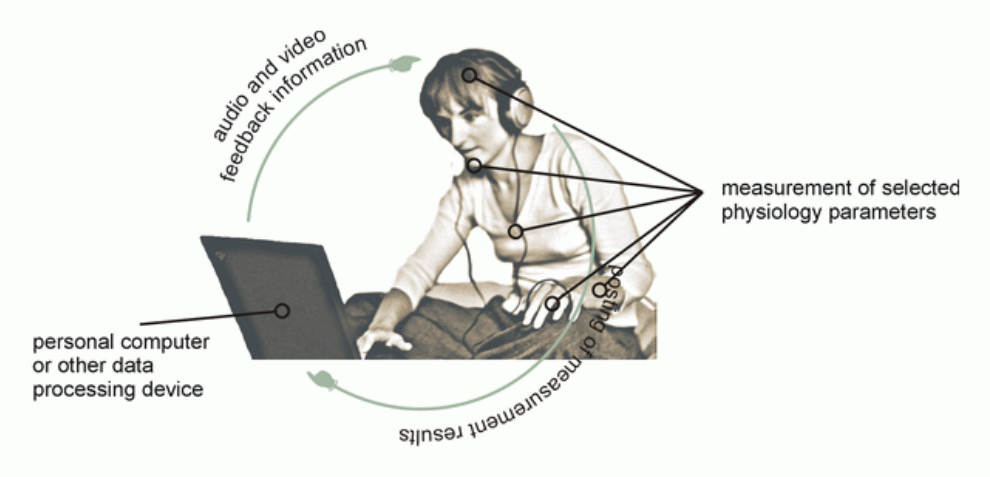
Master thesis:

Bio- and neurofeedback applications in stress regulation



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Abstract

Chronically being stressed has a negative impact on health. Of the ten leading causes to death, stress has been directly implicated in four and indirectly in three diseases. Stress occurs when homeostasis in the body becomes disrupted, for example by a stressful stimulus. To bring the body back into a homeostatic state, a stress response is initiated. The stress response activates the autonomic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis. The autonomic nervous system is divided into three parts, the sympathetic, parasympathetic and enteric nervous system. During a stressful situation, the sympathetic division becomes more active, causing some physiological parameters to change activity. Also adrenaline is released by the sympathetic nervous system. Adrenaline works within seconds, but is short-lasting. For longer periods of stress, or anticipation to a stressor, the HPA axis, causing the release of cortisol is activated.

Several biological parameters (EDA, heart rate, respiration rate) represent stress in the body. These parameters can be used to determine how stressed an individual is. Biofeedback makes use of these parameters to decrease the amount of stress individuals perceive. By measuring the parameters reflecting stress and feeding these back to the individual, the brain should learn that some behaviours or thoughts are rewarding and therefore should be executed more often. Studies showed that this procedure works in decreasing the amount of stress in healthy people and PTSD patients. Biofeedback also showed to change the activity of some brain regions. Especially the dorsolateral prefrontal, anterior cingulate and parietal cortices, amygdala and basal ganglia increase activation after biofeedback relaxation training sessions.

Neurofeedback is a special form of biofeedback and uses the EEG signal. The EEG signal consists of four main frequency bands, namely delta, theta, alpha and beta. Theta and alpha waves are related with relaxation and these waves are therefore often used in neurofeedback sessions aiming to increase relaxation. By feeding back the theta and alpha wave level in the EEG signal; the brain should learn how to permanently increase the amount of these waves. Studies showed that alpha theta neurofeedback training can increase relaxation, but a disadvantage is that these studies have a lot of limitations. In the future these limitations, such as a lack of control groups, have to be solved to get more powerful results. Based on the evidence provided by the current studies, biofeedback seems to be more effective in decreasing stress levels than neurofeedback.

Contents

Chapter 1: Stress

1.1 What is stress?

At present, stress is part of modern consciousness and a new explanation of the interaction of mankind with its environment (Viner, 1999). Stress has become an universal explanation for human behaviour and failure, and is often used by newspapers to explain diseases of civilization. These diseases may be caused by our current way of life, which becomes busier, causing a large pressure on many people. Not all people can deal with this pressure and become chronically stressed. Of the ten leading causes to death, stress is directly involved in four (cardiovascular disease, stroke, musculoskeletal disorders and suicide) and indirectly in three (cancer, chronic liver disease and lung disorders) (Miller & O'Callaghan, 2002). These facts indicate that stress is a major problem and methods have to be developed to solve this problem.

A century ago, stress as an explanation of the cause of several diseases was unknown. The concept of stress started to get a meaning after the discovery by Hans Seyle in 1935 of a phenomenon occurring in laboratory rats (Viner, 1999). After the rats were administered with overian and placental extracts, organ changes such as ulceration of the adrenal cortex and intestines occurred. Seyle believed that his experiments were contaminated and ceased work in despair. However, he mentioned that nature had non-specific healing powers. After some new experiments in which rats were injected with different agents, and the same disease pattern occurred, Seyle described a theory in which stress was the sum of all non-specifically induced changes in a biologic system (Viner, 1999). Until the 1970's researchers speculated about this theory and finally accepted it as a scientific element that should increase the understanding of the cause and prevention of diseases. At present, much more is known about stress and the implications of it at the human body. For example that stress is caused when homeostasis in the body becomes disrupted. Normally, hormonal, behavioural and autonomic adjustments are made to deal with external and internal stressors (Miller & O'Callaghan, 2002). The adjustments are made by body systems that respond to the body state, like sleeping, lying and standing, and to the external environment and promote adaptation to aversive stimuli and activities such as locomotion (McEwen, 1998). These body systems include the autonomic nervous system, the hypothalamo-pituitary-adrenal axis, the metabolic systems and the immune system. All these systems are closely coupled and its physiological responses lead to protection and adaptation to aversive and threatening challenges, a process called allostasis (Figure 1) (McEwen, 1998).

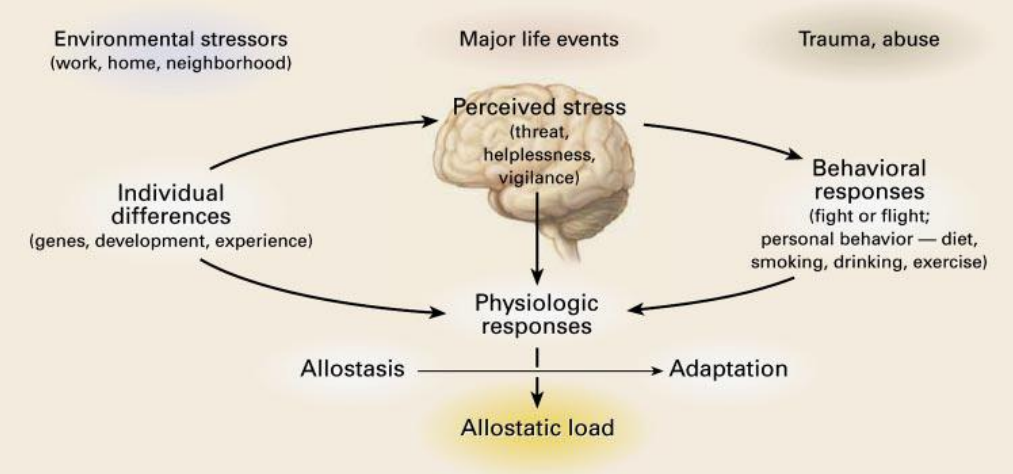

Figure 1. The effect of stressors (environmental, life events, trauma) on the physiological responses of the body. Individual differences determine the amount of perceived stress and the subsequent behavioural responses. These three parameters influence the physiologic responses. When allostasis is not able to successfully adapt the body to the stressor, the physiologic responses causes the occurence of allostatic load. This can eventually result in bodily changes that promote disease. From: McEwen, 2007

The response to a stressor can be divided into a real and anticipatory reaction and also differs per individual (Jankord & Herman, 2008; McEwen, 1998). A real stress response is a reaction to a real sensory stimulus, recognized by somatic, visceral or circumventricular sensory pathways. When these stressors occur, chemical mediators are released and increase heart rate, blood pressure, cause respiratory distress and visceral or somatic pain (Herman et al., 2003; McEwen, 2007). The release of these mediators facilitates the adaptation to the stressor.

An anticipatory reaction occurs when chemical mediators are released in the absence of a real stressor signalling homeostatic disruption (Jankord & Herman, 2008).This anticipatory response is often initiated by comparing a current environmental stimulus to innate programs. Examples are the presence of a predator or the recognition of danger associated with heights. Moreover, an anticipatory reaction can occur to learned stimuli, such as a previous experienced painful or threatening situation.

When a real or anticipatory stress response only occurs for a short time, the body can perfectly deal with it and the psychological burden is low. However, adaptation to an adversity has a price, and the cost of adaptation is called allostatic load (McEwen, 1998). McEwen (1998) defines allostatic load as the wear and tear on the body and brain resulting from chronic overactivity or inactivity of physiological systems that are normally involved in adaptation to environmental challenge. A high allostatic load therefore occurs when the body constantly has to cope with demands outside its operating range (Miller & O'Callaghan, 2002). This can eventually result in bodily changes that promote disease. In cases of high allostatic load, the individual is chronically stressed and its homeostasis is constantly disrupted.

1.2 The stress response

After homeostasis is disrupted by for instance an infection, social stress or emotional distress; a stress response involving the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system is initiated. The stress response can be divided into a relatively fast and slow response (Eriksen et al., 1999). The autonomic nervous system is involved in the quick stress response, while the HPA axis is particularly activated in the slow response.

The stress response originated in our earliest ancestors about 600 million years ago (Nesse & Young, 2000). Probably, these simple life forms only contained two states, activity and rest. This fundamental division is still present in our biochemical and nervous systems. For example, the biochemical pathways can be divided into a catabolic state, in which energy is used, and an anabolic state in which energy is stored and tissues are repaired. Parallel to this division are the two main parts of the autonomic nervous system. One part of the autonomic system increases blood pressure, heart rate, respiratory rate and physical activity, while the other part inhibits muscular activity, stores energy, and shunts blood to digestion and bodily repair (Nesse & Young, 2000).

1.2.1 The autonomic nervous system

The autonomic nervous system is one of the divisions of the stress response and actively involved in maintaining homeostasis and adaptation to stressful stimuli. It especially regulates visceral functions, primarily through interactions with the endocrine system and via autonomic reflexes (Shields, 1993). Autonomic reflexes become induced by sensory information from the viscera. This information, containing visceral function, goes to the autonomic nervous centres in the brain. These centres process and integrate the incoming information and send signals to the autonomic efferent system, which carries out the appropriate autonomic responses. Mainly, visceral function is changed by innervations of smooth muscle, cardiac muscle or glandular secretions (Shields, 1993). In this way, the autonomic nervous system represents the principal neural channels through which the brain and body interact, and therefore is able to quickly respond to changes in the internal environment of the body and maintain homeostasis.

The autonomic nervous system can be divided into three subdivisions, namely the parasympathetic, the sympathetic and the enteric nervous system (Benarroch, 2007; Jänig, 2006; Shields, 1993). All these nervous systems have their own function and affect the activity of the tissue they are directed to. The parasympathetic and sympathetic neurons innervating the target tissue lie mainly outside the central nervous system (Jänig, 2006). The cell bodies of these neurons form structures, called autonomic ganglia. The neurons running from the autonomic ganglia to the target tissue are postganglionic neurons (Benarroch, 2007). Sometimes these neurons are also called peripheral effector neurons. The neurons running from the brainstem or spinal cord towards the autonomic ganglia are called preganglionic neurons. The cell bodies of these neurons are located in the brain

stem or spinal cord. All communication between the preganglionic and postganglionic neurons is done by neurotransmitters. Preganglionic neurons often use acetylcholine, while most postganglionic neurons use noradrenaline for transmission of signals (Shields, 1993; Jänig, 2006).

To determine which postganglionic neurons were stimulated by which subdivision of the autonomic nervous system, researchers started experiments in which nerves were stimulated with an electric current. Other experiments blocked or removed a nerve to discover what its function was. Results of all examinations showed that most organs or tissues are more or less affected by both subdivisions of the autonomous nervous system (Figure 2) (Shields, 1993).

The postganglionic neurons of the sympathetic nervous system are located in the spinal cord (Shields, 1993). Each segment of the spinal cord contains efferent neurons which mostly innervate one particular organ. These neurons become especially active in stressful situations. The sympathetic nervous system is namely responsible for the maintenance of blood pressure, thermoregulation and cardiovascular and metabolic responses in stressful situations (Benarroch, 2007). Sympathetic nerves cause constriction of the blood vessels in the arteries of the heart, skeletal muscle, kidneys, skin and salivary glands. Furthermore, it de-

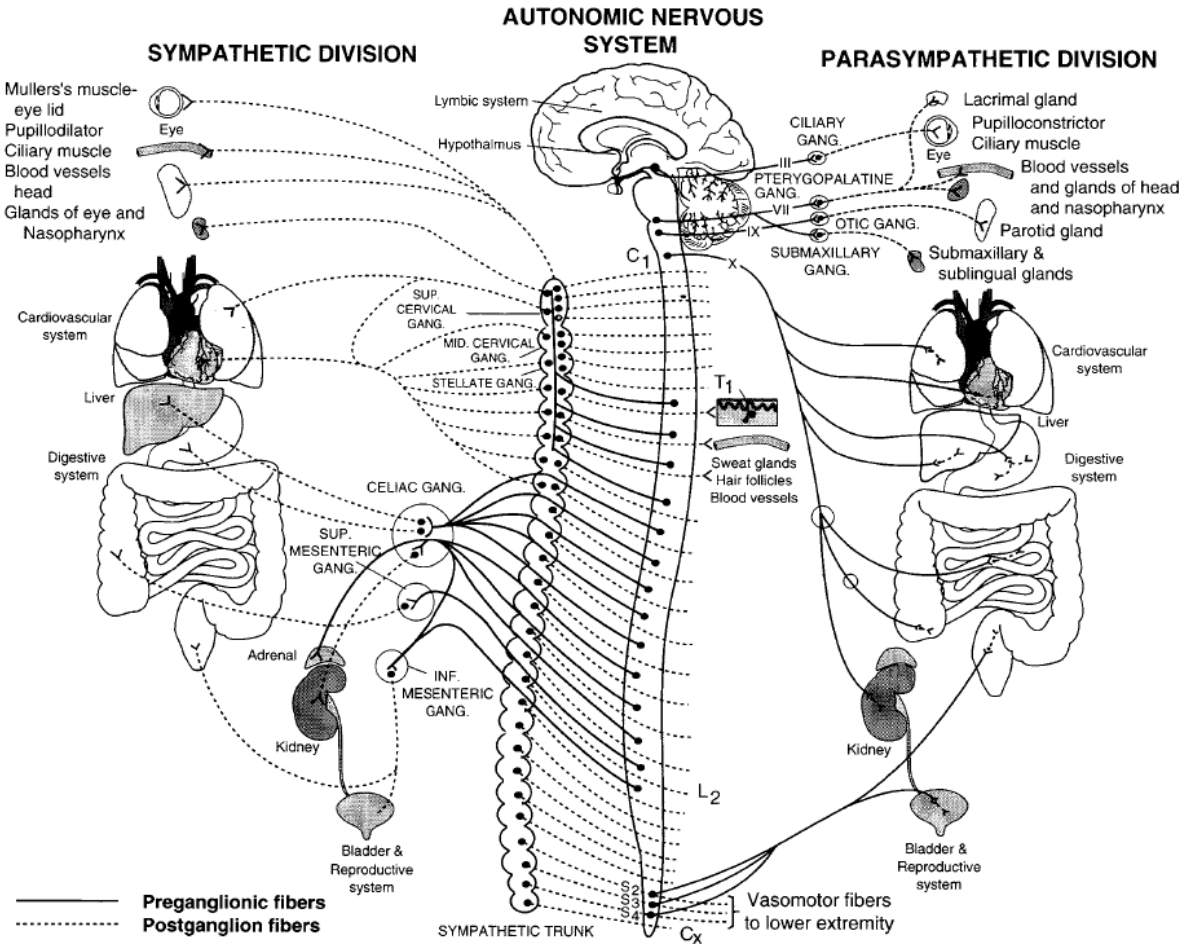

Figure 2. The autonomic nervous system with the sympathetic and parasympathetic division. Only the efferent part of both divisions is shown here. The sympathetic division contains larger postganglionic fibres than the parasympathetic division. From: Shields (1993)

creases the motility of the muscles in the intestine and causes the digestive glands to decrease their secretion. It also induces the contraction of the bladder and pupil of the eye (Jänig, 2006). All these physiological changes are executed to prepare the body for action, which is often needed in emergency situations (Critchley, 2009). Another function of the sympathetic nervous system is to activate the adrenal medulla to produce norepinephrine and epinephrine. These hormones cause an increase in blood pressure and heart rate and also a raised blood flow to the skeletal muscles (Shields, 1993). The muscles therefore, receive more oxygen and energy so that it takes a longer time before they become exhausted.

People who are chronically stressed constantly trigger the sympathetic nervous system, and as a consequence, have high levels of epinephrine in their blood. After some time, the body becomes exhausted and the effects of epinephrine can become problematic. One of such problems is the suppression of the immune system by epinephrine. Chronically stressed people constantly suppress the immune system, and as a result, they often suffer from diseases.

To examine which brain structures are active during the activation of the sympathetic nervous system, a functional magnetic resonance imaging (fMRI) study was executed (Critchley, 2009). Healthy subjects were placed in a scanner and had to make mental calculations which were made too complicated. As a consequence, subjects gave a lot of wrong answers. To make subjects even more aroused, they were told that they were performing very badly compared with other subjects of their age. Results showed that activity within the dorsal anterior cingulate cortex (ACC) correlated with an increase in blood pressure. This finding showed that the dorsal ACC is probably involved in generating sympathetic neural responses.

The parasympathetic nervous system has the opposite effect of the sympathetic nervous system. It is mainly active when the body is at rest or at least not aroused. Unlike the sympathetic nervous system, the cell bodies of the efferent parasympathetic system are situated in the neighbourhood of the target organ (Shields, 1993). This results in relatively long preganglionic nerves and short postganglionic nerves. A preganglionic nerve that is involved in relaying the signals from the central nervous system to the ganglia is the vagus nerve (Benarroch, 2007; Shields, 1993). This nerve runs from the brainstem to the thorax and abdomen. The vagus nerve innervates the heart, pancreas, liver, kidney and secretion of digestive enzymes in the gastrointestinal tract (Shields, 1993). It also innervates the exocrine glands of the head, neck and thorax. Moreover, the vagus nerve innervates smooth muscles of the organs and induces bronchial gland secretion (Jänig, 2006). Other nerves of the parasympathetic nervous system relax the arteries of the skin and intracranial tissues. Furthermore, postganglionic nerves innervate the rectum, bladder and sexual organs (Shields, 1993). Gastric relaxation is also induced by the parasympathetic nervous system. This is to make the body prepared for a meal so that new energy can be taken up.

The last division of the autonomic nervous system is the enteric nervous system. It is composed of several types of sensory neurons, interneurons and motor neurons (Benarroch, 2007). The neurons of the enteric nervous system are primarily located in the wall of the gastrointestinal tract (Shields, 1993). They form relatively independent of the parasympathetic and sympathetic nervous system, local reflex circuits that regulate the motility, secretion and blood flow throughout the gut. Although these reflexes are mainly regulated by the enteric nervous system, the vagus nerve is also able to regulate the activity of the gut (Benarroch, 2007).

1.2.2 The HPA axis

The HPA axis is the second division of the stress response and it works slower than the autonomic nervous system. It is probably the major stress hormonal axis in the body and consists of the hypothalamus, the anterior lobe of the pituitary gland and the adrenal cortices (Pruessner et al., 2009). Each of these structures releases its own hormone and the hormone produced by the hypothalamus initiates the stress response (Figure 3). Corticotropin-releasing hormone (CRH) is synthesized by the paraventricular nucleus (PVN) of the hypothalamus (Herman et al., 2005). After production, CRH is released via an inferior boundary of the hypothalamus, the median eminence, into the blood (Miller & O' Callaghan, 2002). Other mammals and even non-mammalian species show the same production pattern (Denver, 2009). This conserved distribution pattern suggests ancient origins and strong selective forces against mutations that change the sequence of the genes coding for CRH. By contrast, the receptors underwent muta-

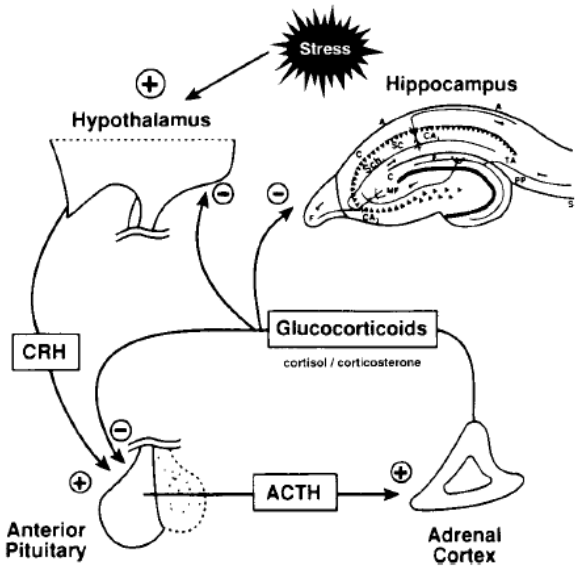

Figure 3. Brain structures and hormones involved in the stress response. Stress acts on the hypothalamus, which secretes CRH. CRH causes the secretion of ACTH in the anterior pituitary. ACTH causes the production of glucocorticoids which inhibit the hypothalamus, anterior pituitary and hippocampus. From: Miller & O' Callaghan 2002.

tions leading to a differentiation of different classes of receptors in target tissues and as a consequence, a specialized response of that tissue to CRH (Nesse & Young, 2000).

In the anterior pituitary, CRH and a co-expressed peptide arginine vasopressin (AVP) cause the secretion of adrenocorticotropic hormone (ACTH) (Herman et al., 2003). Peptide sequences very similar to human ACTH are not only found in mammals, but also in amphibians, reptiles, insects, mollusks and marine worms (Nesse & Young, 2000). The presence of ACTH in simpler life forms indicates that like CRH, ACTH has been conserved over hundreds millions of years. At the level of the hypothalamus, ACTH causes a decrease in the CRH production through negative feedback (Miller & O'Callaghan, 2002). Negative feedback consists of reducing the output of an organ or system back to its normal range. Considering this case, ACTH cause production of glucocorticoids, which indirectly reduce ACTH levels by inhibiting CRH production in the hypothalamus and directly reduce it by inhibiting ACTH production in the anterior pituitary (Figure 3). The negative feedback ultimately results in a suppression of ACTH and the end of the stress response. Except down regulating the stress response, ACTH acts on the adrenal cortex, which produces glucocorticoids, mineralocortocoids and adrenal androgens. In unstressed conditions, glucocorticoid secretion follows a daily rhythm with the highest levels at the waking phase (Herman et al., 2005). However, in stressful situations the glucocorticoid level in the blood can be much higher.

When glucocorticoids are released into the blood, they bind to specific receptors found in every nucleated cell (Miller & O' Callaghan, 2002; Herman et al., 2003). Binding to these cells causes suppression of the innate immunity of the immune organs, inhibition of bone and muscle growth, suppression of reproductive function, behavioural depression and most important, elevation of the glucose level in the blood (Herman et al., 2003). This is of importance, because stressful situations often require a lot of energy. People who do not have an adequate amount of glucocorticoids in emergency situations, for example due to an adrenal insufficiency, can suffer from confusion, lethargy, circulatory collapse and even death. An excess of glucocorticoids in the blood is also not optimal, but less threatening than an insufficiency. People with extreme glucocorticoid levels suffer from adiposity or metabolic problems (Miller & O' Callaghan 2002).

1.3 Brain structures involved in HPA axis regulation

Except hormones, also brain structures are involved in the regulation of HPA axis activity. The hippocampus is a limbic structure, positioned in the medial part of the temporal lobe. Next to the hippocampus are the enthorhinal and perirhinal cortex and the parahippocampal cortex situated (Pruessner et al., 2009). The hippocampus has a high number of mineralocorticoid and glucocorticoid receptors, and exerts negative feedback on HPA axis activity after stress

(Pruessner et al., 2009). Results of studies showed that the hippocampus also plays a tonic inhibitory influence on HPA axis activity. People with hippocampal lesions miss this inhibitory effect and show elevated basal glucocorticoid levels (Jankord & Herman, 2008; Herman et al., 2005; Herman et al., 2003). Studies showed that extreme glucocorticoid levels, caused by chronic stress, can change the morphology and functional reliability of the hippocampus (Pruessner et al., 2009). This can result in problems with memory consolidation and retrieval, since the hippocampus is involved in memory and learning processes.

Studies also showed a relationship between behaviour, HPA axis activity and hippocampus volume (Pruessner et al., 2009). People low in self-esteem often live solitary or withdrawn themselves of social activities. It is known that these people have a higher glucocorticoid stress response to stimuli compared with people with high self-esteem. Moreover, unlike most people, they fail to habituate to a stressor that is repeated over and over again. An experiment demonstrated that only people with low self-esteem showed a significant glucocorticoid release to a stressful task (Pruessner et al., 2009). Furthermore, a significant positive correlation was found between the level of self-esteem and hippocampus volume. So, people with low-levels of self-esteem had higher HPA axis activity, probably causing a decrease in hippocampus volume.

The hippocampus is not the only brain structure involved in HPA-axis regulation. Also limbic structures such as the prefrontal cortex, with the anterior cingulate cortex as a regulatory structure, and the amygdala play a role in the regulation of HPA axis activity (Herman et al., 2003; Jankord & Herman, 2008; Puessner et al., 2009). Considering the prefrontal cortex, it is especially the medial part that reacts to stressful stimuli. After acute or chronic stress, the release of the neurotransmitter dopamine, a precursor of the hormone adrenaline, is increased in this region. Like the hippocampus, the medial prefrontal cortex inhibits the HPA axis response. Lesions in the dorsal part of the medial prefrontal cortex showed that ACTH and corticoid levels are enhanced, due to a decreased HPA inhibition (Herman et al., 2003).

The amygdala consists of a group of nuclei located in the medial temporal lobe. In contrast to the hippocampus and the medial prefrontal cortex, it seems to activate the HPA axis. Electrical stimulation of the amygdala in rats, rabbits and monkeys showed an increased corticosteroid production (Jankord & Herman, 2008). In humans, stimulation of the amygdala results in a higher ACTH secretion (Herman et al., 2003). Eventually, this also leads to a higher corticosteroid level in the blood. On the other hand, a lesion in the amygdala causes a decrease of ACTH and consequently glucocorticoid level. Another effect of the amygdala that is related to the activity of the HPA axis is the activation of autonomic responses, such as an increase in heart rate, blood pressure and respiration frequency (Herman et al., 2005). The involvement of the amygdala in these autonomic responses demonstrates that this brain structure is part of the central autonomic network.

1.4 Which biological parameters reflect stress in the body?

From the above it became clear that the stress response involves two systems, the autonomic nervous system and the HPA axis. Evidence suggests that both systems originated a few hundred million years ago in our earliest ancestors (Nesse & Young, 2000). Throughout the years, both systems remained almost unaffected and retained their distinct function. The autonomic nervous system is involved in the fast stress response that is initiated when immediate action is required. This system was very important for our ancestors because danger could come at any time (Nesse & Young, 2000). For example, when a predator suddenly appeared is was important to run away immediately. The adrenaline provided by the sympathetic division of the autonomic nervous system enabled quick action and a higher survival rate. However, adrenaline is short lasting (Eriksen et al., 1999) and for situations that require a longer period of increased vigilance, another system was needed. The HPA axis is the slower system of the stress response. After a cascade, it eventually causes the release of the hormone cortisol. The HPA axis system is designed to prepare the body for action (Nesse & Young, 2000). This is useful in situations in which action may be needed in the short time. Examples are when a predator is spotted but not forms an immediate threatening situation, when food reserves are depleted and no other food is available or when an athlete knows that he has to run in a few moments. In contrary to adrenaline, cortisol levels can be elevated for a long time.

The environment we live in is completely different from that of our ancestors. Despite this difference, the stress system is still the same. In the environment of our ancestors, probably more often physical stressors occurred (Nesse & Young, 2000; Chrousos, 2009). Their body reacted on these stressors with the release of the short lasting adrenaline. On the contrary, the modern environment almost only contains social and mental stressors, resulting to a frequent stimulation of the HPA axis. Perhaps this frequent or long lasting stimulation may yield net costs and the stress-related diseases and disorders that occur today. Examples of stress related disorders are post traumatic stress disorder (PTSD) and anxiety disorders, such as phobic anxiety and panic attacks. People with phobic anxiety only become stressed when they really perceive the stimulus they are afraid for. This could be classified as a fear disorder, and most probably only activates the autonomic nervous system, so that a quick response is possible. However, generalized anxiety is the prototype of an anxiety disorder and activates the HPA axis. On the other hand, PTSD is a mixture of a fear and anxiety disorder (Grillon, 2008). PTSD patients not only show conditioned fear responses to discrete cues that act as a reminder of the trauma, but also exhibit persistent symptoms of sustained anxiety. In PTSD patients, both stress systems become activated. By diminishing the activation of the involved stress system(s), the disorders may be cured. One of the ways to diminish the activation of the

Table 1. Some biological parameters that change during arousal as an effect of the stress response. EDA = electrodermal activity. HRV = heart rate variability.

Biological parameter	Change during arousal/stress response
EDA	EDA increases
HRV	increase in heart rate → decrease in interbeat interval
Blood pressure	Higher blood pressure
Respiration	Respiration rate increases

stress system is by biofeedback and neurofeedback. The exact procedures will be discussed in chapter two and three, but to start with bio- and neurofeedback it is of importance to first find parameters that define stress levels in the human body.

From the outside it is difficult to determine whether people are stressed or not. And when they say they are stressed, it is difficult to examine how stressed they really are. Several biological parameters change during stress and can be used to determine the level of arousal (Table 1). Body changes that occur during the stress response cause this parameter change. In modern times, this is often a chronically elevated cortisol level, but an increased level of adrenaline can also cause a parameter change. By giving the individual information about its changed parameters, it learns how such a state feels like. After practising how the parameters can be shifted back to normal, the individual's stress response including HPA axis activity should be lowered again.

One of the parameters that can give information about the level of arousal is electrodermal activity (EDA) (Critchley, 2002, 2009). It is measured at the skin and represents an autonomic measure that reflects sympathetic neural responses, without that it becomes disturbed by parasympathetic activity or circulating hormonal factors, such as adrenaline. When people become aroused, the sympathetic nervous system causes the sweat glands to excrete. The excreted sweat modulates the conductance of the skin current.

There are slow and fast changes in skin conductance (Critchley, 2002). Slow shifts in skin conductance are measured by the skin conductance level (SCL), while relatively fast shifts are measured by the skin conductance response (SCR) or the galvanic skin response (GSR). The EDA includes both the slow and fast shifts of skin conductance.

In humans, sweating is also used for thermoregulation and a reaction to emotional stimuli. Therefore, the EDA is sometimes used to measure emotional arousal (Critchley et al., 2001). EDA responses are easily induced by threatening stimuli, such as a loud noise or scary pictures. Before the stimulus, the EDA level shifts around a horizontal baseline. After the stimulus, the EDA increases to a much higher level indicating that the subject became aroused by the stimulus (Critchley, 2002). The higher the EDA, the more the subject becomes aroused.

The EDA response seen after a stressful stimulus is initiated by activity of several brain regions. Research showed that direct electrical stimulation of the cingulate, lateral prefrontal cortex, medial temporal lobe including the amygdala and hippocampus, and the middle temporal gyrus affects the EDA (Critchley 2002). Lesions in the lateral, ventral and medial prefrontal cortex, anterior cingulate and right parietal lobe result in a decreased EDA response (Critchley, 2002). Furthermore, it seems that the right hemisphere influences EDA the most, because damage to the right hemisphere has a larger influence on the EDA response than when the left hemisphere is damaged. Taken together, these results show that EDA is correlated with sympathetic arousal and that some brain regions are involved in regulating sympathetic arousal and thereby also regulate the skin conductance. In this way, EDA can be used to measure the individual's level of arousal.

Another parameter that is sometimes used to reflect arousal level is heart rate variability (HRV). The clinical relevance of HRV was discovered in 1965 when researchers noticed that alternations in interbeat intervals predicted fetal distress (Malik, 1996). Normally, the heart beats at a regular interval. One heart beat is characterized by a kind of waveform, called the QRS complex (Figure 4). This

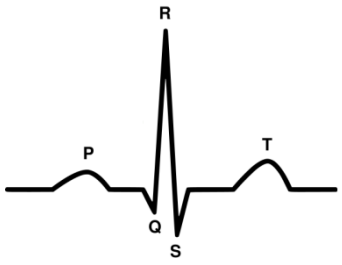

Figure 4. A schematic representation of a normal heart beat. The QRS complex is the highest peak and it is preceded by a P wave and followed by a T wave.

QRS complex is preceded by a P wave and followed by a T wave. The P wave represents the depolarization of the atria. After this depolarization, the ventricles become depolarized. This is represented by the QRS complex and because the ventricles contain more muscle than the atria, the QRS wave is larger than the P wave. The T wave following the QRS complex corresponds to the recovery of the ventricles. After the T wave, a new heart beat can occur.

HRV makes use of the time between two heart beats. Mostly, the time between two R peaks is used to calculate the interbeat interval (Malik, 1996; Ahuja et al., 2003). This interbeat interval changes during stressful situations because the heart is innervated by the sympathetic and parasympathetic nervous system. During aroused situations, activity of the sympathetic nervous system results in an increase in heart rate. This increase in heart rate is reflected in a shorter interbeat interval and therefore affects the HRV. In this manner, aroused people have a lower HRV than people who are in autonomic homeostasis (Zucker et al., 2009).

The blood pressure level can also be used to get an idea of how stressed people are. When someone is aroused, the sympathetic nervous system causes the blood vessels to constrain. This results in a higher blood pressure. During periods of acute stress, the systolic blood pressure raises more rapidly than the diastolic blood pressure (Noble, 2002). However, the effect of chronic stress on blood pressure is less obvious, primarily because there is an adaptation of the blood pressure controlling systems. Despite this adaption during chronic stress, blood pressure is often used an indicator of how stressed a person is.

1.5 Summary

A lot of people suffer from stress related problems, perhaps caused by an inability to pursue all goals they committed their selves at once. Stress causes a disruption of homeostasis and after the body noticed this, a stress response is initiated. The stress response consists of a relatively fast autonomic reaction and a slower HPA axis response. The autonomic nervous system is divided into three divisions and the sympathetic system becomes more activated during stressful situations. This result in a lot of physiological changes, including constriction of blood vessels, suppression of the immune system and an increase in blood pressure and heart rate. It also leads to the release of adrenaline and the ability to undertake action very quickly. The HPA axis response produces cortisol that last longer than adrenaline. Several brain structures are involved in the regulation of the HPA axis. These are the hippocampus, prefrontal cortex and amygdala. To measure the effect of stress on the body, several biological parameters can be used. These parameters measure and reflect the amount of the stress or arousal in the body. Examples are the electrodermal activity of the skin, heart rate variability and blood pressure.

Chapter 2: Biofeedback

2.1 What is biofeedback?

Most people unconsciously perceive and control their heart rate, muscle activity or respiration. Through biofeedback people can become aware of these psychological functions (Heinrich et al., 2007). Biofeedback requires a form of learning, called operant conditioning. Operant conditioning became a well-known way of learning after the experiments done by Skinner (Demos, 2005). Skinner trained rats to press a lever to obtain food. In this way, the rats learned that certain behaviour was reinforcing. In humans, thoughts, feelings and physiological responses are consequences of behaviours (Schwartz & Andrasik, 2003).

For a long time, people thought that only the central nervous system, consisting of brain and spinal cord, was influenced by operant conditioning. The idea was that the autonomic nervous system functioned automatically without any voluntarily control (Moravec, 2008). However in the 1970s, the first researchers published results that individuals could get voluntarily control over several autonomic functions without that it could be attributed by cognitive factors (Schwartz & Andrasik, 2003). These autonomic functions were blood pressure, GSR and cardiac rates and rhythms. By making subjects aware of these autonomic functions, they were able to increase the perception of their subject's own visceral responses.

An increased perception of the psychological functions of the body is actually one of the goals of biofeedback. The main purpose is that people, after some biofeedback training sessions, are able to self regulate the psychological process that had to be trained (Yucha & Gilbert, 2004). A biofeedback training session starts with the attachment of sensors to the subject. These sensors constantly measure the body's autonomic responses. Most of the time, the measured autonomic responses are converted into visual or acoustic signals which are fed back in real time (Heinrich et al., 2007). This makes it easier for the subject to interpret the data. The feedback given to the subject is always positive. For example, when the subject achieves a relaxed state, indicated by a low heart rate and blood pressure, it receives a reward in the form of a sound, or the level of a bar that is presented on a computer screen increases. In this way, the brain should learn that some behaviours or thoughts are rewarding and therefore should be executed more often.

The amount of biofeedback training sessions that a person needs to alter its psychological responses differs per situation (Yucha & Gilbert, 2004). For instance, an individual with urinary incontinence may only need a few sessions,

while a person with attention deficit disorder may require fifty sessions before improvement is seen.

Nowadays, biofeedback is more and more often used in the treatment of disorders. Examples are headache, hypertension, attention disorders, anxiety, asthma, cardiovascular disorders and duodenal ulcers (Conde Pastor et al., 2008; Horowitz 2006). Biofeedback is used by physicians, nurses, psychologists, counsellors, physical therapists and occupational therapists (Yucha & Gilbert, 2004). Some people favour biofeedback over a medical intervention, while others undergo biofeedback sessions as a last resort.

2.2 How can biofeedback be used to reduce the amount of stress?

Now stress plays an increasing role in our modern society, the regulation of it has become a topic in biofeedback research. Today, several scientific studies are executed to determine the effect of biofeedback in stress regulation. Chronic stress is caused by a constant activity of the HPA axis and/or the autonomic nervous system. Most biofeedback therapies aim to decrease the activity of these systems by making people aware of their heart rate, blood pressure or respiration. Other studies make use of the EDA.

2.2.1 EDA

An example of a study using EDA for biofeedback applications is the study by Critchley et al. (2001). This study used EDA measurements to examine the influence of cognitive intent on sympathetic relaxation. Normally, the peak in EDA differs per person and per situation. If the measurements are taken in a hot environment, the results will be different from EDA measurements that are administered under cold conditions. Another problem is that most people show a decreased response after the stimulus is repeated a few times. This is a normal habituation response. To use EDA for biofeedback sessions, these problems have to be overcome. Eventually, it was solved by providing an objective quantitative measure in the form of latency, or rate of decreasing sympathetic tone (Critchley et al. 2001). These quantitative measurements are independent of the differences in the amplitude of the responses.

In the experiment of Critchley et al. (2001) subjects had to watch a thermometer of which the height indicated the EDA. As the subject became more relaxed, its EDA level decreased and the level of the thermometer dropped. However, in some experimental tasks the thermometer did not show the subject's EDA. There were four different task conditions in total. In the first task, subjects got the instruction to bring the level of the thermometer down as low as possible. This could be achieved by relaxation. The second task required the participants not to relax and prevent a downward drift of the thermometer. The third and fourth tasks were control conditions. In these tasks, the thermometer did not show the subject's EDA but fluctuated randomly. In the third task, sub-

jects received the instruction to relax, while the fourth task required subjects not to relax.

During the tasks subjects were scanned in a magnetic resonance imaging (MRI) scanner. In this way, the researchers were able to measure which brain areas were active in every task condition. Comparing the relaxation tasks with the non-relaxation tasks showed some differences in brain activity. A significant increase in activity was seen in the left anterior cingulate and the globus pallidus. These regions are associated with intentional relaxation (Critchley et al., 2001). The left anterior cingulate is also especially involved in autonomic responses. Enhanced relaxation related activity was also seen in the inferior parietal lobule (Critchley et al., 2001). Furthermore, there was an increased activity in the cerebellar vermis and the anterior/medial prefrontal cortex when the influence of biofeedback on intentional relaxation was examined. As mentioned in chapter one, the prefrontal cortex is involved in inhibiting the HPA axis response. The higher activation of the prefrontal cortex probably shows that people become more relaxed during the biofeedback sessions. This would indicate that EDA biofeedback can decrease sympathetic arousal and support people in becoming less stressed.

Another study that used EDA to examine the distributed network of brain areas supporting the volitional regulation of autonomic states is a study done by Critchley et al. (2002). This study also represented the EDA by a thermometer and subjects had to decrease the level of the thermometer as much as possible. The study consisted of four different biofeedback tasks in which sometimes the accuracy and/or the sensitivity of the thermometer were manipulated. The thermometer was not manipulated in the first task and a decrease of factor one in EDA corresponded to a decrease of one on the thermometer scale. However, in the third and fourth task, a decrease of factor two in EDA corresponded to a factor one decrease on the thermometer. In the second and fourth task, the accuracy of the thermometer was manipulated. The hypothesis was that by manipulating the thermometer different brain regions would be activated. Results of the study showed that subjects had more difficulty with relaxing when the accuracy or sensitivity of the thermometer was manipulated. The discrepancy between the visual information of the thermometer and the internal representations of bodily arousal that is caused by the manipulation impaired cognitively driven modulation of the EDA (Critchley et al., 2002). Subjects were scanned during the tasks and results demonstrated that during the manipulated accuracy tasks, insula, amygdala and cingulate showed enhanced activity. This is probably caused by a conflict between representations of internal state and external indications of arousal (Critchley et al., 2001). However, during the sensitivity tasks not a significant effect in brain activity was seen.

Results of the study also showed an association between biofeedback relaxation and an increase in activity of several brain regions such as dorsolateral prefrontal, anterior cingulate and parietal cortices, amygdala and basal ganglia. These brain structures probably regulate the integration of the intention to relax

and the corresponding body responses. The study also found a clear indication that the activity of the pons, thalamus and above mentioned brain areas, except the amygdala, was negatively correlated with the EDA. In other words, a decrease in sympathetic arousal, reflected by the EDA, resulted in an increased activity of these brain areas. It is known that being exposed to a stressor results in a deactivation of specific parts of the limbic system (Pruessner et al., 2009). If the same correlation counts for other brain regions, the negative correlation found by Critchley et al. (2002), probably indicates that due to biofeedback, the activity of some brain areas increases, resulting in a decrease of sympathetic arousal. Another indication for this correlation is that Critchley et al. (2002) found no brain areas that showed a decreased activity when EDA decreased. This probably demonstrates that by giving people EDA biofeedback, sympathetic arousal decreases and brain activity changes.

Except EDA, some studies use SCL as a parameter reflecting sympathetic arousal. One of such studies is a study executed by Nagai et al. (2004). They used a biofeedback setting to determine which brain structures are associated with biofeedback relaxation and biofeedback arousal. SCL of subjects was continuously measured and it was represented by a visual display of horizontal lines. These lines moved downwards to reflect changes in skin conductance in the direction intended by the task. If the skin conductance did not change in the intended direction, the lines remained static. In the biofeedback relaxation task, subjects received the instruction to attempt to move the horizontal lines in a downward direction by relaxing their mind and body. In the biofeedback arousal task, similar instructions were given, only in this task subjects had to block relaxation by mental alertness. During the tasks, subjects were scanned in a MRI scanner so that afterwards, shifts in neural activity could be calculated. Results showed that almost all subjects could decrease their SCL during the relaxation task. The biofeedback arousal task showed more distributed results, but all subjects demonstrated substantial periods of ramping of SCL arousal over the course of the experiment. Brain regions correlated with a decrease in SCL in both relaxation and arousal tasks were the ventral medial prefrontal cortex (VMPFC) and the orbitofrontal cortex (OFC). These structures showed an increased activity when SCL decreased, suggesting a task-independent representation of autonomic state. This is further supported by the fact that the VMPFC and OFC are closely connected to homeostatic control centres within hypothalamus and brain stem, mediating a default homeostatic state of brain activity. In contrast with above brain regions, activity relating to increases in SCL was observed in distributed cortical and subcortical areas. This activity is probably caused by the recruitment of volitional motor circuitry that directly influences peripheral sympathetic arousal (Nagai et al., 2004). Rapid changes in SCL were observed in anterior cingulate and insular cortices, thalamus, hypothalamus and lateral regions of prefrontal cortex and anterior striate and extrastriate visual cortices. An increased activity in some of these regions was also found by Critchley et al. (2002).

Brain regions that demonstrated enhanced brain activity during both tasks included the left mid-OFC and the right-parieto-occipital junction. An increased OFC activity is related with the presence of rewarding stimuli. This could mean that an increased mid-OFC activity may mediate self generating reward, serving to reinforce behaviour combining the external influence of biofeedback, the accompanying internal representation of autonomic arousal state, and the cognitive representation of it.

To conclude, EDA and SCL biofeedback can enhance relaxation and affect activity of several brain regions. By repeating these biofeedback training sessions a several times, brain activity may be altered for a long time.

2.2.2 HRV Biofeedback

A second application of biofeedback is heart rate variability biofeedback. HRV biofeedback aims to increase and strengthen one of the body's most important reflexes, namely the baroreflex (Lehrer & Vaschillo, 2003). The baroreflex is a homeostatic reflex that makes part of a complex system controlling blood pressure. It is regulated by stretch receptors in the aorta and carotid arteries. These stretch receptors cause a decrease in heart rate and vasodilatation when the blood pressure increases, and the opposite when blood pressure decreases. The process of vasodilatation, vasoconstriction and increases or decreases in heart rate produces an oscillatory rhythm in heart rate, vascular tone and blood pressure. This rhythm oscillates with about 0.1 Hz in heart rate and 0.03 Hz in vascular tone (Lehrer & Vaschillo, 2003).

Some decades ago, the rhythmical oscillations were viewed as noise, but today it is seen as a measure of autonomic activity and of parasympathetic and sympathetic balance. This knowledge is used in the application of heart rate biofeedback. Heart rate variability biofeedback elicits high amplitude oscillations in cardiovascular functions, and thereby stimulates the baroreflex (Vaschillo et al., 2006). By improving the regulative function of this reflex, the balance between the parasympathetic and sympathetic nervous system becomes more tightly regulated, and when the autonomic balance is disturbed, it will be restored again. The baroreflex can most easily be stimulated by breathing at the heart rate oscillation frequency of 0.1 Hz (Vaschillo et al., 2006). Respiration is associated with heart rate oscillations; inhalation causes an increase, while exhalation causes a decrease. This phenomenon is known as respiration sinus arrhythmia (RSA). However, in most people, the heart rate oscillations do not occur in phase with the respiration. This can only be achieved by breathing at the resonance frequency of the heart, which is about six breaths per minute and much slower than the average breathing rate of 12-20 breaths per minute (Lehrer & Vaschillo, 2003). The danger of this slow breathing rhythm is that people begin to hyperventilate and thereby disturb the cardiovascular regulation (Vaschillo et al., 2006). To prevent hyperventilation, it is important that people do not breathe too deeply.

A study of Lehrer et al. (2003) showed that breathing at the heart's resonance frequency has indeed some effect. The study made use of healthy people who were taught to breathe at their individual resonant frequency and a control group. Their blood pressure, heart rate and respiration were monitored during ten biofeedback sessions. Results of the study showed that the biofeedback group was able to increase both the heart rate variability and baroreflex gain. This gain is calculated as the change in heart period per unit change in blood pressure (Lehrer & Vaschillo, 2003). The study of Lehrer et al. (2003) showed that after biofeedback, healthy people can chronically increase baroreflex gain without being depended on breathing rate and volume. This means that biofeedback can change the baroreflex, perhaps by changing its modulatory systems higher in the brain. It is known that the hypothalamus is involved in mediating the baroreflex gain. A decrease in baroreflex gain is often correlated with diseases, ranging from cardiovascular diseases to hypertension and anxiety (Lehrer et al., 2003; Lehrer & Vaschillo, 2003). Hypertension and cardiovascular diseases can be caused by stress. If people suffering from these diseases are also able to increase their baroreflex gain through biofeedback, it becomes a useful tool to reduce the symptoms of these diseases and eventually decrease the amount of stress. To conclude, there is evidence that HRV biofeedback can change the baroreflex gain, which restores the balance between parasympathetic and sympathetic activity, and that this restored autonomic balance may reduce the amount of stress.

HRV biofeedback is also used to treat posttraumatic stress disorder (PTSD). PTSD is an often chronic, psychiatric disorder that is characterized by an intense response of fear or helplessness to trauma exposure (Zucker et al., 2009). The intense response is caused by a set of biological modifications found in patients with PTSD (Yehuda, 2001). These modifications primarily involve the HPA axis. The HPA axis becomes highly sensitized in PTSD patients and eventually cortisol levels are decreased. Furthermore, chronic CRH release leads to an altered responsiveness of the pituitary gland, as is more often seen in patients with anxiety disorders. Patients with PTSD also have a higher level of glucocorticoid receptors. This results in an enhanced negative feedback inhibition of the hippocampus, hypothalamus and pituitary, with low cortisol levels and an attenuated baseline ACTH as a consequence (Yehuda, 2001). These modifications lead to a heightened response to stress, and symptoms of increased startle and physiologic arousal (hyperarousal). Except hyperarousal, PTSD patients also suffer from intrusive re-experiencing and maladaptive avoidance of the trauma (Zucker et al., 2009).

An elevated heart rate is the most prominent autonomic feature of PTSD. A study found that two-third of a PTSD and non-PTSD patient sample could be classified according to their heart rate. Additionally, a recent study demonstrated that an elevated heart rate and respiratory rate may predict the onset of PTSD (Zucker et al., 2009). Furthermore, some studies have found a significant association between PTSD and low heart rate variability. The purpose of a study of Zucker et al. (2009) was to discover whether respiration sinus arrhythmia (RSA)

biofeedback could increase HRV and thereby reduce PTSD symptoms. They compared the effectiveness of RSA biofeedback with guided progressive muscle relaxation (PMR).

Results of the study showed that the RSA biofeedback group had a significant greater reduction in depression scores than the PMR group. However, both groups had a reduction in PTSD symptom severity. This means that PMR works, but that RSA biofeedback works better in decreasing PTSD symptoms. When HRV was taken into account, the RSA group showed an increased baseline HRV that was significantly higher within the normal range for healthy adults, relative to the PMR group. The increase in HRV was significantly associated with PTSD symptom reduction. This association would mean that RSA biofeedback helps to reduce the hyperarousal of which PTSD patients suffer. However, Zucker et al. (2009) argued that the increase in HRV was probably mediated by a decrease in resting respiration rate. This indicates that the patients learned to breathe slowly, as is proven successful in the HRV biofeedback protocol of Lehrer et al. (2003). So, perhaps a slow breathing rhythm is important to influence the heart rate variability and reduce the amount of stress. However, Zucker et al. (2009) demonstrated that on its own RSA biofeedback decreases PTSD symptoms.

2.2.3 Respiration

Respiration is one of the functions that can be regulated by biofeedback to achieve relaxation. Mostly, except the HRV biofeedback protocol of Lehrer et al. (2003), subjects are told to achieve a general state of relaxation and not how they should breathe. Conde Pastor et al. (2008) wanted to know whether subjects would gain higher relaxation levels in a biofeedback session when they were previously told how to breathe compared with a group that did not receive any instructions. To determine the subject's relaxation level, the skin conductance level (SCL) was continuously measured. From previous studies it was known that when the respiratory pattern was exactly three respiration frequencies below the baseline of the subjects, SCL was reduced the most (Conde Pastor et al., 2008). SCL was decreased even more when the exhalation time was longer than the inhalation time. Taken together, the respiratory pattern utilised by Conde Pastor et al. (2008) is different from that of Lehrer et al. (2003) because in the latter the respiration frequency is much lower than in the former. This difference is probably caused by the biological parameter that is used. Conde Pastor et al. (2008) make use of the SCL while Lehrer et al. (2003) use heart rate variability to reduce psychophysiological activation.

In the experiment of Conde Pastor et al. (2008) the control group received exact instructions how to breathe according to their optimal respiratory pattern. Red and blue screens on a computer screen indicated when they had to inhale or exhale. The control group also had a second monitor on which a series of lights reflected their SCL level. They had to decrease this level as much as possible. This was also the instruction, the experimental subjects received, however they only had the monitor with the lights. Before the biofeedback training started,

baseline respiration frequency and SCL were measured. Results of the study show that those individuals who had been given precise respiration instructions showed greater reductions in SCL than those who had not been given these instructions. This indicates that by giving exact respiration patterns, people can relax even more than with only the feedback of a biological parameter, such as SCL or heart rate. Therefore respiratory biofeedback can be used to reduce activation levels of individuals that are easily stressed or aroused. In combination with other feedback methods such as EDA biofeedback, respiration biofeedback may be even more effective.

2.2.4 Biofeedback and hypertension

Hypertension is often caused by chronic stress. Longitudinal studies of more than 3,000 Europeans showed that chronic stress for several years predicts high blood pressure in three to seven years of follow-up (Rainforth et al., 2007). For this reason, a lot of biofeedback research is done to reduce blood pressure and stress levels. However, until know the results of these biofeedback studies are not so promising. The studies are no more effective than drugs and compared to other relaxation methodologies, biofeedback does not have a higher relaxation rate (Linden & Mosely, 2006).

A study of Nakao et al. (2003) compared biofeedback treatment of hypertension with a control group that did not receive any treatment and a sham intervention group. The outcome of the study reported a significant effect in decreasing blood pressure for biofeedback compared with relaxation training, but not for biofeedback on its own. However, Nakao et al. (2003) concluded that biofeedback treatment is at least better than no treatment. Almost the same conclusion was found in a study of Yucha et al. (2005). This study combined RSA biofeedback, thermal feedback and electromyography (EMG) biofeedback with deep breathing and muscle relaxation. EMG biofeedback makes use of electrodes that measure muscle action potentials. These action potentials lead to muscle tension and by feeding this back to the subject, it can learn how muscle tension feels and reduce it. Yucha et al. (2005) showed that combined biofeedback and relaxation therapies can reduce systolic blood pressure in some people. However, it is not clear whether the combination of biofeedback and relaxation therapies caused this effect or that only one or two components of the therapies are responsible for the reduction is systolic blood pressure.

Despite a lot of research, it seems that biofeedback cannot decrease blood pressure more than other relaxation therapies or drugs. This indicates that biofeedback is not effective in the treatment of every disease related with stress. But biofeedback can be used to prevent hypertension, by applying biofeedback when the individual is stressed. By reducing the amount of stress, also the chance for hypertension to occur becomes reduced.

2.3 Summary

This chapter showed that people can better perceive their own psychological functions through biofeedback. By giving positive feedback about these psychological functions to the subject, the brain should learn that some behaviours or thoughts are rewarding and therefore should be executed more often. This principle is also used when biofeedback is applied to reduce the amount of stress in individuals. Several physiological functions can be regulated by biofeedback to achieve relaxation (Table 2). These functions are mainly regulated by the autonomic nervous system.

Table 2. Psychological functions of the human body that can be regulated by biofeedback. To decrease stress, the functions should be decreased in activity and to increase stress, the functions should increase activity.

Physiological function	Regulated by biofeedback to decrease stress level
Respiration	Decrease respiration rate to optimal individual respiratory pattern
Heart rate	Decrease heart rate
Blood pressure	Decrease systolic and diastolic blood pressure
Skin conductance	Decrease skin conductance reflected in EDA, SCR or GSR level

One application that proved to be effective is EDA biofeedback. Showing subjects their actual EDA leads to changed activities of some brain structures. Especially the activity of the dorsolateral prefrontal, anterior cingulate and parietal cortices, amygdala and basal ganglia changes when EDA changes. It seems that there is a correlation between the activity of these areas and EDA, namely when EDA decreases, the activity of these areas increases. Previous studies found that limbic areas of the brain showed a decreased activity when the body is exposed to a stressor. The above mentioned correlation would in that perspective mean that the increased activity of the brain areas indicate that the body became more relaxed and less stressed due to the biofeedback sessions.

Another biofeedback application that regulates stress is HRV biofeedback. HRV biofeedback elicits high amplitude oscillations in cardiovascular functions, and thereby stimulates the baroreflex. By improving this reflex, the autonomic nervous system becomes more tightly regulated, and when the autonomic balance is disturbed, it will be restored again. The baroreflex can be trained the best when people breathe with 6 breaths per minute. This is much slower than the normal 12-20 breaths per minute and the danger is that people begin to hyperventilate. However, when people breathe at the right pace, HRV biofeedback demonstrated to be effective. After some sessions, baroreflex gain increased and the balance between the sympathetic and parasympathetic nervous system became restored. So, when people have a hyperactive sympathetic nervous system, HRV biofeedback makes them relaxed again. This is actually what happens with

PTSD patients. They are hyper aroused and react strongly to stressors. However, by undergoing some RSA biofeedback sessions, PTSD symptoms reduced.

A third biofeedback application is respiration biofeedback. This form of feedback works better in combination with another kind of feedback, such as EDA feedback. By letting people breathe in a certain rhythm, their SCL decreases more than when they do not take respiration into account. So, maybe respiration rhythms are more important for relaxation than many people think. Anyhow, by getting feedback about the respiration it is possible to reduce stress levels.

Biofeedback can reduce stress through several applications. However, the possibilities of it are not unlimited. Hypertension is a disease that is often caused by stress. Researchers studied whether biofeedback could decrease blood pressure. Results of these studies showed that biofeedback is no more effective than other relaxation strategies or drugs. So, biofeedback cannot solve all stress-related problems.

Chapter 3: Neurofeedback

3.1 What is neurofeedback?

Neurofeedback is a special and sophisticated form of biofeedback. It is based on specific aspects of cortical activity (Vernon, 2005). Sometimes, neurofeedback is called electroencephalogram (EEG) biofeedback because it is based on the strength of the EEG signal.

3.1.1 The EEG signal

The EEG signal is first described in 1929 by the German psychiatrist Hans Berger who studied correlations between the intake of drugs and mental state (van den Bergh, 2007). Berger realized that if the pattern of oscillating activity recorded from the human scalp could be used to measure and define biological markers corresponding to human behaviour, the technique could prove to be useful diagnostically and therapeutically. Today, it seems that Berger's prediction was right, because the technique is used more and more often to treat people with diverse disorders.

Although the EEG signal is measured at the human scalp, the neurons that display oscillatory behaviour are located in the thalamus. The thalamus is one of the oldest structures of the brain and it constitutes the main part of the diencephalon. It relays signals between the cortex and multiple other brain areas (Cantor, 1999). The thalamic nuclei in the thalamus consist of three main types of neurons. The thalamo-cortical neurons (TCR) whose output is projected to the cortex, the reticular nucleus neurons (RE) that provides inhibitory feedback to the TCR neurons, and the local intrinsic neurons (Lopes da Silva, 1991). Both the TCR and RE neurons have the ability to show oscillatory behaviour. These oscillations can lead to spindle generation and eventually the typical oscillation pattern found during EEG recording.

3.1.2 Brain waves

Several oscillation frequencies can occur during an EEG recording. These oscillation frequencies are often called brain waves. There are four main categories of brain waves (Hammond, 2006). The alpha wave (8-12 Hz) was the first brain wave frequency to be discovered by Berger and was therefore called alpha, according to the first letter of the Greek alphabet. Subsequently discovered brain wave frequencies were also named to Greek letters, namely delta, theta and beta. Alpha waves are associated with a state of relaxation, but the brain is able to respond quickly when needed (Hammond, 2006; Cho et al., 2007). It appears

that alpha forms a bridge between the conscious and subconscious. When people close their eyes for a few seconds, their alpha activity already start to increase (Norris & Currieri, 1999). Alpha waves are generated in the parieto-occipital cortex and in the visual thalamus, particularly in the lateral geniculate nucleus (LGN) and the pulvinar. From these thalamic nuclei, the pulvinar appears to have the strongest influence on the alpha activity of the cortex (Lopes da Silva, 1991).

Delta waves are the slowest brain waves (0.5-4 Hz) with the highest amplitude and primarily occur during sleep (Hammond, 2006). However, there is some evidence that delta waves also dominate when people are in an empathetic state. A study showed that delta waves are present in relatively higher amounts in psychotherapists, counsellors and other healers. People with these jobs are often in an empathetic state, and this let some researchers conclude that delta waves are probably associated with empathy and reflect the unconscious mind (Norris & Currieri, 1999). Theta waves (4-8 Hz) are faster than delta waves and represent a daydream-like state of mind that is associated with mental inefficiency (Hammond, 2006). Furthermore, the occurrence of theta waves is related with creativity and intuition and is also predominant during meditation, prayer and periods of increased spiritual awareness (Norris & Currieri, 1999). When theta waves occur at very slow levels, the brainwave activity is very low and corresponds to the twilight zone between sleep and wakefulness. The last category of brain waves is the beta wave. Beta waves (above 13 Hz) are small and the fastest brain waves, often related with a state of mental and intellectual activity (Norris & Currieri, 1999; Hammond, 2006). For example, judgement, decision making and problem solving are tasks which generate a lot of beta waves. Also tasks that demand outwardly focused attention and concentration are associated with an increase in beta waves.

Despite a particular type of brain wave can dominate during certain feelings, the four types of brain waves are always present in different parts of the brain (Hammond, 2006). For instance, during a drowsy state, more delta and slow theta waves are present in the brain, but alpha and beta waves are not completely absent. The same applies to a conscious state in which beta waves are more present than delta and theta waves.

The brain waves that are present in different parts of the brain are measured by electrodes placed on the scalp. Each electrode records the mass activity of neural dendrites in the underlying cortex (van den Bergh, 2007). If the electrodes are placed too close to each other, some will record the same electrical fields and do not enhance the spatial resolution of the measurement. To prevent that the distance between electrodes is too large or too small, a standard for the placement of electrodes was established. Nowadays, often a cap with electrodes placed according to the 10-20 International System of Electrode Placement is used (Cantor, 1999). Nineteen electrodes are used for recording cortical areas, whereas two others are used as reference electrodes. Most of the time, the earlobes are used as a reference. The electrodes at the scalp are divided into five

regions and are indicated with the letters F (frontal), C (central), T (temporal), P (parietal) and O (occipital). Each letter corresponds to the cortical region in which it is placed. Numbers are used to distinguish electrodes placed on the left hemisphere from those on the right hemisphere. Odd numbers refer to electrodes at the left hemisphere and even numbers to right hemisphere sites.

3.1.3 Aim of neurofeedback

The principle of neurofeedback was discovered in the late 1960s when researchers noticed that cats trained to produce 12-15 Hz activity in the cortex, were better resistant to induced epileptic seizures than non-trained cats (Angelakis et al., 2007). Later, the same effect was shown in humans. Due to this discovery, researchers realized that the electrical activity of the brain, which is reflected in the EEG signal, represented mental states. Moreover, the idea arose that the electrical activity of the brain reflected the relationship between brain and behaviour and that by altering brain wave activity also the behaviour could be changed (Heinrich et al., 2007). To teach an individual how to modify a specific brain wave activity and how to activate such state voluntarily is an important goal of neurofeedback. This is often realized by extracting the relevant components of the EEG signal and feed these back to the individual (Vernon, 2005). There are different feedback signals by which the individual can be informed about its brain wave activity. Especially in children, often computer games or movies are used as a feedback signal. The goal is then to let a popular character jump over obstacles or let the movie play (Heinrich et al., 2007). In adults, changes in audio or visual information are used as a way to keep them updated about their performance. Positive feedback is given when the brain wave activity moves in the desired direction. Therefore, neurofeedback corresponds, just as biofeedback, to an operant conditioning paradigm (Angelakis et al., 2007; Egner & Gruzelier, 2001; Heinrich et al., 2007; Vernon et al., 2003).

Neurofeedback treatments often start with the administration of a quantitative electroencephalogram (QEEG). A QEEG can objectively and scientifically asses a person's brainwave function (Hammond, 2006). The procedure consists of placing a cap with electrodes on the head measuring the electrical activity coming from the brain. In the meantime, the person rests quietly with the eyes open or closed. Sometimes the person has to make tasks, such as reading or pressing a button. After the artefacts are removed, the data is compared to a normative database that shows how the brain should function at the client's age. If the brainwave patterns are different from normal, the deviant brain wave levels can be trained in the desired direction. During the 1970's and 1980's, a great deal of experimentation with QEEG started. This lead to standard documentary that helps in the evaluation of conditions such as mild traumatic brain injury, ADHD, learning disabilities, depression, obsessive-compulsive disorder, anxiety and panic disorder (Hammond, 2006).

3.2 Neurofeedback and relaxation

Neurofeedback training sessions are often used to treat diseases and disorders (Heinrich et al., 2007). Examples are epilepsy, ADHD and anxiety. Most neurofeedback training sessions trying to reduce anxiety and improve relaxation use alpha or theta training. These brainwaves are selected because alpha and theta waves are related with relaxation (Peniston & Kulkosky, 1999; Egner et al., 2002).

One of the first studies reporting a raise in alpha brain wave level could increase relaxation was a study done by Nowlis & Kamiya (1970). They investigated whether subjects could learn to control alpha brain wave levels without instructions how to do so. Before the real experiment, subjects underwent some practice sessions in which they were left free to learn control in any manner they chose. The feedback consisted of a tone coming on and off. What the subjects did not know was that the presence of a tone indicated high alpha levels and no tone, low alpha levels. After practicing, a baseline test was administered with the instruction to remain still and keep eyes closed. This baseline test was followed by a 15 min period in which the subjects could experiment with the tone. After this relaxed period of experimentation, the real experiment started, and subjects received the instruction to keep the tone on in the first trial and keep it off in the second trial. Both trials had a duration of two minutes and if more time was left, further trials were ran. Subjects had to close their eyes during the real experiment; only subjects with a very high initial baseline for alpha with eyes closed were given a second baseline with eyes open prior to experiencing feedback. These subjects had to do the experiment with eyes open.

Results of the experiment showed that all 26 subjects were having more alpha during the tone on trials than during the tone off trials. Furthermore, 21 of the 26 subjects had a higher amount of alpha during the tone on trials than during the relaxed baseline period. Also 19 of the 26 subjects had a decreased amount of alpha in the tone off condition compared with baseline level. The eyes open and eyes closed results were analysed separately, and those subjects that controlled alpha brain wave levels with eyes open achieved somewhat greater success than those who trained with eyes closed. However, Nowlis & Kamiya (1970) argue that this is possibly caused by an extra baseline of two minutes, during which time the eyes open group could hear the tone. At the end of the experiment, all subjects were asked what their strategy was to keep the tone on and off. Most subjects reported that to keep the tone on, they relaxed, did not focus visually, were aware of inhalations and exhalations and just let it go. To keep the tone off, they were alert and vigilant, visually focussing or tried to get agitated. Subjects who were able to control alpha spontaneously reported mental states reflecting relaxation and pleasant affect with maintaining alpha. All in all, these results show that people are able to regulate brain waves without being cognitively aware of doing so. It also demonstrates that an increase in alpha brain wave level corresponds to a raised feeling of relaxation. The results could have been

stronger when Nowlis & Kamiya (1970) used a control group with did not hear a tone, but only were instructed to relax. If this group reported significant lower alpha levels than the experimental group, the experiment showed that the addition of feedback facilitated learning and therefore an increase in alpha level.

The experiment of Nowlis & Kamiya (1970) showed that by increasing alpha levels, relaxation increases and that it probably is a useful approach in the treatment of stressed people. Egner et al. (2002) not only used alpha waves but also theta waves to test whether people changed their activation levels after training. The experiment consisted of a real feedback group and a mock feedback group. The real feedback group received alpha theta feedback. The aim of this kind of feedback is to facilitate a state of deep relaxation, resembling a meditative state, by teaching subjects to raise theta over alpha activity (Egner et al., 2002). A successful progression within an individual alpha/theta session would be defined with an increase in the theta/alpha (t/a) ratio across time. The mock feedback group resembled the real feedback condition as closely as possible. Instead of their own theta alpha ratio, subjects of the mock feedback group received a recording of a typical a/t session with auditory feedback. The hypothesis of the study was that the group receiving a/t feedback would display higher and steeper t/a ratios within and between sessions, and that these effects would be accompanied by differences in activational phenomenology.

Subjects were told to relax with their eyes closed and without body movement. Before the experiment started, a baseline measurement of two minutes, in which subjects underwent eyes closed feedback free relaxation, was administered. During the real experiment subjects received auditory feedback with the volume adjusted to the subjects' liking. Each session consisted of five periods of 3 minute duration and in total 5 sessions were carried out 2 or 3 times per week. Before and after each session, subjects filled out activational self-report measures.

Results showed that within sessions, the mean t/a ratio of the real feedback group increased across periods. On the other hand, the mean theta/alpha ratio of the mock feedback group remained the same during the periods. The difference in t/a ratio between both groups became significant at the last two periods of three minutes. The progressive increase in t/a ratios leading to higher t/a ratios than the mock feedback group, indicate that subjects learn to increase their t/a ratio, as a consequence of the operant feedback loop. However, between sessions, results were less convincing. The t/a alpha ratio was significantly higher in the real feedback group in sessions 2 and 4, but not in the other sessions. In contrast to the within-session data, there was no significant linear trend evident in the t/a alpha ratios of either group. Egner et al. (2002) argued that a variety of variables could have caused the lack of significance. For example, they did not control for the subject's emotional state or amount of sleep during the previous night.

The subjective judgement of changes in activational state after training sessions also showed no significant difference between both groups. Both groups

showed a decrease in general activation and high activation, and an increase in general deactivation and deactivation sleep. These results show that subjects became more relaxed after a training session, but that the group to which they belonged to did not matter. This is also supported by the finding that the significant changes in subjective activational phenomenology did not covary with the mean t/a ratio displayed within sessions. Egner et al. (2002) stated that the EEG changes in the real neurofeedback group detected by the t/a ratio measure were too minute in phenomenological terms to induce a subjective state significantly from mock feedback relaxation. This may have become clearer when Egner et al. (2002) had used a third group that received no feedback. If this group shows the same amount of relaxation as the real and mock feedback group, than the changes in activation level are caused by the instruction to relax and not by the feedback procedure. If the no feedback group shows no or significant lower relaxation levels, than the relaxation level of the mock feedback group might be caused by the placebo of undergoing a neurofeedback training and receiving feedback. The mock feedback subjects than probably had expectations that some improvement in relaxation should happen.

Egner et al. (2002) showed that alpha theta neurofeedback training can increase t/a ratio within sessions. This knowledge was used by Batty et al. (2006) to examine whether alpha theta neurofeedback could increase hypnotic susceptibility. Hypnotic susceptibility is a measurement how easy a person can be hypnotized. The research of neurofeedback and the effects on hypnotic susceptibility started in the 1970's. In 1974, London et al. published a paper in which they demonstrated that neurofeedback could increase hypnotic susceptibility. Two groups were used in the study; an alpha neurofeedback training group and a mock feedback group that received a pre-recorded EEG tape of a single subject. After a baseline measurement and practising what a tone made going on and off, subjects got the instruction to relax and keep the tone on as long as possible. Results showed that pre-training baseline measurements and hypnotic susceptibility values were equal between both groups. However, after training, the alpha production of the neurofeedback group was significantly higher than the mock feedback group, although this group also showed an increase in alpha level across sessions. The raise in alpha level correlated with a significant increase in hypnotic susceptibility. London et al. (1974) concluded that learning occurred more frequent in the neurofeedback group than in the control group. Moreover, they mentioned that the increase in alpha level of the control group was probably caused by the kind of mock feedback. The recorded feedback could coincidently concur with the actual production of alpha by the control subject. To prevent this from happening again, London et al. (1974) proposed to use different degrees of pseudo feedback. This is actually what Batty et al. (2006) did in their experiment. They compared the effects of alpha theta neurofeedback with a group receiving progressive muscle relaxation and a group undergoing self-hypnosis. The idea is that hypnotic susceptibility can be increased by alpha theta neurofeedback, because this neurofeedback protocol facilitates relaxation. Relaxation,

on its turn, facilitates parasympathetic activity, focusing of attention and the vividness of imagery (Batty et al., 2006). It is believed that these last two factors are prerequisites for hypnosis, and by training the initiation of these factors, hypnotic susceptibility will be higher.

Results of the study demonstrated that all groups increased their hypnotic susceptibility with about the same level. This indicates that alpha theta neurofeedback is not more effective in increasing hypnotic susceptibility than the other relaxation methods. This would mean that relaxation on its own is more important for an increase in hypnotic susceptibility than raising theta/alpha levels. However, alpha/theta training can raise relaxation levels and is therefore effective in increasing hypnotic susceptibility.

In all groups, about half of the subjects did not respond to the training, and as a result did not show an increase in hypnotic susceptibility. The majority of these non-responding subjects had low susceptibility scores at the beginning of the experiment. Batty et al. (2006) came to the conclusion that hypnotisability is heritable and not all people can equally enhance their hypnotic susceptibility. However, they did not come up with the point that people with low susceptibility scores may not want to be hypnotized. When someone does not believe in, or is not open for hypnosis, it becomes very difficult to increase its hypnotic susceptibility scores. Therefore, the willing to be hypnotized could also be an explanation for the fact that people with low susceptibility scores did not show an improvement. To conclude, alpha theta neurofeedback can increase hypnotic susceptibility, but also other relaxation interventions can increase this value. An increased hypnotic susceptibility can be helpful for stressed and anxious people to become more relaxed, but whether neurofeedback is the best option is not clear yet.

Alpha theta neurofeedback is used to induce a state of relaxation. Therefore, it is sometimes used as a therapeutic intervention. One example is the Peniston & Kulkosky brain wave neurofeedback therapy (PKBNT) (Peniston & Kulkosky, 1999). The PKBNT uses alpha theta neurofeedback to get patients more relaxed. It contains a lot of therapeutic procedures and starts with an admission and an EEG assessment. After the assessment, all patients who are candidates for the PKBNT are administered a battery of psychological tests and are rated for baseline production of beta, alpha and theta brain wave frequencies. Before the real training starts, patients first undergo some biofeedback temperature and respiration sessions to achieve relaxation of the body and a quiet, inward turned state of mind. They also try to visualize an increase in their alpha brain wave level. The alpha theta brain wave training starts with a 5 minute baseline rating of alpha rhythm amplitude, and the percentage of alpha and theta brain waves with eyes closed is obtained. The patient is then instructed to open his eyes and concentrate on an object in the room for 5 minutes. During this period, beta rhythm sensitivity threshold is set to encourage 40-50% of beta rhythm presence. After all thresholds are set, the patient closes his eyes and is required to imagine an increased alpha rhythm amplitude or scenes of the normalization

of his personality. Furthermore, the patient is asked to sink down in the theta state, while keeping the mind quiet and alert, and the body calm. The feedback consists of a sound that changes in volume. Alpha and theta level are represented by different sounds, so patients can hear which of the two brain waves is high or low. Sessions takes about 30 minutes and in total 30 sessions are undergone across a duration of 28 days. At the end of each session, the average alpha rhythm amplitude and the cumulative percentage of duration of feedback for each brain wave is recorded. Eventually, all data is summarized and reviewed and the patient can be discharged when the alpha rhythm amplitude, and alpha and increased theta rhythm production are detected from a comparison of baseline and final EEG assessments (Peniston & Kulkosky, 1999).

3.3 Neurofeedback in stress related disorders

The Peniston & Kulkosky brain wave neurofeedback therapy is sometimes used in the treatment of alcoholism. The rationale of using a relaxation procedure for the treatment of a substance abuse is that the abuse is often caused or exacerbated by stress (Peniston, 1998). Furthermore, it seems that relaxation training is effective because it reduces anxiety and increases perceived control over stressful situations (Klajner et al., 1984). Thus, reducing the stress level of the alcoholics may subsequently result in a decrease of stress-related drinking or craving.

An experiment used the PKBNT in the treatment of alcoholics (Peniston, 1998). There were three intervention groups, a PKBNT group, a group that received traditional psychotherapy and a non-alcoholic control group. Results of the intervention showed that after treatment, the PKBNT group had enhanced alpha and theta waves in the EEG's compared with pre-treatment values. The group also showed a gradual increase in alpha and theta activity as the thirty experimental sessions progressed. The control groups did not show such increase.

In a 36-month follow-up study, the PKBNT group showed a sharp reduction in self-assessed depression and sustained abstinence with significantly less relapses than the traditional psychotherapy group (Peniston, 1998). Furthermore, the traditional group had higher beta-endorphin levels at the end of treatment compared to their pre-treatment levels as well as to the levels of the non-alcoholic control group. A raised level of beta-endorphins is associated with stress and the elevated level of the traditional control group can indicate that this group experienced stress due to the abstinence and fear of relapse. The PKBNT group did not show an increase in beta-endorphin levels, but instead showed stabilization. This indicates that the PKBNT group did not perceive the neurofeedback training as a stressful event. The good results of the Peniston & Kulkosky neurofeedback therapy shows that alpha theta relaxation training can change the drinking pattern of alcoholics. This indicates that neurofeedback might be a good application in the treatment of disorders caused by stress.

Another stress related disorder treated by neurofeedback training is PTSD (Hammond, 2006). A group of PTSD Vietnam combat veterans received, in addition to their traditional hospital treatment, thirty alpha theta neurofeedback sessions of 30 minute duration. Results of the group were compared 30 months post-treatment with a group of veterans that only received traditional treatment. Of the alpha theta neurofeedback treatment group, only 3 of the 15 patients showed relapse, while all 14 traditional treatment patients had relapsed and been re-hospitalized. Another outcome measure involved psychotropic medication requirements. The medication requirements of all patients in the neurofeedback treatment group had decreased by follow up. On the contrary, among the patients receiving traditional treatment, only one decreased medication, two reported no change and ten increased their need for psychiatric medications (Hammond, 2006). The results of this study show that alpha theta neurofeedback training decreases the symptoms of PTSD in a better way than conventional treatment.

In another study with Vietnam veterans, 20 veterans with PTSD and alcohol abuse were randomly selected (Hammond, 2005). All patients showed frequent occurrence of PTSD symptoms and had about five times been hospitalized for PTSD. Patients received thirty alpha theta neurofeedback training sessions of 30 minutes each. Until 26 months after the intervention, the veterans were followed and in that period only 4 of the 20 patients reported a few recurrences of PTSD symptoms, such as nightmares or flashbacks. The rest of the patients did not show a relapse or reoccurrence of the symptoms. The study shows that neurofeedback can reduce PTSD symptoms, but there are some limitations. One limitation of the study was that it did not report anything about the alcohol abuse of the PTSD patients. This was especially interesting, because in alcoholics, neurofeedback showed to be effective in reducing the amount of drinking. The lack of a control group is another limitation that made the results of the study less convincing. All in all, neurofeedback shows to be probably efficacious in the treatment of PTSD. However, still much research has to be done.

Like PTSD, phobic anxiety disorders are also sometimes treated by neurofeedback. People with phobic anxiety show increased fear and the accompanying neural responses when they perceive a particular object. Neurofeedback can decrease the occurrence of this stress response. A study showed that the group receiving alpha neurofeedback produced 33 percent more alpha after the study and demonstrated a significant reduction in test anxiety (Hammond, 2005). However, the control groups receiving muscle biofeedback and alpha plus muscle feedback also showed this significant reduction. On the other hand, the untreated control group and the relaxation training group did not experience a significant reduction. This indicates that a biofeedback procedure is necessary to decrease anxiety, but that is does not have to be neurofeedback per se.

In a second study, subjects received a combination of alpha enhancement training and muscle biofeedback training (Hammond, 2005). Results showed that alpha scores increased from 64 to 78 percent and anxiety scores dropped significantly for the treatment group, compared with a nontreatment group.

However, a limitation of the study was that there was no group that only received neurofeedback. Therefore, the current study design does not make it possible to separately assess the effect of alpha neurofeedback and muscle feedback on anxiety scores.

A third study examined the effect of alpha neurofeedback training on the anxiety scores of anxiety patients of which most were also alcoholics (Hammond, 2005). The control group did not receive feedback and consisted of anxious patients, most of whom were also alcoholics. Although the study did not evaluate drinking status, patients of the neurofeedback training group showed significant changes in state and trait anxiety compared with controls (Hammond, 2005). This was accompanied by an increase in eyes-closed alpha, and at 18 months follow-up, these results were still present. So, the effects of alpha neurofeedback showed to be long lasting.

3.4 Summary

Neurofeedback is a special and sophisticated form of biofeedback and based on the EEG signal measured from the scalp. The EEG signal can be divided into four main frequency waves, delta, theta, alpha and beta. Alpha and theta waves

Table 3: Summary of studies using neurofeedback training to decrease stress levels.

Study	Feedback protocol	Results
Nowlis & Kamiya (1970)	Alpha training	Increase in alpha and relaxation level
Egner et al. (2002)	Alpha-Theta training	T/A ratio increased in experimental group. Both the experimental and mock feedback group showed increased relaxation after treatment.
Batty et al. (2006)	Alpha-Theta training	T/A ratio increased in experimental group. No difference in hypnotic susceptibility between groups.
Peniston & Kulkosky brain wave neurotherapy (1999)	Alpha-Theta training	Alcoholism: PKBNT group showed increased alpha and theta activity, and lower beta-endorphin levels than control group. PTSD: Less relapse of PTSD symptoms in PKBNT group compared with control group.
Hammond (2005)	Alpha training	Anxiety: Anxiety scores significantly dropped in the experimental group.

are most used in the neurofeedback interventions aimed to increase relaxation. An overview of the studies discussed in this chapter is presented in Table 3.

A study of Nowlis & Kamiya (1970) showed that by increasing alpha levels, relaxation increases. The effect of alpha theta training aiming to increase relaxation is less clear. Egner et al. (2002) demonstrated that alpha theta training works to increase the relaxation level, but also the mock feedback grouped showed increased relaxation. This was also the case in a study of Batty of et al. (2006). All three groups showed an increased hypnotic susceptibility, probably reflecting a high level of relaxation. However, alpha theta training was not more effective than the other relaxation paradigms. Alpha theta training is also used for therapeutic purposes. Especially the Peniston & Kulkosky brain wave neurotherapy showed to be effective in the treatment of alcoholics and PTSD. Patients suffering from these disorders showed a significant improvement in their disease pattern, compared with controls that were not treated with the PKBNT. Anxiety disorders are also treated with neurofeedback training. Results of these studies showed that alpha increases, and that most of the time, anxiety scores dropped. Thus, neurofeedback can help in initiating a relaxed state, but it is not completely clear whether it is more effective than other relaxation methods.

Chapter 4: Discussion

Biofeedback and neurofeedback are interventions that are used in the regulation of stress. The previous chapters provided evidence that bio- and neurofeedback can indeed regulate stress. But which method is the most effective?

There is much more known about biofeedback than about neurofeedback in the field of stress management. There are more biofeedback methods (e.g. EDA, HRV and respiration biofeedback) and also more research is done using biofeedback than neurofeedback. EDA biofeedback showed to be effective in decreasing arousal, and was also able to change activity in some brain areas (Critchley et al., 2001, 2002). These changes in brain activity were visualized using fMRI, and the affected brain structures were especially associated with the integration of the intention to relax and the corresponding body responses. Compared to biofeedback, neurofeedback studies almost never use fMRI to examine brain changes caused by neurofeedback training (Heinrich et al., 2006). The only studies combining neurofeedback and fMRI are studies determining the effect of neurofeedback training on the neural substrates of children with attention deficit hyperactivity disorder (ADHD). Neurofeedback studies aiming to decrease stress-levels did not use fMRI to examine which brain areas change activity as a consequence of the training. Until now, most neurofeedback studies only measure EEG and behavioural changes. This is a pity; because fMRI can strengthen the evidence that neurofeedback might be effective. fMRI measurements provide good spatial images, but on the temporal scale these are less accurate. EEG measurements on the other hand, are very accurate on the temporal scale, but much less on the spatial scale. By combining EEG and fMRI, researchers cannot only examine brain changes on a temporal scale, but also spatially determine where in the brain these changes take place. An explanation why not many studies combine EEG and fMRI, might be that MRI measurements are expensive, cannot be administered everywhere and a lot of preparation is needed before a measurement can start. However, some well executed experiments could strengthen the effectiveness of neurofeedback, and give fewer opportunities to sceptics.

Some people in the world are not convinced of the effectiveness of biofeedback and especially neurofeedback. They come with the argument that most neurofeedback studies have a lot of limitations and that all articles can be summarized with the sentence ‘Neurofeedback is promising, but further research is needed’ (Koppenaal, 2007). Maybe this is a bit exaggerated, but it is not completely untruthful. Many neurofeedback studies do not have a good control

group or miss control groups at all, and as a consequence, results are less powerful because they can also be caused by a placebo effect. Studies without or with not enough control groups cannot rule out this possibility.

Another limitation of many neuro- and also biofeedback studies is that the researchers are aware of the training paradigm subjects undergo. By knowing which subject belongs to which group, researchers can unconsciously influence the subject. This can be by body language or treating the subject in a different way. Examining double-blind studies, in which the subject and researcher interacting with the subject, do not know the group to which the subject belongs, increases the validity of the experiment.

Sceptics of biofeedback come also with the point that there are almost no follow-up studies (Koppenaal, 2007). This was certainly true in the beginning of the bio- and neurofeedback experiments, but nowadays many follow up studies are carried out, showing that the effects of bio- and neurofeedback can be long lasting. Thus, not all things sceptics assert are true.

To come back to the question which method, bio-or neurofeedback, is more effective, is difficult to answer. Both methods have their limitations, as is mentioned above. However, compared to neurofeedback, there seems to be more direct evidence that biofeedback works in the regulation of stress. Biofeedback uses respiration, heart rate and sometimes blood pressure as parameters indicating stress levels. A change in these parameters works directly on the activity of the parasympathetic and sympathetic nervous system. For example, when the feedback is aimed to reduce stress, a decrease in respiration and heart rate will be trained. This results in a decreased activity of the sympathetic nervous system and an increased activity of the parasympathetic division of the autonomic nervous system. Thus, biofeedback especially targets the short-lasting branch of the stress response. However, a study of McGrady et al. (1987) in hypertensives showed that EMG biofeedback decreased blood pressure and also cortisol levels. This means that the amount of glucocorticoids decreased, and glucocorticoids are mainly produced by the HPA axis. So, perhaps biofeedback also influences the activity of the HPA axis.

Neurofeedback training sessions attempt to induce changes in the EEG. This does not as directly influence the autonomic nervous system as biofeedback does. By stimulating the brain to make more alpha and theta waves, general relaxation should occur, and as a consequence a decreased heart rate, blood pressure and respiration rate. So, these parameters are not directly trained, as is the case in biofeedback training procedures. No study in literature mentions whether neurofeedback influences both the HPA axis and autonomic nervous system. If it influences the HPA axis, cortisol levels should decrease, but until now no study measured the effect of neurofeedback relaxation training on cortisol levels.

The studies examining whether alpha-theta neurofeedback training is effective in inducing relaxation showed that the experimental groups increased theta alpha ratio, but that relaxation levels were the same as the different control groups. These control groups varied from a mock feedback group to other re-

laxation therapies, such as self-hypnosis. This indicates that any relaxation therapy can be applied to reduce stress-levels, and that alpha theta neurofeedback is one of them. Neurofeedback does not prove to work better than the other relaxation methods. In contrary to neurofeedback, biofeedback relaxation procedures showed to induce higher relaxation levels, reflected by the HRV or respiration, in the experimental group than in the control group. This means that biofeedback aiming to increase relaxation, works better than for example progressive muscle relaxation (Zucker et al., 2009). In this respect, biofeedback showed more evidence that it increases relaxation than neurofeedback and is therefore perhaps more effective than neurofeedback.

4.1 Future research

Biofeedback and neurofeedback make part of a relative new field of research. It showed to be effective in some clinical applications, but in the area of stress-regulation, still much research has to be done. One example is that the paradigms which are used today, should be optimized. As already mentioned above, the procedures contain some limitations which in the future have to be solved. For example, every study should get at least one control group and it would be recommended that the study is carried out double-blinded. Furthermore, the study should use enough subjects, resulting in a more powerful statistical analysis. It would also strengthen the results of a study when they examine a follow-up study. Follow-up studies can demonstrate whether the processes induced by neurofeedback or biofeedback are long-lasting or not.

An idea for future research is the combination of bio- and neurofeedback, or using a biofeedback intervention based on two biological parameters instead of one. This would be especially beneficial for patients who after only bio- or neurofeedback training do not show enough improvement. By giving them two relaxation interventions, there might be a larger chance that they become relaxed and achieve the optimal improvement. For the treatment of epilepsy, slow cortical potential (SCP) training, which gives information about the activity of the underlying cortical regions, already showed to be successful in combination with a behavioural self-management program (Heinrich et al., 2007). Combined approaches should also be developed for other clinical disorders and stress management programmes. One approach is the combination of GSR and HRV biofeedback (Ahuja et al., 2003). The galvanic skin response shows relatively fast shifts in skin conductance (Critchley, 2002) and therefore reflects the stress-level. However, the response of the heart in conditions of stress is unavailable with this method. By measuring the GSR and ECG signal, and subsequently computer interface these signals to get the GSR and HRV, will provide patients a good biofeedback intervention under conditions of stress and anxiety.

It is known that individuals tend to differ in terms of the physiological systems in which they manifest stress. This phenomenon is known as individual response stereotypy (Gould & Urdy, 1994). Some people can for example react

to stress through an increase in heart rate, while another person increases its muscular tension. Providing biofeedback with responses of more than one physiological system might reduce the amount of individuals that do not show improvement after training. This would be another benefit of combining two biofeedback interventions.

Most of the time, feedback is adjusted to reduce the amount of stress. This reduction procedure is often applied because people have the feeling that they are too stressed and want to prevent stress-related diseases that may occur after long periods of stress. On the other hand, very little research is done to increase arousal by bio- or neurofeedback. Increasing arousal levels can be useful for athletes who must become more energized to achieve their optimal level of performance (Gould & Urdy, 1994). A controlled laboratory study showed that preparatory arousal techniques, such as getting mad or charging up, facilitated performance more than control-rest, imagery and cognitive distraction conditions, on strength tasks. The study suggests that it is possible to elevate arousal and enhance performance. This provides an opportunity for biofeedback to be used in the athletic field. By giving athletes the opposite feedback of what is given in a training session aiming to increase relaxation, arousal can probably be increased. This might be a new future application of bio- and neurofeedback.

Nowadays, most neurofeedback applications and devices are not very practical. If in the future these devices become more practical, they become available for the broad public. Today, neurofeedback training sessions often require the adjustment of a cap with electrodes. It takes time to place the electrodes on the exact positions of the scalp and the electrodes only make contact when gel is injected. This is not practical for everyday or self utilization. An option is to make a device in which the electrodes are built in and do not have to make contact with gel. Other improvements may be devices that work wireless or are not sensitive to movements. Eye blinks and muscle tension produces artefacts in the EEG which have to be rejected afterwards. This causes data losses and when a lot of artefacts are present in the EEG, few data is left to analyze. Devices that are not sensitive to movements can also be easier applied in children. They now have to sit still for minutes, and this is especially difficult for children with ADHD. Therefore it is important that new devices are developed so that it has less constrains and more people can use it.

To conclude, literature studies provide evidence that neuro- and biofeedback can reduce stress and improve relaxation. The results of these studies provide a basis on which future studies can build. However, still a lot of limitations have to be solved in the future to get more powerful results and more insight into the effectiveness of bio- and neurofeedback.

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