

# Central Nervous System (CNS) Autonomic and Endocrine Regulation: a Homeostatic Hierarchy

## A Homeostatic Hierarchy in the Central Nervous System

Homeostasis is not only innate to living organisms, but increases in complexity, sophistication, flexibility and range of responses in parallel with similar (phylogenetic) developments of the nervous system (Williams et al., 1989).

Inherent to homeostatic systems are control loops that include sensors or receptors, afferent pathways, at least one integration and control centre, efferent pathways, and effectors. As nervous systems became more complex, simple loops became coupled together to form integrated hierarchies of control loops (Williams et al., 1989). These are homeostatic control hierarchies.

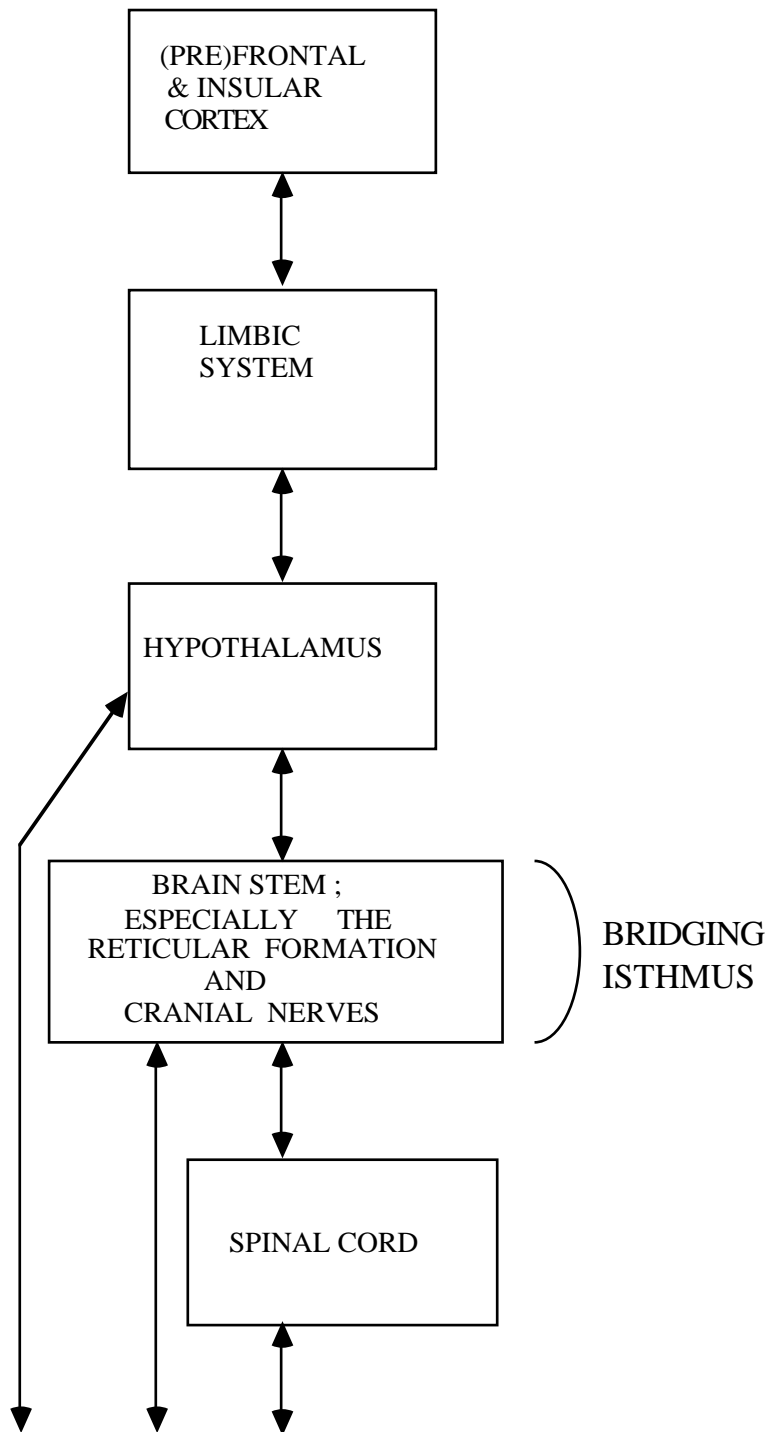
The broad homeostatic hierarchy of the central nervous system in humans is represented (rostral to caudal) by the cerebral cortex (frontal and insular), limbic system, hypothalamus, brain stem and spinal cord, mediated peripherally by autonomic and endocrine effector mechanisms (Williams et al., 1989). This is illustrated in Figure 1.

The concept of a hierarchy is inherent in language which refers to 'lower' or 'higher' centres of autonomic control, although such centres are commonly just individual focal regions (nuclei or groups of nuclei) with a number of afferent and efferent connections, often in series with other focal regions, all of which contribute to a general overall function - for example, respiratory rhythm, or cardiovascular control (Williams et al., 1989).

The concept of a hierarchy is relevant, particularly as experimental transection of the brain stem shows that more effective homeostasis is retained as such transections are made at progressively more rostral levels (Anand, 1970; Williams et al., 1989). Transection at the level of the rostral midbrain retains relatively simple reflex adjustments to the cardiovascular, respiratory and alimentary systems, but these are not integrated and temperature control is not maintained (Anand, 1970).

Transection rostral to the hypothalamus which separates it from the limbic system and the rest of the forebrain retains effective homeostasis over a moderate range of conditions. Visceral and endocrine control are integrated, and innate drives and motivated behaviour such as drinking, feeding, satiation and copulatory behaviour are retained (Anand, 1970). But when environmental stress becomes more extreme, such as persistently high or low temperatures, homeostasis fails (Anand, 1970). Motivated behaviour also becomes inappropriate or abnormal, such as copulating with inappropriate objects.

When the neocortex only is removed, so that the limbic system, hypothalamus and caudal structures are retained, normal homeostasis is preserved over a wide range of conditions (Anand, 1970).



With Mediation at the Periphery by the Endocrine System and the Autonomic Nervous System  
(adapted from Gray's Anatomy, 37th Ed., 1989, p. 1011)

**Figure 1 Homeostatic Control Hierarchy of the Central Nervous System**

## **The Model and the Homeostatic Hierarchy**

The activity of tier two of the model mainly occurs in the hindbrain, midbrain and diencephalon, but to some extent also in the spinal cord. It therefore includes the vast majority of homeostatic control mechanisms, particularly hypothalamic and caudal brain stem structures. More rostral limbic structures such as the amygdala are not included in tier two, although they do participate in visceral control.

Neural regions which participate in central autonomic and endocrine regulation are hypothesised to house the functional activity and interactions of the Meridians and Wu Xing, and are thought to be key participants in the Zang Fu (refer to the paper on the model). These regions are reviewed below.

Deriving from this view is the idea that tier two functions as a coordinating homeostatic fulcrum. It is from integration and control regions of this tier that connections are established to tiers one and three.

By linking components of each tier into functional 'Orbs' (Porkert, 1974; Davis, 1994a, 1995), inter-tier connections contribute to the Zang Fu. Each TCM Organ is thought to incorporate functional and structural components of the body (in tier one), emotional and behavioural components (mainly tier three), as well as its pertaining Meridians (mainly tier two). [Refer to papers on web page 'TCM Theory' and other papers on the model].

Figure 2 incorporates the homeostatic hierarchy into the model. It is an elaboration of figures 1 to 4 in the paper on the model.

The idea of a coordinating physiological fulcrum is a key aspect of the model as stimulation of acupuncture points (and Meridians) on the periphery is hypothesised to have its most direct impact in tier two via neural pain and temperature pathways (access to the homeostatic hierarchy is thereby gained via tier two), with the clinical impact of acupuncture being referred to tier one in reflex homeostatic loops - to the structures of the body which mediate homeostasis, or in rostral pathways of the central homeostatic hierarchy to tier three - to emotional and behavioural areas such as the limbic system. In this way all three tiers are able to receive the impact of acupuncture therapy, and all aspects of a Zang Fu may thereby receive treatment.

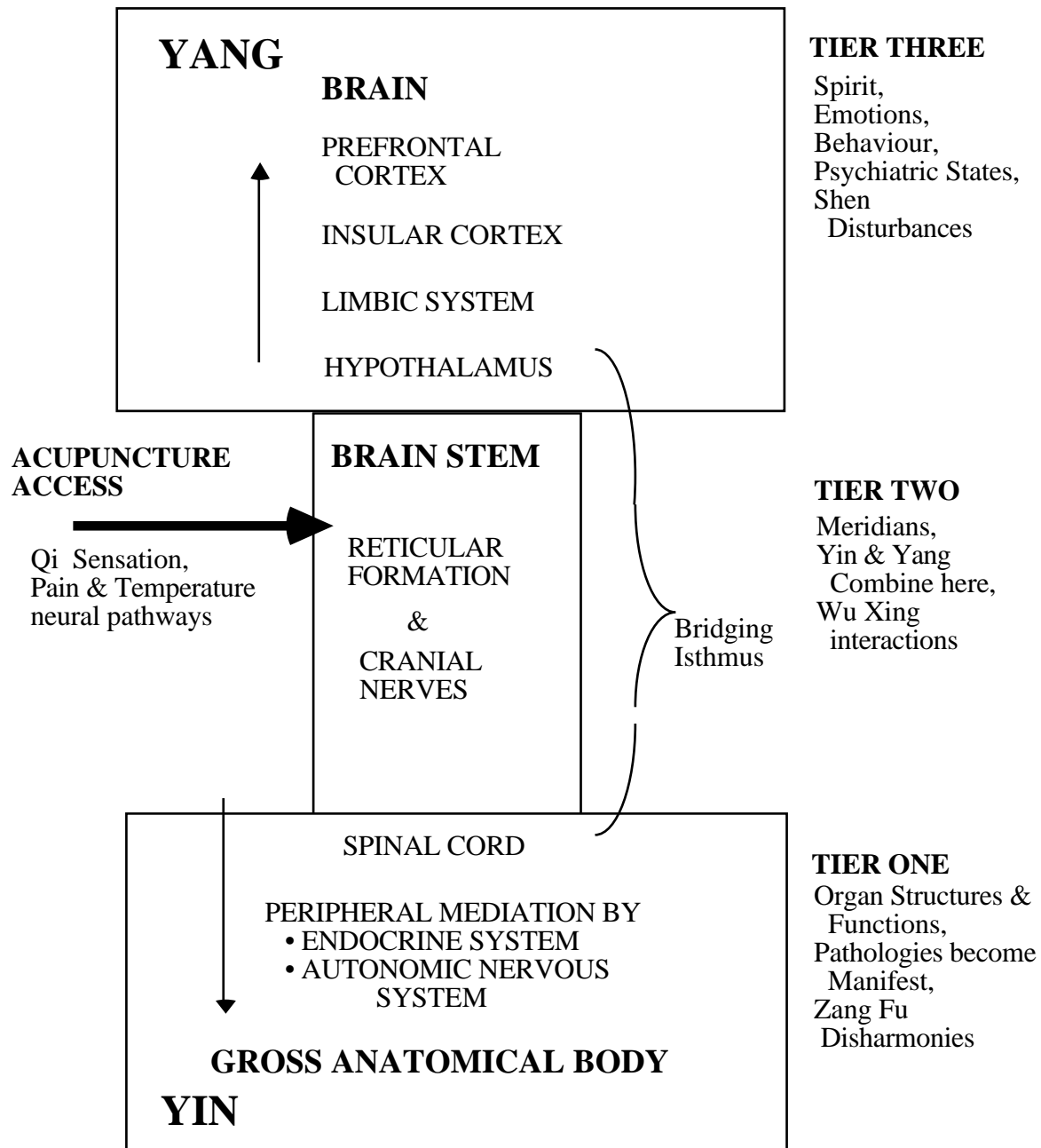
Clearly it is essential that the model embraces the neural (homeostatic) and endocrine anatomy of the brain stem and diencephalon, and the central nervous system generally. The works of Loewy (1990), Loewy and Burton (1978), Loewy et al. (1979, 1986), Harris and Loewy (1990), Strack et al. (1989a,b) have been influential in the development of the model.

## **The Central Autonomic Hierarchy: review & overview**

There is an important conceptual distinction to be drawn between central autonomic circuits which act as relatively simple reflex arcs that produce specific, detailed control of end organ function, and those which interconnect along the more rostral neural axis, possibly as high as the cerebral cortex, to provide a central CNS control network or hierarchy (Loewy 1990).

The complexity and interconnectedness of the central hierarchy provides the necessary neural substrate for integrated autonomic, neuro-endocrine and behavioural responses (Loewy 1990).

The activity of these regions is hypothesised to contribute directly to (participate in) the Jing Luo, and therefore becomes an essential component of the Zang Fu.

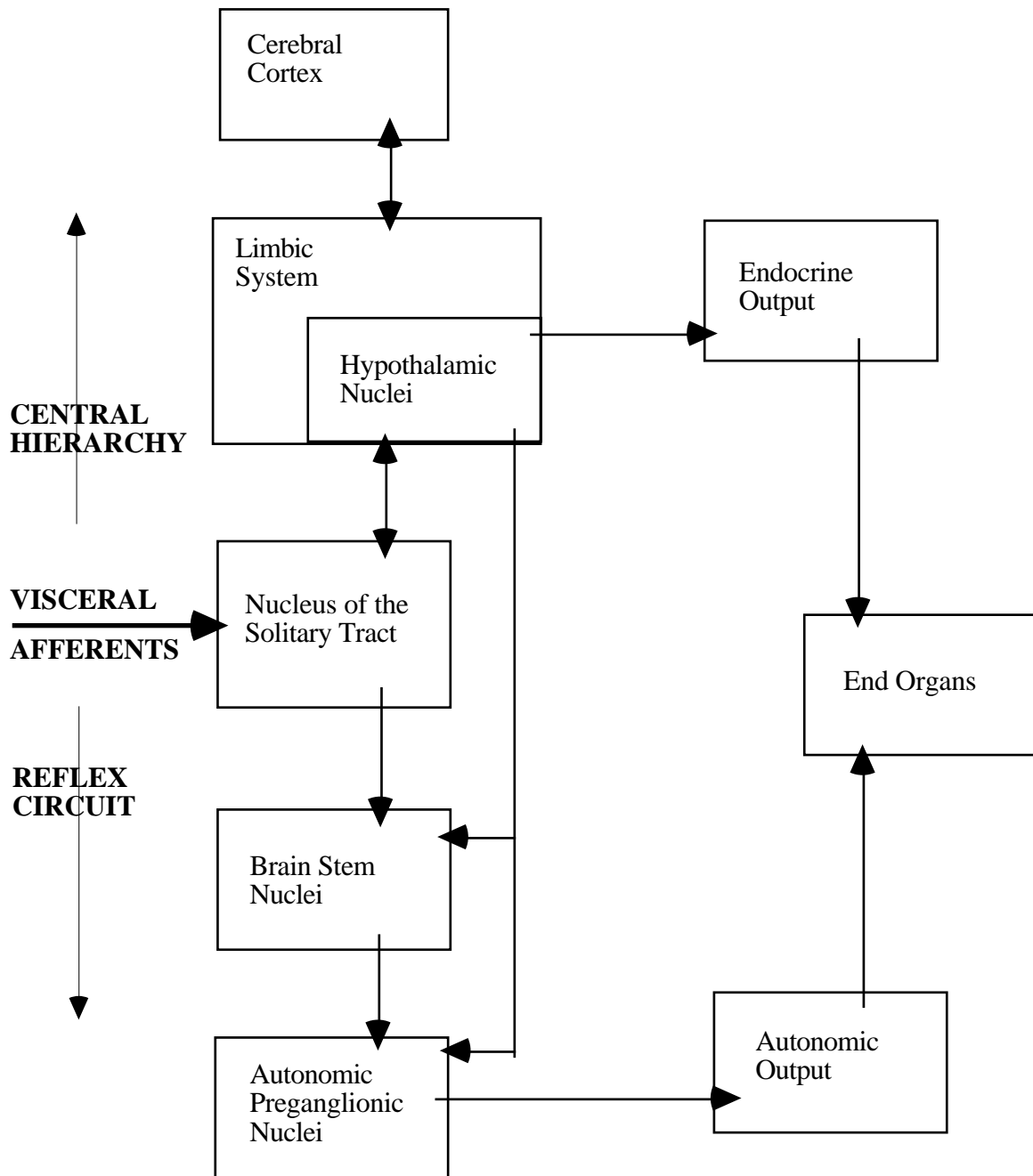


**Figure 2 CNS Homeostatic Hierarchy and the Model**

This conceptual distinction may be represented diagrammatically, refer figure 3, but *in vivo* such a distinction is not really apparent. There is simply integrated physiological activity which encompasses all components of autonomic and endocrine control.

An example of a reflex pathway is provided by the control mechanism for blood pressure, the sensory limb of which arises from the carotid sinus and aortic baroreceptors. There may be as few as four neurons in the parasympathetic arm of this reflex, while the sympathetic arm may only have six (Loewy 1990, Loewy & Spyer 1990).

In the central control network, ascending projections from the nucleus of the solitary tract (NTS) carry a range of visceral sensations (special and general, conscious and subconscious) to various brain stem and forebrain nuclei, where this information is integrated and various autonomic and neuro-endocrine responses are integrated and initiated.



**Figure 3** Conceptual Distinction between Simple Reflex Homeostatic Circuits and more complex Central Circuits

(adapted from Dodd & Role, 1991, p. 767; and Loewy, 1990)

Due to its connections with the limbic system and cerebral cortex, the central control network may be involved in various complex behaviours including food and fluid intake, temperature regulation, and the social behaviours which may be associated with these - indeed all behaviour in which the limbic system is involved (Loewy 1990).

## **Nucleus of the Solitary Tract**

The nucleus of the solitary tract (NTS) is a key participant for both the reflex loop and the CNS control hierarchy. It is the major visceral sensory relay cell group of the medulla, receiving input from all major visceral organs (Loewy 1990).

Three regions or zones of the NTS are identified - rostral, intermediate and caudal. These are defined in relation to the area postrema of the medulla. While they do not correspond exactly with underlying nuclei, these zones provide delineation and definition of regions, which serves to guide discussion.

The NTS is located in the medulla oblongata immediately ventral to the dorsal column nuclei. It consists of a number of subnuclei which differ in terms of cytoarchitectonics (Loewy 1990; Carpenter 1991). These subnuclei may be classified into two main groups on the basis of their location relative to the solitary tract itself - medial and lateral, but more specific terminology such as dorsolateral NTS and ventrolateral NTS is also used (Loewy 1990, Carpenter 1991).

## **Summary of NTS Connections**

Two broad categories of visceral afferent fibres projecting to the NTS may be distinguished:

- i) an organ-specific pattern which projects to individual subnuclei, and
- ii) overlapping afferent fibres which project to a NTS region/zone.

The NTS receives input from a variety of sources. One of these is the sensory component of autonomic nerves which project directly to this nucleus. Others involve multisynaptic afferent spinal pathways, and efferent projections from various nuclei of the brainstem and forebrain. Another source is the area postrema, a circumventricular organ which functions as a sensor of the chemical environment of plasma and CSF (Loewy, 1990; Carpenter, 1991).

Efferent projections from the NTS appear to be organized to allow two modes of response (Loewy 1990). Projections are made to:

- i) Nuclei in the caudal brain stem which regulate autonomic preganglionic neurons, both sympathetic and parasympathetic.
- ii) Forebrain nuclei participating in the regulation of autonomic and neuro-endocrine functions. These projections include limbic and cortical connections, hence this network appears to be involved in behavioural and cognitive functions (Loewy 1990).

NTS subnuclei receiving organ-specific afferent information probably only project to the particular lower brain stem nuclei involved in reflex autonomic adjustments, although the evidence for this is not complete (Altschuler et al. 1989, Jordan and Spyer 1986, Loewy 1990).

Most visceral afferent fibres not only connect with their main organ-specific subnuclei but also send collaterals to other NTS subnuclei. One NTS area, the commissural nucleus of the

caudal NTS zone and the medial region of the intermediate NTS zone (which may be considered a continuous single region), is unique in that it receives input from all major visceral systems except those related to pelvic organs (Loewy and Burton 1978, Ricardo and Koh 1978, Loewy 1990).

Visceral afferents from the respiratory, cardiovascular, and gastrointestinal systems, project to the commissural-medial NTS region in an overlapping and possibly convergent manner (Loewy 1990). It is mainly neurons in this region which project to higher CNS areas. These projections are likely to have a viscerotopic organization (Loewy, 1990). For example, central taste information is carried along specific pathways to the insular cortex (Cechetto and Saper 1990), especially from the rostral region of the medial NTS.

The idea of two levels of complexity of autonomic response is contributed to by this identification of parallel reception and processing in the NTS - individual NTS subnuclei on the one hand (NTS intermediate zone) and a common recipient area on the other (NTS medial-commissural area).

### **General Visceral Afferent Pathways**

The NTS receives afferent information from many visceral organs. Cardiovascular, pulmonary, respiratory tract and gastrointestinal receptors all project to specific areas in the NTS (Jordan and Spyer 1986).

In the intermediate region of the NTS, afferent fibres from the pharynx, larynx, trachea and bronchi (ie. air passages) project largely to the interstitial NTS. Cardiovascular afferent projections terminate mainly in the dorsolateral NTS. Pulmonary fibres project largely to the ventral and ventrolateral NTS. Gastrointestinal afferents project largely to the parvocellular NTS (alternatively called the subgelatinosa or subpostrema NTS - Loewy 1990).

The commissural-medial region of the intermediate and caudal NTS receives input from all of these organs (Kalia and Mesulam 1980, Altschuler et al. 1989).

#### ***Cardiovascular Afferents***

Baroreceptor and chemoreceptor afferent information from the carotid sinus and aortic arch projects to three areas of the NTS (Housley et al. 1987):

- i) the dorsolateral NTS in the intermediate zone
- ii) the medial NTS in the intermediate zone
- iii) the commissural NTS of the caudal zone.

Baroreceptor afferent fibres terminate in a more restricted area of the medial NTS than chemoreceptor fibres, however both generally have overlapping projections in the medial and commissural NTS (Czachurski et al. 1988).

Cardiac projections terminate in the dorsolateral NTS (intermediate zone), with a lighter input to the medial and commissural NTS (Kalia and Mesulam 1980).

The role of individual NTS nuclei in the reception and processing of this cardiovascular information is not clear, but output from the medial-commissural NTS projects to the brainstem

and to the hypothalamus, which in turn project to various regions of the autonomic network including direct fibres to sympathetic preganglionic neurons (Loewy 1990).

### *Respiratory Tract Afferents*

Afferent fibres carrying information from receptors in the larynx, trachea and bronchi terminate in the intermediate and caudal NTS regions - in particular these fibres project to the interstitial, ventrolateral, and medial-commissural NTS. The most significant group of these fibres terminate in the interstitial NTS (Kalia and Mesulam 1980). These fibres very likely participate in reflex vagal (CN X) control of smooth muscle and mucus secretion in the bronchial tree (Widdicombe 1982, Loewy 1990).

There are also rapidly adapting afferents from the airways which mediate protective reflexes (Spyer 1990). The receptors for these are considered to be irritant receptors.

### *Pulmonary Afferents*

Afferent vagal fibres from the lung project to the ventrolateral, ventral, medial areas of the intermediate NTS, and the commissural area of the caudal NTS (Kalia and Mesulam 1980). These are known to exert strong influences on both the cardiovascular and respiratory systems (Spyer 1990).

Afferents arising from lung stretch receptors have been classified as slowly adapting and rapidly adapting (Spyer 1990).

### *Slowly Adapting Pulmonary Afferents*

Pulmonary afferents which adapt slowly to inflation of the lung (ie. to stretch), are thought to have a marked impact on the cardiovascular system (Daly 1985), particularly by influencing other reflex inputs concerned with the regulation of heart rate.

In both the cat and the rabbit, the major projection of these fibres is to the medial region of the intermediate NTS (Donoghue 1982). There is also significant (but less) input to the lateral and ventrolateral NTS. One group of inspiratory neurons ( $R_{\beta}$ ) situated in the ventrolateral NTS is described as being monosynaptically activated by pulmonary afferents (Averill et al. 1984, Backman et al. 1984, Berger and Dick 1987). These  $R_{\beta}$  neurons increase their activity with inspiration and project to phrenic respiratory motor neurons (Backman et al. 1984, Berger and Dick 1987). These appear to participate in a relatively simple reflex circuit.

In a spike-triggered averaging study (Averill et al. 1984), the major projection of slowly adapting pulmonary afferents was to the medial NTS.

Evidence also exists for a widely dispersed afferent input to NTS neurons, called 'pump cells'. This input is monosynaptic, is excited by lung inflation, but does not have a pattern of discharge correlated with central respiratory rhythm (Averill et al. 1984, Berger and Dick 1987).

### *Rapidly Adapting Pulmonary Afferents*

Rapidly adapting pulmonary afferents project to the NTS with quite a different pattern to that of slowly adapting fibres (Davies and Kubin 1986). Although there is widespread projection to caudal regions of the NTS, the most dense projection is to the medial and commissural regions. In this case there is also a marked contralateral, medial NTS projection. There is less dense

innervation to the lateral and ventrolateral areas of the intermediate zone (Davies and Kubin 1986, Spyer 1990).

Rapidly adapting pulmonary afferents are thought not to be involved in direct modulation of respiratory motor neurons (Davies and Kubin 1986).

### ***Gastrointestinal Afferents***

A majority of gastrointestinal afferents project to the parvocellular NTS, where a viscerotopographic representation of the upper gastrointestinal tract has been demonstrated (Altschuler et al. 1989). Some fibres also terminate in the medial-commissural NTS (Gwyn et al. 1985, Leslie et al. 1982, Shapiro and Miselis 1985).

Afferent fibres from abdominal areas project to discrete regions of the parvocellular NTS. For example, hepatic afferent fibres lie dorsal and medial to gastric afferents in the NTS (Rogers and Hermann 1980, Shapiro and Miselis 1985).

Gastrointestinal afferents provide information about sodium balance, fluid balance, and general digestion and absorption. The liver may possess specialized receptors for sodium, glucose and osmolarity (Lautt 1980). Receptors in the portal vein monitor sodium concentration and osmolarity (Contreras and Kosten 1981). Small intestine receptors monitor glucose concentration, which is transmitted in the vagus. This is an important link in the central control of carbohydrate metabolism (Nijjima and Mei 1987).

### ***General Visceral Afferent Convergence***

Loewy (1990, p. 93) states that:

"Afferents from thoracic and abdominal viscera converge on neurons in the commissural-medial NTS, thus providing information regarding the physiological state of major visceral organs. This information is then transmitted via the ascending NTS pathways to a CNS autonomic network to produce a broad range of autonomic, endocrine and behavioural effects."

### **Special Visceral Afferent Pathway: Taste**

An example of the two levels of complexity (reflex arc and central circuit) is provided by gustatory pathways.

At a basic level, there is a reflex loop in which gustatory NTS nuclei project to areas adjacent to the brain stem motor nuclei controlling chewing, swallowing and salivation - cranial nerves V, VII, IX, X, and XI, are involved (Norgren 1978, Travers 1988, Travers and Norgren 1983).

Most gustatory afferents arise from four main sensory fields (Norgren 1984):

i) Fungiform papillae on the anterior two thirds of the tongue. The corda tympani nerve (CN VII) transmits this information via the geniculate ganglion to the superior gustatory nucleus in the rostral NTS.

ii) The soft palate area. The greater petrosal nerve (CN VII) transmits this information via the geniculate ganglion to the superior gustatory nucleus.

iii) Circumvallate and foliate papillae on the posterior one third of the tongue. The lingual branch of CN IX transmits this information via the petrosal ganglion to the inferior gustatory nucleus.

iv) The laryngeal surface of the epiglottis. The superior laryngeal nerve (CN X) transmits this information via the nodose ganglion to the inferior gustatory nucleus.

Gustatory information is received in viscerotopic pattern in the NTS. The anterior two-thirds of the tongue and soft palate having overlapping areas of termination in the superior gustatory nucleus. The posterior one-third of the tongue and epiglottis are represented in the inferior gustatory nucleus (Norgren 1984).

Somatosensory afferents arising in the oral cavity also terminate in the rostral NTS, in the same area as the gustatory afferents (Hamilton and Norgren 1984).

In midbrain transected rats, the basic ability to select or reject food substances on the basis of taste is preserved (Grill 1980), indicating that the lower brain stem (ie. reflex) neural circuitry is sufficient for this capability. Control of swallowing however, involves sites in the forebrain (Jean 1984), indicating that more complex behaviour requires higher order neural connections.

The NTS projects fibres rostrally to sites in the brain stem, diencephalon, and cerebral cortex. The medial parabrachial nucleus (PBN) receives a significant input from the NTS, onto a region called the pontine taste area. This area acts as a secondary relay nucleus for afferent taste information (Norgren 1984).

The NTS and medial PBN give rise to parallel pathways for ascending gustatory information, both of which project to the diencephalon and telencephalon, especially the insular cortex. In the thalamus, a portion of this parallel pathway synapses in the ventroposterior nucleus (Cechetto and Saper 1990). Neurons in both the NTS and PBN which make up this pathway are immunoreactive for cholecystokinin, enkephalin, neurotensin, somatostatin and substance P (Mantyh and Hunt 1984).

Ascending taste fibres from the NTS also project to the lateral hypothalamic area, the paraventricular hypothalamic nucleus, the central nucleus of the amygdala, the bed nucleus of the stria terminalis, and the substantia innominata (Norgren 1984). There are very similar projections from the medial parabrachial area (Saper and Loewy 1980).

Both the lateral and paraventricular hypothalamic areas have been implicated as sites which regulate the uptake of specific types of food (Leibowitz 1986).

## **Central Autonomic Network**

### **NTS: Central Projections**

Loewy (1990, p. 94) states "...the NTS projects to a number of key nuclei in the lower brain stem that regulate the autonomic preganglionic neurones of the sympathetic and vagal systems as well as projecting to (brain stem and) forebrain nuclei in the central autonomic network that are capable of regulating both autonomic and neuroendocrine functions. This network also provides connections to limbic and neocortical areas and quite probably effects behavioural and cognitive functions."

Ascending pathways from the NTS transmit a range of visceral information to nuclei of the forebrain (Loewy 1990; Carpenter 1991).

The central nucleus of the amygdala and the paraventricular hypothalamic nucleus both receive baroreceptor and chemoreceptor input (Cecchetto and Calaresu 1985, Ciriello and Calaresu 1980).

The median preoptic nucleus of the hypothalamus, which regulates the release of vasopressin (Harris and Loewy 1990, Johnson and Loewy 1990), also receives input from the NTS.

The NTS projects osmoreceptor signals to the paraventricular hypothalamic nucleus, the lateral hypothalamic area, and the zona incerta (Kobashi and Adachi 1988).

Loewy (1990) suggests that other fibres which project to the forebrain from the NTS also affect ingestive functions.

The commissural nucleus of the caudal NTS is the main site in the medulla receiving general visceral sensations via cranial nerves IX and X. It projects fibres to nuclei of the pons, midbrain and forebrain which control autonomic and neuro-endocrine systems (Loewy 1990).

The commissural nucleus also receives afferent input from the spinal cord, brainstem, forebrain generally and cortex in particular.

Inputs to the NTS from the spinal cord originate from neurons in Rexed laminae I, V, and X. Spinal inputs may carry both somatic and visceral information (Menetrey and Basbaum 1987).

Furthermore, the spinal trigeminal nucleus, which receives somatic afferent fibres from the head, tongue, soft palate and pharynx, also projects to the NTS (Menetrey and Basbaum 1987).

Hence the NTS is an important sensory linkage where both visceral and somatic information from the internal and external environments of the body is received, and transmitted to higher neural centres for autonomic and endocrine responses.

The commissural NTS has reciprocal connections with several cell groups that provide direct inputs to both sympathetic and vagal preganglionic neurons. These include the A5 cell group, caudal raphe nuclei, rostral ventrolateral medulla, periaqueductal grey matter, and paraventricular and lateral hypothalamic regions (Loewy et al. 1979, 1986; Thor and Helke 1987a,b; Luiten et al. 1985; 1987).

The central amygdaloid nucleus, the bed nucleus of the stria terminalis, and the insular cortex have reciprocal connections with the NTS, however these forebrain centres project mainly to the dorsal nucleus of vagus and so influence parasympathetic outflow to the gastrointestinal system (Hopkins and Holstege 1978, Holstege et al. 1985).

### **Parabrachial Nucleus - a Parallel Pathway**

The parabrachial nucleus (PBN) of the pons/midbrain is another major brain stem relay centre for visceral information. The main source of its input arises from specific regions of the NTS (Herbert et al. 1990).

The general pattern of connections is as follows. The medial PBN receives input from the gustatory region of the NTS. The lateral PBN area receives input from the general

visceroreceptive region of the NTS, and the ventral PBN, the Kölliker-Fuse nucleus, receives input from the respiratory region of the NTS (Herbert et al. 1990).

The medial and lateral PBN project topographically to more rostral areas of the brain. The ventral PBN is part of a brain stem network which controls respiration (Caille et al. 1981).

The medial PBN (in the pontine taste area) has direct connections with the frontal, infralimbic, and insular regions of the cerebral cortex (Saper and Loewy 1980). The medial PBN also projects to the ventroposterior thalamic nucleus, the zona incerta, the central nucleus of the amygdala, and the bed nucleus of the stria terminalis.

Pathways deriving from the lateral PBN are thought to be mainly involved in autonomic and neuroendocrine responses (Loewy 1990), but more complex functions may be effected because of indirect connections with the cerebral cortex.

For example, an important pathway from the lateral PBN projects to the intralaminar thalamic nuclei (including the parafascicular, paracentral and central lateral thalamic nuclei). This lateral PBN-thalamic pathway may have quite particular cortical influences, as the parafascicular thalamic nucleus projects to the frontal cortex, and the paracentral and central lateral thalamic nuclei project to the parietal cortex (Loewy 1990).

The lateral PBN also connects with the centromedial nucleus of the thalamus, which in turn, has connections with the cingulate gyrus and anterior limbic areas (Loewy 1990, Carpenter 1991). This suggests it may have some involvement in emotions and related behaviours.

The lateral PBN also projects to the paraventricular thalamic nucleus, so it may be involved in widespread variations in cortical function (Loewy 1990).

One region of the lateral PBN projects mainly to the ventromedial hypothalamic nucleus, suggesting that it may be part of the major ascending pathways affecting food intake, as this nucleus of the hypothalamus has been shown to regulate food intake (Shimizu et al. 1987, Loewy 1990).

The lateral PBN also projects to the zona incerta, the lateral hypothalamic area, the paraventricular hypothalamic nucleus, the substantia innominata, the median preoptic nucleus, the central nucleus of the amygdala, and the bed nucleus of the stria terminalis (Fulwiler and Saper 1984).

These projections parallel those which arise from the commissural-medial region of the NTS. There is no doubt the lateral PBN is involved in processing general visceral information (Loewy 1990). The parallel nature of the projections from the NTS and PBN are illustrated in figure 4.

### **Locus Coeruleus**

The efferent fibres of the locus coeruleus project in an extensive divergent pattern throughout the entire central nervous system (Jones and Yang 1985). In contrast, afferent fibres projecting to the locus coeruleus arise from two sites in the medulla oblongata - the nucleus prepositus hypoglossi, and the rostral ventrolateral medulla (Aston-Jones et al. 1986, Ennis and Aston-

Jones 1986, 1987). The rostral ventrolateral medulla is strongly implicated as a cardiovascular control centre (Guyenet 1990).

The functions of the locus coeruleus are not clearly understood (Loewy 1990), but because of the highly divergent nature of its efferent projections, it has been implicated in almost every known function of the brain (Loewy 1990).

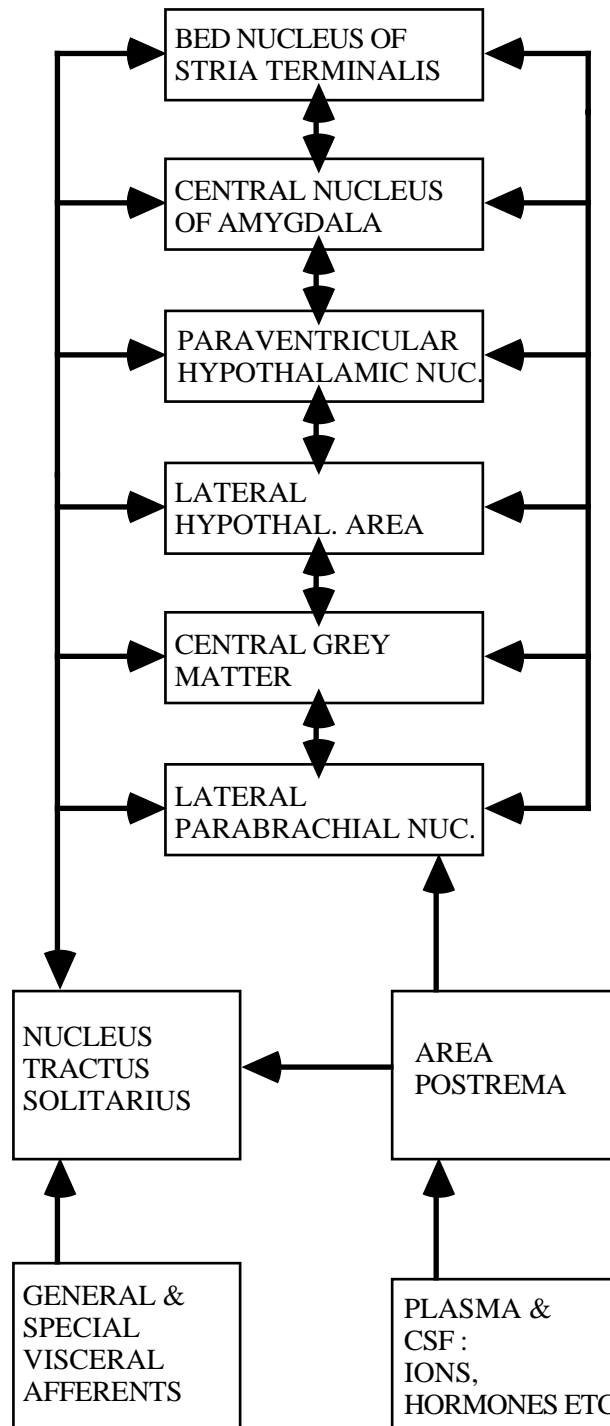


Figure 4

Central Autonomic Network

(adapted from Loewy, 1990, p. 93)

One suggested function is that the locus coeruleus acts as a relay centre which monitors afferent information from both the internal and external environments (Aston-Jones 1985, Aston-Jones et al. 1984). It is thought that the activity levels of its neurons vary with different stages of the sleep-wakefulness cycle, with its neurons recording a high level of activity during the waking state, and progressively lower levels at deeper stages of sleep (Parmeggiani and Morrison 1990). During some sleep stages, almost all neuronal activity in locus coeruleus neurons ceases (Aston-Jones 1985, Parmeggiani and Morrison 1990).

However during behavioural patterns such as grooming or drinking in the cat, the level of activity in locus coeruleus neurons decreases (Aston-Jones 1985). This activity level is not simply related to the level of arousal, but correlates more directly with the level of vigilance or surveillance of the external environment (Aston-Jones 1985).

The locus coeruleus also receives afferent information via multisynaptic pathways from a wide variety of internal receptors from sources such as the splanchnic, pelvic and vagal nerves (Elam et al. 1984, 1986; Svensson and Thoren 1979).

Although it has a highly divergent pattern of efferent projections, the locus coeruleus does not project directly to autonomic preganglionic nuclei such as the intermediolateral cell column of the spinal cord, vagal preganglionic neurons (Jones and Yang 1985), or to the nucleus of the solitary tract (Thor and Helke 1987). But Sved and Felsten (1987) have shown that microinjections of L-glutamate into the locus coeruleus of rats cause a decrease in blood pressure and heart rate that is eliminated by local 6-hydroxydopamine injections. Hence indirect pathways must provide the explanation for the impact on the central autonomic network (Loewy 1990).

Possible pathways which may explain this response are ascending projections from the locus coeruleus to the lateral hypothalamic area and to the bed nucleus of stria terminalis (Jones and Yang 1985). Both of these have been implicated in central autonomic control.

## **Descending Regulation of Sympathetic Outflow**

Sympathetic preganglionic neurons in the spinal cord are the final CNS output for this division of the autonomic nervous system. The integration and central processing of the sympathetic aspect of the homeostatic hierarchy is represented in the output of these neurons.

Five areas of the brain stem and hypothalamus have been shown to be involved in all levels of the preganglionic sympathetic outflow and are consequently considered to be key areas active in its control (Strack et al. 1989b; Coote 1988).

These areas are (Strack et al. 1989b):

- i) the paraventricular hypothalamic nucleus
- ii) the A5 noradrenergic cell group
- iii) the caudal raphe region
- iv) the rostral ventrolateral medulla, and
- v) the ventromedial medulla.

It is unclear whether neurons in each of these nuclei regulate the entire sympathetic outflow, or whether these projections are topographically organized, as has been demonstrated with the paraventricular hypothalamic nucleus (Strack et al. 1989b).

It is possible that particular nuclei or regions at times may control the entire outflow, for example in the defense reaction, or the sleep/wakefulness cycle (Loewy 1990).

It is also possible that specific chemically coded patterns of innervation exist for the various descending pathways (Loewy 1990). For example Strack et al. (1989a), found a variety of neuropeptide-containing neurons in both the medulla and the paraventricular hypothalamic nuclei which innervate the sympathoadrenal preganglionic neurons (Edwards 1990).

It should also be noted that interneurons in the intermediate grey matter of the spinal cord (laminae VII and X) innervate sympathetic preganglionic neurons at all segmental levels which have sympathetic outflow (Strack et al. 1989a). Interneurons from primary sensory neurons are also probably present in the dorsal horn (Loewy 1990).

Because of the presence of these local segmental interneurons, there may be intrinsic spinal pathways which modulate the sympathetic outflow. However relatively little is known about these (Schramm 1986).

## Overview of the Hypothalamus

The hypothalamus is essential for life and is a complex integration centre of somatic, autonomic, emotional and endocrine functions. It controls and regulates many bodily functions such as appetite, metabolism, thirst and water balance, cardiovascular functions, temperature, sleep/wake cycle, reproductive organs, sexual behaviour, and emotional expression (Nolte, 1988; Freeman, 1995; Kandel et al., 1991). Tables 1 and 2 provide a general overview of hypothalamic functions. They summarise hypothalamic involvement in neural and endocrine regulation.

The hypothalamus is necessary for the maintenance of homeostasis which it does through control of the endocrine and autonomic nervous systems. It may be viewed as a rostral participant in (extension of) the activity of the reticular formation and is the major output region of the limbic system (Nolte, 1988; Freeman, 1995; Kandel et al., 1991).

## Hypothalamic Inputs

Afferent fibres to the hypothalamus are received from two general areas (Nolte, 1988):

- 1) the diencephalon and telencephalon, especially from limbic regions. Input from the limbic system involves the hypothalamus in affective states, which may, and very often do, have autonomic, somatic and endocrine expression;

- 2) the brainstem. Input from the brainstem conveys visceral and somatosensory information to the hypothalamus.

Table 1

**NEURAL PROCESSES REGULATED BY  
THE HYPOTHALAMUS**

<b>Process</b>	<b>System or Activity</b>	<b>Effect</b>
Autonomic	Cardiovascular	Blood flow ( ↓ or ↑)* Vasodilation or vasoconstriction
	Thermoregulatory	Blood flow, shivering, panting
	Visceral	Digestive acid secretion ( ↑ )
Behavioral	Sexual	Sexual receptivity ( ↑ )
	Maternal	Nest building
	Emotional	Aggression ( ↑ )
	Ingestive	Eating and drinking ( ↑ or ↓ )

\* ↑ , increase; ↓ , decrease

(Reproduced from Freeman, 1995. p. 262)

Table 2

**NEUROENDOCRINE REGULATORS OF HYPOTHALAMIC ORIGIN**

<b>System Regulated</b>	<b>Site of Regulation</b>	<b>Action</b>	<b>Hypothalamic Regulator</b>
Thyroid gland	Adenohypophysis	Stimulation of thyrotrophin secretion	Thyrotrophin-releasing hormone
Adrenal cortex	Adenohypophysis	Stimulation of adrenocorticotrophin secretion	Corticotrophin-releasing hormone
Gonads	Adenohypophysis	Stimulation of luteinizing hormone and follicle-stimulating hormone secretion	Gonadotropin-releasing hormone
Muscle, bone, liver	Adenohypophysis	Stimulation or inhibition of growth hormone secretion	Growth hormone-releasing hormone, somatostatin
Milk synthesis and secretion from the mammary gland	Adenohypophysis	Inhibition of prolactin secretion	Dopamine
Cardiovascular, renal	Vascular smooth muscle, renal tubule	Vasoconstriction, water reabsorption	Vasopressin (antidiuretic hormone)
Mammary gland, uterus	Smooth muscle of mammary ducts and uterus	Increase intramammary pressure, inducing milk ejection; increase uterine contraction in labor	Oxytocin

(Reproduced from Freeman, 1995. p. 263)

Input to the hypothalamus is very often indirect. Olfactory information is received via the olfactory bulb and cortex. Gustatory information is received via the nucleus of the solitary tract in the medulla. Visual input is received via the optic pathway, such as that to the suprachiasmatic nucleus which influences the endocrine system and biological rhythms. General sensory afferents such as nociceptive and autonomic afferents are received from the brainstem and spinal cord (Brown, 1988; Freeman, 1995).

Autonomic input from cranial nerves and the spinal cord reaches the hypothalamus mainly via the reticular formation. Input is also received from blood vessels and cerebrospinal fluid, which allows control of variables such as blood osmolarity and pH, and body temperature. Endocrine feedback to the hypothalamus also occurs.

Reticular input to the hypothalamus arises mainly, but not exclusively, from the midbrain (Guyton, 1987; Brown, 1988).

### *Forebrain Afferents*

Several forebrain regions project afferents to the hypothalamus. These include the septal area, the hippocampal formation, the amygdaloid body, the orbital cortex, the thalamus and the retina (Nolte, 1988; Freeman 1995; Brown, 1988).

The septal area, adjacent to the septum pellucidum and a component of the limbic system, projects fibres to the hypothalamus in the median forebrain bundle (Freeman 1995).

The fornix is the main output tract of the hippocampal formation, a major component of the limbic system. This tract follows an extended 'C' shaped route. It projects from the hippocampal formation, reaches the hypothalamus which it enters, and synapses in the mammillary body (Freeman 1995; Carpenter, 1991).

The amygdala, another major component of the limbic system, is very well connected to the hypothalamus. It projects fibres to it through two main routes. These are i) the stria terminalis which accompanies the caudate nucleus, and ii) a diffuse ventral pathway (amygdalofugal) which passes more directly to the hypothalamus, inferior to the lentiform nucleus. The ventral pathway is mainly efferent. Both pathways terminate near the ventromedial nucleus of the hypothalamus (Nolte, 1988; Freeman, 1995).

Fibres from the orbital cortex of the frontal lobe project directly to the hypothalamus in the median forebrain bundle. The dorsomedial nucleus of the thalamus projects periventricular fibres to the hypothalamus. This is an indirect route by which the frontal lobe may influence the hypothalamus, as the prefrontal cortex is extensively connected to the dorsomedial thalamic nucleus (Nolte, 1988; Freeman, 1995).

### *Brainstem Afferents*

Afferent pathways to the hypothalamus from the brainstem are not completely understood, but follow various routes. Direct input is received from the solitary nucleus of the medulla, and the parabrachial nuclei of the pons. Indirect input is received via parts of the reticular formation and periaqueductal grey (Nolte, 1988; Freeman, 1995).

Collateral afferents from pathways such as the spinothalamic tract also reach the hypothalamus (Nolte, 1988).

## Hypothalamic Outputs

Efferents fibres from the hypothalamus project to the brainstem reticular nuclei, particularly the periaqueductal grey and tectal regions, the spinal cord, and to autonomic cranial nerve nuclei (CN III, VII, IX, X) in the brainstem. Control exerted by the hypothalamus may be both direct and indirect, with indirect control in the brainstem occurring via the reticular formation (Nolte, 1988).

In general, anterior and medial areas of the hypothalamus control parasympathetic activity, while sympathetic activity is controlled from lateral and posterior regions. The limbic system projects to both the medial and lateral regions of the hypothalamus (Freeman, 1995; Nolte, 1988).

To a considerable extent efferent pathways from the hypothalamus are reciprocal to the afferent pathways, with afferent fibre bundles commonly carrying efferent projections. Hence the septal area, the hippocampus, the amygdala, and the dorsomedial and anterior thalamic nuclei (which are all components of the limbic system), all receive efferent hypothalamic projections (Freeman, 1995; Nolte, 1988).

Two efferent pathways arising in the hypothalamus control the pituitary gland (refer below). The hypothalamus plays a major role in the control and modulation of the endocrine system (Freeman, 1995; Nolte, 1988; Guyton, 1987).

## Associated Tracts

The median forebrain bundle (MFB) includes functionally diverse groups of fibres that pass through the lateral and preoptic areas of the hypothalamus. It extends from the septal region of the basal forebrain to the midbrain tegmentum, with fibres entering and leaving it along its course. Descending fibres originate in the basal forebrain, including the olfactory cortex, the preoptic area, the septal area, the nucleus accumbens, and the amygdala (Freeman, 1995; Nolte, 1988; Brown, 1988).

Some fibres of the MFB terminate in the hypothalamus, some originate there, and many pass through. Those of hypothalamic origin ascend to the septal nuclei (medial septal nuclei, diagonal band of Brocca), descend to the midbrain reticular formation, or interconnect different hypothalamic nuclei (Nolte, 1988).

The ascending fibres of the median forebrain bundle arise from the spinal cord and reticular formation, and visceral, taste and monoaminergic nuclei in the brainstem (Nolte, 1988; Freeman, 1995).

The dorsal longitudinal fasciculus (DLF) runs between the hypothalamus and the medulla. It contains thinly myelinated fibres from the medial and paraventricular regions of the hypothalamus (many of which terminate in the midbrain), and hypothalamic afferents from the periventricular and periaqueductal grey of the brainstem. Fibres in the DLF are thought to be mainly concerned with olfactory, gustatory and emotional influences on salivation, lacrimation and oral, facial and visceral reflexes (Freeman, 1995; Nolte, 1988; Brown, 1988).

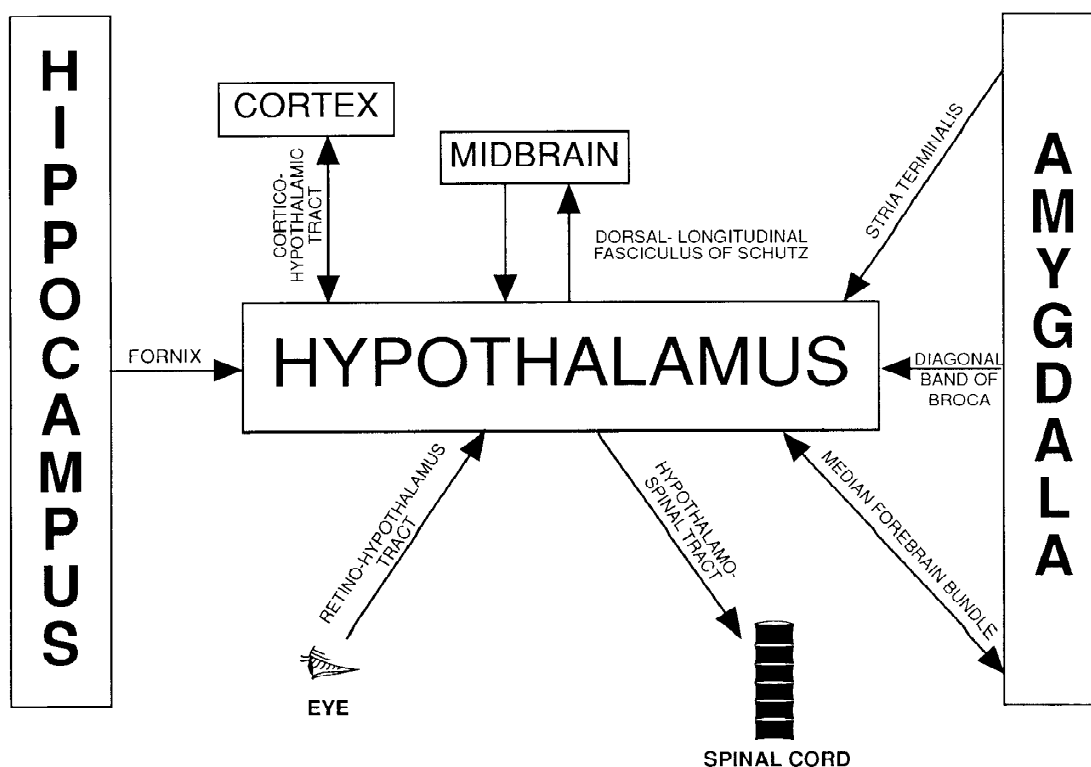
The stria terminalis and a diffuse ventral pathway provide reciprocal connections between the hypothalamus and the amygdaloid body, although the majority of fibres are afferent to the hypothalamus (Nolte, 1988).

Some ganglion cells in the retina project to the suprachiasmatic nucleus via the retinohypothalamic tract (Freeman, 1955).

The hippocampal region of the temporal lobe provides considerable input to the hypothalamus via the fornix. The majority of these fibres pass through the hypothalamus to the mammillary body, and this information is relayed from there to the anterior nucleus of the thalamus in the mammillothalamic tract. The anterior thalamic nucleus projects to the cingulate gyrus (Nolte, 1988), - part of the limbic lobe.

The mammillotegmental tract passes caudally to reticular nuclei of the midbrain. The mammillary peduncle receives reciprocal input from the midbrain reticular formation in the mammillary-pudendal tract (Freeman, 1995; Nolte, 1988; Brown, 1988).

Two hypothalamic tracts control the pituitary gland, the tuberoinfundibular tract and the hypothalamohypophysial tract (Brown, 1988).



**Figure 5 Major neural connections of the hypothalamus, illustrating the importance of limbic connections.** (Reproduced from Freeman, 1995. p. 268).

The tuberoinfundibular tract mainly arises from the tuber cinereum (arcuate nucleus, periventricular nucleus) and terminates on capillaries in the median eminence. Fibres secrete releasing or inhibiting factors which control endocrine cells of the anterior pituitary via hypophysial portal veins. The tuberoinfundibular tract controls the release of prolactin, growth hormone, thyroid stimulating hormone, follicle stimulating hormone, luteinising hormone,

adrenocorticotrophic hormone, and melanocyte stimulating hormone (Freeman, 1995; Nolte, 1988; Brown, 1988).

The hypothalamohypophysial tract arises from neurosecretory cells of the supraoptic and paraventricular nuclei of the hypothalamus, passes through the infundibulum, and releases oxytocin and antidiuretic hormone (ADH) in the posterior pituitary lobe (Nolte, 1988; Brown, 1988).

Many cells of the supraoptic and paraventricular nuclei project fibres to the dorsal motor nucleus of the vagus (CN X) [parasympathetic], and the intermediolateral cell column of the thoracic spinal cord (hypothalamospinal tract). Preganglionic sympathetic nerves arise in the intermediolateral cell column, so the hypothalamospinal tract must surely be involved in this aspect of autonomic function (Brown, 1988; Freeman, 1995).

Figure 5 illustrates some of the more important neural connections of the hypothalamus. Connections with two major structures of the limbic system are emphasised, those with the hippocampal formation and amygdaloid body.

### **Specific Autonomic Nuclei of the Forebrain**

Specific forebrain nuclei thought to participate in a central autonomic network include the paraventricular hypothalamic nucleus (PVH), the lateral hypothalamic area, the central nucleus of the amygdala, and the bed nucleus of the stria terminalis (Harris and Loewy 1990, Swanson 1987, Price et al. 1987, Weller and Smith 1982, Holstege et al. 1985, Loewy 1990).

These nuclei are reciprocally connected to both the nucleus of the solitary tract and to the parabrachial nucleus. This is a significant feature of the central autonomic network. In fact, almost every site which receives an NTS input also sends projections back to the NTS (Loewy 1990). Such interconnectedness suggests that a feedback system is in place at virtually all levels of the network.

Further, the PVH and the lateral hypothalamic area project to the dorsal vagal preganglionic neurons as well as to sympathetic preganglionic neurons. The central nucleus of the amygdala, and the bed nucleus of the stria terminalis project mainly to the dorsal vagal preganglionic neurons (ie. parasympathetic) (Loewy, 1990).

#### **Paraventricular hypothalamic nucleus (PVH)**

The PVH is made up of several functionally distinct subnuclei which affect both autonomic and endocrine responses (Harris and Loewy 1990, Swanson 1987). Some groups of PVH neurons are involved in anterior and posterior pituitary regulation. Others are involved in autonomic control.

For example, one subnucleus synthesises corticotropin-releasing hormone, which regulates ACTH release from the anterior pituitary. Another group of PVH neurons releases antidiuretic hormone (ADH) into the vascular system. Others give rise to descending autonomic pathways to the brain stem and spinal cord.

The descending PVH pathways project to the periaqueductal grey matter, the locus coeruleus, the PBN, the NTS, the dorsal vagal nucleus, the nucleus ambiguus, and the

intermediolateral cell column of the spinal cord (Luiten et al. 1985), all of which have been implicated in autonomic control (Loewy 1990).

However it is not clear which particular functions are regulated by these connections, although anatomical evidence suggests that the PVH is one of only a few sites in the brain which regulate the entire sympathetic outflow (Strack et al. 1989b).

Certainly PVH neurons regulate a large variety of autonomic and visceral functions. For example, microinjections of L-glutamate into the PVH evoke an increase in adrenal nerve activity and a decrease in renal nerve activity and blood pressure (Katafuchi et al. 1988). And lesions and injections of various peptides into the PVH causes overeating and obesity in rats (Leibowitz et al. 1981, Leibowitz 1986), indicating a role in the control of food intake.

### **Lateral Hypothalamic Area**

It is not entirely clear whether the functions attributed to the lateral hypothalamic area derive from axons which project through it, or whether they result from stimulation of cell bodies located within the area itself (Swanson 1987).

However techniques which employ the use of injection have attempted to selectively effect the excitability of cell bodies, and it has been found that microinjections of L-glutamate into the lateral hypothalamic area of rats causes a decrease in blood pressure, heart rate and cardiac output, with the changes in heart rate and cardiac output being mediated by both sympathetic and parasympathetic mechanisms (Spencer et al. 1989).

### **Central Nucleus of the Amygdala**

The amygdala is thought to be involved in a range of autonomic, neuroendocrine, and behavioural functions (Price et al., 1987). Neuroanatomical studies indicate that the central nucleus of the amygdala receives dense inputs from the NTS (Ricardo and Koh 1978, Norgren 1978), the PBN (Saper and Loewy 1980), and several other areas (Russchen 1982b).

This anatomical evidence suggests that the central nucleus of the amygdala is involved in processing autonomic information.

It projects to several nuclei known to be involved in autonomic processing, such as the lateral hypothalamic area, periaqueductal grey matter, and autonomic nuclei of the pons and medulla (Hopkins and Holstege 1978, Krettek and Price 1978, Price and Amaral 1981, Wallace et al. 1989).

Projections to the brain stem arise from separate cells within the central nucleus of the amygdala (Thompson and Cassell 1989). Some project directly to the C1 adrenergic neurons which have been implicated in autonomic control (Cassell and Grey 1989, Guyenet 1990).

These descending projections are predominantly to autonomic centres such as the PBN, the NTS, and the motor nuclei of the vagus, however projections are also made to dopamine neurons of the substantia nigra and the ventral tegmental area of the midbrain. Both these latter areas may be involved in motor functions (Wallace et al. 1989).

Areas of the cerebral cortex which provide direct input to the central amygdala nucleus include the orbitofrontal and insular regions. Both of which are implicated in autonomic function, refer to discussion below.

Indirect cortical connections derive from the lateral amygdaloid nucleus, which receives input from a wide range of sensory areas of the cerebral cortex.

Given the broad range of direct and indirect input into the central amygdaloid nucleus, it is most likely that the activity of these neurons is modulated as a consequence (Loewy 1990).

### **Bed Nucleus of Stria Terminalis**

This nucleus has similar connections to those of the central nucleus of the amygdala (Weller and Smith 1982, Holstege et al. 1985). Knowledge of its overall functions is at a similar level to that nucleus (Loewy 1990).

## **Cerebral Cortex and Autonomic Control**

Three regions of the cerebral cortex have been implicated in autonomic function - the insular cortex, the medial prefrontal cortex, and the somatic sensorimotor cortex (Cechetto and Saper 1990).

### **Insular cortex**

The insular cortex has many connections with subcortical sites implicated in autonomic control. Afferents to this area arise directly from the PBN and the lateral hypothalamic area (Saper 1982a,b, 1985; Shipley and Sanders 1982).

Efferents from the insular region project to the NTS, the PBN, the lateral hypothalamic area, and the central nucleus of the amygdaloid body (van der Kooy et al. 1982, 1984; Ross et al. 1981, Ruggiero et al. 1987, Shipley 1982, Saper 1982a,b, Yasui et al. 1985).

The NTS receives topographical projections from the insular cortex. The insular taste area projects to the gustatory nucleus (rostral NTS), while the general visceral insular area innervates the general visceral (caudal) NTS.

The PBN and the lateral hypothalamus receive insular innervation mainly to subnuclei which have reciprocal connections with the insular cortex (Saper 1982a,b, Fulwiler and Saper 1984). This may be considered a feedback mechanism which modulates ascending sensory input (Cechetto and Saper 1990).

Insular neurons also innervate areas of the PBN and the lateral hypothalamus which have extensive descending projections to autonomic preganglionic cell groups in the medulla and spinal cord (Berk and Finkelstein 1982; Hosoya and Matsushita 1981; Luiten et al. 1987; Miura et al. 1983; Saper et al. 1976; Saper and Loewy 1980).

The central nucleus of the amygdala receives a significant number of projections from the insular cortex (Saper 1982a; Russchen 1982a; Otterson 1982; Cechetto et al. 1983).

Together with the nucleus of the solitary tract, the parabrachial nucleus, and the lateral hypothalamus, the central nucleus of the amygdala innervates reticular areas of the medulla which are involved in coordinating autonomic responses (Fulwiler and Saper 1984; Loewy and Burton 1978; Luiten et al. 1987; Price and Amaral 1981; Ricardo and Koh 1978; Saper and Loewy 1980).

In the monkey some neurons in the central nucleus of the amygdala may send projections directly to the spinal cord (Mizuno et al. 1985).

### **Medial Prefrontal Cortex**

It has been suggested that the infralimbic area of the medial prefrontal cortex may function as a visceral motor cortex (Hurley-Gius and Neafsey 1986). This area receives extensive input from the limbic system but only sparse visceral sensory input. There are massive inputs from the hippocampus, amygdala, and prelimbic cortex but relatively few from the spinal cord, NTS, PBN, and visceral nuclei of the thalamus (Cechetto and Saper 1990).

Furthermore, the hypothesis that it is a visceral motor area, can be supported by the fact that its anatomical position is on the medial surface of the frontal lobe, adjacent to motor areas (Hurley-Gius and Neafsey 1986).

However stronger evidence is probably required from studies using evoked potentials, chemical stimulation, and neuroanatomical localization for this hypothesis to gain greater credence (Cechetto and Saper 1990).

### **Somatic Sensorimotor Cortex**

The degree of participation of the motor cortex in autonomic nervous system control remains unclear. Definitive evidence of the pathways involved would help clarify the nature of the cortical motor/autonomic relationship (Cechetto and Saper 1990).

Considerable evidence does exist however, of visceral (sympathetic) afferent impulses entering the thoracic spinal cord, converging with somatosensory afferent information in the dorsal horn, and then being processed by the nervous system as thoracic somatosensory input, including representation in the somatosensory cortex (Blair et al. 1984; Ammons et al. 1985; Cechetto and Saper 1990).

In these cases, participation of the autonomic nervous system seems largely coordinated with ongoing somatic motor and sensory processes, suggesting that these are integrated rather than functionally separate (Cechetto and Saper 1990).

## **Discussion**

It seems clear that modern understanding of neuro-endocrine structures and relationships along the neuraxis of the central nervous system quite validly allows the concept of a homeostatic hierarchy (HH) to be portrayed in terms of three interconnected parts - the three tiers of the model.

Central autonomic and endocrine regions such as the reticular formation, the nucleus of the solitary tract, the parabrachial nucleus, the locus coeruleus and the hypothalamus play key roles in tier two.

In tier three the amygdala, insular cortex, medial prefrontal cortex, and possibly also the somatic sensori-motor cortex, play significant roles in autonomic regulation.

Tier one embraces the structures and functions of the gross anatomical body. It is through these that the influences of tiers two and three are mediated and made manifest, as well as organ function and reflex activity in tier one itself. In this way all three tiers contribute to and participate in the normal (or abnormal!) events and vicissitudes of daily life.

So all tiers impact upon the functions of the heart, lungs, various structures of the gastrointestinal tract, blood vessels, endocrine and immune systems, temperature control, emotions, sleep/wake cycles, reproductive behaviour, blood osmolarity and pH, and so on.

The final manifestation of events in tier one can only ever be the summation of activity which occurs in all three tiers. This defines the activity of tier one. It is nothing less than the final common pathway/ exposition which displays the integrated impact of all the tiers.

Of course dividing bodily identity and functions into three interconnected tiers is somewhat artificial. It is really only of use if it leads to clarity of thought and understanding - if it facilitates analytical penetration in juxtapositional discussion.

Table 3, Individual Identity, summarises the activities of the three tiers, and displays the notion of hierarchy in this view of individual identity.

<b>Tier 3</b>	Determination and establishment of almost all the complexities of individual personality and character, including cognition and emotions, occurs in this tier. Activity in this tier is 'built' upon, is dependent upon, the activity of the other tiers.
<b>Tier 2</b>	Integration of information/ activity from tiers 1 & 3 occurs in this tier. Balance, visual coordination, hearing, taste, homeostasis, autonomic and endocrine control, skeletal muscle modulation, etc. There is a 'gatekeeper' role carried out in tier 2, balancing, integrating and coordinating the exigencies and requirements of tier 1, with those of tier 3.
<b>Tier 1</b>	Manifestation of individual identity via the gross anatomical body in the 'real' three dimensional world occurs in this tier. Activity and intentions deriving from tiers 3 & 2 receives expression in tier 1.

**Table 3: Individual Identity, expressed in terms of three tiers.**

While this is all well and good, and may even be recognised as providing an interesting portrayal of an individual's identity, the real issue which arises is;

Of what use is this view to juxtapositional analysis? How does it facilitate 'western' understanding of the Zang Fu, Jing Luo and Wu Xing?

The paper on the model makes it clear that these three major TCM theoretical constructs may be viewed, in juxtapositional terms, within the context of the three tiers. [It may be appropriate to read that paper (available on this web page) if the reader has not already done so].

In this approach, the Zang Fu are considered to be made up of components of each tier, the Jing Luo is considered to be focused mainly in tier 2, and the interactions of the Wu Xing are thought to mainly occur in tier 2 as well. [Remember that although the various Meridians

making up the Jing Luo have separate identities in TCM theory, the twelve primary Meridians are at the same time, integral components of individual Zang Fu].

Further, consideration of individual Zang Fu and their related Disharmonies shows that each one typically encompasses functions centred in the gross anatomical body - tier 1 (e.g. mucus production in the respiratory tract), various Meridians - tier 2, as well as emotions, personal attributes, temperament, virtues, sounds, spirit attributes and various modes of behaviour, etc. - tier 3.

The tiered structure of the model allows these various qualities to be sensibly embraced (from a WMB stance) within a unifying framework.

Certainly, there is no *a priori* reason why an Organ (or an 'Orb'), cannot be defined to include the functional activity of a physical structure (ie. of an anatomical entity in tier 1), *plus* its neural and endocrine homeostatic control substrates, as well as behavioural and emotional components. The diverse location in the CNS of tier 2 and 3 components is not really an issue, as TCM invariably takes a functional view of Organ identity rather than a somatic-based one.

It is also important to appreciate the magnitude and significance of brainstem and diencephalic activity in the modulation of homeostatic control. Life is not possible without tier 2 activity. So *in vivo*, an individual without Meridian activity can not survive, and the idea that an Organ should be thought of as existing (in functional terms) without its control substrate is at best, of academic interest.

It is the view of the writer that this understanding is precisely that which is embraced within the parameters of traditional Chinese medicine. Its inherent genius is to recognise these distinctions, and to separate them out for separate consideration and therapeutic access via the Meridians of the Jing Luo. Establishing reliable and reproducible therapeutic access to precise regions of tier 2 is the essence of acupuncture.

Does it make sense to view the Zang Fu this way? There is really no reason not to. At its core is a functional approach to individual identity. They certainly include the emotions and behaviour (refer to the paper on Concordances, TCM Theory page), which modern neuro-endocrine science knows to be very difficult to separate from reflex homeostatic activity lower in the hierarchy.

Indeed viewed from the stance of the model, this embrace of homeostatic control mechanisms, emotions, behaviour, etc., confirms the integrity of the TCM approach. These attributes simply cannot be left out just to suit the somatic-based approach to the human body which has become so well established in the WMB mind over the past three or four hundred years.

It would appear this presentation of the TCM world view very much reflects the real *in vivo* functional integrity of an individual - real CNS functional integration of neuroanatomy and physiology.

With the Meridians and Zang Fu approached in this way, acupuncture points, point functions, and many aspects of TCM theory should begin to make sense to the western mind.

Groups of points, point categories, various types of meridians, Zang Fu syndromes etc., are all worthy of investigation in this light. These are issues to be addressed in future papers.

By way of illustrative example it is worthwhile to have a brief look at the point He Gu (LI-4). [The TCM information given here derives from the paper on Large Intestine Points which may be found on the TCM Theory page of Acu Centre’s web site].

**He Gu (LI-4)**

<b>TCM Point Qualities &amp; Information</b>		<b>Some Juxtapositional Observations</b>
<p><b>He Gu (LI-4) Location</b></p>	<p>In the centre of the flesh (high point) between the first and second metacarpal bones in the first dorsal interosseus muscle. This is approximately midway along the length of the second metacarpal bone.</p> <p>The point may be located by placing the transverse interphalangeal crease of one thumb at the margin of the webbing between the thumb and index finger of the opposite hand - the point is where the distal end of the thumb touches.</p>	<p>The point is located on the dorsum of the hand and is itself clearly in tier 1. It is located in the 1st dorsal interosseus muscle.</p> <p>Qi sensations are carried into the central nervous system mainly by nociceptive and thermal neural pathways.</p> <p>They are carried higher in the central nervous system (in the first instance) mainly via spinothalamic, spinoreticular, and spinomesencephalic neural pathways - tier 2.</p> <p>Proportional measurements are considered by this writer to ‘standardise’ input into the central nervous system - necessary due to great differences in the physical size of the gross anatomical body (tier 1) between individuals.</p>

<p><b>He Gu (LI-4) Features &amp; Categories</b></p>	<p>Yuan-Source point of the Large Intestine Channel; Regional Command point of the face and mouth. One of the nine needles for returning Yang. A Heavenly Star point of Ma Dan-Yang.</p>	<p>As one of the 9 needles for returning Yang, Hegu (LI-4) may very well participate prominently in enlivening the ascending reticular activating system (ARAS) of the brainstem - tiers 2 &amp; 3.</p> <p>As a command point of the face/ mouth it would seem to have a significant impact on the complex and extensive neural substrate which has functional control over these complicated anatomical regions - tiers 2&amp;3.</p> <p>As the Large Intestine Channel Yuan point it may very well have a significant neuro/ endocrine/ immune impact too - tier 2.</p> <p>Its status as a Heavenly Star point indicates clinical experience of efficacy over considerable time (centuries). This suggests the impact of needling Hegu (LI-4) is well distributed and integrated throughout a number of homeostatic hierarchies in tier 2.</p>
<p><b>He Gu (LI-4) Functions</b></p>	<p>Frees the Channels and quickens the Connecting Vessels; disperses Wind and resolves the Exterior; clears Lung Heat; stimulates dispersal function of the Lungs; relieves pain and calms the Shen.</p>	<p>Without becoming too involved in the detail of TCM theory, a juxtapositional view here would suggest that Hegu (LI-4) is able to modulate various aspects of respiratory function (whether upper or lower respiratory tract, the lungs themselves, or aspects of breathing patterns), because needling sends a volley of action potentials into tier 2, thereby having an impact on those neural regions which have homeostatic control over lung/ bronchial/ respiratory functions. This then gets expression in tiers 3 &amp; 1- particularly the latter.</p> <p>Modulation of pain is a well-known attribute of the brainstem (tier 2), and the ability to calm the Shen suggests an impact on the limbic system - tiers 3, 2.</p>

<p><b>He Gu (LI-4)</b> <b>Indications</b></p>	<p>Headache; painful swelling and reddening of the eyes; nosebleed; swelling of the face; nasal obstruction or congestion; runny nose; sore, swollen throat; throat Bi; parotitis; common cold; deafness; hypertonicity of the fingers; pain in the arm; neck pain; toothache; wryness of the eyes and mouth; facial paralysis; hemiplegia; neurasthenia; sweating or absence of it in Heat diseases; tidal fever; amenorrhoea; prolonged labor; diarrhoea; dysentery; pain generally; diseases of the sensory organs; motor impairment of upper limb.</p>	<p>Not only are many of these indications reflective of respiratory tract, lung and breathing homeostatic modulation (the Large Intestine Fu is paired with the Lung Zang in the Metal Element), but several are also indicative of an impact on the face and mouth, which reflects the path of the primary LI Channel. Those on the upper limb also reflect this.</p> <p>Less obvious indications relating to the lower Jiao and other aspects of TCM theory may be explained by neural interactions within the brain stem which involve other homeostatic hierarchies. Remember that interactions such as these have always been part of TCM theory (via the Wu Xing and Jing Luo ).</p> <p>This view would appear to suggest that WMB should now be able to come to terms with the subtlety of TCM's understanding of bodily functions and variations <i>in vivo</i>.</p>
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The next three papers discuss the tiers in some detail, and apply the content of these ideas to the model, particularly the concept of tier two functioning as a coordinating physiological fulcrum. The reticular formation is also discussed in this context.