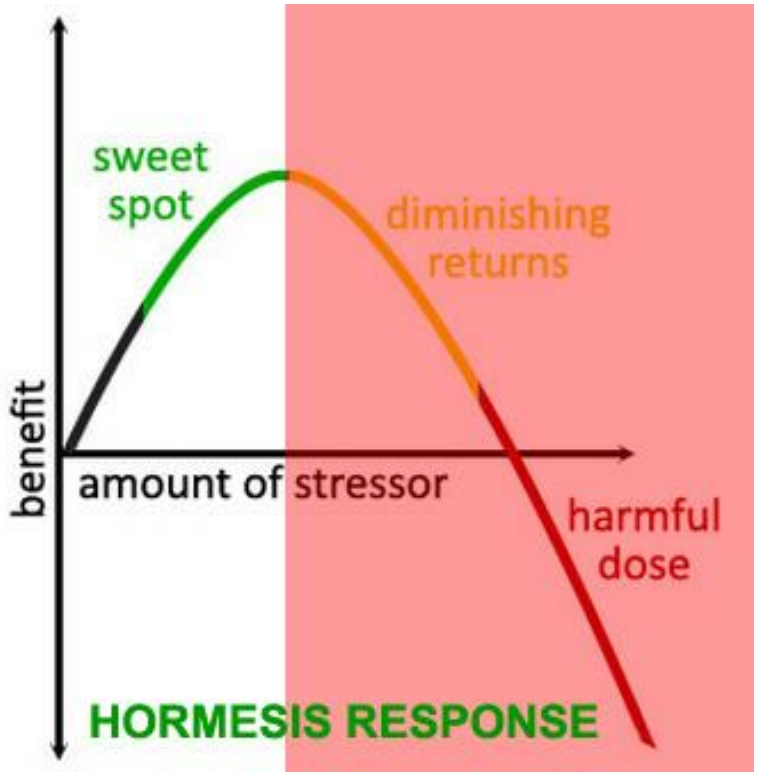


<u>Hormesis can be defined as a biphasic response to a stressor - where a low dose of the stressor results in a beneficial effect and a high dose results in a toxic effect</u>. For example, while a large 'dose' of the stress of caloric restriction (lack of food) results eventually in starvation and a collapse of our major biological systems such as metabolism and immunity, a smaller dose (i.e. fasting) activates biological repair mechanisms, builds resilience, and regenerates the brain and body by upregulating the vitagenes.

Hormesis underlies Nietzsche's maxim:

'What doesn't kill you makes you stronger'!

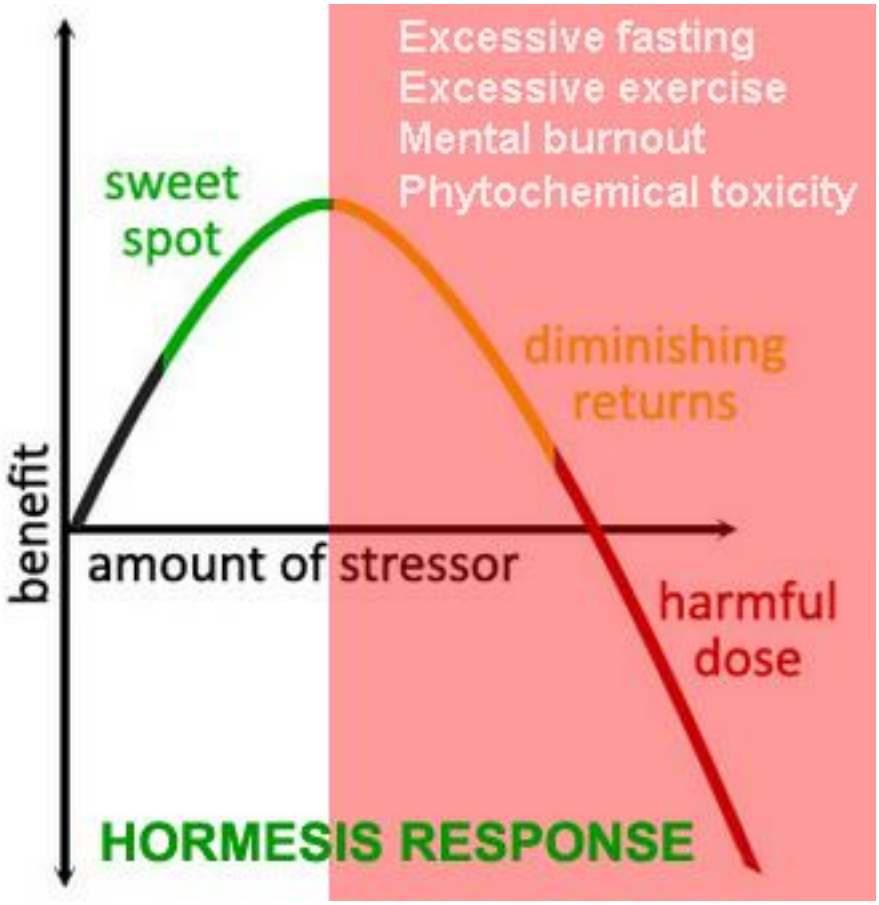
What does 'biphasic response' mean in scientific terms? The general *biphasic response curve* for hormesis is shown in this diagram.



As the dose of the stressor (e.g. lack of food, exercise, cognitive challenge) is increased, beneficial vitagenes are upregulated within a certain range – the 'sweet spot' of the hormesis response. If the stressor goes beyond the sweet spot it can result in harmful biological outcomes.

The Right Dose of Stress

The doses are absolutely critical. It is easy to overshoot, and damage our biological systems and brain health with inappropriate doses of the stressors. And individuals all differ in these dynamics. While one person might be able to fast for 24 hours and reap a lot of biological benefits, someone else might be over-stressed by 8 hours of fasting, with adverse effects on the immune function and metabolism.



And by regularly activating the hormesis response *at the **right dose***, the ability to take on increasing intensities of stressors increases. The response is *adaptive*. The curve shifts to the right as we become adapted to higher levels of stress, **increasing the depth of our resilience** and broadening the range of conditions over which we can remain healthy and perform at an optimal level.

Summary

Stress – in the right doses and applied at the right times – is highly beneficial for the brain and body. We can harness it in brain cross-training programs. Without stress, the vitagenes and adaptive cellular stress responses don't kick into action to build resilience, health and better brain functioning.

And while the 'good stress' practices of fasting, exercise and taking on mental challenges are all known to promote our health and brain function, we see the opposite effect too: deteriorating health, immune function and neuroplasticity resulting from overeating, a sedentary lifestyle and cognitive inactivity.

Hormesis is a cornerstone of IQ Mindware's **brain cross-training** programs. In the following eBooks I will be looking at these programs in more detail.

IQ Mindware Apps

If you are interested in finding out more about the IQ Mindware app **i3** for brain performance, resilience and health you can do so at this website.

This app is designed to harness the hormesis response, and can be combined with exercise, fasting, and other brain cross-training strategies.

Appendix 1

The Adaptive Cellular Stress Response

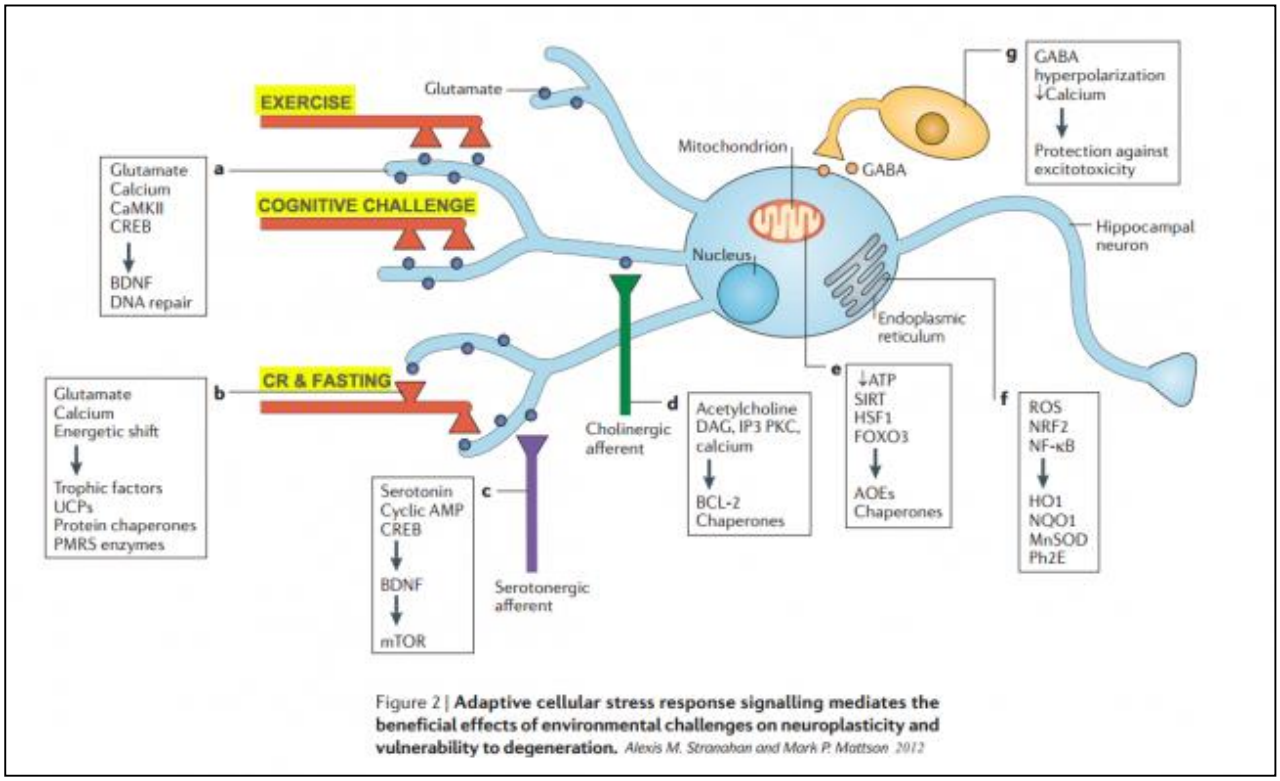


Figure 2 | **Adaptive cellular stress response signalling mediates the beneficial effects of environmental challenges on neuroplasticity and vulnerability to degeneration.** *Alexis M. Stranahan and Mark P. Mattson 2012*

Specific pathways of the adaptive cellular stress response include the following:

- Activation of **neuroprotective proteins** such as brain-derived neurotrophic factor (BDNF) (a).
- Increased **brain tissue growth and neuroplasticity** by the activation of BDNF (c).
- Activation of proteins (e.g. UCP) that **help regulate blood glucose energy** and prevent **diabetes** (b).
- Activation of anti-apoptotic proteins (e.g. BCL2) that **prevent the destruction of immune (white blood) cells** (d).
- Activation of protein chaperones and other proteins that **protect cell structures against stress** (b, d, e, f).
- Activation of **DNA repair and stabilization proteins (a, f)**.

- Release of GABA during exercise and brain training **reduces excitotoxicity** (g) – the toxic effects of over-active neurons.
- Lower cell energy (ATP) levels during fasting **activate antioxidant enzymes** (PMRS, AOEs) (b, e, f). These enzymes protect against **oxidative stress** which is damage to cell structure and cell function by overly reactive (**free radical producing**) oxygen-containing molecules and chronic **inflammation**.
- Activation of ATP involving enzymes (kinases) and other proteins that increase **removal of damaged cells and cell parts** (a, d, e).
- Activation of **anti-inflammatory enzymes** (e.g. HO1) (f).