**Neuroplasticity & Addiction Within Neural Network Therapy®: A Literature Review**

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**Neuroplasticity & Addiction Within Neural Network Therapy®: A Review of Literature**

Researchers have been examining how aspects of the brain can help within therapy and clinical treatment for many years. Neuroplasticity, the ability for brain cells to change and reorganize its structure, function, and connections in response to internal and external stimuli (Cramer et al., 2011), is one of those aspects. Understanding the mechanisms of neuroplasticity and implementing it within therapy is likely connected with benefits of changes in behaviour and improvements in an individual's mental health and well-being. In this literature review, the biological basis of neuroplasticity, the effects of stress on neuroplasticity, and regulating neuroplasticity are examined. By examining the current literature on neuroplasticity, it can assist us in identifying a gap in the current literature regarding neuroplasticity, especially in the area of the use of neuroplasticity in the clinical setting.

Relating to neuroplasticity, the topic of addiction in the brain is examined. Addiction in the brain is a complex topic, but there is some research to support that neuroplasticity plays a part in this process and possibly in the treatment of addiction. Examining addiction in the brain, brings up the important relationship between specifically the amygdala and prefrontal cortex in the brain. Increasing our understanding of the brain, including its prominent connections when it comes to understanding neuroplasticity and addiction, can assist in working towards new therapy techniques.

Neural Network Therapy® is a holistic therapy approach created in 1997 by Canadian Family Health Counselling that focuses on making new habits in place of unwanted ones. Neural Network Therapy® (Sargent, 2023) is based around research that has been done within the topics mentioned above with a big emphasis on neuroplasticity. The goal of one of the core exercises "Playdough Brain" is to gain an understanding of neuroplasticity (Sargent, 2023). Another core

exercise is “The Crocodile” and this is based around the idea of the “Reptilian Brain” and is used to explore how the body responds to stressful situations (Sargent, 2023). “The Crocodile” exercise explains the “Old Brain” as the amygdala and the “New Brain” as the prefrontal cortex and recommends thinking and making decisions using your prefrontal cortex (Sargent, 2023). This literature review will examine the research basis related to these core exercises and the ability for Neural Network Therapy® to promote changes in behaviour and cause improvement in an individual’s mental health and well-being, specifically if there’s any benefit for those struggling with a form of addiction (Sargent, 2023).

## Neuroplasticity

### *Biological Basis of Neuroplasticity*

The brain is a highly complex and dynamic organ that goes through synaptic reorganization, these reorganizations can influence an individuals behaviour due to the experiences that an individual goes through. The composition of neural networks include dense systems of neurons that are attached to one another with synapses at the junctions. There are many factors that go into synaptic plasticity such as psychoactive drugs (Kolb et al., 2003), gonadal hormones (Kolb et al., 2003; Herrera-Morales et al., 2019), disease (Goto et al., 2010), and stress (Kolb et al., 2003). Memory is strongly affected by the modifications of the synapses through the Hebbian process, which specifies three mechanisms for synaptic plasticity which are synaptic scaling, spike-timing dependent synaptic plasticity, and synaptic redistribution (Abbott & Nelson 2000). Hebbian plasticity is a function of how new information is added to an individual’s memory that will then be preserved in neurons to work in a positive-feedback response. Synaptic scaling modifies the strength of synapses, spike-timing dependent synaptic plasticity is focused on the rates at which the postsynaptic firing, and synaptic redistribution

improves the amplitude of synaptic transmission (Abbott & Nelson 2000). Hebbian plasticity leads to fiber bundles within the brain being stimulated, making it essential for learning and creating new memories (Lazari et al., 2022). The internal processes of learning are elaborate and Hebbian plasticity allows for efficient modifications. Presynaptic axons and postsynaptic dendrites are critical for ensuring that the pathways among the neurons are functioning well and provides a framework for synaptic plasticity (Hiratani & Fukai 2018). Hebbian plasticity is important for developing memories as it strengthens the pre- and postsynaptic neurons to create new pathways. The function of neuroplasticity has been shown to have a link in the hippocampus as it supports memory encoding and consolidation, and the regulation of learning. Within the hippocampus, neurotrophins secrete proteins to aid in the development and function of neurons when new connections are being formed (Lu & Chow 1999). It has been seen that brain-derived neurotrophic factors (BNDF) are critical for synaptic functions in the hippocampus, as it regulates long-term potentiation (the consistent strengthening of synapses involved in memory formation (Lu & Chow 1999). Long-term potentiation is strengthened through CA3-CA1 synapse, which indicates that secreted form of the amyloid precursor protein induces the fluctuation of learning (Lu & Chow 1999; Ishii et al., 2021). Considering that the CA1 region is responsible for memory retrieval, while CA3 is responsible for rapid memory encoding through vesicular exocytosis (Ishii et al., 2021). The findings suggest that Calcium-dependent activator protein for secretion 1 is involved in the cellular mechanisms that rely on synapses in the hippocampus (Ishii et al., 2021).

The molecular mechanisms and background for neuroplasticity have been a prominent area of study, primarily the purpose of calcium (Cavazzini et al., 2005; Inglebert et al., 2020), acid receptors (Wang et al., 2012), and histones (Geng et al., 2021; Gupta et al., 2010). In the

past synaptic plasticity has built one of its pillars of understanding upon it being a calcium-dependent process, a dependency that relies on an influx of voltage- or ligand-gated calcium to change neuronal activities (Cavazzini et al., 2005). It was determined that the strength, duration, and timing of the signals change the synaptic plasticity (Cavazzini et al., 2005). Calcium in the brain plays a role in neuroplasticity where it encodes the timing for pre- and postsynaptic activities. It also helps with the growth and development of neurons and functional advancement of synapses (Inglebert et al., 2020). Calcium in the brain is also responsible for the release of the neurotransmitters that are critical for the promotion of learning and encoding of memories (Inglebert et al., 2020). The regulation of neuroplasticity is important for understanding what needs to occur for changes in the brain. Various histone modifications will enforce change to be made in the structure of chromosomes as well as how it has the potential to alter gene expression from its original expression pattern (Gupta et al., 2010; Geng et al., 2021). Adaptations to environmental changes are crucial to understanding the mechanisms that correlate to the formation of learning and memory (Gupta et al., 2010; Geng et al., 2021). These mechanisms have been studied and have shown that the creation of new ways of learning and the creation of memories require histone codes. The methylation of histones is regulated within the hippocampus to promote memory consolidation in the long-term (Gupta et al., 2010). Histone codes are important in the modification of genes because it is a hypothesis for the transcription of genetic information that is continually regulated by chemical modifications. The regulation of neuroplasticity is kept up by histone modifications by the activation and inhibition of transcription - there are many modifications that are responsible for this regulation, such as phosphorylation and acetylation (Geng et al., 2021). The brain is able to alter its molecular chemistry based on what it experiences and it does this by negative-feedback pathways of its

neural networks. A literature review from Wang et al. describes the primary way in which synaptic plasticity occurs, that being through the *a*-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (Wang et al., 2012). The purpose of this receptor is to regulate the plasticity of synapses and the remodelling of the brain when learning new activities and going through new experiences (Wang et al., 2012). By understanding how neuroplasticity occurs on a molecular level, it can assist in developing exercises to help with addiction treatment.

Sex hormones have the ability to influence neuroplasticity. Estrogen is a large contributor to memory as in female mice as the hippocampus is quite sensitive to concentration changes of this hormone (Schecter et al., 2023). Introducing the use of female mice to be used in experiments has greatly impacted the scientific community as in the past only male mice had been used. This was due to scientists assuming a likeness across the sexual differences that could be applied to both males and females and also due to the fact that males do not have an ovulation or menstruation cycle, which means that they do not experience hormone fluctuations in the way that the female mice do. Having both sexes used in experiments is incredibly beneficial as it provides researchers with the knowledge of how human females respond to certain experiences and how their brain networks are subject to change. Sexual activity, like any experience, can strengthen or weaken connections between various synapses that are found throughout the brain and are involved with learning and memory. As individuals become more sexually experienced, their sexual behaviour has the possibility of altering and this idea has been present within the scientific communities for a number of years (Herrera-Morales et al., 2019). Steroid sex hormones (i.e. estrogens, progestogens, and androgens) influence the central nervous system as they are able to circulate throughout the brain (Herrera-Morales et al., 2019; Celik et al., 2022).

The sex hormones create neuronal plasticity because of the crossing of the blood brain barrier by the sex hormones which induces cellular change of the synapses (Herrera-Morales et al., 2019). It is found that mechanisms, such as sex hormones, changes to signalling pathways, and neurogenesis, are responsible for this synaptic plasticity and sexual behaviour change (Herrera-Morales et al., 2019; Celik et al., 2022). A weakness that this review highlighted is that there is minimal research found concerning how female sex hormones change with sexual activity (Herrera-Morales et al., 2019). This article is relevant to the study of Neural Network Therapy® because the remodelling of the brain is a central idea of the therapy and researching various ways that this remodelling can occur is helpful to understanding why experiences induce plastic changes within the nervous system and thus alter learning. In a paper by Kim and Strathearn they speak on how mothers' brain plasticity changes during and after pregnancy due to the effects of oxytocin and how the maternal brain faces challenges when it comes to the disruption of typical oxytocin release (Kim and Strathean 2016). Oxytocin is a primary agent to the bond between mother and child and can also influence how the mother acts towards the child (Kim and Strathean 2016). The oxytocin pathway influences synaptic plasticity in the paraventricular and supraoptic nuclei and medial preoptic area which heightens structural changes in neurons (Kim and Strathean 2016). The synaptic changes that occur in the hippocampus are important for the development of the fetus and for its survival out of the uterus (Celik et al., 2022). The neuronal systems become more dense and the transmission between the synapses becomes altered (Celik et al., 2022). This is due to the estrogen receptors in the hippocampus responding to new synapse formation from learning and memory (Celik et al., 2022) and the blood brain barrier changes in permeability (Celik et al., 2022; Herrera-Morales et al., 2019), which was also noted in the literature review by Herrera et al. (2019). This is relevant

to the study of Neural Network Therapy® because the remodelling of the brain is a central idea of the therapy and researching various ways that this remodelling can occur is helpful to understanding why experiences induce plastic changes within the nervous system and thus alter learning.

Neural networks are extensive and the changes that occur at the synaptic level can explain some aspects of psychiatric disorders. In a study reviewed by Goto et al. (2010), it was suggested that a deficit in synaptic plasticity induction within the prefrontal cortex has the possibility of influencing various psychiatric disorders, such as schizophrenia, drug addiction, mood disorders, and Alzheimer's disease (Goto et al., 2010). Influencing or moderating the synaptic plasticity in the PFC through monoamines like dopamine could be a promising therapeutic approach for these psychiatric disorders (Goto et al., 2010). Disruptions to synaptic disruptions contribute to neurodegenerative diseases (Huntington's disease, Alzheimer's disease, and Parkinson's disease) (Goto et al., 2010; Murphy et al., 2000; Quirion et al., 2019; Rebelo et al., 2019; Gengler et al., 2010) and neuropsychiatric conditions (autism spectrum disorder, major depression disorder, and schizophrenia) (Goto et al., 2010; Granerud et al., 2022; Rygvold et al., 2022). Within the synapse networks at the CA1 location, changes can contribute to phenotypic observations in carriers of Huntington's disease (Murphy et al., 2000; Quirion et al., 2019). In autism spectrum disorder, it is now understood that an individual with this disorder has a different brain arrangement than individuals without this disorder (Granerud et al., 2022). The learning takes a longer amount of time for these individuals as their synapses do not function like a non autistic individual's brain (Granerud et al., 2022). Another study examined the dysregulation of the corticotropin releasing factor (CRF) system can lead to psychiatric disorders like substance use disorders (Haas-Koffler & Bartlett 2012). This is because it enhances some

drug effects and enhances potentiating drug-induced neuroplasticity during withdrawal (Haas-Koffler & Bartlett 2012). The CRF system plays a large role in synaptic plasticity in the ventral tegmental area (VTA) and the amygdala which impacts drug addiction and stress-induced compulsive behaviours in addiction (Haas-Koffler & Bartlett 2012). Moderating the CRF system is a possible therapeutic strategy to treat the positive reinforcement of substance abuse and negative reinforcement of withdrawal (Haas-Koffler & Bartlett 2012). Understanding the role of the CRF system is important to the intersections of stress, addiction, and neuroplasticity.

*Effects of Stress on Neuroplasticity*

A key consideration in neuroplasticity is how stress affects the brain. A study by Bloss et al. (2010) investigated the interaction between stress and aging on neuroplasticity through the use of male rats. It has long been hypothesized that stress was an accelerator of cognitive aging, and thus causing the impairment of memory and learning (Bloss et al., 2010). The structure of neuronal networks within the prefrontal cortex (PFC) is extensive and can change over time, both positively and negatively (Bloss et al., 2010). Remodeling of neural networks of the PFC in the rats occurred from the exposure of stress, however, there showed a possibility of reversibility (Bloss et al., 2010). The capacity for experience-dependent, stress-related neuroplasticity occurred with the shortening of apical dendrites, especially in the middle-aged and aged rats as their brains are not plastic enough to reverse the destruction of the neurons from the stressors (Bloss et al., 2010). These findings suggest that the structural plasticity of the PFC is influenced by both stress and aging (Bloss et al., 2010). By understanding how stress can influence neuroplasticity, it can help with understanding the signals of stress that lead to the alteration of neurons. This has been shown in a review by Regev and Baram (2013) in which they explored how stress signals promote neuroplasticity as well as how corticotropin releasing factor (CRF) is

involved in the process (Regev & Baram 2013). These stress signals have been imperative to the survival species over the years as the restructuring of neurons leads to the perception of dangers and helps to adapt to surroundings. CRF is expressed in various neurons within the brain and contributes to the regulation of autonomic and endocrine functions, emotional regulation, promotion of learning, and memory encoding (Regev & Baram 2013). CRF acts on specific receptors to induce plastic changes from the stress signals and can lead to maladaptive consequences in learning and emotion (Regev & Baram 2013). The CRF interacts with dopamine and glutamate during high stress times, which are both involved in reward-related addiction and learning (Regev & Baram 2013). Regulating CRF gives potential to therapeutic strategies towards treating addiction and emotional impairment (Regev & Baram 2013). The maladaptive synaptic plastic changes can lead to the persistence of the symptoms of individuals experiencing psychiatric disorders. As seen in a study by Rădulescu et al. (2021), chronic stress puts individuals at developing depression due to the persistent activation of the main stress response system, the hypothalamic-pituitary-adrenal system (Rădulescu et al., 2021).

With pharmacological and therapeutic interventions to lower stress and depression levels, individuals can induce positive synaptic and neuronal changes within their brains (Rădulescu et al., 2021). After experiencing stress, it is beneficial to engage in a period of recovery as it can reverse maladaptive neuroplastic changes that have occurred (Gray & McEwen 2013). Significant exposure to stress, however, can make it increasingly more difficult to reverse these changes since chronic stress lowers the possibility of the brain being able to recover and create beneficial plastic changes (Gray & McEwen 2013). An intervention for mood disorders related to stress is lithium, it has the ability to counteract the effects of stress on the brain by facilitating neural plasticity through regulating the cytoskeletal and glutamate system (Gray & McEwen

2013). Understanding how neuroplasticity relates with stress and lithium, it can help us understand how this affects those with mood disorders like bipolar disorder. Neural Network Therapy® could be a beneficial resource to explore these therapeutic interventions.

The experience of stress in early life can be detrimental to development into adulthood as it can produce psychiatric disorders (Herpfer et al., 2012). When individuals experience trauma and stress early in their lives, it can affect the brain in various ways, such as hippocampal volume, neurogenesis, and synaptic plasticity (Herpfer et al., 2012). The traumatic events that are described to cause the brain plasticity include complications experienced at birth, physical, sexual, and emotional abuse (Herpfer et al., 2012). Once the individual has reached adulthood, their brain is able to return the hippocampal volume and neurogenesis back to normal, however, synaptic plasticity remains impaired and is thought to lead to dysfunctions in adulthood (Herpfer et al., 2012). A neuropeptide that is involved in the regulation of brain plasticity is substance P, which is secreted by neurons in the central nervous system, that may help to explain the regulation of brain plasticity from early life stressors (Herpfer et al., 2012). If the stress experienced early in life is severe enough to cause an impairment of synaptic plasticity in adulthood, these individuals may exhibit dysregulation of mood, cause affective disorders, and psychiatric diseases. A psychiatric disorder that can be induced by stress is substance use disorders as the CRF induces the bahaviour linked to this addiction from the stress (Haas-Koffler & Bartlett 2012). Substance abuse disorders are denoted by repetitive cycles of use, abstinence, and relapse (Haas-Koffler & Bartlett 2012). The stress that the brain is subjected to comes primarily from the withdrawal period as the CRF produces behaviours corresponding to anxiety and a stress response (Haas-Koffler & Bartlett 2012). Reducing the possibility of relapse could

be explored by alleviating stress-induced addiction seeking behaviours (Haas-Koffler & Bartlett 2012).

Learning and memory has long been shown to affect the plasticity of synapses within the hippocampus as it induces biochemical and morphological changes within the CA1 and CA3 regions of this area (Stewart et al., 2005). Stress induction reduces the ability for learning to create changes within the brain, as was seen in the study by Stewart et al. (2005) in which the rats that were exposed to stressors experienced a more difficult time of spatial training when placed in a Morris water maze (Stewart et al., 2005). It was found, through the experiment, that stress inhibits synaptic plasticity within the hippocampus, while the prevention of this decrease in synaptic plasticity can occur with learning (Stewart et al., 2005). Learning is also able to promote recovery of maladaptive synaptic plasticity in the hippocampus (Stewart et al., 2005).

*Regulating Neuroplasticity*

Many efforts to regulate neuroplasticity within a clinical setting have been made. The concept of neuroplasticity has often been associated with and thought of as building new habits and breaking old habits, which has been found to be an effective approach. A study by Cleo et al. (2019) examined the effectiveness of two habit-based weight-loss interventions, one called Ten Top Tips that focused on forming new habits and one called Do Something Different that focused on breaking old habits. Treatment plans that were designed to both develop new habits and break poor habits were seen to be an important and effective factor in individuals with the goal of weight loss and for maintaining the weight loss (Cleo et al., 2019). By building these habits and strengthening and weakening targeted neural pathways related to these habits, results support that undesirable behaviours can be decreased (Cleo et al., 2019) By learning these new habits, it has been found to also increase cortical growth in specific areas of the brain (Romeo et

al., 2021). Romeo et al. (2021) examined language development and cortical growth through an intervention to enhance language environments for adolescents and children in families with low socioeconomic status (Romeo et al., 2021). The findings suggested that conversational turns, a back and forth conversation between an adult and child, used in these interventions supported language development as increases in cortical growth in language and social processing areas of the brain were observed (Romeo et al., 2021). This response to neuroplasticity-based intervention studies in children and adolescents has suggested that these early interventions can promote neuroplasticity and maximize the potential for positive outcomes (Weyandt et al., 2020). A literature review by Weyandt et al. (2020) further supported that neuroplasticity plays a big part in the development and recovery of both cognitive and motor skills in children and adolescents. By having targeted treatment interventions especially in these age groups, it could lead to structural and functional changes within the brain that could have lasting effects (Weyandt et al., 2020).

Many factors have been further researched into their influence on neuroplasticity. Factors that cause the brain to form and strengthen dendritic connections are known as positive neuroplasticity and factors that cause the brain to weaken dendritic connections are known as negative neuroplasticity (Vance et al., 2010). Factors that have been found to promote positive neuroplasticity include education, physical activity, social interaction, intellectual pursuits, and cognitive remediation (Vance et al., 2010). Whereas factors that have been found to promote negative neuroplasticity are poor health, poor sleep habits, poor diet, substance abuse and depression or anxiety (Vance et al., 2010). Some behaviours can affect neuroplasticity in both positive and negative ways like sexual behaviour (Herrea-Morales et al., 2019). As individuals gain sexual experience, their sexual behaviour changes and is altered resulting in the

strengthening or weakening of the connections between synapses in the brain that are involved in learning and memory (Herrea-Morales et al., 2019). By understanding how lifestyle and behaviours can affect neuroplasticity it can assist in working towards optimal cognitive health through methods to increase positive neuroplasticity and avoid negative neuroplasticity (Vance et al., 2010).

Psychologists have a big role in driving and increasing the use of neuroplasticity-based practices in a positive direction through their training in evidence-based behavioural techniques (Shaffer, 2016). When clinicians use the neuroscience findings on neuroplasticity and brain-plasticity strategies to inform the treatments they provide to clients, they can increase the compliance of their clients to make lasting lifestyle changes that can enhance brain plasticity (Shaffer, 2016). There is some research examining some of these evidence-based interventions for positive neuroplasticity changes in an effort to improve one's general health including environmental stimulation and novel challenges (Shaffer, 2016). Possible benefits could also be observed in an effort to promote neuroplasticity through mindfulness meditation and calorie restriction (Shaffer, 2016). Although continued development of better methods of assessing neuroplasticity in humans is needed, it is important to use current knowledge of neuroscience to inform our practice and incorporate brain-plasticity based strategies into clinical practice (Cramer et al., 2011; Shaffer, 2016). Neuroplasticity has such a big effect within humans and has the possibility to impact clinical applications and become effective clinical therapies (Cramer et al., 2011). By examining a neuroplasticity-based approach in action, findings suggested that neuroplasticity skills training can improve outcomes in behaviour, but it must be maintained through continued exposure to therapy (Cramer et al., 2011). For neuroplasticity-based interventions to become more common, therapeutic exposures have to reliably show behaviour

changes in humans from neuroplasticity and there should be better ways to assess neuroplasticity changes in humans like using biomarkers to see responses to treatment (Cramer et al., 2011). Further research should examine neuroplasticity focused therapies and look into the effects when combined with other therapies (Cramer et al., 2011). Neural Network Therapy® could be a prime example of brain-plasticity based strategies in clinical treatment.

Biological methods in an effort to regulate neuroplasticity have also been examined. As the regulation of neuroplasticity is kept up by histone modifications through the activation and inhibition of transcription, histone codes that are important in the modification of genes can be chemically modified (Geng et al., 2021). Through this chemical modification, it could be possible to activate or inhibit specific histone modifications in an effort to regulate neuroplasticity though more research is needed into this topic. Though brain plasticity is very dynamic and many other factors can affect neuronal structure (Kolb et al., 2003). Kolb et al. (2003) found that factors that affect neuronal structure included pre and post natal experiences, psychoactive drugs, gonadal hormones, maturation, aging, diet, disease, genetics, stress, and injury. The main two examined were the effects of experience and psychoactive drugs, both of which are involved in clinical practice (Kolb et al., 2003). Researchers examined the effects of early experiences on brain development and found that early experiences, even prenatal experiences, later affected brain development (Kolb et al., 2003). As well, the use of psychoactive drugs is predicted to cause an increase in dendritic material in areas of the brain related to the reward system which could explain synaptic organization in those struggling with addiction (Kolb et al., 2003). Lasting neuronal change has also been associated with moderating synaptic plasticity in the prefrontal cortex through monoamines (Goto et al., 2010). A deficit in synaptic plasticity in the prefrontal cortical neurons, that appear to have the ability for synaptic

plasticity, is thought to be a contributing factor to developing psychiatric disorders like schizophrenia, drug addiction, mood disorders, and Alzheimer's disease (Goto et al., 2010). Monoamines like dopamine can influence the prefrontal cortical neurons and have the possible ability to increase synaptic plasticity and help in the treatment of some psychiatric disorders (Goto et al., 2010).

**Addiction in the Brain**

The brain is sensitive to various substance and non-substance addictions and parts of the brain will respond differently. The epithalamic lateral habenula is a portion of the brain that is especially vulnerable to addiction and is partially responsible for withdrawal from substance-based addictions (Clerke et al., 2021). The lateral habenula becomes altered when addiction arises and negative behaviours that begin to develop are associated with this alteration (Clerke et al., 2021). The changes that are found within this structure are glutamatergic transmission, synaptic plasticity, as changes to the GABA receptor-mediated neurotransmission (Clerke et al., 2021). Understanding this structure is critical to developing strategies to target addiction and addiction withdrawal as the cellular and synaptic modifications that occur during this period are related to how individuals experience their addiction (Clerke et al., 2021). The lateral habenula plays an important role in building modifications to inhibit responses to specific stimuli (Clerke et al., 2021). Interventions for the alterations that occur within the lateral habenula are potential avenues of research towards mitigating the negative behaviours of addiction and addiction withdrawal. The lateral habenula is involved in the habenula-frontal circuit that contributes to decision making based upon the ascribed value that each choice has received from the decision-maker (Duan et al., 2022). Addictive drug use is the attribution of unfavourable decision-making due to a flaw within the habenula-frontal circuit (Duan et al.,

2022). With repeated drug abuse, the strength of the habenula-frontal circuit increases and this is reflected by the development of negative behaviours and decisions (Duan et al., 2022). Understanding the difference between addictive drug use and recreational drug use provides an avenue for treatment development. Another region of the brain that is involved with addiction, specifically nicotine addiction, is the ventral tegmental area (VTA) (Grieder et al., 2014). This region is recognized for its purpose in the reinforcement of drug abuse (Grieder et al., 2014). The VTA expresses corticotropin-releasing factor (CRF) within humans and rodents and overtime the abuse of nicotine leads to corticotropin-releasing hormone (Crh) mRNA levels which causes the disorganized response to stress from nicotine (Grieder et al., 2014). The response from this leaves the brain with negative effects (Grieder et al., 2014).

Addictions can take many forms and lead to disruptions within the brain's reward systems. Olsen (2011) wrote a review that highlights connections between drug and non-drug (such as eating, exercise, sexual behaviour, and gambling) addictions (Olsen 2011). The manifestation of addiction causes neuroplasticity within the brain and the various addictions show adaptations in the same brain regions (Olsen 2011). These regions include the amygdala, which is responsible for the negative reinforcement and behaviours of addiction, and the mesocorticolimbic system, which is involved in the sensitization of addictive substances. Due to the same brain regions being affected by different types of addictions for the processing of rewards, non-drug rewards have the ability to influence neuroplasticity (Olsen 2011). As these regions are the same for both drug and non-drug addictions, the avenues of treatment are similar (Olsen 2011). In addiction, an individual's reward system can become disrupted leading to the partaking in addictive substances (Koob & Le Moal 2001). The continuous susceptibility to relapse in addiction is influenced by allostasis, the process of bringing the body back to

homeostasis and altering the levels of physiological systems when responding to the external environment (Koob & Le Moal 2001). The use of addictive substances in excess disrupts the brain's reward and stress system exponentially, and leads to a motivation for using these addictive substances (Koob & Le Moal 2001). In a study by Hollmann et al. (2012), it was found that the desire for food affects the brain's ability to control the desire for certain foods (Hollmann et al., 2012). The brain has mechanisms that are involved in the regulation of food desire; Hollmann et al. (2012) used functional magnetic resonance imaging (fMRI) to view the areas of the brain that contribute to this conscious regulation (Hollmann et al., 2012). The brain regions activated when regulating food include the dorsolateral prefrontal cortex (dlPFC), pre-supplementary motor area, inferior frontal gyrus (IFG), dorsal striatum (DS), bilateral orbitofrontal cortex (OFC), anterior insula, and the temporo-parietal junction (TPJ) (Hollmann et al., 2012). The study found that when individuals possess a higher level of cognitive restraint, there is a tendency to regulate hedonic foods (Hollmann et al., 2012). The activation of the valuation and reward systems as well as a response inhibition within the brain occurs when an individual reassesses unhealthy foods (Hollmann et al., 2012). Alcohol addiction has the potential to cause remodelling within the brain with histone modifications (Pandey et al., 2008). Histone modifications play a role with the regulation of gene expression when suffering with addiction and an individual's brain chromatin is susceptible to remodelling when the modification of histones is occurring (Pandey et al., 2008). Brain plasticity is heightened from alcohol addiction due to the enzymes histone acetyltransferases and histone deacetylases that are present in the regulation of chromatin structure (Pandey et al., 2008). The researchers in this study determined that histone deacetylase inhibition is a beneficial therapy towards treating the symptoms that individuals experience when going through withdrawal of alcohol as these

individuals often face histone modifications leading to chromatin brain remodelling (Pandey et al. 2008). Illicit drug use, specifically cocaine, causes restructuring within the brain from excessive use (Sadri-Vakili et al., 2010). Cocaine addiction causes histones to be modified through acetylation, thus inducing the remodelling of chromatin (Sadri-Vakili et al., 2010). These modifications lead to the changes in gene expression, namely transcription, DNA repair, and replication, while brain-derived neurotrophic factor becomes increased within the medial prefrontal cortex and this variation leads to the understanding of how to better treat addictions (Sadri-Vakili et al., 2010). The understanding of how various addictions influence the reward system and disrupt regulatory pathways can help with the knowledge of how addictions affect learning.

Addiction has the ability to influence reward-related behaviour and influence learning and memory due to the modification to neural processes. The major components that are involved in persistent drug use are cellular and molecular mechanisms of memory-making within the circuits of the forebrain (Hyman et al., 2006). Illicit substances mimic the effects of neurotransmitters: opiates, psychostimulants, nicotine, alcohol, and marijuana which mimic endorphins, dopamine, acetylcholine, GABA glutamate, and anandamide, respectively (Hyman et al., 2006). The mimicking of these neurotransmitters give addiction the ability to exhibit aggressive rewarding effects that cause the reinforcement of desiring these substances (Hyman et al., 2006). With continuous use of addictive substances, the memory storage that an individual possess diminishes as the experience-dependent plasticity of the brain affects the areas involved with this (Hyman et al., 2006). Addiction can cause memory loss and reduced capacity for learning due to the rewiring of the brain's pathways inducing plastic changes. The research that has been conducted within the realm of smartphone addiction and learning is extensive. It has been found

that this type of addiction leads to negative consequences in an individual's daily life (Park & Lee, 2012), especially with the capacity to learn (Yildiz Durak, 2018; Rozgonjuk et al., 2018). Since the introduction of the smartphone, this usage has caused individuals (typically those of elementary to university age) to perform worse in academics (Yildiz Durak, 2018; Rozgonjuk et al., 2018). The study of addiction and how it influences neuroplasticity, memory, and learning is important to begin to develop treatments for specific addictions, be it substance or non-substance addictions.

The treatment of addiction can be a long process as individuals can experience multiple relapses within their treatment. In a publication by Haas-Koffler & Bartlett (2012), they reviewed the effects of CRF and how exploring ways to regulate this system can lead to possible treatments for addiction (Haas-Koffler & Bartlett 2012). CRF regulation could help with the treatment of addiction as it would treat the positive reinforcement that is experienced with the use of addictive substances as well as the negative reinforcement of withdrawal in addiction (Haas-Koffler & Bartlett 2012; de Guglielmo et al., 2019). The neurons that are present within the CRF system are the neurons that comprise most of the central nucleus of the amygdala and these neurons are responsible for aspects of withdrawal from alcohol (de Guglielmo et al., 2019). Inactivating the CRF-dependent amygdalofugal pathway reverses the behaviours expressed from addiction of alcohol (de Guglielmo et al., 2019). Substance use and non-substance use addiction impact the brain's reward system, alters levels of neurotransmitters, and affects regions of the brain that are involved in memory and learning. Research in these areas have revealed many developments for possible treatments and restore the brain back to its normal cognitive functioning.

**Relationship Between the Amygdala & Prefrontal Cortex**

The amygdala and prefrontal cortex in the brain are highly connected. The amygdala is part of what is known as the primal brain which includes the hindbrain and the medulla (Šimić et al., 2021) This primal brain has been retained for the survival of the human species to be able to distinguish between threatening and non threatening situations (Šimić et al., 2021). This highlights the role of the amygdala in learning, synaptic plasticity, and fight-or-flight responses which is a function that has remained in the human brain throughout evolution (Šimić et al., 2021). Previous research has examined the relationship between the amygdala and specifically the dorsomedial prefrontal cortex (Moses-Kolko et al., 2010). Mothers with postpartum depression have shown less dorsomedial prefrontal cortical activity and reduced effective connectivity between the dorsomedial prefrontal cortex and the amygdala (Moses-Kolko et al., 2010). When there's more activity in the amygdala and less in the prefrontal cortex, we tend to experience more fight-or-flight emotions or stress like that of postpartum depression (Moses-Kolko et al., 2010).

The amygdala also plays a role in making appropriate behavioural responses (Cohen & Paz, 2015). Context information is encoded by amygdala neurons similarly to the way they are encoded in the prefrontal cortex suggesting that the amygdala and prefrontal cortex actively work together to maintain abstract cognitively relevant information (Cohen & Paz, 2015). When abstract context information was not maintained in the amygdala, it resulted in behavioural failures suggesting that the amygdala is very important in the process of making appropriate behavioural responses (Cohen & Paz, 2015). It's important when examining the relationship between the amygdala and prefrontal cortex to acknowledge that they are highly connected and the context of the information matters (Cohen & Paz, 2015). Thus careful separation of

reinforcement driven computations and abstract rule-based representations are needed to examine the amygdala and prefrontal cortex (Cohen & Paz, 2015).

The connectivity between the amygdala and frontal cortex is integral to examine in the context of other psychiatric disorders including social anxiety disorder (SAD). Patients with SAD have shown to have reduced connectivity between the amygdala and the rostral anterior cingulate cortex (ACC) and dorsolateral prefrontal cortex (DLPFC) when perceiving fearful stimuli and at rest with the absence of the fearful stimuli (Prater et al., 2013). This suggests that the relationship between the amygdala and DLPFC is a phasic abnormality that is dependent on the presence of a social threat (Prater et al., 2013). Since dysregulated amygdala connectivity with the DLPFC was only seen when perceiving threatening stimuli, it could be due to a decrease in emotion regulation and increase in response to the threatening information in SAD (Prater et al., 2013). The amygdala in social anxiety disorder (SAD) has also been examined through neuroimaging (Klumpp & Fitzgerald, 2018). Pre-treatment functional connectivity between the frontal areas of the brain and the amygdala have predicted improvement suggesting that with treatment, the connections between them support emotion processing and regulation (Klumpp & Fitzgerald, 2018). In the pre-to-post treatment studies, there has been a decrease in amygdala responses and altered functional connectivity in the pathways of the amygdala regardless of the treatment individuals received suggesting that the amygdala is a potential effective treatment target (Klumpp & Fitzgerald, 2018). These results showed that those with SAD often have a very active amygdala as they are often in fight-or-flight mode, but treatment can help to decrease the amygdala responses and increase connectivity between the amygdala and other areas of the brian like the frontal structures (Klumpp & Fitzgerald, 2018). This suggests that often there's a decrease in connectivity between the amygdala and prefrontal cortex when individuals are

suffering from different psychiatric disorders, but through treatment increased connectivity can be achieved.

**Conclusion**

Neuroplasticity in the brain has been thoroughly researched for many years and has the possibility to have positive impacts in clinical treatment. Neuroplasticity, the ability for the brain cells to change and reorganize its structure, function, and connections in response to internal and external stimuli (Cramer et al., 2011) has been examined to understand the biological basis, its relationship and stress, and efforts to regulate neuroplasticity. By understanding these mechanisms of neuroplasticity and previous efforts to implement it into clinical settings like therapy, the connected benefits of changes in behaviour and improvements in an individual's mental health and well-being can be seen. By examining the current literature on neuroplasticity, it revealed the gap in the current literature regarding neuroplasticity being implemented and used in clinical settings and practice. Gaps that were identified in the studies concerning neuroplasticity are that there are shortcomings in the understanding of spike-timing dependent synaptic plasticity (Abbott & Nelson 2000) and how the calcium code is interpreted by sensors within the brain to influence neuroplastic changes (Cavazzini et al., 2005). There is also a gap in the knowledge for how permanent the synaptic changes will be and if the exercises developed to influence beneficial behavioural changes will remain permanent from the neuroplastic modifications (Kolb et al., 2003). This literature review also examined addiction in the brain as it relates to neuroplasticity and important connections in the brain between the amygdala and prefrontal cortex. Research supports that addiction and connectivity in the brain between the amygdala and prefrontal cortex are complex topics, but neuroplasticity plays a part in this process and suggests that neuroplasticity based practices could be used in the treatment of

addiction (Clerke et al., 2021; Olsen 2011; Shaffer 2016). By furthering our understanding of neuroplasticity and the connection between the amygdala and prefrontal cortex in the brain, it helps work towards new therapy techniques and research that may provide support for them like that of Neural Network Therapy®.

Neural Network Therapy® is a holistic therapy approach created in 1997 by Canadian Family Health Counselling that focuses on making new habits in place of unwanted ones. The literature examined provides support for two of the core exercises used in Neural Network Therapy®, “Playdough Brain” and “The Crocodile” (Sargent, 2023). The one core exercise “Playdough Brain” strives to gain an understanding of neuroplasticity and uses it to build habits (Sargent, 2023). The other core exercise “The Crocodile” explores how the body responds to stressful situations by considering the “Reptilian Brain” and the connection between the amygdala, the “Old Brain”, and the prefrontal cortex, the “New Brain” (Sargent, 2023). Although much more research is needed to understand how to implement neuroplasticity-based therapies and the implications of using these approaches in practice, Neural Network Therapy®, which is currently being used in practice at Canadian Family Health Counselling, could allow us to examine these exercises and the scientific basis behind them to start to fill the gap in research of neuroplasticity being implemented into clinical practice to promote changes in behaviour and cause improvement in one's mental health and well-being including in those struggling with addiction.

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