Chapter 7.1

A selective overview of the ANS

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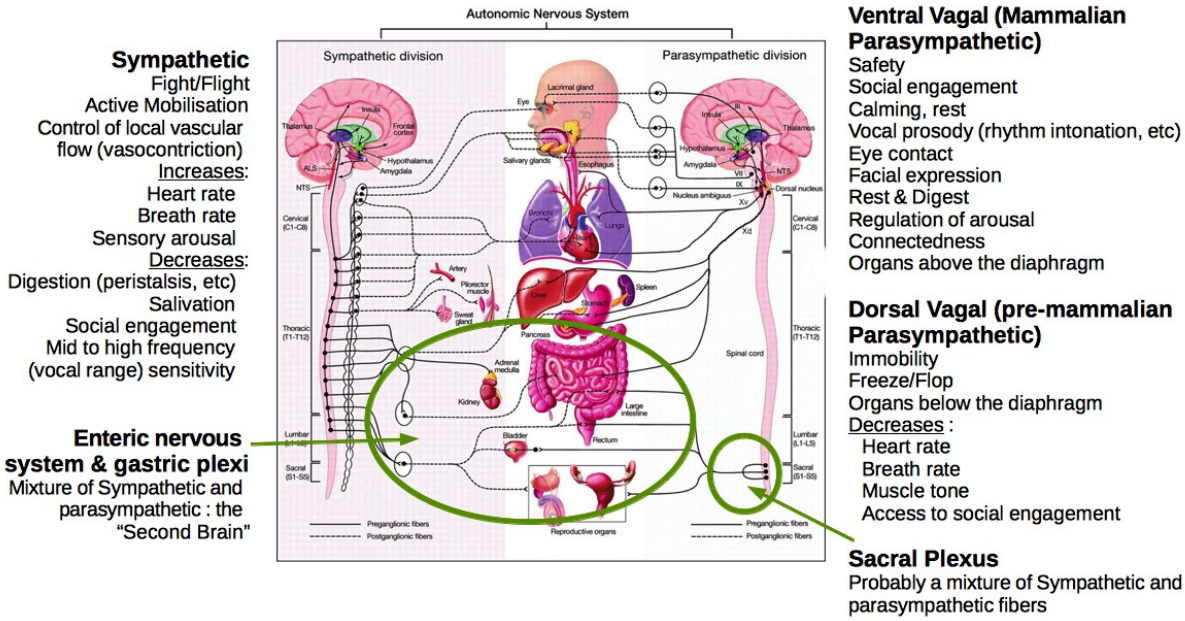
I once had a sparrow alight on my shoulder for a moment when I was hoeing in a village garden; and I felt I was more distinguished by that circumstance than I should have been by any epaulette I could have worn.
– Thoreau

The ANS : an introduction

"Autonomic" = *auto* (self-) + *nomic* (laws) …

Or translated into plain speak, the Autonomic Nervous System (ANS) is something of a law unto itself. The ANS is a branch of the peripheral nervous system that *generally speaking, for most people in most circumstances, in most normal states of waking consciousness* is not under direct volitional conscious control. And is nominally concerned with the physiology of the body and is distinct from the motor nervous system (the part of the nervous system that organises movement of locomotor muscles). As we shall see later on, these simplistic distinctions found in many anatomy books rapidly break down when investigated in any detail.

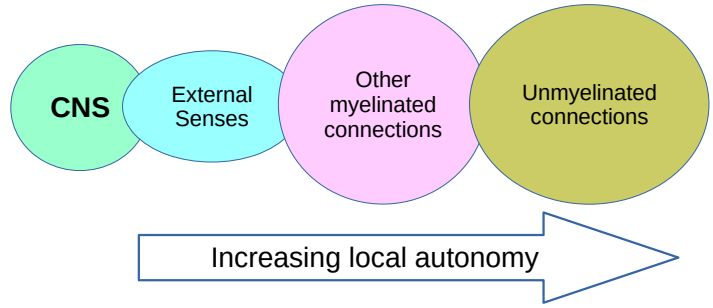
Overview of the Autonomic Nervous System (ANS)



Text adapated from Kathy Kain & Stephen Terrell (2018) Nurturing Resilience : Helping Clients Move Forward from Developmental Trauma--An Integrative Somatic Approach. Publ. North Atlantic Books ISBN-13: 9781623172039 Figure 2, p. 64
Figure adapted from O'Callaghan, Susan & Kenny, Rose. (2016). Neurocardiovascular Instability and Cognition. The Yale journal of biology and medicine. 89(1) pp59-72 PMID: 27505017 Figure 1

When compared to the motor (muscular system), the ANS reveals itself as a visceral body with a primitive brain. The motor muscles receive a direct myelinated connection from the spinal cord because muscles are controlled more fully by the central nervous system and have somewhat less of an intelligence of their own compared to the ANS. The brain connects to everything under less conscious control via ganglia and plexi –

small concentrations of neural tissue distributed round the body. If one considers myelinated connections from the brain to be the "core" nervous system, then accumulations of neural tissue with unmyelinated connection are relatively independent. They have more of a local intelligence, and the central brain is (for the most part) a means of coordination and regulation as much as it is a means of control.



The autonomic nervous system's unmyelinated fibres are extensions from these ganglia and plexi – i.e. there is a complex network of small interconnected (autonomic) brains connected to the core in slightly different ways. The Parasympathetic nervous system is the oldest from an evolutionary point of view, and so its local brains sit close to their "target" organs, with long myelinated nerves (the Vagus nerve being about one metre long) reaching out to them from the central nervous system. Or perhaps it would be better to say that they reach out to the CNS, because about 80% of Vagal nerve fibres are sensory (afferent). The sympathetic nervous system is a later evolutionary addition, so its small brains are much closer to the spine, their unmyelinated connections can be quite long, they follow another structure (the arterial system) instead of having their own distinct pathways, and some of them use a different neurotransmitter (noradrenaline) instead of acetylcholine. The sympathetic (or *splanchnic*) nerves can be thought of as an analogy to cranial nerves. The adrenal medulla – the gland that produces adrenaline – is actually a specialised sympathetic ganglion that produces adrenaline for the whole body instead of just noradrenaline for itself.

For the human body-mind, the ANS is a major conduit for the two-way stream of information: top-down (regulatory/controlling or "*efferent*"), and bottom-up (sensory or "*afferent*") between brain/mind and body/soma/viscera. The ANS arises from several distinct nuclei in the brainstem that have evolved to have specific but interrelated functions. Whilst many of these nuclei have unique connections to the periphery, there is a large degree of cross-connections between nuclei, and between their peripheral nerves at peripheral plexi. So whilst it would be neat to say *this* nucleus carries out *that* specific task, for the most part (other than for very basic survival functions such as the gag reflex) it isn't quite that simple. The ANS sits at a confluence of biological processes (metabolism / homeostasis, and the management / use / conservation / storage / absorption of energy and other resources), the sensory system (along with the brain-functions of recognition and meaning, including the recognition of safety and danger), instinctive biological behaviour, emergency survival responses, socialisation (emotions, facial expression, inter-personal relationships) and *both* consciously and

unconsciously directed movement. The ANS can therefore can be accurately considered to be a major *part of* the means by which the human body and mind are stitched together. The ANS has received increasing attention in therapy because :

- *It provides a relatively simple qualitative lens (or analogy) through which the complexity of the body-mind can be viewed, understood and* ***recognised***.
- It is one of the primary *means by which* socialisation responses are innervated and tied into physiology. In fact it is pretty well impossible to engage in any relational response or behaviour without there being physiological consequences; and physiological states prime the body-mind towards particular ranges of relational-behavioural responses. So an understanding of the ANS results in a better understanding of socialisation, and the biological aspects of relationship.
- Its location on the nexus of physiology and consciousness makes the ANS a relatively easy target for interventions that have physical and/or mental-emotional effect – particularly collaborative ones in which the patient learns how to proactively manage their ANS and their body-mind. Or perhaps it is more accurate to say that a simplified mapping of the ANS creates a mental model that allows one to navigate with sufficient accuracy the vast range of possible mental-emotional states that we can experience; and to devise simple interventions that have a useful effect.
- It controls or interfaces with every part of the body, and - as has been recognised more and more – it is the body that stores and replays memories from the past, and its is the body that must be addressed in order to create the right conditions for self-regulation in cases of PTSD-spectrum dysregulation.
- In particular, a major cause of physical and psychological pathologies – possibly the greatest cause – is trauma held in the body. This is simply because trauma always plays out through the ANS - and so trauma is essentially *physiological* (rather than "mental") in nature. Any significant and lasting return to health requires that the "rules" by which the ANS works are understood, so that the primitive hyper-aroused physiological and sensory systems can be re-calibrated.

In modern anatomy, the ANS is now considered to have five major branches, four arising from the hindbrain :

1. The **Sympathetic** (or Orthosympathetic) Nervous System (S-ANS), consisting of a bilateral chain of nodes sitting either side of the spine immediately anterior to the spinal facet joints of the ribs, and innervated mainly via the thoracic spinal nerve roots (T1 - L2). These nodes/ganglia are linked in a chain that extends the full length of the spine, as far as the upper neck, and down as far as the coccyx.

2. The **Dorsal Vagal** (or Parasympathetic) Nervous System (V_D-ANS), arising in the Dorsal Motor Nucleus of Cranial Nerve X (DMN.X). The V_D-ANS mainly innervates the digestive system (subdiaphragmatic viscera) as far as the transverse colon/large intestine, but also has some input into the thoracic (heart/lungs).

3. The **Ventral Vagal** (or Social) Nervous System (V_V-ANS) is a recent major mammalian adaptation to Parasympathetic physiology. The V_V-ANS begins in the Nucleus Ambiguus (NA) – an evolutionary extension of the DMN.X. It is particularly responsible for efferent innervation of the face and neck muscles (in socialisation/facial expression and sensory orientation), and regulates the heart and lungs (supradiaphragmatic viscera). It <u>also</u> provides sensory (afferent) innervation to the skin of the ear and larynx, and visceral sensation from the heart and abdominal viscera, taste from the epiglottis and root of the tongue, muscular innervation to the pharynx, soft palate and larynx.

4. The **Sacral ANS** is subject to some controversy[1, 2, 3]. It has traditionally been thought of as part of the Parasympathetic nervous system, but an investigation of its early embryological origins (as the initial cells are formed in the neural crest) suggests that it could be more strongly related to the Sympathetic Nervous System (S-ANS). Its function is certainly different from that of the Vagal ANS in the upper two thirds of the body, and at the very least it would seem that it is a complex mix of both Sympathetic and Parasympathetic, or maybe something that should be given a unique category in its own right. The Sacral ANS is itself strongly linked to the lower plexi of …

5. The **Enteric Nervous system**. Both the descending and sacral branches of the ANS (both V-ANS & S-ANS) connect directly to the plexi and ganglia of the Enteric (or Visceral) Nervous System (E-ANS) : the oldest part of the nervous system from an evolutionary point of view. A small brain in its own right (or more accurately, a distribution or constellation of small interconnected brains) capable of independent function and complete with its own blood-brain

barrier; the E-ANS is richly and intimately connected to both Vagal and Sympathetic branches of the ANS, but particularly to the Vagus. It is capable of running itself; but is modulated by the ANS so that the activity of the digestive system, mesentery and E-ANS are integrated into the activity and fluid/energy balance of the rest of the body. The E-ANS communicates with the gut microbiome, and is *one of the pathways* used by the gut microbiome to communicate with the CNS. And, of course, vice versa, in that mood affects the microbiome – though emotion is also somewhat physiological and is less dependent on cortical activity than is usually thought.

Unlike the muscular system (and its motor nerves), the ANS is not fully lateralised. Some connections to brainstem nuclei are contralateral, and others ipsilateral. Laterality tends to be stronger for the upper body – particularly the head and neck. Further down, the thoracic Vagus has an estimated 5% - 20% of its fibers crossing and connecting between "Left" and "Right" Vagus nerves; and there is very little laterality at all below the diaphragm in the mess of abdominal plexi, except in that specific target organs physically lie more on one side of the body or another. As an example, most motor connections from the *nucleus ambiguus* related to swallowing are contralateral, but the soft palate innervation (e.g. to the uvula) is ipsilateral.

Strongly associated with the ANS are other Cranial Nerves CN.V (Trigeminal), CN.VII (Facial), CN.IX (Glossopharyngeal), CN.XI (Spinal Accessory), & CN.XII (Hypoglossal). It is possible to argue that <u>all</u> cranial nerves either have an important contribution to the ANS responses, or are important pathways for both afferent and efferent ANS nerve fibers. So, for instance, the Spinal Accessory nerve CN.XI (supplying the supposedly voluntary Trapezius and Sterno-Cleido-Mastoid/SCM muscles) is innervated by the special motor branches of the ANS to enable a non-conscious reflex orienting/startle response. Similarly the three motor nerves for the eye CN.III, IV and VI are also part of that reflex-orienting system and are necessary for the involuntary action of *saccading (the way that the eye scans the world as a series of focussed dots joined together with a less focussed peripheral image)*. For the eye,

i. the accommodation reflex (eye focus) is a largely autonomic function that can be cognitively overriden, and

ii. light adaptation (iris sphincter muscle), not available to conscious control

are innervated via Parasympatheic fibers in CN.III and are modulated by noradrenaline; whilst the lacrimal glands have Parasympathetic innervation via the Trigeminal Nerve CN.V (and are modulated by noradrenaline). The Facial nerve CN.VII is (for most people) far more under control of the ANS (socialisation, startle/orienting, grimace/fight-flight) than it is under conscious control. The senses of smell (Olfactory

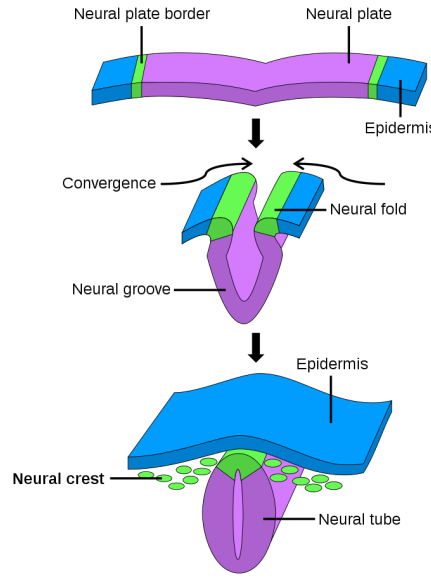
CN.I) has a powerful effect on the pleasure/disgust survival arc, and also contributes very significantly to the socialisation/safety functions mediated by the Ventral Vagus nerve CN.X. And so on.

So whilst this chapter is removing the ANS from the body and inspecting it like one might do in a dissection room, in fact that dissection requires that we remove attachments – sometimes unknowingly discarding synergies and a sense of the ANS's place in the whole organism. The end result inevitably tends to either a cartoon-ish simplification or a labyrinthine detail. Truth be told, the main reason that the ANS receives so much attention now in the study of trauma and dissociation is Stephen Porge's ability to steer a path between these two opposites. In his book PolyVagl Theory[4] he presented sufficient scientific detail and yet also had sufficient eye on the global meaning – such that something very valuable emerged. As he implicitly acknowledged this process is not wholly scientific (in the reductionist definition of the word), because attention to synergy and wholeness requires that more dots have to be joined than can be fully accounted for by experimental evidence. One has to not only look at the research results, but also ask how that research was carried out, what were the *a priori* assumptions that might have constrained or distorted it, what does it mean in the greater context, and – since we are investigating something that is on our bodies as well – how does that relate to our direct experience as living organisms?

There are still many unanswered questions, and the detailed intricacies of *physiological range* (as opposed to unnaturally forced or introduced) interactions in homeostasis, the ANS and the production and effect of neurotransmitters, hormones and other forms of signalling are nowhere near fully understood. One particular gap - now being addressed to some degree - is the implicit assumption made in many physiological studies that everyone is the same (or even that humans in general have the same internal arrangement as a specific laboratory-bred strain of mouse or nematode or locust. For starters, it is now becoming obvious that female metabolism is different from male – but US pharmacological trials only required women to be included since 1993[5]. The differences between male and female physiology are sometimes surprising[6] – such as the activity of major intestinal and hepatic metabolic enzymes, plasma protein binding, elimination pathways, and the way compounds are distributed through the body. The topic is given a little more attention below (e.g Oxytocin) – though less than I would like, for there are clearly very different responses between men and women to stress and trauma[7]. Ssimilarly there are distinct patterns *more likely* to be (i.e. not exclusively) either male or female in the manifestation of and response to dissociation. And there has been very little work undertaken looking at physiological differences in non-biological and binary genders – who constitute a significant proportion (somewhere around 5%) of the total population. *In addition to* gender differences, there are also very significant changes according to age, genetic population

differences (i.e. family's continents of origin and blood groups) and differences brought about by cultural beliefs and attitudes, diet, environmental considerations, family cohesiveness, and lived relationship to ancestors.

Neural Crest Cells



During the very early development of the embryo, the first stage is the formation of a flat bi/trilaminar plate – the top/ectoderm (roughly = skin & central nervous system), the bottom/endoderm (the lining of the digestive tract – topologically the inside surface of the human donut), and the middle/mesoderm (musculoskeletal and connective). Then a tube – the notochord – forms, and then the ectoderm folds and fuses round this axis, forming the outer skin and inner neural tube, leading to the CNS. The place where the folded plate meets is the "neural crest". Cells from this area then migrate to form a vast array of different structures – the thymus, the bony/cartilaginous structures of the head and face, the ear, teeth, melanocytes in the skin, dorsal root ganglia (spinal afferent/sensory nerve roots), the sympathetic chains, the adrenal medulla, the aortic plexus, the enteric nervous system, parasympathetic ganglia (i.e. target ganglia connected to the Vagus nerve) and various structures in and around the heart. The migration and diversification of function of neural crest cells is one of the unexplained marvels of embryological development, that appears to express purpose. Some cells leave the neural crest already[8] "fate restricted" whereas others remain pluripotential until they have reached their final location in the body; but all populations of final cells begin in specific locations and have distinct migration pathways, many connecting to their targets before migration even begins[9]. The "Vagal" crest is also the source of 99.9% of the ENS[10], of cardiac crest/cells (which also end up as the thymus, thyroid and muscular tunics of the main arteries), and of glia for much of the peripheral nervous system.

Although various signalling mechanisms have been identified (Netrins, Slit proteins, Semaphorins, Neurotrophins) that can guide the growth cones of the Autonomic axons[11], it is a marvel that the Vagus, one of the longest nerves in the body, grows towards and then locates and innervates all the viscera and tissues that it "should" by finding the various neural crest cells (or being found by them). The connections are not simple – for example, the Enteric nervous system of the four distinct layers of the gastrointestinal tract have to be connected via both efferent and afferent fibres. This task is made (perhaps?) a little easier in that the brain seems to know what is connected

to what, as if it has an internal electrician who carries out connectivity tests when commissioning the circuit, and can re-wire itself (if that is the correct analogy – perhaps re-organise might be better) if necessary so that its function matches its target. It is perhaps not a coincidence that the structures of the face and inner ear so central to the relational/socialisation and neuroceptive functioning of the ANS also share embryological origins with the ANS.

The several most significant plexi and ganglia that serve the ANS and E-ANS are shown in Table 7.1 below in approximately descending (or cranial → caudal) order. The efferent (outgoing) fibers of the ANS coordinate E-ANS activity with that of the rest of the body, and the afferent fibers of the ANS coordinate the central nervous system with the E-ANS and its microbiome. The relationship between ANS/ E-ANS and CNS is completely holistic, mutual and more reminiscent of a symbiosis than a hierarchy - particularly since the gut is virtually a primitive animal in its own right. It has recently been found that the developing embryo already has its own microbiome[12], and it may be that the embryonic plate stratifies into an endoderm and meso/ectoderm specifically because it is already populated with bacteria, presumably arriving with the sperm.

If the ANS were to be defined by only one characteristic, it would have to be energy management – and that is a specific case of **resource management** and **adaptation**. When we are in the window of normal adaptation, there is greatest freedom of choice of allocation of energy and other resources. In a general sense, the five greatest areas of energy expenditure in the body are :

- Active usage, mainly dealing with the external world : **(1)** movement via skeletal muscle and **(2)** the brain
- Homeostatic processes, mainly regulation of the internal homeostatic environment around the demands of dealing with the external world : **(3)** circulation (cardiac beat plus vascular constriction), **(4)** thermoregulation, and
- **(5)** digestion

A very close second to the energy management role of the ANS comes its function of central coordination of body physiology. Many aspects of body physiology (such as liver function) are capable of running themselves through local control, but this does not make for an efficient whole- organism response to the external world. So the ANS integrates the external and internal responses, coordinates the internal world (homeostatic balance) to best suit external demand, and modulates local processes by providing integrative feedback loops from other local processes elsewhere in the body. This is not only a top-down (afferent) system. The ANS actively detects changes in its target systems both through afferent (sensory) nerves and through chemodetectors in its major nuclei. So for instance, regulation of exocrine and endocrine functions for the

pancreas is achieved by both sympathetic innervation (arising from from several brain areas including the hypothalamus) and parasympathetic (Dorsal Vagal) control… But *pancreatic polypeptide* released by the pancreas circulates in the blood, and receptors in the Dorsal Motor Nucleus (DMN.X) also respond (i.e. in addition to Vagal afferent/sensory inputs)[13] - creating a highly synergistic feedback system.

The afferent (sensory) system of the Vagal complex is very diverse. *Chemoreceptors* responsive to a very wide range of neurotransmitters, peptides, and local metabolic conditions are widely distributed, from brainstem nuclei through to peripheral nerve endings on membranes, small groupings of cells in visceral organs, and possibly even white adipose tissue (fat cells) – though this is subject to some vigorous debate. In a very real sense there are taste receptors not only on the tongue, but also in the pharynx, oesophagus, and all the way through gut. The Vagus nerve is also the conduit of signals from *mechanosensors* that detect touch (e.g. to the face or scalp), tension (e.g. of the stomach wall or major blood vessels) and the motion of serous membranes. There are *temperatures sensors* deep in the body whose purpose is not fully understood, but whose action can be readily experienced during hypothermia. *Osmosensors* detect the balance between fluid and major ions. Vagal afferents have a complex relationship with nocioception (the detection of pain), partly being the effect of local and systemic ANS reflexes on promoting and de-escalating inflammation. And the Vagus nerve also has *transduction mechanisms*, whereby changes to its local environment cause a release from specialised Vagus endings of a range of signalling chemicals that affect local targets, or that feed back into central various control mechanisms. Afferent fibers generally have both local reflex action and more central effects.

Specific balances between activity in branches of the ANS are (amongst other things) associated with specific states of consciousness and brain activity, internal physiological status, movement/passivity and sensory focus. Indeed, all of these anatomical sub-groupings of the nervous system exist in such closely coupled feedback loops that it can be difficult to separate them in the lived human (or animal) experience. Most cells in the human body have a 24 hour clock which tends to drift, and needs to be constantly synchronised with the whole-organism clock. Clearly the master internal clock must be synchronsied itself to the external environment, the most obvious signal being the cycle of day and night. However, food/meal times are also a strong environmental signal, and I guess if food is more available at certain times it would make sense to coordinate the body around that rather than the path of the sun. So research has shown that cells *and genetic expression* different parts of the body can end up being synchronised to both the sun and to meal times, causing a metabolic conflict between parts wanting to be awake and other parts wanting to be asleep (sleep being a time for cleansing, immune system activity and tissue repair). Which in turn leads to accumulation of triglycerides in the blood, potentially increasing the risk of

heart disease, diabetes, and stroke. The food-oriented clock signal that can dominate (or seriously disrupt) the diurnal clock of the central nervous system that determines sleep patterns - originates in the Liver[14], and so is likely to be communicated by afferent Vagal fibres, but is also generally part of the conversation between the gut microbiome and the brain.

Whilst neurological connections between specific muscles and areas of skin can be mapped fairly accurately back to specific spinal (motor and sensory) nerve roots with relatively little variation between individuals, the Enteric ANS is far less visibly structured. It is more akin to a 3-dimensional version of the network of roads in a group of cities that have evolved into one big conurbation – not unlike the urban area of West Yorkshire, where the cities of Leeds, Bradford, Huddersfield and several other major towns have grown into each other. Fields remain largely hidden behind strip urbanisation, making it less continuous than the many different boroughs that comprise Greater London. A few recognisable trunk roads enter and leave, but in the centre of the cities the individual streets make local connections, and provide routes both to and between trunk roads, or even meander off into the countryside on their own. You can trace these roads back from the countryside to a particular city, but the choice of major road you follow at certain junctions might be slightly arbitrary, and that direct A-B mapping disappears completely once in the city centre.

Where it is	Name	What it does
Behind the wisdom teeth (in between the palatine and pterygoid wings of the sphenoid)	Pterygopalatine Ganglion	The largest parasympathetic ganglion in the face, associated with the Maxillary and Facial CN.VII Nerves, supplies the nose, eyes and face. Also with sympathetic efferents.
C2/3, behind the jugular vein and carotid artery	Superior cervical ganglion	Sympathetic supply to the head, *including* the Pineal gland, Choroid plexus (CSF production), Carotid body & **Cardiac Plexus** (cardiovascular regulation) eye, facial skin capillaries (inc some socialisation responses), Vestibular system, etc. Connections to internal & external carotid nerves and CN.II, III IV, VI & IX)
Middle pharyngeal constrictor muscle (roughly at tongue level, in front of jugular vein and carotid artery).	Pharyngeal plexus of vagus nerve	Serves the palate and pharynx. Mainly sensory, includes branches from CN.IX, X (Vagus) and XI. Connected to the Superior cervical ganglion
Anterior to C6 (when present)	Middle cervical ganglion	Larynx, trachea, pharynx and upper oesophagus, plus fibers to the **Cardiac Plexus**
C7/T1 (innervated from T1 to as low as T6)	Inferior cervical ganglion	Branches to the subclavian and vertebral arteries and to the **Cardiac Plexus**
Anteriolateral to thoracic vertebrae **T1 - T12**	Top of Sympathetic chain	Sympathetic supply to body
Two closely connected parts: (1, superficial) lies in the concavity of the aortic arch, and (2, deep) between the aortic arch and the trachea.	Cardiac plexus	Serves the heart and lungs, innervated from the Vagus nerve and the Sympathetic NS (Superior, Middle and Lower/T1 cervical ganglia).
Sides and front of the Aorta	Thoracic Aortic Plexus	Innervated from the Sympathetic chains

Table 7.1a : Major concentrations of the peripheral ANS : Supradiaphragmatic (head & thoracic)

Where it is	Name	What it does
Behind the stomach, roughly at the level of L1	Celiac plexus (solar plexus)	Mainly serves the upper solid viscera (liver, spleen, pancreas, adrenals). Includes the Hepatic, Splenic, Gastric, Pancreatic and Suprarenal plexi, and substantially innervates the Renal, Testicular / ovarian and Superior mesenteric plexi.
Sides and front of the Aorta	Lumbar Aortic Plexus	Innervated from the Sympathetic chains & the Celiac Plexus, and receiving fibres from the lower abdominal plexi
Lies within the walls of the intestines, on the outside of the intestinal circular muscle.	Auerbach's plexus (myenteric plexus of the E-ANS)	Serves the gastrointestinal tract. Part of the Enteric Nervous System, and capable of functioning independently of the CNS. Includes taste receptors! Strongly linked to the brain/CNS and coordinates digestive and CNS function, uses over 30 different neurotransmitters and stores about 90% of the body's serotonin. Also produces VasoIntestinal Peptide (VIP) : qv. Candace Pert.
Lies within the walls of the intestines, on the inside of the intestinal circular muscle.	Meissner's plexus (submucosal plexus of the E-ANS)	Serves the gastrointestinal tract. Part of the Enteric Nervous System, and capable of functioning independently of the CNS. Local muscle intestinal secretion, local absorption, and local contraction.

Table 7.1b : Major concentrations of the peripheral ANS : Infradiaphragmatic (Abdomen & pelvis)

> A recognized fact which goes back to the earliest times is that every living organism is not the sum of a multitude of unitary processes, but is, by virtue of interrelationships and of higher and lower levels of control, an unbroken unity[15].
>
> Walter Rudolf Hess (Nobel Prize-winning physiologist)

Reworking

Our culture has some quite ingrained ways of thinking of the body as being largely unchangeable once it has fully developed – a machine-like entity that reaches a peak of perfection in the teens to early 20's, and then starts to degrade. Certain parts are not quite so unforgiving, in that skin heals from superficial wounds and broken bones and other parts of the musculoskeletal system can heal. But I see a large number of people in my clinic who don't even have a sense that their body is capable of healing other than through application of creams or antibiotics to cuts, or through surgical replacement of parts. This is the end result of a technology-oriented culture that has separated itself from a meaningful relationship with life. In particular it is common to talk of neurological functions as being "hardwired" – especially functions that arise in the more "primitive" (i.e. less conscious) hindbrain. However, both the (open-minded) lived experience and scientific evidence says otherwise. Spinal injuries are usually thought of as being particularly irreversible. However, the progression is not so devastatingly absolute. Whilst it is true that in the short term (a couple of weeks after spinal cord severance) there is about 50% loss of volume of the spinal ANS sympathetic ganglia, clinical observation has found that these then return to normal volume[16] over the course of up to several months! And there is a more general plasticity of organisation that can ameliorate particularly severe injury[17]. Which has interesting implications. The ANS (at least the SNS) is constantly re-making itself based on usage. This is an extraordinarily hopeful message - all one has to do is be presented with a new experience, and the ANS will rapidly re-structure itself. Or stop using the ANS in a particular way, and it will re-structure itself to the new usage. Within a matter of days. How extraordinary is that? Perhaps we shouldn't be surprised … the general principle is well known in remedial medicine, that greater sensory (afferent) activity tends to reconnect damaged motor (efferent) circuits. It's a little strange that this principle is so pigeonholed, and the more general principle – that the entire neural system operates in a plastic and self-reorganising set of interwoven feedback loops – is largely invisible. The most important question should be – how does conscious use of the sensory (i.e. the afferent) part of that loop feed back? *What kinds of conscious or reactive engagement with any parts of these feedback loops have the most constructive (and destructive) effects on the entire organism?* We do potentially have some conscious control over how we place our attention on senses, and also how we engage with the "voluntary" parts of the motor system. My experience clinically is that our culture as a whole tends to lead people to engage with these feedback loops in a way that – at the least – does not make optimal use of their potential. I was being slightly mealy mouthed there. Most body-mind usage "instructions" common in western cultures cause problems and tend to amplify pathology.

Hypothalamus

The Hypothalamus is central to the functioning of *all* branches of the ANS - and consequently to the coordination of survival responses via the HPA (Hypothalamus-Pituitary-Adrenal) axis. It is a critical structure that links mid and hind-brain functions to the endocrine system via the pituitary gland. In particular, it sits directly above and controls the pituitary gland and is important for the regulation of hunger, thirst, body temperature, attachment behaviours and sleep. It *also* produces a set of primary hormones including **Vasopressin**, antidiuretic hormone (or **ADH**), important for fluid and major ion balance, **Oxytocin** (Oxt, a peptide that mediates social bonding, reproduction and mother-baby bonding – also see later), **Somatostatin**, growth hormone-inhibiting hormone (or **GHIH**), Thyrotropin-releasing hormone (**TRH**, controlling thyroxine and ATP production), and Corticotropin-releasing hormone (**CRH**, a peptide that controls release of *both* cortisol and DHEA).

Cortisol, Androgen, Aldosterone (& DHEA)

Cortisol, Androgen & Aldosterone are all produced by the cortex (outer sheath) of the adrenal gland. Cortisol is a multifunctional hormone produced during "stress" (either "danger" kinds of stress or metabolic stress due to starvation/low blood sugar), which has receptors in most cells of the body. It affects mood and emotion (tending to create anxious and "wired" mental-emotional states), but also has significant metabolic effects. It shuts down inflammation, digestion and even growth, and chronically high concentrations can reduce fertility (fertility is not a major consideration when being pursued by a sabretooth tiger). Further functions of cortisol and other adrenocortical hormones include :

- Acute energy management : Increases blood sugar from non-carbohydrate sources in the liver (gluconeogenesis : which process may make the body either warm or cold, depending on its specific energy supply), accompanied by a reduction in insulin sensitivity in peripheral tissue, and a systemic increase in the metabolic sensitivity to glucose-releasing hormones such as adrenaline and glucagon.
- Chronic energy management : (chronic stress), the cortisol-induced insulin resistance causes a higher release of insulin, which initiates breakdown of proteins and fats in the body, leading to muscle wastage. Cortisol is a nice example of the ambivalent nature of emergency survival physiology on the meaning of hormones and other biochemical signals – in that its function is very contextual and may even reverse. For instance, cortisol may in some

situations decrease fat production and initiate a muscle-burning metabolic response (proteolysis), or in other circumstances it may either increase or decrease the burning of fat (lipolysis). Thus, some stressed people can eat as much as they like and they don't get fat, whereas for others there is an uncontrollable accumulation of abdominal fat (metabolic syndrome) almost regardless of diet.

- Immune modulation : Usually the greatest everyday threat from infection is through the skin and the orifices - mainly via air entering the lungs and food or water ingested through the mouth, so the immune system is usually geared to mainly respond to these kinds of threats. Cortisol suppresses release of inflammatory substances, generally weakening the immune system, reducing Interleukin-1 and shifting it from Th1 to a primarily Th2[18] response. The Th1 state is required to deal with parasites, toxins, and general extracellular bacterial infections, being more likely to be present in open wounds. But a Th2 immune bias tends towards allergies. It might seem strange that the body suppresses the inflammatory response[19] and repair of damaged tissue in a fight-flight situation. The principle is that fresh wounds need to drain to flush out infection, but that flushing would also potentially lose blood, as it increases blood flow to injured areas. So inflammation (and associated fluid loss) is a response that is only really useful when danger has passed. It is not unusual for people in emergency situations to not bleed (even from major wounds) or feel pain until their adrenaline levels start to fall. The release of fluid from capillaries during inflammation carries immune cells, and endotoxic (gram-negative) bacteria have evolved to force the hypothalamus to release CRH. Thus, a "stress" response may actually be induced by an infection, and/or an opportunistic infection may enhance and maintain a stress response via the HPA-axis!

- Oxidising enzymes as an acute/emergency immune response : Cortisol stimulates copper-based enzymes, including (i) lysyl oxidase – an enzyme that is useful for rapid emergency patching of wounds, but otherwise causes cumulative scarring of connective tissue by cross-linking elastin and collagen, and (ii) superoxide dismutase - that is aggressive to human cells as well as bacteria i.e. short term expedient measures rather than something you would want active in your body all of the time.

- Increases blood capillary formation – more suited to emergency repairs, because in the long-term this is one potential cause of cancer..

- Loss of medium to long-term repair capacity : such as reduction in bone

formation and dietary calcium absorption[20], reduction in synthesis of collagen and proteins – neither being of major concern when fighting off a cave bear.

- Cortisol is also a diuretic, and it is not unusual for someone to wet themselves if very frightened… However, another adrenocortical hormone – *aldosterone* - *regulates* water-salt balance by increasing transport of potassium from cells to blood[21], retention of sodium and water (leading to general fluid retention issues, lymphodema, etc). This response increases blood pressure (BP), and is the primary way in which the total fluid-salt balance in the body is maintained. An abnormally high BP is *also* useful when in fight-flight, because a higher static fluid body pressure is a form of armouring against physical impact. The body tends to be experienced as being stronger and more self-supporting[22]. Aldosterone also loops directly into the Angiotensin II control of blood pressure. Low blood pressure can arise from Dorsal Vagal stares (see later) which then cause stimulation of the adrenal cortex to retain fluid/salt – and so (apparently) paradoxically create a stress response.

  > *"Cortisol's original purpose may have been sodium transport. This hypothesis is supported by the fact that freshwater fish use cortisol to stimulate sodium inward, while saltwater fish have a cortisol-based system for expelling excess sodium."*

- Digestion : strangely, cortisol stimulates production of gastric acid – perhaps as a way of compensating for a reduced T-cell immune response. But this is balanced by the fact that adrenaline reduces Vagal tone and so decreases general function and motility of the GIT. It could also be that this higher stomach acid is related to the fact that cortisol has a diurnal cycle, because of its association with adrenaline which is higher in the morning for that early get up and go. Thus, protein and fats are best consumed and absorbed in this morning period.

- Negative feedback : As cortisol levels rise, they are detected by the hippocampus and hypothalamus, which then inhibit cortisol in a negative-feedback cycle. Thus, stressors have to remain present, otherwise the HPA-axis stress response simply (sensibly) shuts itself down.

- Androgen : Increase in body hair, muscle bulk, and aggressive characteristics in men, a reasonable adaptation in chronic very long term stress situations. I am reminded of the high proportion (compared to the UK) of very masculine muscle-bound, hairy men that can be seen living in typical middle eastern (war zone) countries. The higher male/female libido induced by androgen is another evolutionarily sensible chronic stress adaptation – resulting in a higher birth

rate to offset higher a higher death rate. This also reminds me of my own experience of how stress can induce a vulnerable but compulsively driven sexuality – a state that Ursula LeGuin called "*kemmer*" in her book *Left Hand of Darkness*. Even more chronic stress leads to epigenetic changes in offspring[23] for the next few generations[24], making their baseline metabolism more immediately calibrated to a dangerous environment – and presumably leaving them with higher baseline levels of androgen. Thus it's possible that violence in general, or trans-generational (epigenetic) stress adaptations lead to a higher incidence of (male) sexual violence simply because of the effect of androgens.

Exactly what happens when Cortisol is released – appears to depend on the intensity (and maybe even specific external details) of the Fight-Flight response, and/or the stage of starvation. Cortisol is persistent, and even if there are no further stressful incidents the Cortisol released by just a few minutes of anger might take up six hours or more to be fully reabsorbed. A combination of Cortisol and Epinephrene (Adrenaline) lays down very clear and detailed memories of emotionally charged events – and so is the basis for PTSD flashbacks[25]. Thus we have a direct evolutionary relationship between survival-critical internal fluid and electrolyte balance (if you recall, the original function of adrenaline was to regulate salt-water balance in primitive fish), the kidneys and the adrenal glands – which then progresses to a system dealing with other survival-critical situations using the same biochemistry. It is impossible to ignore the fact that Traditional Chinese Medicine – devised well before the development of modern physiology, evolutionary biology and endocrinology – sees the kidneys as being associated with salt-water balance, internal "Yin" reserves (which translates more or less as the ability to adapt homeostatically to any situation), and the processing of fearful emotions.

The fact that a high Cortisol level is only meant to exist in the body during short-lived emergencies is particularly apparent, in that – as Cortisol levels rise, DHEA levels go down (and vice versa). DHEA (Dehydroepiandrosterone), another endogenous steroidal hormone produced by the deepest layer of the adrenal cortex is associated with extended cell life – i.e. longevity. In particular it is one of a family of proteins (neurotrophins) that improves survival, development (growth of new neurons/brain plasticity), and function (by selective apoptosis/thinning of brain cells – e.g. in infant development) of the central nervous system. DHEA is considered to be anti-inflammatory, anti-carcinogenic, moderates lipid production, anti-diabetic, anti-obesic, and immunomodulating. DHEA may be a proto-form of the general class of neuropeptides (see Molecules of Emotion by Candace Pert). It neutralises some aspects of pain nocioception (particularly excess sensitivity to heat/cold and burning pains via

TRPV1). DHEA increases when in a grateful/appreciative mental-emotional state, with increased exercise, and on a healthy calorie-restricted diet[26]. It mediates puberty. It may also be important for construction of microtubules[27]. DHEA also inhibits both G6PDH (an enzyme implicated in cancer development) and NADPH (a co-factor that is involved in cholesterol synthesis; and which helps remove toxicity from cells, but at the same time produces potentially dangerous free radicals).

The Hypothalamus-Pituitary-Adrenal (HPA) Axis

The HPA axis is central to regulation of the stress response, in which the anterior pituitary affects the kidneys and thence the adrenal glands (which sit on top of the kidneys). During stress the hypothalamus produces **CRH**, which in turn signals the pituitary to release **ACTH** (adreno-corticotropin hormone) into the blood stream. When the cortex (outer layer) of the adrenal gland detects ACTH, it produces **cortisol** – the steroidal "stress hormone".

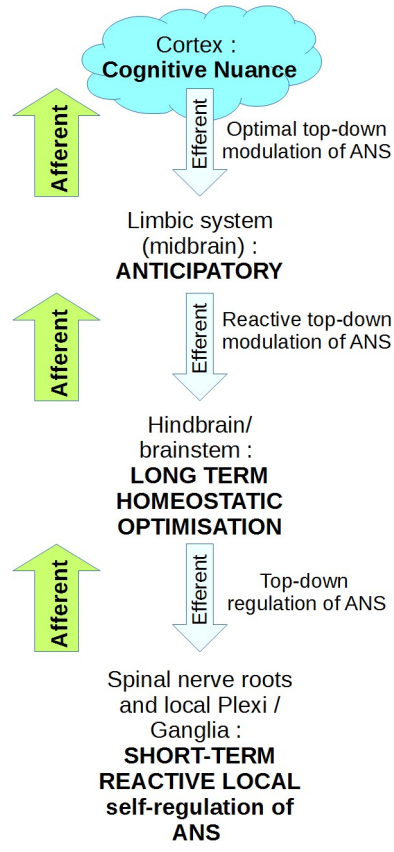
Whilst the adrenal cortex is triggered by hormones in the blood stream, the HPA-axis is also driven by neural signalling to the adrenal medulla, which then produces adrenaline/noradrenaline. In a general sense, neural signals generate a faster response, and blood-based signalling tends to be more related to background environmental factors – the blood being a soup that signals a moving average status assessment from various systems in the body/brain.

Hierarchy of control of the ANS

There is a hierarchy of control of the ANS that works in a series of feedback loops according to factors of immediacy, longer term homeostatic agendas, connectivity, etc:

a) Some regulation is possible locally in plexi and spinal nerve roots, but one could say that these local feedback loops do not have sufficient oversight to understand larger scale (whole-body) dynamics, and so if this level of control is dominant (e.g. spinal cord severed above C6), there are serious consequences.

b) As described previously there are hormonal/peptide/neurotransmitter signals via the blood stream that are more persistent than neurological signalling, which connect different organs and physiological states in



different ways and work in positive or (more usually) negative feedback loops with the neurology. These signalling proteins are produced locally as well as systemically, and many of them are produced by the microbiome, or create a response by the microbiome that then affects afferent Vagal pathways.

c) The brainstem contains nuclei that control the ANS centrally, and so ***brainstem → local*** will maintain a regulation of sorts, but it is not sufficiently connected to the sensory system to be able to have a true picture of the outside world, so it is dependent on local (internal) feedback loops for information. If this loop is in control, then the body physiology is stable, but is largely unresponsive to changes in external circumstances.

d) Longer term control comes from ***hypothalamus → brainstem → local***, and allows for reactive response to the general emotional state; and so is connected (albeit poorly) to the external world and controls long term homeostasis.

e) On top of this, there is modulation through ***limbic system → hypothalamus → brainstem → local***, which integrates thermoregulation, emotions, memory, and non-cognitive sensory reflexes and allows for ***anticipation*** (e.g. an increase in dietary fructose signals autumn, and so the body prepares for winter by laying down more fat).

f) Finally, there is the *possibility of* cognitive control (via a two-way feedback loop) of some aspects of the limbic survival responses and survival-meaning interpreted by the sensory system, that feed into the limbic system and hypothalamus. Note that there are far more afferent (incoming) ANS nerve fibers than efferent (outgoing) ones. Therefore, unless the mind-body connection is actively managed, the body (e.g. the ANS) tends to exert a significant control over what are normally considered to be mental processes.

The Enteric Nervous System and the digestive tract are almost capable of existing without reference to higher levels of control, and are a special (and substantial) exception to the above hierarchy. Research into the gut microbiome is still in its infancy[28]

The Vagus Nerve

The **Vagus nerve** or *Wanderer*[29] is the main nerve trunk of the Parasympathetic or Vagal branch of the Autonomic Nervous System (V-ANS). It is an ancient[30] means of regulation of body physiology and digestion in vertebrates[31]. The Vagus Nerve (the 10th Cranial Nerve / CN.X) travels down into the abdomen along the sides of the oesophagus, completing a 90 degree rotation; so at diaphragm level the right Vagus lies at the front of the oesophagus, and the left Vagus lies behind the oesophagus[32].

The right/anterior/Ventral Vagus specifically innervates the sinoatrial node of the heart and posterior cardiac plexus, and tends to slow the heart, and may cause very slow (<60bpm) heart rates (bradycardia). Whereas the left/posterior/Dorsal Vagus has a greater innervation of the anterior cardiac plexus and inhibits the sinoatrial node (the heart's electrical pacemaker), which in extreme conditions can lead to AV block, (where the generation of the electrical pace-making signal in the heart completely stops).

There is a clear evolutionary progression of physiological control through a common set of neurotransmitters and via something resembling Vagus nerve back to the most primitive of organisms; such that that invertebrates (e.g. nematodes[33] and grasshoppers) are used in research as analogues of human metabolic process in hibernation research. So although strictly speaking a Vagus Nerve arises from the central nervous system in a vertebrate, it (along with the Sympathetic nervous system) has functional equivalents in far more "primitive" organisms that do not require the presence of a significant brain. And the Vagus Nerve in turn controls (?coordinates) biochemistry and other aspects of homeostasis physiology that are evolutionarily continuous down to the level of a single cell. Each level of complexity is a direct adaptation of preceding metabolic functions. Whereas external sensory organs such as the eye have evolved separately several times in different ways; fundamental metabolic processes cannot so easily redesign themselves in this way, are far more constrained in the plasticity of their form, and tend to have a much more consistent, direct and sequential (though not necessarily linear) evolutionary hierarchy.

Estimates vary, but the Vagus nerve is thought to be (depending on which authority you consult) 70-90% afferent – i.e. sensory – so its function is far more about informing the CNS of what is happening in the body than relaying instructions from the CNS to the Viscera. Afferent fibres of the Vagus inform the CNS about inflammation and other immune activations/responses in the digestive system - which may then trigger immune responses within the Blood-Brain-Barrier (BBB) of the CNS. Taste centres not only in the tongue/mouth but all through the upper digestive tract give indications as to the

nutritional content of food, along with associated satiety/hunger. And part of this information is also relevant to functioning of the liver and other digestive organs/processes that give information about energy metabolism. Efferent Vagal fibers regulate secretion of gastric juices, digestive enzymes, and gut motility and overall smooth muscle tone (capacity) of the digestive tract. Really, we have only just scratched the surface in understanding the ANS and its synergy with both the CNS and the microbiome – the Gut-Brain Axis. For example, it has now been demonstrated that :

- Chemical compounds released by the gut microbiome are in direct contact with the E-ANS, which signals to the brain stem via the ANS, and this signal then relays back to the E-ANS to regulate gut motility[34]. Meaning that the gut bacteria actively control gut motility as a means to regulate their environment, and the ANS/brainstem uses this signal as an indirect means to sense the presence of fatty acids.
- There is a feedback loop via the Vagus Nerve that associates inflammatory GI disorders (e.g. Ulcerative Colitis and Crohn's Disease) with psychiatric disorders (major depression, PTSD), due to common brain areas being affected : the thalamus, medulla oblongata, amygdala, locus coeroelus and nucleus tractus solitarii (NTS) – and on to the hypothalamic–pituitary–adrenal (HPA) axis[35]. So the interventions that improve physical pathologies affect psychological ones – and vice versa.
- The Vagus nerve acts as a conduit for exchanges between the E-ANS and the hippocampus[36] - the part of the brain important for learning (particularly geographic memory) and emotions. This link between environment, location mapping, emotion and the gut/Vagus nerve is part of Porge's principle of "*neuroception*" (see later), and is particularly important for recalibration of the survival-alarm systems.

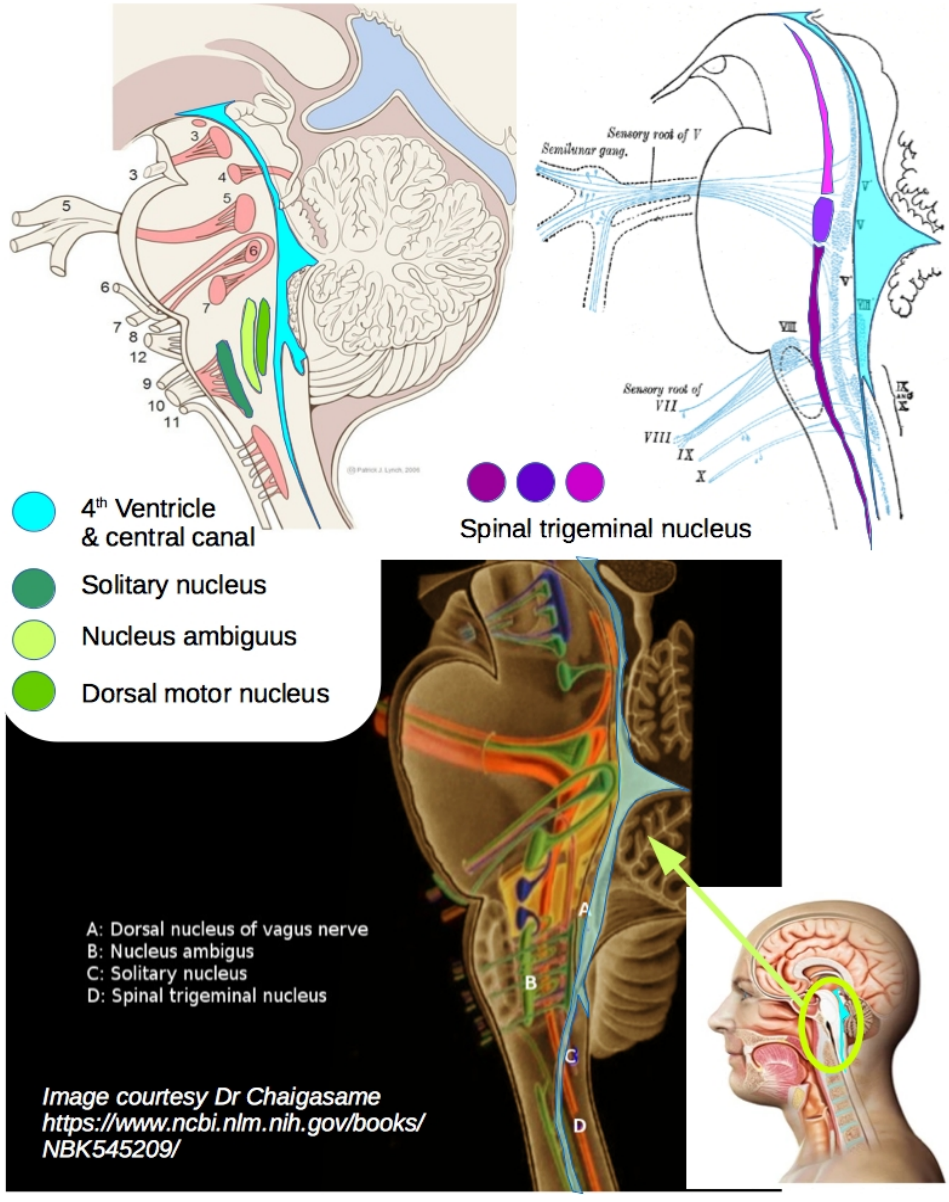
The following diagrams give some indication as to the interconnections of the Vagus Nerve (CN.X) :

1. Major parasympathetic brainstem nuclei
2. Nucleus ambiguus (NA)
3. The dorsal motor nucleus (of the Vagus) (DMN.X)
4. The Solitary nucleus and the Gag reflex
5. The spinal trigeminal nucleus

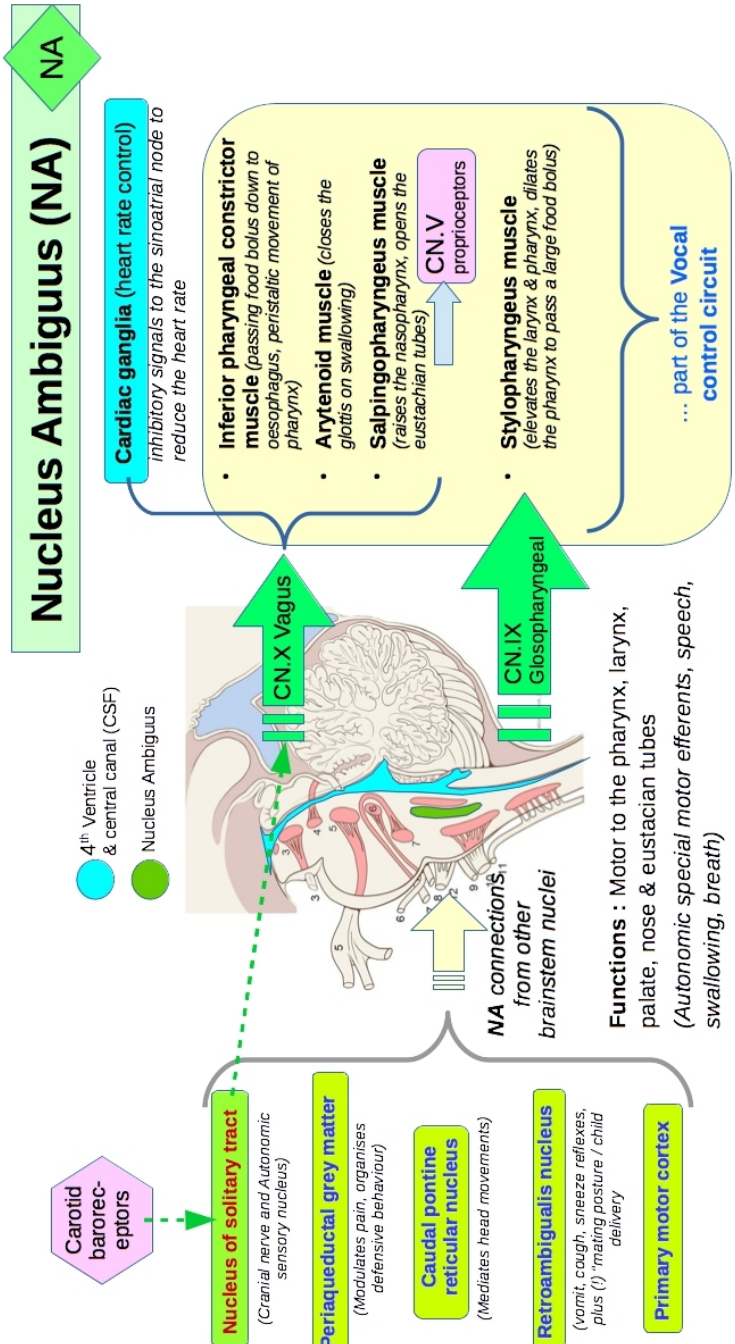
Remember when looking at these that Parasympathetic branches also (probably) arise from the Sacrum, and that this vegetative system cannot really be understood without also reference to the energy-consuming Sympathetic system (which we will cover in the next section)…. You will also find that if you inspect the various diagrams carefully

there are some discrepancies between the connections between various brain areas and nucleus bodies. The fact is that connectivity in the brain (and therefore between the brain and the autonomic nervous system) is not an exact science. And if an inspection of the various interconnections is to reveal anything at all, it is the labyrinthine complexity of the ways that the ANS integrates with itself and with the other functions of the central nervous system.

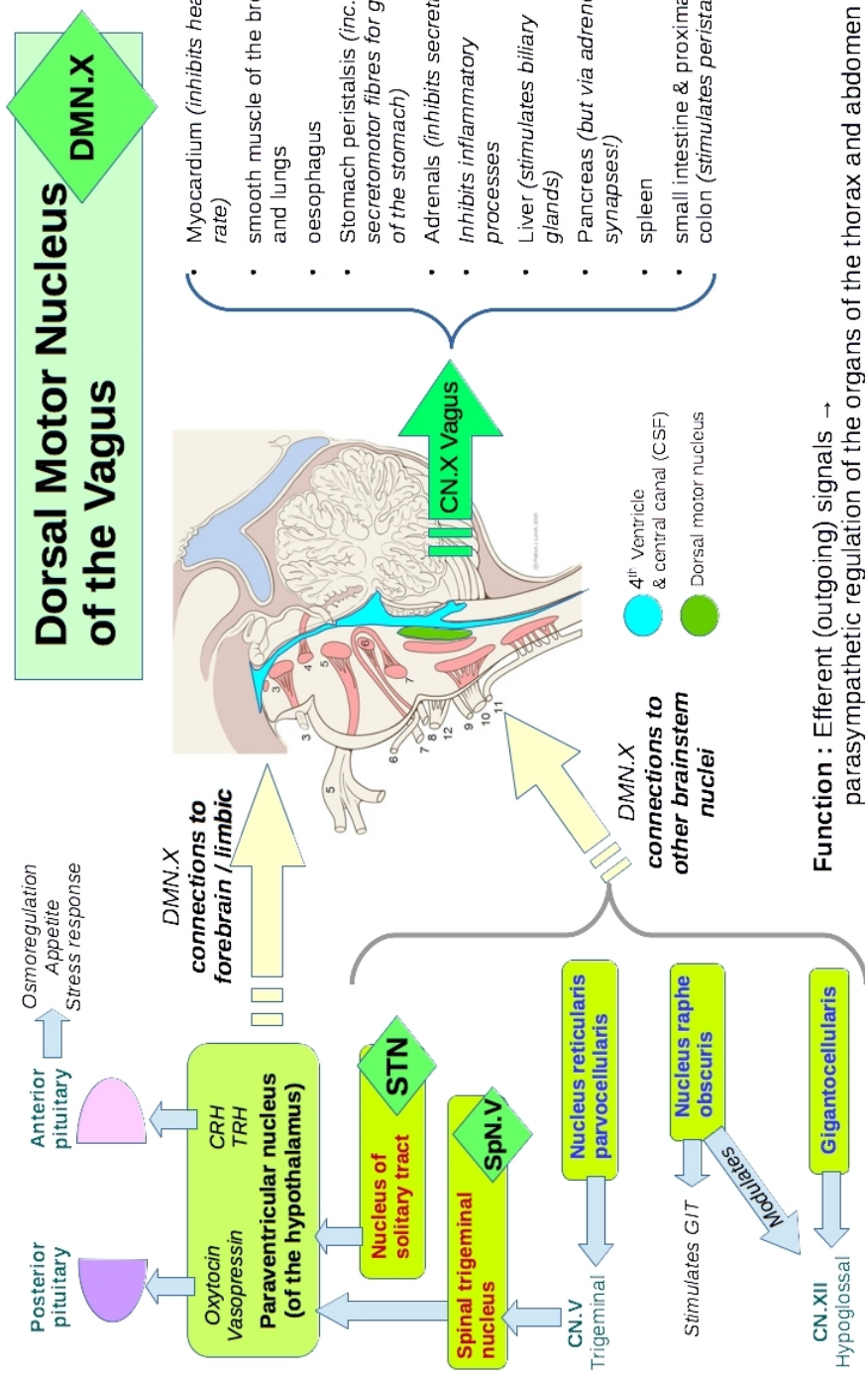
1. Parasympathetic nuclei



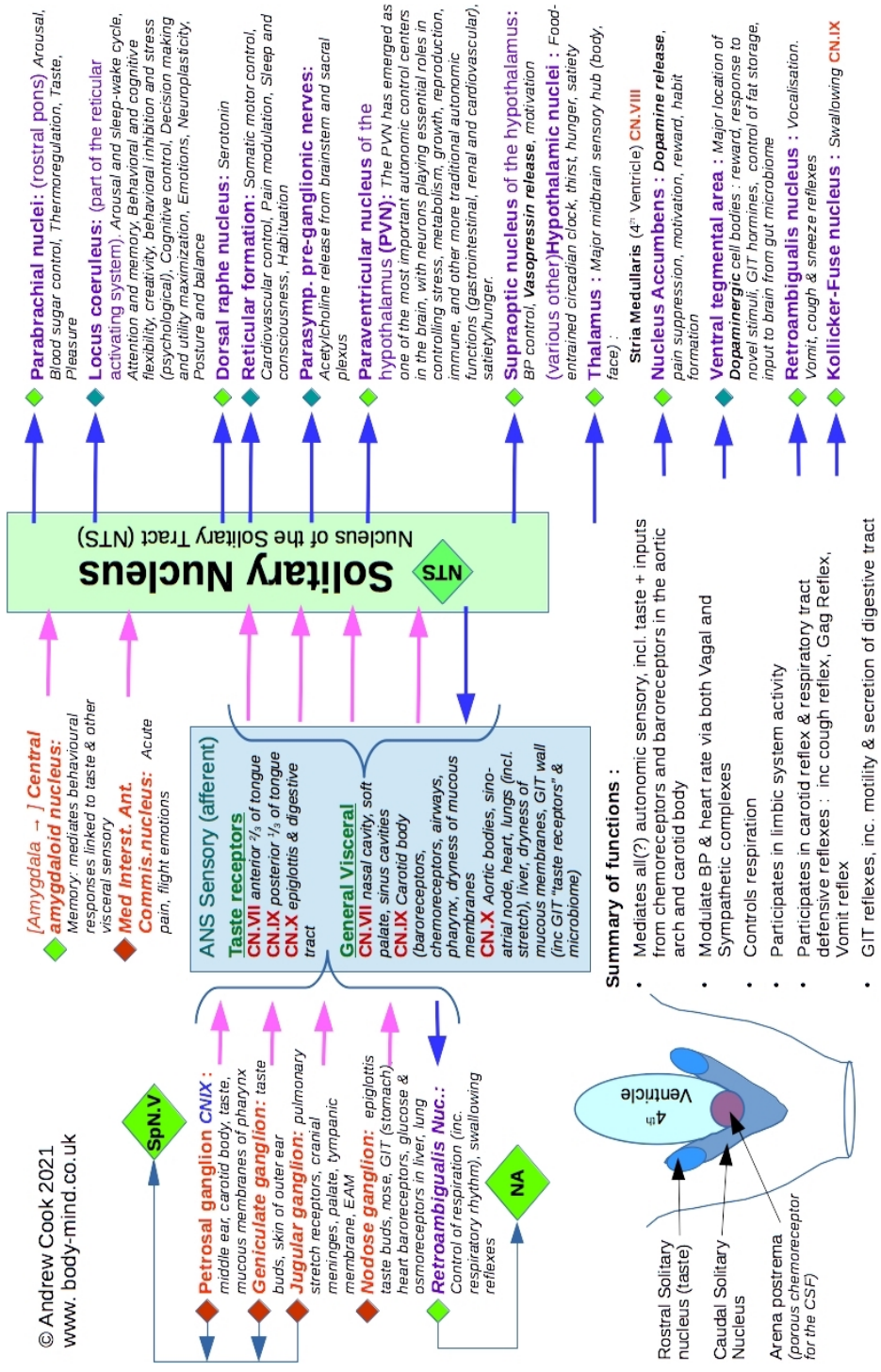
2. Nucleus ambiguus (NA)

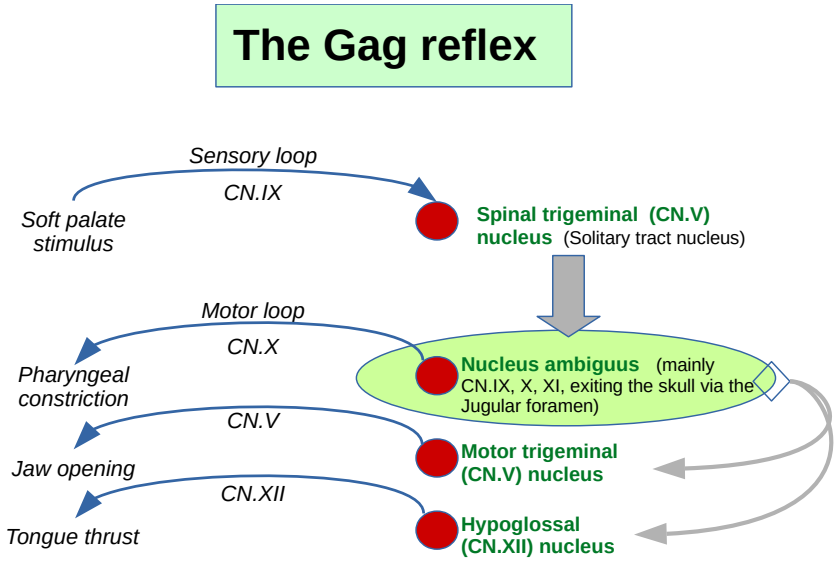


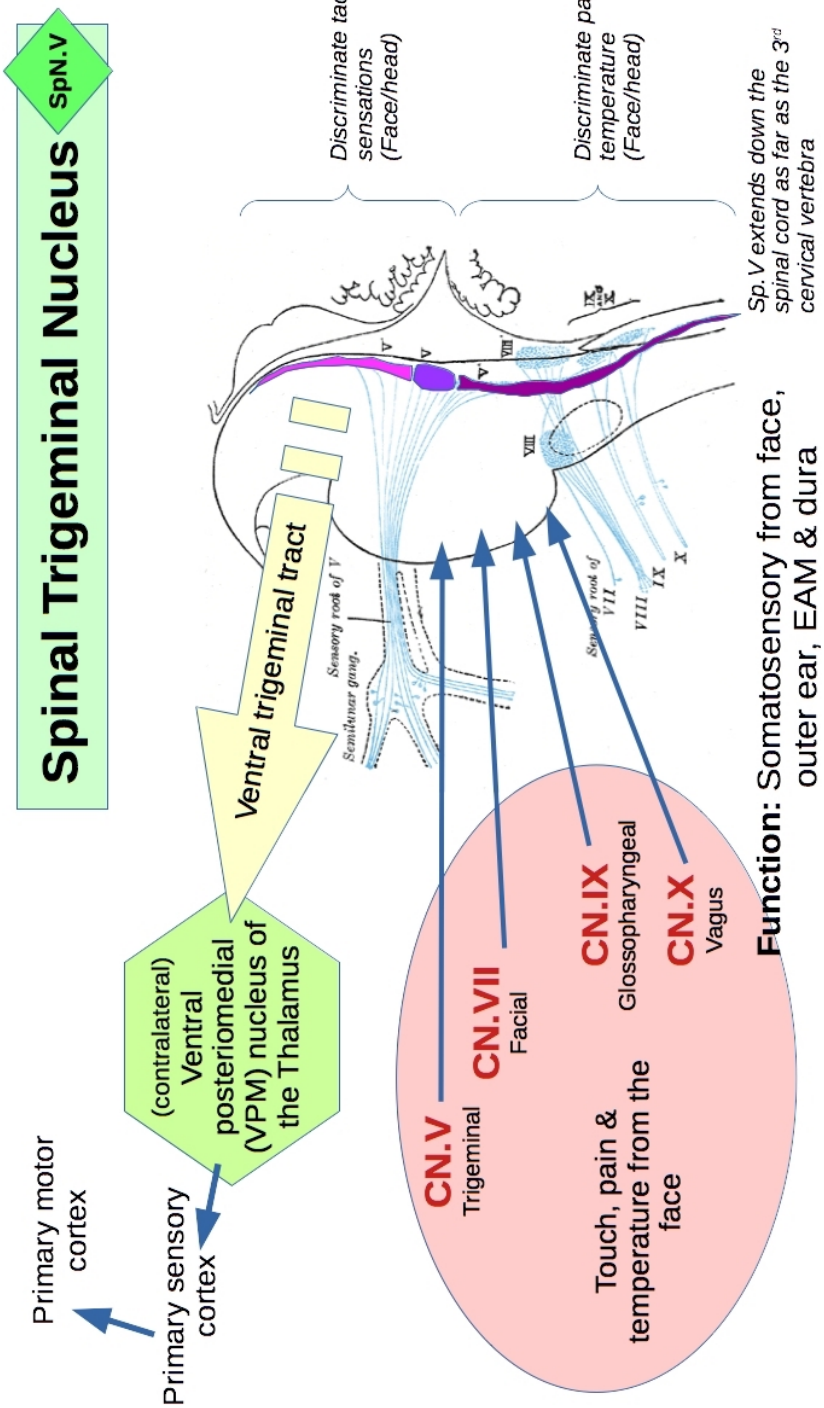
3. The dorsal motor nucleus (of the Vagus) (DMN.X)



4(a). The Solitary nucleus




The Gag reflex
Sensory loop
CN.IX
Soft palate stimulus
Spinal trigeminal (CN.V) nucleus (Solitary tract nucleus)
Motor loop
CN.X
Pharyngeal constriction
Nucleus ambiguus (mainly CN.IX, X, XI, exiting the skull via the Jugular foramen)
CN.V
Jaw opening
Motor trigeminal (CN.V) nucleus
CN.XII
Tongue thrust
Hypoglossal (CN.XII) nucleus


Spinal Trigeminal Nucleus
SpN.V
Discriminate tactile sensations (Face/head)
Discriminate pain & temperature (Face/head)
Sp.V extends down the spinal cord as far as the 3rd cervical vertebra
Ventral trigeminal tract
(contralateral) Ventral posteriomedial (VPM) nucleus of the Thalamus
Primary motor cortex
Primary sensory cortex
CN.V Trigeminal
CN.VII Facial
CN.IX Glossopharyngeal
CN.X Vagus
Touch, pain & temperature from the face
Function: Somatosensory from face, outer ear, EAM & dura

The Sympathetic Nervous System

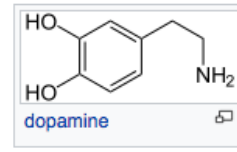
The **Sympathetic** branch of the Autonomic Nervous System (S-ANS) is mainly specific to vertebrates, and allows a rapid release of energy to muscles. The V-ANS and S-ANS systems are synergistic and opposite in function – so (in a very general sense) when the activity/expression of one increases, the activity/expression of the other decreases (and vice versa). In reality it is not possible to switch the Vagal/Parasympathetic system off, because of its vital role in coordinating critical homeostatic and metabolic functions. And when active and awake all animals much have a functioning S-ANS – because this controls the flow of oxygenated blood so that it is delivered wherever it is needed. So the shift between S-ANS and V-ANS is relative and proportional (rather than being absolute or extreme). The mammalian relationship between them (described in more detail later) is that the S-ANS nervous system is on all the time *to a degree*, and is inhibited by V-ANS activity – the "Vagal brake".

The S-ANS consists of two chains of nerve plexi that lie slightly in front and to the side of the thoracic vertebral column - with important secondary plexi rising up into the neck and head from T1, and connecting to the various ANS plexi and ganglia listed in Table 1 above. Nerve fibres from the thoracic spine enter this pair of chains, and from there follow arterial blood vessels to virtually every part of the body. One of the main functions of the S-ANS is to release and assist the distribution of energy for the purpose of moving in the external world. Therefore S-ANS activity is about release of energy and so is intimately connected to thyroxine and adrenal production (in fact, the adrenal glands are modified nodes at the bottom of the sympathetic chain), and to sugar metabolism and insulin production. Energy is used for movement primarily though use of muscles[37]. The S-ANS is also required for vital homeostatic functions related to cardiovascular activity and blood circulation, digestion, running the brain (the most energy-hungry organ of the body) and **thermoregulation** (Chapter 7.4). Humans are quite unusual in the animal kingdom - in that we sweat through our skin to reduce body temperature. Therefore there Is also an important relationship between energy metabolism, thermoregulation, blood flow to the skin capillary bed, and whole-body fluid/salt balance.

One of the main ways energy distribution is achieved is by control of blood flow, which in turn carries sugar, oxygen, other important building blocks such as taurine and cholesterol, metabolites, and regulatory hormones/neurotransmitters. Minor arteries and capillary beds are restricted by the S-ANS in parts of the body that do *not* require energy[38] , so that blood moves more easily to other areas of the body as required – one reason the peripheral S-ANS is very closely associated with peripheral arteries.

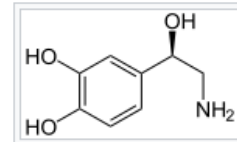
So, for example, if you use your brain more intensively by thinking, the brain uses more energy; and so the arteries to the rest of the body are slightly contracted by the S-ANS, therefore passing more blood to the brain. It is as if the entire organic emphasis swings brain-wards, and this metabolic emphasis can even be experienced as a slight whole-body contraction (accompanied by a shift in awareness and sensory availability away from the body. Re-focussing attention to a receptive (as opposed to active "thinking") use of the senses *feels* soft partly because the S-ANS and its associated adrenaline are not restricting (i.e. tightening) arteries and capillaries in the rest of the body. In a slightly different manner, if you eat food, the gut needs more energy to function; but also needs more blood flow so that the products of digestion can be transported to the liver. Therefore less blood flows to the limbs and brain, making us slightly sluggish after a heavy meal, requiring a parallel reduction in the blood concentration of noradrenaline. As the S-ANS modulates blood flow to certain parts of the body, so it and the Vagal system, and various other central (hindbrain) and peripheral feedback mechanisms (e.g. vasopressin and vasodilators such as NO_2) also work together to modulate breathing, heart rate and the volume of cardiac contractions to properly meet these aspects of energy metabolism. Thermoregulation along with associated issues of vasoconstriction, vasodilation and core vs peripheral metabolism are major topics in their own right, and will be dealt with in a separate chapter. It is thought that the Vagal/Parasympathetic ANS evolved first, and the S-ANS originally existed as few chromaffin cells (i.e. neuroendocrine cells that produce catecholamines) scattered throughout the organism, with no traceable interconnections[39].

Dopamine, Adrenaline & Noradrenaline



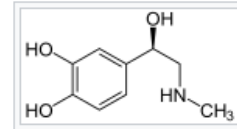
dopamine

It's worth reviewing the three signalling molecules of the sympathetic nervous system[40]. These are all catecholamines, a benzene ring with two hydroxyl molecules attached to an amine – see figure right, produced by the brain and the adrenal medulla :



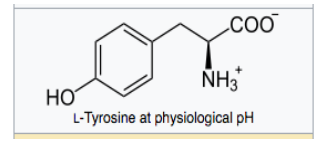
norepinephrine
(noradrenaline)

- adrenaline (also called epinephrene)[41] : a hormone produced by chromaffin cells located near the S-ANS chains – and particularly concentrated in the ad-renal *("attached to the kidney")* medulla
- noradrenaline (also called norepinephrene) : has the same (sympathetic ganglia) sites of production as adrenaline, but also by nuclei in the brain associated with the stress response - particularly the locus coeruleus (LC) of the brainstem. LC activity increases markedly under unpleasant or painful stimulation. Noradrenaline is the neurotransmitter that activates postganglionic neurons I the S-ANS.



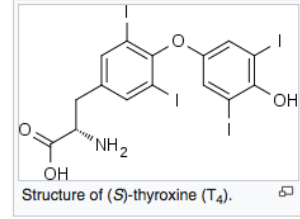
epinephrine
(adrenaline)

- dopamine : is produced mainly by two structures in the floor of the midbrain, the *ventral tegmental area* and the *substantia nigra*. But it is also synthesized in the kidneys, pancreas, GIT and immune system, and acts on the cells immediately local to its production.

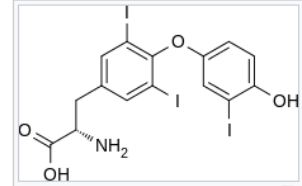


L-Tyrosine at physiological pH

They all act as *both* hormones and neurotransmitters vital to the maintenance of homeostasis. They have a half-life of only a few minutes when circulating in the blood, so unlike most other hormones, adrenaline does not need to self-regulate by means of a negative feedback loop. The catecholamines are directly related in that dopamine is a precursor to noradrenaline, which in turn is a precursor to adrenaline. Catecholamines all prepare the body and brain for action (e.g. fight-flight), and are produced as a result of emotions and/or environmental stressors (including extreme intensities of light and sound) and as a means to rectify low blood sugar levels. Being such a simple molecule they are bound to have a long evolutionary history, and are found in many plants in which they function as precursors to alkaloids – a major group of active substances in medicinal herbs.



Structure of (*S*)-thyroxine (T_4).



(*S*)-triiodothyronine (T_3, also called liothyronine).

Adrenaline has a very direct relationship to fear, but a somewhat ambivalent relationship to other emotions. In the case of fear, adrenaline enhances the laying down of long term memories (particularly in PTSD), which may then be re-triggered by elevated blood adrenaline. Adrenaline and noradrenaline are synergistic, secreted in stress conditions, and target the heart (raising BP and HR), muscles and blood vessels.

The action of adrenaline is complex and a little contradictory. It relaxes/dilates smooth muscle in the lungs, and increases BP – initially by increasing heart rate - to improve perfusion pressure of O_2 at a cellular level. Adrenaline also ramps up tetanic (10Hz) muscle oscillation, and feeds back to sustain the action of noradrenaline. In low physiologic concentrations adrenaline dilates skeletal muscle arteries; but as its concentration increases its action changes, constricting the smooth muscle of arterioles to increase the total peripheral vascular flow resistance to maintain optimisation of cellular O_2 perfusion.

Noradrenaline concentration has a diurnal cycle, being lowest during sleep. With even slightly elevated levels, noradrenaline causes an increase in vigilance, alertness, attentive capacity, and arousal; improves accessibility and formation of memory; and as its concentration increases is associated with restlessness and anxiety. So for instance, the LC is stimulated to produce more noradrenaline if the bladder is full, so having a full bladder can induce quite strong feelings of anxiety.

Physiologically noradrenaline *constricts* blood vessels in areas of the body that are not critical for motion such as the digestive system and skin; opens/dilates the eye pupils and the lungs; increases heart rate and volume of blood pumped; and decreases GIT motility and E-ANS activity. On a cellular level, noradrenaline is strongly adaptive in its effects – both inhibiting and activating a secondary cell signalling molecule related to ATP (cAMP); and its overall physiological action is strongly linked to ATP. Its physiological effects also include moisturising the eyes (and production of tears), increasedATP throughput in brown adipose tissue (thermogenesis), a complex set of inhibitions and activations of the immune system, vasoconstriction (increase of BP), release of glucagon from the pancreas to increase production of glucose by the liver, increase in glucose uptake by skeletal muscles, lipolysis (conversion of stored fat to useful energy). Noradrenaline (and its analogue, octopamine) is present in insects, jellyfish and protozoa.

Dopamine, the "reward hormone" might seem to be the odd man out in this trio of catecholamines. Like adrenaline, its use can be traced back to plants in which it is a paracrine messenger, allowing individual cells to coordinate groups of cells. In the CNS it is a neuromodulator (essentially the same except with neural cells) - which probably gives cause to its importance in the proper control by inhibition of muscle tremor. So Dopamine can be seen to be critical to the ability of large multicellular organisms to function in a coordinated and coherent manner – but also has far wider implications for brain function, e.g. with altered dopamine activity being associated with schizophrenia (another kind of loss of coherence).

Physiologically, dopamine inhibits norepinephrine release in blood vessels and acts as a vasodilator; increases sodium and urine output from the kidneys; reduces (pancreas)

insulin production; reduces GIT motility; benefits intestinal mucosa; and reduces lymphocyte activity. Both psychologically and physiologically, dopamine conveys a rather un-nuanced, black-and-white survival "meaning". As such, it is crucial to **neuroception** (see PolyVagal Theory below) – the means by which the ANS decides how to respond to an event, object, or situation. Technically its action is one of "*motivational salience*" – turning the organism towards a desired outcome and away from an undesired one. So far as the brain is concerned, the *ventral tegmental area* both produces dopamine and assesses *positive valence* – i.e. the "goodness" of an event, object, or situation. This again is of direct importance for neuroception. It is possible to easily intuit how this generically translates into the control of fixed oscillatory (i.e. meaningless) tremor to give directional (meaningful) action to muscles. Placed in this light, the presence of Dopamine in the triad of catecholamines makes absolute sense, because there is a direct mutual relationship between valance – the (perceived) goodness or badness of something – and action – the response. Response requires energy (adrenaline/noradrenaline), and it is only the valence provided by dopamine that gives meaning to action – or provides meaning that then initiates action. Thus, the direction, frugality and elegance of the metabolic cascade

dopamine (valence/meaning) →

*(add **OH**, becomes…)* **noradrenaline** (immediate response) →

*(add **CH_2**, becomes…)* **adrenaline** (sustained response)

is also totally relevant to their function (as would be expected, given a billion years or so of evolution of this almost universal metabolic building block).

Acetylcholine

Whereas noradrenaline is the main signalling hormone/neurotransmitter for the sympathetic arousal nervous system, **acetylcholine**[42] (**ACH**) is the equivalent neurotransmitter used by the Parasympathetic or Vagal ANS and the Motor nervous system. One of the building blocks of ACH is glucose, so ACH production is favoured when glucose is not prioritised as a fuel for sympathetic activity. ACH synthesis takes place in the mitochondria in nerve endings(!), but ACH is also present in almost all non-neuronal cells. It must be catalysed at nerve synapses by ***acetylcholinesterase*** to its constituent parts as soon as it is used, otherwise the buildup of ACH prevents further synapse activity, and paralysis ensues. Organophosphorous nerve gases and pesticides are toxic because they prevent synthesis of acetylcholinesterase.

The general metabolic effect of ACH is complex. Its effects are felt across the Central and Peripheral nervous systems, affecting Motor nerves, and all branches of the ANS

(i.e. not only the Parasympathetic ANS). In the CNS, Acetylcholine mediates "higher" cortical functions, being important for memory formation and retrieval, alertness, engagement in the world, and behavioural plasticity. Either through direct action or modulation of other neurotransmitters (serotonin, dopamine, noradrenaline) it influences important higher level cognitive processes related to the exercise of free will (choice of action, judgement, etc) and planning[43]. ACH also activates skeletal muscle (underlining the importance of physical movement for good quality mental health). It also activates preganglionic neurons in the S-ANS, again indicating something of the evolutionary progression of the peripheral nervous system. Although the sweat glands are innervated sympathetically, they are triggered by ACH – just one example of how both water/major ion metabolism and thermoregulation are deeply tied into to ANS regulation of all aspects of homeostasis. At a cellular level, ACH can both inhibit or excite (as a "second messenger"), and is important for ATP metabolism and cross-membrane transfer of sodium, potassium, and calcium ions.

From an evolutionary point of view, ACH is present in almost all kinds of life, including bacteria and fungi. Choline was probably used as a signalling agent by the very first life-forms to exist over 2.5 billion years ago, and is a basic ingredient used to synthesise cell membrane phospholipids.

Adaptive ranges

It could be generalised that the S-ANS expends energy and is largely focussed on providing the energetic means to act in the **external** world. In contrast, the Vagal or Parasympathetic nervous system is often called the "Vegetative" system, absorbing and storings (conserving) energy - and is more focussed on maintaining the **internal** environment on good order. Clearly, blood circulation is indispensable for homeostatic function, so the functions of the S-ANS and V-ANS are not just complementary to each other – the are deeply interwoven. It would, however, be a mistake to think of one of these systems being purely focussed on the internal or external. From an evolutionary point of view, the Vagal system came first, and therefore must also *necessarily* have the capacity to express functions that relate to the external world, and not just to baseline homeostasis. So for instance, when we (or a rat or a honeybee) finds something very nutritious in our environment, it is signals from Vagus nerve that lay down memories of where that food, and that coordinates activity in the hippocampus was so that we can return to the same place at a future date[44]. Even more, it seems that the Vagal afferents are important for laying down memory through production of new neurons – a rather interesting twist on the idea of having a "gut instinct".

All branches of the ANS have a ***normal adaptive range*** *of function, inside which they*

work together, optimise energy expenditure for the whole human organism and are coordinated by the central nervous system.

They can also enter **emergency-survival adaptive states**. In such emergencies, one branch of the ANS becomes much more dominant – depending on the specific circumstances of the emergency. In more extreme emergencies there is generally less coherence between the various branches of the ANS and the CNS; as parts of the body are left to get on with their job unsupervised as attention focusses on the specific survival issue on hand. This reduced synergy and increased compartmentalisation of physiological function under extreme stress/danger allows a more efficient generic response to the danger at the expense of whole body and wide-ranging adaptive capacity. The more extreme the survival adaptation, the less adaptive capacity there is for anything else. Broadly speaking, these survival states see a real and qualitative change in the degree of integration of the entire body-mind. There is a loss of nuance, a certain rigidity and increasing central control on the one hand, whilst on the other hand peripheral systems and physiological feedback loops tend to become less centrally coordinated, less coherent with each other, and less connected to ("aware of") higher end regulatory feedback.. There is less of a unified organism and more of an ad hoc executive committee. In these emergency adaptations, the body is much less interested in homeostasis or long term requirements - and much more interested in more short-term reactive and specialised ranges of physiology that might increase the chances of survival from *immediate* mortal threats. The drawback of these high-end (or even last-ditch) physiological survival response zones is that they are not gracefully adaptive to normal "business as usual, everything is OK" life. They are either physiologically inefficient and burn too much energy too quickly (S-ANS survival range) , or are too efficient and too conservative of energy. Extreme survival adaptations are generally unsustainable beyond a short timeframe or outside narrow ranges of external circumstance.

In these extreme emergency states, signalling proteins – neurotransmitters, peptides, hormones, etc. – may have very different biological meanings, sometimes even opposite meanings to the ones that they have in the normal adaptive range.

Thyroid hormones and Calcium metabolism

In addition to important roles during development and growth, the thyroid hormones (**thyroxine** or T4 and triiodothyronine or **T3**) increase the body's sensitivity to the catecholamines *when the physiology is more or less in a normal adaptive range*. In this role they accelerate the release of heat and energy for movement. They also regulate protein, fat, and carbohydrate metabolism. However, T3/T4 have the opposite effect in deep DV-ANS states, and can cause a severe drop in body temperature and assist entering hibernation. The importance of T3/T4 at a cellular level is shown by the fact that they cannot easily cross the cellular wall, but there are at least 10 different genetically modulated kinds of cell transporter that act on them, ensuring that cell concentrations are higher than those in blood plasma. Triiodothyronine/T3 :

- Increases cardiac output
- Increases heart rate and respiratory rate
- Increases basal metabolic rate
- Potentiates the effects of catecholamines (i.e. increases sympathetic activity)
- Potentiates brain development
- Thickens endometrium in females
- Increases catabolism of proteins and carbohydrates

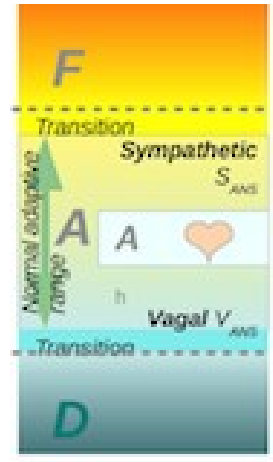
The Thyroid also produces **Calcitonin**, which buffers excess blood Calcium (Ca) to bone, and acts in opposition to Parathyroid hormone (PTH), which releases Ca and P from bone (q.v. cortisol). Blood Ca is one of the critical homeostatic values, having a very narrow healthy metabolic range of 2.2 - 2.6 mmol/L, so the various hormones that affect calcium metabolism have to be balanced by others in a complex set of interdependent effects. Since Ca is necessary for sodium transport across cell membranes (q.v. cortisol again), intracellular signalling and muscle contraction, it makes sense that Ca is released from bone during high S-ANS activity[45, 46, 47] (through both blood-plasma noradrenaline, and autonomic innervation leading to local production of noradrenaline from cortical bone). That is – it makes sense assuming S-ANS activity is only meant to be of short duration. The reverse is also true – in that Parasympathetic activity[48] favours loading-based accrual of bone mass via the inflammatory/immune/autorepair signalling agent IL-1. Thus, taking the specific case of Calcium, we have very clearly demonstrated principle that is general to the entire workings of the ANS – namely that the body optimises for acute high-end S-ANS activity (*fight-flight*) by de-prioritising critical homeostatic functions such as tissue

repair, major ion conservation, and immunological response to infections. Chronically high-threat environments produce a shift in Cortisol metabolism, and some (but not all) of the worst excesses of this short-term contingent metabolism are – ameliorated.

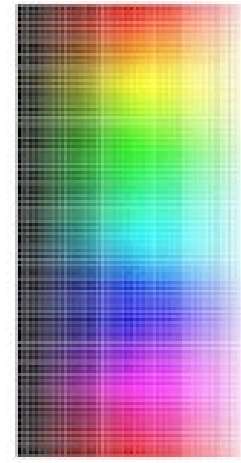
The Enteric Nervous System and the Microbiome

The Enteric Nervous System (E-ANS) is a relatively recent discovery, is not described in all anatomy texts, and is the brain of the most autonomous part of the entire body. It consists of a mesh-like collection of neurons surrounding the intestinal walls, that also organise into major plexi in the abdomen. Thinking of the E-ANS in a very simplistic and mechanistic way, its main overt task is to coordinate peristalsis and other functions of the gastrointestinal tract, including the production of enzymes. The E-ANS and its plexi are sometimes called the "Second Brain", and consist of about half a billion neurons (compared to about 100 million neurons in the Brain). Although spread across a large volume of the abdomen, the E-ANS is almost identical in many ways to the CNS - having supporting astroctyes (specialised immune cells), producing and using the same 30-plus neurotransmitters that the brain uses, and having a diffusion barrier round supporting capillaries in a way that echoes the blood-brain barrier.

The E-ANS is connected to the hindbrain (which regulates body physiology and maintains homeostasis) through both the Vagal and Sympathetic ANS. Indeed, there is almost ten times as much (afferent) information flowing up the Vagus nerve back into the brain – as there are (efferent) signals leaving the brain through it to the rest of the body. The Enteric nervous system can also function independently of the central nervous system if its connections to it are severed.
So the gut and its microbiome are almost separate entities in their own right, a primitive digestive-tract-creature (with its own dedicated brain) living within its companion body. The lining of the gut even originates from its own specialised layer of cells (the Endoderm) in the developing embryo. Most nerve connections in the "second brain" are local between the gut and E-ANS. Of the non-local connections, there are more afferent (sensory) fibers bringing information from the gut to the brain – than there are efferent (control) fibers leading from the brain to the gut. If the spinal cord is severed, the body's and homeostatic mechanisms and organs (such as the heart and lungs) may continue to work, but they rely on central regulation in the brain, and



The ANS model
(nice clear, neat zones)



The ANS reality
(transitions, ambiguities, complexity, multiple states)

small sensory inputs such as stroking the skin can send them into chaotic behaviour. However, provided they are supplied with oxygen and blood, the gut and the E-ANS are self-sufficient, and have no need for central control from the brain. It"s almost as if we have a separate animal living inside us.

Another peculiarity about the gut (or more precisely, the digestive tract, from the mouth through to the anus) is that it contains roughly as many bacterial cells as there are human cells in the body. These bacteria live in an ecological balance, the health of which affects the health of the entire body, including the brain. It was once thought that the immune system keeps bacteria on the outside of an otherwise "human" body; so the bacteria of the digestive tract would be firmly contained inside the digestive tract, and skin bacteria would be contained on the outside surface of the skin. This has been found to be incorrect. Skin bacteria naturally live inside the epidermis, and are part of the antibiotic response that kills most bacteria that come into contact with the skin. And gut bacteria have been found to migrate throughout the body and are now known to be associated with many illnesses. Bacteria from the gut have even been found inside the brain.

A simplified model of ANS response zones

When describing the holistic function (of the entire) ANS it is easiest to begin with the core elements – the Sympathetic and Parasympathetic (Vagal) branches - which usually act in a reciprocal and mutual synergy. Once this balance is understood, the Ventral Vagal and Enteric systems can be added on to the core model as relatively simple extensions.

When conceptualising adaptive responses mediated by the ANS, it is convenient to divide them into a few discrete zones (such as Fight-flight, or Freeze). In reality this is a multidimensional landscape of combinations and nuances, much more like a three-dimensional RGB or CMYK colour chart than a simple diagram. The point of simplification is that – just as we can identify the presence of certain colours in a colour chart – reds, blues, black, yellows,

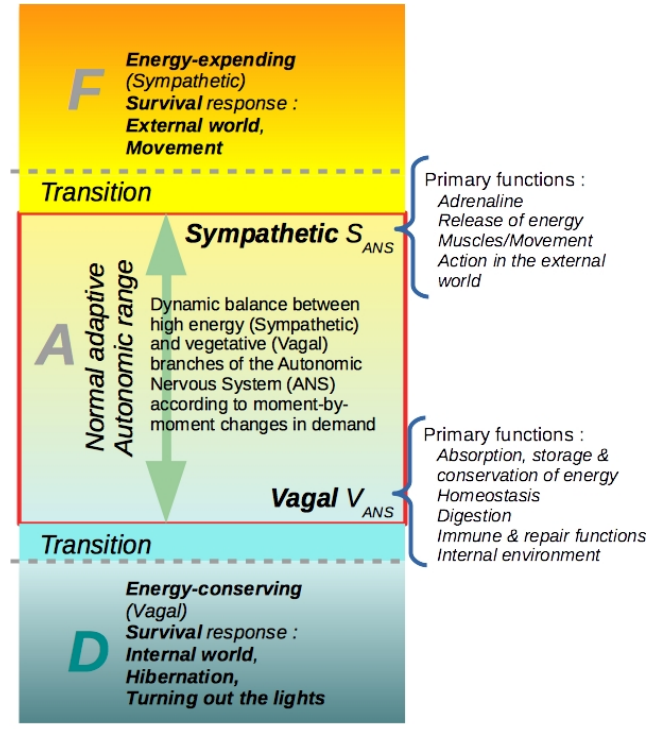


Figure ANS-1 : A simple map of Autonomic ranges

etc. - a simplified categorisation of the ANS allows us to recognise certain kinds of response; and recognition helps us to navigate this shifting and sometimes ambiguous terrain.

Normal Adaptive Range

Figure 1 shows the basic kinds of adaptive response available to the ANS. This consists of three major zones, and three sub-zones. The central major zone **A** is the **normal adaptive range** of response available when the world is a relatively safe place (i.e. there are no significant perceived or imagined mortal threats to existence).

The total width of this (normal adaptive) window is an indicator of overall mental, emotional, psychological, physical and physiological resilience and adaptive capacity... So the wider the window of **A**, the more extreme situations can be dealt with – without needing to enter an emergency-survival adaptive state. In trauma psychology, zone **A** is sometimes called the "*Window of Tolerance*", because emergency response states outside this window are in-tolerant and non-adaptive in the usual sense of the word.

In this normal range **A**, the interplay between the two branches of the ANS (Sympathetic and Vagal) is fully adaptive, and always in dynamic balance. At any one time (**Figure ANS-2**) the external expression of one or the other branch will be more dominant, depending on the current priority. If the priority is movement, then the sympathetic branch will tend to be more active. Otherwise the Vagal branch dominates. The balance also shifts according to factors such as the circadian clock (Chapter 3).

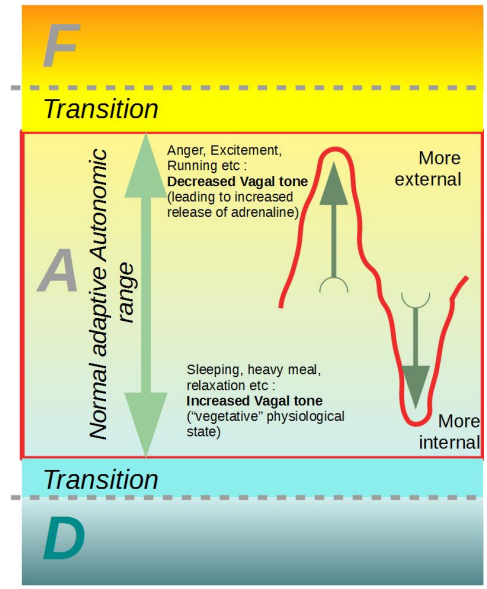


Figure ANS-2 : Moving in the normal Autonomic range during everyday life

In mammals, the mechanism by which this adaptive balance is regulated is not quite so intuitive. The Sympathetic nervous system is turned <u>on</u> at all times, ready for action. Compared to our evolutionary ancestors, the constant availability of adrenaline creates a greater capacity for dynamic response and sustained output from the heart and lungs, along with heat to control body temperature. But if this were running all of the time, we would need a vast and inexhaustible supply of food, and would burn out burn quickly. So the constantly available mammalian Sympathetic nervous system is usually down-regulated (inhibited) by a high Vagal tone - termed the **Vagal Brake**[49] - which is a part of the ANS model described by PolyVagal Theory (see Chapter 7.2). Practically speaking, all that needs to happen if more energy is needed –

is for the brake to be released.

The constant availability of the high energy Sympathetic / Adrenal response provided by the Vagal brake comes at a cost – because it burns more energy at rest than does the reptilian metabolism of (e.g.) a crocodile. But the survival benefits for mammals – of greater responsiveness, more ability to sustain motion or to redirect energy towards homeostasis and temperature control (**thermoregulation**) – far outweigh the disadvantages in most circumstances. The increased adaptive capacity that comes with a Vagal brake is reflected in the way in which mammals have expanded into almost every environment on Earth – including many places where reptiles simply cannot live.

The inhibitory nature of the Vagal brake is itself a means to conserve energy and resources. By using a Vagal brake, the mammalian organism does not expend its resources on everything at once, but rather there is a means to prioritise *either* Sympathetic/Adrenal physiology (higher energy, more externally directed movement) *or* Vagal physiology (digestion and other vegetative processes). This prioritisation allows for fine control, and retains energy in reserve. As an analogy, it's a little like having a controller that ensures your oven and central heating cannot both be switched on at the same time, or at the very least, never usually takes more than a total of 3kW of electricity – whilst the wiring supply to the house is still organised so it can provide 30kW peak load if absolutely necessary. The Normal Adaptive Range provides a vast range of possible physiological, behavioural, social, sensory, mental and emotional states. One of these of particular importance is the **Immobilisation** response, described later.

Extreme adaptive responses

Above zone **A** in Figure ANS-1, we have the "Fight-Flight" Sympathetic / Adrenal **emergency response** zone **F**. And at the bottom, below zone **A** we have the Deep (or Dorsal) Vagal emergency response zone **D**. These two physiological windows (beyond the dotted lines) are <u>not</u> accessible (i.e. they cannot be turned on to any significant extent) through any act of conscious *will*; though we still remain conscious through most of their functional range. Rather, at some degree of threat, a profound biological switch is thrown by a primitive part of the body-mind. This propels us into physiological and mental-emotional states that transcend any normal experience of what we might be capable of[50].

Both of the extreme adaptive ANS zones induce a change in state of consciousness in which the mind is not so much directing action as modulating action, and is relegated much more to the role of observer. There is less Agency, and more Reactivity. Both also involve a certain reduction in somatic awareness – but for very different reasons.

There are many recorded instances of soldiers being shot and being oblivious to the bullet wound – which normally would be totally incapacitating[51]. Many people who have broken bones in car and sports accidents also experience a complete lack of awareness of the injury (even to the point of being able to move a broken arm in a completely normal way) – until they realise what has happened. As they "*come to their senses*", the pain suddenly hits them. Intense deep and uncontrollable shaking often sets in at this point. And interestingly, it is not unusual for severe bleeding to also begin at this point – so the body had also somehow contained and sealed off damaged blood vessels as part of its temporary adaptive response. The painless somatic oblivion experienced during extreme Fight-Flight appears to be induced by Endorphins (endogenous opioids), which may sometimes also be accompanied by emotions of exhilaration, excitement and triumph, along with a remarkable clarity of mind. The unpredictable and uncontrollable way in which this transition to high adrenaline physiology occurs is attested to by the many people who did not experience a bullet as being (at least initially) painless[52].

Fight-Flight

> Instead of dropping dead as I expected him to, the tiger went straight up into the air above the bushes for his full length, falling backwards onto a tree a foot thick which had been blown down in a storm and was still green. With unbelievable fury he attacked this tree and tore it to bits, emitting as he did so roar upon roar, and what was even worse, a dreadful blood-curdling sound as though he was savaging his worst enemy. The branches of the tree tossed about as though struck by a tornado, while the bushes on my side shook and bulged out, and every moment I expected to have him on top of me, for he had been looking at me when I fired, and knew where I was.
>
> – from "*Man Eaters of the Kumaon*" by Jim Corbett

The fight-flight state (**F**) results in an availability of energy that may release almost superhuman powers. When compared to the early days of human evolution during the last ice age, when sabretooth tigers, dire wolves, short faced bears and other huge predators were still around ... the modern world is relatively safe. But there are still real stories of people entering extreme adrenal states and being able to lift a heavy car off somebody, or fight off a fierce animal. The Viking berserkers were trained to enter this hyper-adrenal state. Aron Ralston (who survived by sawing his own arm off with a blunt penknife[53]) could probably only do that because his blood stream was filled with adrenaline and painkilling endorphins. Or there is the simultaneously entertaining and hair-raising

account of Mr DC Robertson, who in 1898 successfully escaped a lion by cycling with a buckled front wheel up a steep hill[54]. Or Lydia Angyiou, who (weighing in at at 90 pounds) attacked and fended off a 700lb polar bear that had wandered into her garden long enough for her children to escape – and survived.

The fight-flight response is primarily a means to deal with short-term acute and physically present mortal dangers in the **external world** by **moving**/using muscles, and by releasing a large amount of energy to support that movement. People who have experienced a true high adrenaline Fight-Flight state are often (in retrospect) surprised at the strength they have expressed and the things they have done. Movement requires a certain degree of conscious attention. But too much conscious attention will slow down reflexes. Movement is always faster if it is unconscious - because thinking of a movement before it happens creates inhibitory impulses in the antagonist muscles, due to activity in the mirror neurons of the premotor cortex. So in strong fight-flight responses the frontal (cognitive) lobes of the cortex tend to be turned off by being flooded with norepinephrine.

The fight-flight state may be characterised by a very matter of fact frame of mind in which time may appear to slow down, or a mindless state in which time speeds up, or an uncontrollably racing set of (panicky) thoughts. The neurochemistry of these states is very ill-defined because they are so hard to reproduce in a laboratory. Although – to an external observer - decisions may be taken, in fact the person is almost passively observing themselves taking actions with very little consciously controlled mental activity. It is very similar to (if not the same as) the heightened mental states described by high level martial artists – who achieve this altered state of consciousness without entering an emergency fight-flight ANS zone. In a similar vein, soldiers who are selected for special forces units are chosen because they are extremely resilient – their window of tolerance is far wider, and so they rarely enter extreme fight-flight, and can still think clearly and objectively in situations in which most people's brains would be shutting down. High intensity emotions (emotions are NOT thoughts!) can also occur during fight-flight; in which case they will dominate the mental experience, and may be anything from ("*blind*" or "*seeing red*") rage through to ("*mind-numbing*" or "*blind*") terror. The words and phrases in common usage are an accurate experiential description of the way in which normal conscious thought processes are overridden.

An interesting personal account of the transition to fight-flight (and its superhuman strength), to deep parasympathetic and its wound-healing capacity, and then back to health - is given by a survivor of a tiger attack in Jim Corbet's "*Man eaters of the Kumaon*" :

"Do you see that pine tree, sahib, at the bottom of the grassy slope on the shoulder of the hill? Yes, the pine tree with a big white rock to the east of it. Well, it was at the upper edge of the grassy slope that the man-eater attacked me. The grassy slope is as perpendicular as the wall of a house, and none but a hillman could find foothold on it. My son, who was eight years of age at the time, and I had cut grass on that slope on the day of my misfortune, carrying the grass up in armfuls to the belt of trees where the ground is level.

"I was stooping down at the very edge of the slope, tying the grass into a big bundle, when the tiger sprang at me and buried its teeth, one under my right eye, one in my chin and the other two here at the back of my neck. The tiger's mouth struck me with a great blow and I fell over on my back, while the tiger lay on top of me chest to chest, with its stomach between my legs. When falling backwards I had flung out my arms and my right hand had come in contact with an oak sapling. As my fingers grasped the sapling, an idea came to me. My legs were free, and if I could draw them up and insert my feet under and against the tiger's belly, I might be able to push the tiger off, and run away. The pain, as the tiger crushed all the bones on the right side of my face, was terrible; but I did not lose consciousness, for you see, sahib, at that time I was a young man, and in all the hills there was no one to compare with me in strength. Very slowly, so as not to anger the tiger I drew my legs up on either side of it, and gently inserted my bare feet against its belly. Then placing my left hand against its chest and pushing and kicking upwards with all my might, I lifted the tiger right off the ground and, we being on the very edge of the perpendicular hillside, the tiger went crashing down and belike would have taken me with him, had my hold on the sapling not been a good one.

"My son had been too frightened to run away, and when the tiger had gone, I took his loincloth from him and wrapped it round my head, and holding his hand I walked back to the village. Arrived at my home I told my wife to call all my friends together, for I wished to see their faces before I died. When my friends were assembled and saw my condition, they wanted to put me on a charpoy and carry me fifty miles to the Almora hospital, but this I would not consent to; for my suffering was great, and being assured that my time had come, I wanted to die where I had been born, and where I had lived all my life. Water was brought, for I was thirsty and my head was on fire, but when it was poured into my mouth, it all flowed out through the holes in my neck. Thereafter, for a period beyond measure, there was great confusion in my mind, and much pain in my head and in my neck, and while I waited and longed for death to end my sufferings my wounds healed of themselves, and I became well."

Immune aspects of Fight-Flight

While ANS balance remains in a Fight-Flight / adrenal state, the entire immune function turns towards temporary "*patch up and make do*", and away from self-healing - with current infections or other health issues being put "on hold" and **encapsulated** so they can be attended to properly when all the reserves of the body do not have to be so available for immediate survival. The way that illnesses may be temporarily put into cold storage in highly stressful (i.e. dangerous) times is well recognised. At the onset of both the London Blitz and the siege of Kosovo, when external threat became high, hospital admissions changed almost immediately with far fewer people being admitted due to illness. This wasn't because ill people were staying away to give more beds to the injured. It was a direct result of the change in immune function that comes with high stress. Another well recognised example of this is "teacher's flu" - the tendency for illness to "begin" as soon as stress is removed (in this case, weekends and holidays). Actually, the illness has been there for some time, and has been suppressed and contained by the immune system - rather than being properly addressed.

Musculoskeletal aspects of Fight-Flight

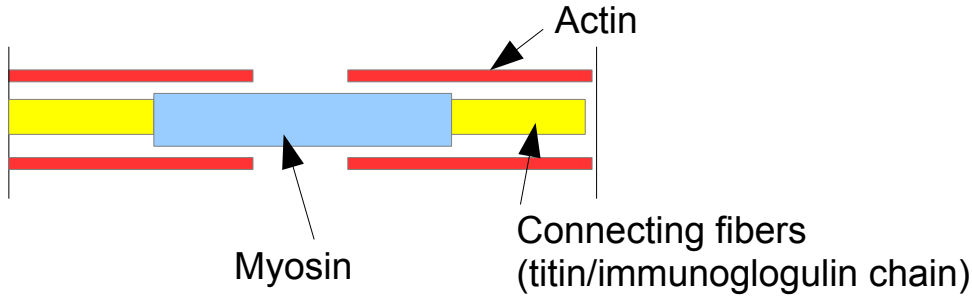
The specific muscles used during fight-flight depend on the choice of action. If "Flight" is chosen (with usually a dominant emotion of fear), it is the leg and buttock muscles that will be used most of all, and if a predator catches up, it is the buttock muscles, neck and rear shoulders that will most likely be bitten first. So fight-flight responses (and stress) are often strongly expressed by tension and armouring in the trapezius, gluteals and hamstrings. One of the most vulnerable locations on the human body is the 2cm gap between the base of the skull and the first vertebra – the only section of the spinal cord not protected by bone and thick cartilage[55]. So every stress reaction includes tightening of the muscles of the base of the skull. Even babies are born – surprisingly often – with a chronically tight atlo-occipital junction.

"Fight" requires a very different set of muscles – in particular the hands (fists/claws), arms, shoulders and mouth/jaw (biting/growling) as the enemy is faced directly. These muscles also often become overtight and armoured during stress and are the dominant zones of somatic awareness during anger and rage[56]. As humans we are defined by a set of anatomical features that ultimately relate to the jaw. It was only by relinquishing the large teeth and powerful jaws of large apes that allowed the skull to become thinner, the falx to become membranous, and the parietal and frontal lobes of the brain to expand. Although we do engage our teeth and jaws and associated muscles (especially *temporalis*) when in a fight response, it may be that the lack of large canines also comes with associated changes in endocrine response. Predator and Prey occupy

very different adaptive zones within the fight-flight spectrum. On the other hand, one of the peculiarities of humans is that we can adopt fight-flight-freeze gestures from more or less any animal – predator or prey (see later discussion on Freeze-Immobilisation).

Fight-flight also includes **armouring** (also see Chapter 9.1 : The element of Metal) – the state in which muscles become hard, rigid and resistive to external force. It is strange that muscles can become hard and still most of retain their normal range of motion, and there are two possible mechanisms that might be happening to create this effect (I suspect that this is not an "either-or", but a "both"). The first is differential contraction of different contractile elements of the muscle sarcomere (cell), and the second mechanism is hydraulic engorgement, using fluid pressure as a form of skeletal scaffolding.

Pollack (2001)[57] & (2012)[58] proposes that biologically bound fluid is in a fourth, quasi-crystalline gel-like state - that he calls "EZ", because the structure of the water creates an exclusion zone, pushing any suspended solids and salts to the periphery. In this state the mechanisms of cells – including muscle contraction – can be viewed in a rather different light, and the three different components of a muscle cell – the Actin, Myosin and Titin – are each theoretically capable of acting somewhat independently. And indeed, connective tissue itself has contractile capacity, but muscle cells being specialised for contraction are more effective. Soft elongation of the muscle is a high energy state in which the cell is "fully charged", containing ATP stored ready to fire the muscle into action. This is reminiscent of Martial Arts training, in which the aim is to move with completely relaxed muscles that only tense up in short explosive bursts, and then return immediately to a state of relaxation and elongation. Another example of this applied by the pianist Lubomyr Melnyk[59] in his "kung fu" piano technique (up to



The three contractile elements of a single sarcomere/muscle cell (after Pollack, 2001)

19 notes per second!) Defensive armouring could be said to be a form of immune response. Curiously, Titin – usually considered to be a passive element of the sarcomere – is an immunoglobulin.

Which indirectly takes us to fluid pressure, because under Pollack's model, connective tissue (i.e. the collagen-elastin matrix, as opposed to the isolated muscle fibres originally identified by Scliep[60, 61, 62]) is also contractile – though not so much as muscle. Each fiber, fascicle, bundle and entire muscle is invested in a pocket of connective tissue, which is not only contractile, but also contains extracellular fluid. So one model for muscular action is that the force exerted by the muscle is partly derived from the change in fluid volume within the connective tissue pocket as both the muscle and surrounding connective tissue contract and change shape. This is one mechanism that would allow muscles to exert a small positive (i.e. anti-contractile) force – something that can be experienced (and cannot be explained by a system of antagonist purely contractile muscles) if one experiments with elongating the body.

Furthermore, each cell, each connective tissue compartment in the body are potentially able to change their internal pressure – either through small shifts in membrane polarity (resulting in a relatively large shift in osmotic potential). And tissues containing arterial vasculature are able to engorge as a direct consequence of elevated blood pressure. Some research into the evolutionary origins of the ANS[63] indicates that the rest-recuperation cycle can be seen in mollusks who increase their heart rate and blood pressure (BP) so to harden and inflate their tongue when eating their prey (i.e. a psuedo-S-ANS state), and subsequently reduce BP in order to digest (i.e. a quasi-Vagal state):

> *"5-Hydroxytryptamine (**5-HT**) elevates heart rate whereas it lowers the digestive movements, just as [noradrenaline] does in mammals. This suggests that 5-HT plays a similar role to [noradrenaline] in mammals . ACH has similar effects in both Aplysia and mammals, reducing the heart rate while increasing digestive movements."*

Slugs (closely related to molluscs) can also be observed to enter a contracted rigid armoured state when threatened. If one considers that their body is full of a water-like (i.e. incompressible) fluid, one has to ask how they contract this to harden, and Pollack's phase change is one possible mechanism. This use of fluid for expansion/contraction can also be seen in whelks as they contract to lock themselves to the side of a rock, and inflate their foot (by increasing BP/heart rate) to walk. The gestures of contraction / hiding / withdrawal (Vagal submissive) and movement / expansion (Sympathetic, higher BP/heart rate) are also seen (of course!) in humans. We have returned once again to Stanley Keleman's principle of pulsation as the fundamental and universal basis for the expression of life. The evolutionary origins of

molluscs (about 500 million years ago) gives some indication as to the physiological depth of this gesture. We therefore see a continuity of immune function from micro (bacteriological and viral) scale up to macro (whole-body) scales. One can think of body armouring through muscle contraction, the maintenance of "body space"/territory, along with social and familial organisation - as normal extensions of the immune function.

The Deep (Dorsal) Vagal

> *"I heard a shout. Starting and looking half around, I saw the lion just in the act of springing upon me. I was on a little height; he caught my shoulder as he sprang and we both came to the ground below together. Growling horribly close to my ear, he shook me as a terrier does a rat. The shock produced a stupor similar to that which seems to be felt by a mouse after the first shake by a cat. It caused a sort of dreaminess in which there was no sense of pain or feeling of terror, though quite conscious of all that was happening. It was like what patients partially under the influence of chloroform describe, who see all the operation but feel not the knife. This singular condition was not the result of any mental process. The shake annihilated fear, and allowed no sense of horror in looking around at the beast. The peculiar state is probably produced in all animals killed by carnivora; and if so, is a merciful provision by our benevolent Creator for lessening the pain of death."*
>
> *David Livingstone (1872) Adventures and Discoveries in the Interior of Africa*

The Deep Vagal / Hibernatory response (Zone D) is also associated with a reduction in sensation, through release of endogenous opioids, along with some degree of loss of utility of the musculoskeletal system. Opioids have a very different effect when the adrenal response is inhibited. Numb, blank, absent and empty feelings are common (instead of the euphoria that might accompany adrenaline) - which may progress to dizziness / disorientation / lack of coordination and distortion of proprioception. **Depersonalisation** is another common phenomenon associated with Deep Vagal release of endorphins, and is not unlike an opium or morphine trip (which is not surprising, because it's more or less the same chemical). Sections of the body may be experienced as larger or smaller than reality, or to lie in a physical position that does not tally with their actual position. In depersonalisation, the world feels slightly alien or cardboard-like or distant and impossible to grasp, experiencing everything as if watching oneself on a television set or through a thick glass window. Even direct touch and physical contact can feel distant, opaque, unreal and somehow intangible - sometimes even skin and muscle are difficult to identify as sensations, or have a slightly fuzzy and metallic or cardboard-like numbness. The ground can feel an unnervingly long way off, as **dissociation** usually begins most strongly at limb extremities, particularly the legs and feet; sometimes leaving the person feeling as if they are on stilts or are a head floating round in a virtual world. Maybe Livingstone was right, and this opioid-driven loss of somatic sensation is one way that animals do not feel the pain when they are eaten. Even further down into the Deep Vagal, exhaustion sets in - not because there is an intrinsic lack of energy, but because the ANS is squirrelling it all away, prioritising energy usage towards repair, immune functions and for maintaining

internal homeostasis.

The Deep Vagal state is probably less familiar than Fight-Flight. It is primarily a means to resolve *internal* physiological emergencies that cannot be dealt with through fighting or running away. Examples of the kind of emergency that it might be used for include :

- *suffocation and drowning (lack of oxygen / excess carbon dioxide and/or restriction, blockage or damage to the respiratory tract),*
- *hyper- or hypo-thermia (excess heat or excess cold),*
- *uncontained infections : bacteria, viruses and fungi that are no longer controlled by the normal processes of the body's ecosystem*
- *toxicity such as Botulinum or Diptheria Toxin, heavy metal poisoning, etc*
- *dehydration or other major water-electrolyte imbalances,*
- *major loss of homeostatic control of internal fluids – such as CSF or blood pressure*
- *starvation,*
- *limb loss, major blood loss and other catastrophic injuries, etc…*
- *Psychological factors such as uncertainty, loss of control*

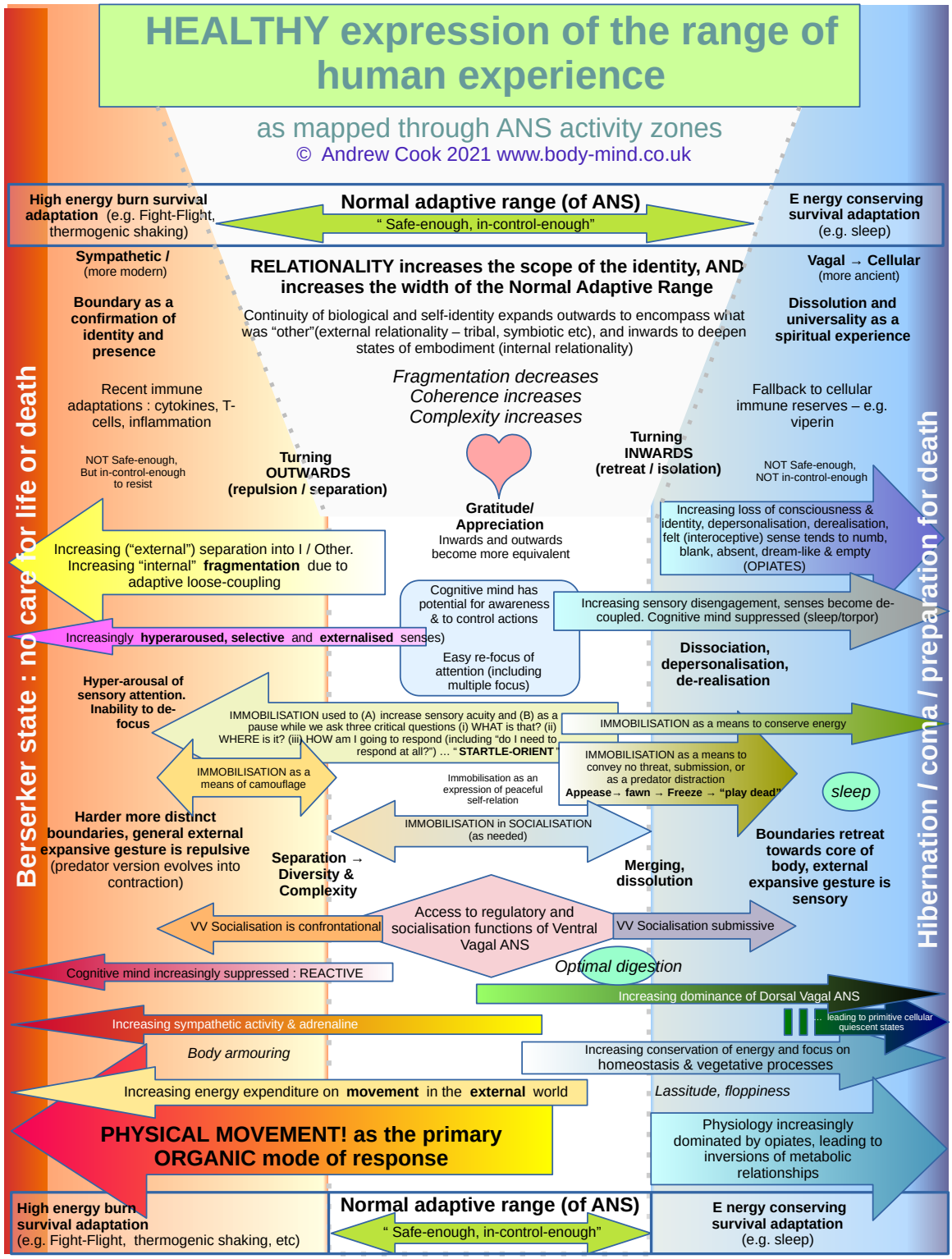
> The research literature has identified three factors that universally lead to stress for human beings: uncertainty, lack of information, and loss of control. To these we may add conflict that the organism is unable to handle and isolation from emotionally supportive relationships'.
>
> Gabor Mate (The realm of the hungry ghosts)

All of these are essentially forms of overwhelm. Most are also types of emergencies generically common to the most primitive of life forms; and the kind of physiological states that we enter in the Deep Vagal state are sometimes more reminiscent of those adopted by primitive single celled organisms – rather than complex multicellular ones. As the emergency Vagal response deepens, coma and quasi-hibernatory states can start to become apparent. Fainting (i.e. a drop in blood pressure) is one fairly common version of this kind of response. The metabolism required to deal with an internal infection or to conserve already-scarce body fluids is not the same one that is applicable for normal day-to-day life. Therefore, the self-healing metabolic shifts required may sometimes appear to be potentially dangerous illnesses[64]. Amputees during the Crimean war often suffered symptoms we now associate with multiple organ failure, and entered a coma. Whilst some did not survive this medical emergency, others re-emerged from this hibernatory state with their wounds healed and their body

metabolism returned to normal.

The deep vagal states also tend towards flaccidity (floppiness) of muscles. If one thinks of a general movement away from mammalian metabolism towards the physiology of a reptile or even more primitive animal, that provides a good clue as to the general effects. Lizards conserve energy by becoming passively still as they wait for their prey to come to them (whereas most mammals proactively go out looking for food). The external senses may be switched on, but this is a passive openness to detecting change (and the body starts to energise when change is detected) – in contrast to the slightly hyperaroused expectant sensory engagement that mammals in the wild often have with their environment.

A generalised map of ANS zones – primarily focussed on human experience - is presented in the figure below. The central white zone is the normal (physiological) adaptive range NAR (or "window of tolerance" WoT in psychotherapy). We would normally bob around in this most of the time, occasionally enter fight-flight (left) when presented with a strong external threat, or enter the deep vagal (right) when (e.g.) we have to heal from an infection and sleep). Then we would normally return to the NAR/WoT. Trauma is when these normal adaptive responses become jammed in survival adaptation states (usually through overwhelm) so that more context-appropriate responses are less available. BUT ALL of the mapping shown below is healthy – if the context is congruent to the response. The primary and normal adaptation to anything is movement, so self-immobilisation is particularly critical. Everyone has experienced that self-immobilisation in surprise ("Hey! They sell ice-cream!"). It is instructive and very useful to consider healthy adaptive responses – this gives a far broader and balanced view of internal states.


HEALTHY expression of the range of human experience
as mapped through ANS activity zones
© Andrew Cook 2021 www.body-mind.co.uk
High energy burn survival adaptation (e.g. Fight-Flight, thermogenic shaking)
Normal adaptive range (of ANS)
" Safe-enough, in-control-enough"
E nergy conserving survival adaptation (e.g. sleep)
Sympathetic / (more modern)
Vagal → Cellular (more ancient)
RELATIONALITY increases the scope of the identity, AND increases the width of the Normal Adaptive Range
Continuity of biological and self-identity expands outwards to encompass what was "other"(external relationality – tribal, symbiotic etc), and inwards to deepen states of embodiment (internal relationality)
Boundary as a confirmation of identity and presence
Dissolution and universality as a spiritual experience
Fragmentation decreases
Coherence increases
Complexity increases
Recent immune adaptations : cytokines, T-cells, inflammation
Fallback to cellular immune reserves – e.g. viperin
NOT Safe-enough, But in-control-enough to resist
Turning OUTWARDS (repulsion / separation)
Turning INWARDS (retreat / isolation)
NOT Safe-enough, NOT in-control-enough
Gratitude/ Appreciation
Inwards and outwards become more equivalent
Increasing ("external") separation into I / Other. Increasing "internal" fragmentation due to adaptive loose-coupling
Increasing loss of consciousness & identity, depersonalisation, derealisation, felt (interoceptive) sense tends to numb, blank, absent, dream-like & empty (OPIATES)
Cognitive mind has potential for awareness & to control actions
Increasing sensory disengagement, senses become de-coupled. Cognitive mind suppressed (sleep/torpor)
Increasingly hyperaroused, selective and externalised senses)
Easy re-focus of attention (including multiple focus)
Dissociation, depersonalisation, de-realisation
Hyper-arousal of sensory attention. Inability to de-focus
IMMOBILISATION used to (A) increase sensory acuity and (B) as a pause while we ask three critical questions (i) WHAT is that? (ii) WHERE is it? (iii) HOW am I going to respond (including "do I need to respond at all?") … "STARTLE-ORIENT"
IMMOBILISATION as a means to conserve energy
IMMOBILISATION as a means of camouflage
Immobilisation as an expression of peaceful self-relation
IMMOBILISATION as a means to convey no threat, submission, or as a predator distraction
Appease → fawn → Freeze → "play dead"
sleep
IMMOBILISATION in SOCIALISATION (as needed)
Harder more distinct boundaries, general external expansive gesture is repulsive (predator version evolves into contraction)
Separation → Diversity & Complexity
Merging, dissolution
Boundaries retreat towards core of body, external expansive gesture is sensory
Access to regulatory and socialisation functions of Ventral Vagal ANS
VV Socialisation is confrontational
VV Socialisation submissive
Optimal digestion
Cognitive mind increasingly suppressed : REACTIVE
Increasing dominance of Dorsal Vagal ANS
Increasing sympathetic activity & adrenaline
… leading to primitive cellular quiescent states
Body armouring
Increasing conservation of energy and focus on homeostasis & vegetative processes
Increasing energy expenditure on movement in the external world
Lassitude, floppiness
PHYSICAL MOVEMENT! as the primary ORGANIC mode of response
Physiology increasingly dominated by opiates, leading to inversions of metabolic relationships
High energy burn survival adaptation (e.g. Fight-Flight, thermogenic shaking, etc)
Normal adaptive range (of ANS)
" Safe-enough, in-control-enough"
E nergy conserving survival adaptation (e.g. sleep)
Berserker state : no care for life or death
Hibernation / coma / preparation for death

Notes : Chapter 7.1

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19 It would therefore seem to be a bad idea for people to be frightened about illness, because this (stress) reduces their immunological capacity to deal with infection.

20 ... leading to osteopenia and osteoporosis – so it seems strange that these conditions are treated by simply trying to cram more calcium into a body that is (via cortisol/stress) reluctant to absorb it. High blood calcium (through diet) is also known to weaken bones by the mechanism of constant calcium buffering. The most common cause of high blood Ca is excess activity of the parathyroid glands, and the thyroid's production of Thyroxine (i.e. the activity of the entire thyroid complex) is stimulated by – adrenaline – i.e. by the stress response! In high stress Ca is important to maintain nerve synapse conduction in muscles to ensure that they fire rapidly, so a high Ca level is not an unreasonable acute fight-flight adaptation.

21 That can lead to hyperkalemia, leading to hypokalemia as potassium and phosphate is lost to urine

22 It seems almost perverse that high BP is "treated" (i.e. suppressed) by use of diuretics and medication such as beta blockers, when the fundamental issue is probably chronic stress.

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25 This was highlighted in 2017 during the appointment hearings for the US supreme court nominee Brett M Kavanaugh. A witness to particular events at a college party some 30 years previously was able to still recall very specific scenes – but have no memory of other details. Christine Blasey Ford's very selective memory is (as she pointed out as an expert witness, being now a professor of psychology at Palo Alto university) typical of traumatic memories that arise under high adrenaline/cortisol conditions. This story was extensively reported in the news – see for example https://www.washingtonpost.com/politics/2018/09/19/worst-is-yet-come-kavanaughs-accuser-take-it-this-sexual-assault-expert/

26 Note again the conditionality – Cortisol goes up (and so DHEA down) when blood sugar is low; but a moderate restriction of calories increases DHEA. Cortisol also increases appetite and fat absorption.

27 See chapter on Consciousness ... microtubules appear to mediate quantum effects related to consciousness.

Notes : Chapter 7.1

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29 This journey of the Vagus nerve can be seen moving from right to left in a recent video (winner of the 2018 Nikon Small World in Motion competition) of the developing nervous system of a zebra fish https://www.youtube.com/watch?v=MGnjvLBwAuUI. (Credit: Elizabeth Haynes & Jiaye He. The brain/central nervous system is on the right of the video image.

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31 Tobias Wang, Evolution of the Cardiovascular Autonomic Nervous System in Vertebrates. In: David Robertson, Italo Biaggioni, Geoffrey Burnstock, Phillip A. Low and Julian F.R. Paton, editors, Primer on the Autonomic Nervous System. Oxford: Academic Press, 2012, pp. 669-674. ISBN-13: 978-0-12-386525-0

32 Part of the development of the embryo consists of a series of rotations – for instance, by week #7 the straight tube that will eventually become the small and large intestines has projected itself ("herniated") into the umbilical cord, where it rotates, and then returns in the form of a loop. Thus, the tube of the intestines can be seen in any anatomy book to have a clockwise arrangement (as seen from the front). Immediately prior to this rotation, the digestive organs are arranged on a membrane that is aligned front-to-back. This also rotates clockwise (as seen from the head end), to place the liver at the front right of the body, and the spleen at the rear left. The Vagus nerve has already grown by this stage, and so ends up with a 90º rotation around the oesophagus. See https://embryology.med.unsw.edu.au/embryology/index.php/Gastrointestinal_Tract_-_Stomach_Development

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37 Although movement is usually assumed to be purely due to the action of muscles, this is not the case. Muscles are specialised cells that are far more efficient at contracting and have a greater range of motion - but in fact *all* tissues are contractile, including the non-cellular parts of connective tissue. Movement also arises from elastic recoil of loaded bones, and the expansive force of fluid in connective tissue compartments.

38 Note – yet another inhibitory form of regulation!

39 Häming (2012) op. cit

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49 This is another facet of the biological tendency to use inhibition as a means to control.

50 However, the point at which this biological switch is thrown (and becomes outside the capacity of the conscious mind) can be altered through various meditation practices. This is particularly so with respect to temperature, and heat generation to survive extreme cold is common to many traditions – e.g. Tibetan Tum-mo, and "Beggar's Qigong" from China. Wim Hof is a more recent example, having trained himself to be at ease in the cold. One of his demonstrations was to complete a half marathon in Finland during winter wearing only shorts (i.e. not even shoes), in temperatures approaching -20ºC.

51 There is a collection of accounts of being shot at https://thoughtcatalog.com/holly-riordan/2017/02/26-gunshot-survivors-explain-exactly-what-the-bullet-felt-like/. One example : "I was shot in the arm when I was young when I got caught in the middle of a drive by shooting. You know in the movies where a gun goes off and there's a sudden look of shock on the victim's face before he looks at the wound? That's very accurate. I did not feel any pain or anything. I heard the gunshot and felt a tight pressure in my arm. I looked and saw the wound and how much blood I was losing, and the next thing I know I'm in the hospital."

52 (Also from the above link...) "I got shot through the thigh with a .45, it burned like a motherfucker. The bullet went through the bone completely and the tendons pulled everything out of place, my leg was about 4 inches shorter than the other. Trying to move it was absolute agony, I was praying to pass out but never did."

53 Aron Ralston's story can be found in the book "Between a rock and a hard place" (2005), Publ Simon & Schuster UK ISBN-13: 978-0743495806, and was made into a film ("127 hours"). A short version in his own words can be seen at

http://www.wideworldmag.com/2010/11/09/127-hours-in-the-life-of-aron-ralston/

54 BBC News (Magazine monitor) Victorian Strangeness: The cyclist chased by a lion. 28 June 2014 https://www.bbc.co.uk/news/blogs-magazine-monitor-28056499

55 Bruce Chatwin goes to some length in "Songlines" (Vintage Classics, 1998, ISBN-10: 9780099769910) to speculate on the relationship between early hominids and big predators – especially cats. He notes that many early hominid skulls have been found with a pair of holes near the top of the neck - that match the teeth of a *Smilodon* / sabretooth tiger. To this day, baboons have a strong antipathy to leopards, and leopards have a strong taste for baby baboon.

56 Nummenmaa, L., Glerean, E., Hari, R., & Hietanen, J. K. (2013). Bodily maps of emotions. Proceedings of the National Academy of Sciences of the United States of America, 111(2), pp646-51. https://dx.doi.org/10.1073%2Fpnas.1321664111

57 Gerald H Pollack (2001) "Cells Gels and the Engines of Life" ISBN 0962689521

58 Gerald H Pollack (2012) The Fourth Phase of Water – beyond solid, liquid and vapour. Publ Ebner & Sons, Seattle ISBN 9780962689536

59 http://www.lubomyr.com/

60 Robert Schleip (2003) Fascial plasticity – a new neurobiological explanation: Part 1. Journal of Bodywork & Movement Therapies 7(1) Jan, pp 11-19 doi:10.1016/S1360-8592(02)00067-0

61 Robert Schleip (2003) Fascial plasticity – a new neurobiological explanation: Part 2. Journal of Bodywork & Movement Therapies 7(2) Apr, pp 104-116 doi:10.1016/S1360-8592(02)00076-1

62 Purslow, P. P., and Delage, J. P. (2012). "General anatomy of the muscle fasciae," in Fascia: The Tensional Network of the Human Body, eds R. Schleip, T. W. Findley, L. Chaitow, and P. A. Huijing (London: Churchill Livingstone), 5–10.

63 Hiroshi Shimizu & Masataka Okabe (2007) Evolutionary origin of autonomic regulation of physiological activities in vertebrate phyla. Journal of Comparative Physiology A 193 pp1013–1019 Nov DOI: 10.1007/s00359-007-0256-4

64 For instance, it is normal for pregnancies to cause mild anaemia due to the increase in blood volume. Provided the anaemia is mild and is not associated with infections, parasites (e.g. hookworm) or other ill health, it is catered for by the body's homeostatic adaptive capacity and does not affect birth outcomes.