Was Freud right? Is intensive psychotherapy needed to harness the brain's natural plasticity?

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Attestation of Authorship

"I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgements), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning".

Signature

Ruth Bradley

Date

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Abstract

Is intensive psychotherapy needed to harness the brain's natural plasticity? In order to throw light on this evidence-based question this dissertation conducts reviews of three bodies of literature:

First it conducts an overview of the neuroscience literature pertaining to the concept of neuroplasticity associated with intensive learning, as psychotherapy is considered an emotional learning experience, to address the question, does intensive learning alter neural structure? The findings from this review indicate that intensive learning does indeed result in significant neural change.

Second, it carries out a systematic review of the neuroimaging literature to answer the following question: What is known about the neural effects of psychotherapy? The neuroimaging studies in this review clearly demonstrate that plastic changes occur not only within brain systems but also at a molecular level and these changes, in response to psychotherapy, are similar to those observed in psychopharmacotherapy treatments.

The third review carries out a systematic review of the psychotherapy/psychoanalytic literature to investigate the question; do more frequent psychotherapy sessions or intensive psychotherapy produce better outcomes? The results of this search draws convincing evidence that demonstrate that intensive therapy produces better outcome, especially in the long term, i.e. lasting changes.

The clinical hypothesis derived from all of these results - a supposition which needs testing - is: intensive psychotherapy (frequent psychotherapy sessions) is more effective in harnessing the brain's plasticity in order to maximise change.

Introduction

> All our provisional ideas in psychology will presumably some day be based on an organic substructure. Freud (1914, p. 78).

I have always had an insatiable curiosity for understanding what brings about change and also for making sense of how things work. This curiosity extends to both the psychology of the mind and the biological sciences. When I studied psychotherapy, although I felt enriched by the programme and the writings of many theorists, I noticed that there was an absence of the biological or neurosciences (apart from one lecture on Neuropsychotherapy on the works of Grawe, 2007). I became curious about how the findings from neuroscience might impact the practice of psychotherapy and have subsequently read widely on the subject. I took the liberty of writing about my interests to some eminent authors namely, Louis Cozolino, Eric Kandel, Norman Doidge, Jonathan Shedler, Allan Schore, James Rose, Margaret Wilkinson and Mark Solms, and was encouraged by them to pursue this project into some potential learning for psychotherapy from neurological research.

In the last decade there has been significant advancements in psychological medicine and the neurosciences, particularly related to our understanding of the brain – these findings have had enormous implications for psychotherapy and the way that it is practiced especially with reference to attachment theory and regulatory disorders. A number of authors and therapists such as Briere, Cozolino, Schore, Solms, Siegel and Wilkinson have drawn on this neurobiological and neuroscientific research, that relates to human emotional development, to make sense of psychopathology and the therapist-patient relationship. We have come to understand, from a biological perspective, how early negative attachment relationships can affect a child's psychological and emotional development. Dysfunctional attachment relationships can have a profound

neurobiological impact on the developing brain and central nervous system. Although this can sometimes result in long term deficits and altered neural structures, it is treatable with psychotherapy. For example, the practice of psychotherapy that takes these neuroscientific findings into consideration may look at ways of helping emotionally dysregulated patients develop a capacity to self soothe using tools such as psycho-education and the also the attachment relationship between therapist and client to facilitate emotional homeostasis (Panskeep, 2009).

Historically, psychotherapy and psychoanalysis have used rich metaphor as a means of articulating psychoanalytic processes and, as an adjunct to this, findings from neurobiology and the neurosciences can provide a means of exploring the physiology beneath these processes. For example, using a neurobiological model, Freud's original theories on free-association can also be thought of as an exploration of interconnected neural pathways in the brain. Doidge (2010) notes that Freud's "law of association by simultaneity" implicitly links changes in neuronal networks with changes in our memory networks – "neurons that fired together years before, wired together, and these original connections are often still in place and show up in a patient's free associations" (p. 223). This wiring of the brain, that was previously thought to be static or hardwired in adulthood, has been found to be malleable in that the brain literally rewires itself in response to stimuli – this concept is called neuroplasticity[1] which has been a key finding in neuroscience (Kandel & Squire, 2000). Berlucchi & Buchtel (2009) mention that "plasticity refers to a change in structure in response to an external force and the maintenance of that shape after removal of the force (as opposed to "elasticity", where the shape returns to its original form after removal of the force)" (p. 318).

[1] The terms 'neuroplasticity', 'neural plasticity', 'synaptic plasticity' and 'brain plasticity' are used interchangeably throughout this study.

According to Hebb, a Canadian neuropsychologist, a fundamental rule of neuroscience is the finding that nerve cells that fire together wire together (Kandel, 2006; LeDoux, 2003; Solms, 2002). In other words, if something is practiced repeatedly, the connections between neurons in the neuronet form a closer relationship with one another. This also occurs in reverse: nerve cells that cease to fire together, no longer wire together and they lose their long term relationship.

What causes the brain to alter its neuronal structures and what influences these changes? Are the rates of change proportional to some external stimuli? I wondered whether this concept of neuroplasticity could be harnessed for more effective clinical practice and if so, how? It might be then that, when psychotherapy provides the patient with a new relational experience, it alters the way in which their neuronets[2] are wired. While I have read numerous research articles in the medical literature that uses the brain's plasticity to better patient clinical outcome in stroke recovery / traumatic brain injury (Cherney, Patterson, & Raymer, 2011; Dombovy, 2004; Hancock, Shepstone, Rowe, Myint, & Pomeroy, 2011), I had not come across any literature pertaining to the use of this concept within the field of psychotherapy. I wondered whether there was any research available that examines how to best to harness the brain's plasticity in response to psychotherapy.

Further to the above, in my clinical practice, I witnessed significant changes in response to psychotherapy, especially more frequent therapy, and have pondered what it was that brought about change and how it occurred. What was it about more therapy sessions per week that enhanced change? Is this related to the neuroplasticity of the brain? Was there any way that I could deepen or better my clinical practice by drawing from the valuable findings within the medical, biological and neuroscientific

[2] The term 'neuronet' is used interchangeably with 'neuronetwork' or 'neural network'.

paradigms? This reminded me of Freud, the founder of psychotherapy, who had had grounding in the biological sciences; I am aware that, in the end, Freud treated his patients five to six times per week for six months. Did Freud know something about the brain's malleability that was ahead of his time?

Freud (1956 [1886]), originally trained as a neurologist and was interested in how psychological syndromes were represented anatomically between different parts of the brain. Although the main law underpinning neuroplasticity of wiring together and firing together is called Hebb's law, this concept was proposed by Freud sixty years before Hebb, in his (Freud's) "Project for a Scientific Psychology" in 1888. Freud's hypothesis is as follows:

> Now there is a basic law of association by simultaneity, which operates in the case of pure ψ activity, of reproductive remembering, and which is the foundation of all links between the ψ neurones. We find that consciousness-that is, the quantitative cathexis of a ψ neurone, α,2-passes over to another, β, if α and β have at some time been simultaneously cathected from ϕ (or from elsewhere). Thus a contact-barrier has been facilitated through the simultaneous cathexis α-β. It follows in the terms of our theory that a Qή passes more easily from a neurone to a cathected neurone than to an uncathected one (1957, p. 318).

In summary, Doidge (2010) notes that "Freud stated that when two neurons fire simultaneously, this firing facilitates their on-going association" and goes on to emphasise that when neurons fire together in time, this creates links between them and, as referred to earlier, this phenomenon he called "the law of association by simultaneity" (p. 223).

Since there was no imaging technology or well developed instruments for studying the anatomical and physiological correlates of psychological phenomena in the "Project for a Scientific Psychology", Freud eventually abandoned this project and diverted his attention to psychoanalysis – predicting that in the future psychoanalysis and neuroscience would become one discipline.

> I shall entirely disregard the fact that the mental apparatus with which we are here concerned is also known to us in the form of an anatomical preparation, and I shall carefully avoid the temptation to determine psychical locality in any anatomical fashion. I shall remain on psychological ground (Freud, 1900, p. 536).

Following on from Freud's original project, there are a number of theorists and psychotherapists who embrace both the biological and the psychological (Cozolino 2006, Grawe, 2007; Kandel, 2000; Peled, 2008, 2011; Schore; 2012, Siegel, 2012; Solms, 2003) and some have written about how both fields of practice would benefit enormously if they could learn from each other. Eric Kandel, being one of these theorists who is a neuropsychiatrist and who won a Nobel Prize for his work, notes the following:

> As I began my residency in psychiatry, I sensed that psychoanalysis could be immeasurably enriched by joining forces with biology. I also thought that if the biology of the twentieth century were to answer some of the enduring questions about the human mind, those answers would be richer and more meaningful if they were arrived at in collaboration with psychoanalysis. Such a collaboration would also provide a firmer scientific foundation for psychoanalysis (2006, p. 365).

With the development of neuroscience in recent years, it is now possible to re-embark on Freud's original project, re-joining psychoanalysis and neuroscience. As Peled notes: "bridging psychoanalysis and neuroscience opens up each discipline to the fruitful advances of the other, substantially increasing our understanding of the human experience" (2008, p. 1).

The Study

> Exactly how the mind changes during the therapeutic process is the fundamental puzzle that the synthesis of neuroscience and psychotherapy seeks to solve (Panksepp, 2009 p. 4).

The purpose of this study is a classic evidence-based-practice study (a derivative of the evidence-based medicine model) where a practitioner conducts a critical systematic review of the literature in order to propose evidence-based notions to inform practice. It explores the concept of neuroplasticity and particularly how it relates to psychotherapy

clinical practice, especially therapy conducted at high frequency. The research is reviewed to find out whether psychotherapy does indeed change neural structures in the brain. Parallels are then drawn between: the psychotherapy / psychoanalytic research on session frequency or dosage, the neuroimaging research that relates to the efficacy of psychotherapy, and the research that pertains to neuroplasticity and learning since psychotherapy is considered an emotional learning experience (Arden, 2009; Cozolino, 2010; Panksepp, 2009; Peled, 2008). I then establish that intensive or iterative learning has profound effects on neuroplasticity and that psychotherapy, as a learning experience, alters the brain significantly. I take something of a leap and consider that it may be that higher session frequency (or referred to as intensive psychotherapy) may be more effective from a neuroplastic point of view than once a week therapy – this notion is consistent with Freud's practice of psychoanalysis five times a week for six months.

Before I embarked on this study, I made contact with a number of important theorists (as previously mentioned), who I will be referencing in this work, to ask for their thoughts on the viability of the leap in finding a relationship between neuroplasticity and session frequency – there is currently no research linking to the two concepts. I felt most grateful to receive responses from these authors who were not only in support of my study - for example, Nobel Prize winning neurobiologist Eric Kandel mentions that: "Your thesis topic sounds terrific. This is exactly what is needed" (personal communication, 11 November, 2011) – but also went to on provide some valuable thoughts around the topic, referenced later in this piece of work. Therefore, although perhaps a leap, it may be an important one especially holding in mind what may prove to be effective in clinical practice.

However, in addition to the above, it feels pertinent to mention that by taking neurology seriously, I am cognisant that the brain is not the mind. Solms (2003) identifies that there has been a large chasm between the lived reality and experience of

the mind and neuropsychology and that this prompted Oliver Sacks, a neurologist, to write that "neuropsychology is admirable, but it excludes the psyche" (Sacks, 1984, p. 164). Cozolino (2010) mentions that it is common to create divide between the brain and the mind and to direct attention to either one or the other, almost as if the other is not relevant. He goes on to say that "the problem with this approach is the barrier it creates to understanding that the human experience of the brain and mind is essentially a unified process" (p. 1). Therefore, I think that given the complexity of the leap made between the neuroscience research and therapy practice, it is important to mention that it is hypothetical in nature and needs to be tested clinically.

Chapter Outline

The chapters in this study are remarkably different from each other as they attempt to link biological concepts with psychotherapy practice. Chapter One outlines the methodology and methods for this study, including its context of Evidence-based Medicine (EBM).

Chapter Two provides an overview of neuroanatomy in terms of neuroplasticity and explains in detail the concept of neuroplasticity. It initially examines the structures of nerve cells within the brain and expands on how these nerve cells connect with one another to form neural networks. Diagrams have been included as reference points for these structures and make it easier to conceptualise the theories. In addition, I have drawn on the medical research, associated with neural plasticity and how the brain is changed by learning experiences, to illustrate the concept of neuroplasticity in action. Having shown the correlations between changes associated with intensive learning and psychotherapy, Chapter Three proceeds to consider how the brain changes in response to psychotherapy which explores the question, is there any literature that demonstrates neural change in response to psychotherapy?

Chapter Three is a systematic literature review which answers the question of whether psychotherapy actually does alter neural structures within the brain or have a significant effect on the brain. While this research was undertaken systematically, due to word count limitations, not all studies will be elaborated on as the purpose of this chapter is to illustrate the findings related to neural changes in response to psychotherapy. However, findings from all the studies will be included in a table that outlines the neural changes in response to each study. Although these studies are around the efficacy of psychotherapy, they are presented from a medical model paradigm with numerous neuroanatomical references which can be confusing at times – I have included brain images as a reference point for the neuroanatomical structures that have been modified by psychotherapy.

In addition to this, I felt struck by the differences between this type of research and the psychoanalytic research (in Chapter Four) which seems to be worlds apart. After conducting research within these two very different paradigms, my reading around the struggles associated with conflict between the two began to make sense – it is no wonder that there is rivalry between the two - they approach the same questions from enormously different standpoints. As the reader, it may be useful to hold in mind your preferential stance and consider the other with an open mind. The findings from this neuroimaging chapter that answers my question of whether psychotherapy changes the brain, led me back to think about neuroplasticity and how this relates to psychotherapy session frequency.

Chapter Four is another systematic literature review of the psychotherapy and psychoanalytic research pertaining to session frequency or therapy dosage (these terms are used interchangeably in the research). There have been very few studies to date that have examined the psychotherapy outcomes in response to intensive treatment, or high frequency treatment vs. low frequency treatment. Although there are few studies, the

ones that have been carried out have suggested remarkable results around the long term outcomes associated with high frequency psychotherapy.

Lastly, this study closes with a discussion around the findings from each chapter and how they link together, as well as the implications that this may have for clinical practice. I also discuss the limitations of the study, caveats associated with the research and suggestions for further study. In addition, there are a number of other avenues that were not able to be included in this research, for example, organic psychiatry, dynamic systems theory, the role of memory (storage and retrieval) in psychotherapy and emotional regulatory systems.

Chapter 1 Methodology and Methods

This dissertation employs the methodology of two systematic literature reviews and one overview. The chapter follows the standard structure for enquiry in the Evidence-based Medicine model and undertakes the first three steps of this framework, as outlined below. The aim is to provide an overview of the neuroscience literature around neuroplasticity, and to systematically review both the neuroimaging literature and the psychoanalytic literature to answer the following research questions which arose from wondering whether Freud was right: "Is intensive psychotherapy needed to harness the brain's natural plasticity?" While the main question will be addressed, a number of other questions also need to be answered in order appropriately synthesise the research. What is known about the neural effects of psychotherapy? Does intensive learning alter neural structure? Do more frequent psychotherapy sessions or intensive psychotherapy produce better outcomes? The search strategies, additional exploration, and consultation with the experts in the field are also outlined below.

The Evidence-Based Medicine Model

> It's about integrating individual clinical expertise and the best external evidence (Sacket et al., 1996, p. 71).

Evidence-based medicine is designed to accurately and conscientiously utilise the best evidence available to guide clinical practice. It plays an important role in bridging gaps between research and clinical practice (Reynolds, 2000) by producing knowledge that assists positive outcomes in patient care while, at the same time, extends "reflective professional discourse" within disciplines (Brown, 1999, p. 4). Evidence-based practice (EBP) was developed from EBM as a model that can be used for research beyond the health sciences. It is an important framework as it provides a sound and proven structure as a tool for guiding intensive investigations into evidence that has been explored and published on

particular subjects across a diverse range of interdisciplinary practices. Abraham Maslow mentions that “if the only tool you have is a hammer, every problem begins to resemble a nail” (cited in Javanbakht, 2011, p. 243). Therefore, without this model, it would be impossible to make informed decisions and recommendations for best practice.

Although critics of EBM assert that it devalues clinical judgment and the art of medicine, clinical expertise continues to carry significant weight in EBM when making decisions about the care of patients by allowing integration between research evidence, patient preferences and clinical state. Gray (2004) suggests that “rather than being "cookbook medicine", EBM actually empowers clinicians to make their own decisions about patient care, guided by the best available evidence to support those decisions" (2004, p. 3). However, despite these 'good things', Alyas & Bhui note “there is still a backlash against EBM from clinicians who feel that the over-reliance on these concepts threatens individual patient care and belittles the use of clinical reasoning based on experience and investigation of pathophysiological mechanisms" (2005, p. 26) - particularly evident in the field of mental health research.

Psychotherapy does not always fit very well within the strict EBM model (Starcevic, 2003) and often conflicts are visible, especially in the area of the usefulness of treatment. Treatment outcomes within the field of psychotherapy are also not as straight forward to measure and, according to Allot (2005), “recovery is a journey as much as a destination. It is different for everyone” (p. 324). Therefore, some practitioners are sceptical of the validity of using an EBM model within psychotherapy and there remains much distrust of the principles of applying research evidence to alter psychotherapy practice (Parry, 2000).

While psychotherapy does not always fit strictly within the EBM, this model is an appropriate model for the research carried out in this project as it provides an excellent framework for a thorough review of the literature available. A systematic literature review is an essential first step of locating answers within the literature as the databases that are searched contain a wide variety of publications from a number of interdisciplinary sources.

This provides valuable input into locating answers to questions from various different angles which I feel is fundamental to employing recommendations for further research or for best practice.

The framework that this study will be based on is outlined in the 5-step EBM process (below) typically used in evidence-based psychiatry, although, given the limitations of this paper, only steps 1-3 will be addressed (Gray, 2004, p. 11).

1. Formulate the question
2. Search for answers (systematic literature review)
3. Appraise the evidence
4. Apply the results
5. Assess the outcome

Systematic Literature Reviews

Systematic literature reviews are employed as an important step within EBM and are considered the top of the hierarchy of evidence (Josette, 2012). According to Dickson (1999) systematic reviews "locate, appraise and synthesise evidence from scientific studies in order to provide informative, empirical answers to scientific research questions" (p.42). It is a methodology which is intended for quantitative studies using randomised control trials (Reynolds, 2000), and is considered the 'gold standard' for assessing the usefulness of treatment within the field of quantitative research (Dickson, 1999).

Although an overview is provided of the neuroscience literature, the main emphasis of this study will be to systematically review the literature relevant to the research questions. An overview differs from a systematic literature review in that it is not necessarily focussed on one particular point and the search strategies and criteria are not explicitly specified and as are typically employed in systematic reviews. In addition, while there are other methods that could have been used to investigate the research questions such as structured interviewing or other evidential sources such as observations, experiences and general literature, which are all valid forms of evidence in

psychotherapy (Goodheart, 2004), the systematic review is most applicable to my research since it includes questions pertinent to the science as well as psychotherapy literature.

Therefore, this review provides a comprehensive framework for appraising the literature, and ascertaining current knowledge in the field and, due to the systematic nature of the review, reduces tendencies toward bias which is necessary especially when the review is being carried out by only one researcher.

Systematic literature review vs. Integrative reviews

Another method often used in conducting research is the integrative review. As with systematic literature reviews, integrative reviews (Noblit & Hare, 1988) are also rooted in the positivist paradigm, but involve techniques such as meta-analysis, which is concerned with the assembling and pooling of data. A basic comparability between phenomena is required so that the data can be aggregated for analysis. This form of review is often employed when a systematic literature review produces enormous and unmanageable amounts of relevant material.

However, given the limited number of relevant articles available in this study, the systematic literature (consistent with the EBM model), provides the best structure for means of synthesising and appraising the literature.

The EBM Question(s)

This study is guided by a wondering – *was Freud right?* From this emerges the main research question: *Is intensive psychotherapy needed to harness the brain's natural plasticity?* While the main question will be addressed, a number of other questions also need to be answered in order appropriately synthesise the research. *What is known about the neural effects of psychotherapy? Does intensive learning alter*

neural structure? Do more frequent psychotherapy sessions or intensive psychotherapy produce better outcomes?

In accordance with the EBM model, a systematic review will be carried out to examine the neuroimaging literature to find out whether psychotherapy alters neural structure and to relate this to the systematic review of the psychotherapy literature on session frequency.

Combining Science and Psychotherapy Research

This study contains two systematic literature reviews (SLR), chapter three and four, and one overview (Chapter Two) of the literature. An exhaustive search has been carried out to locate relevant literature using not only the comprehensive EBM model, but using Internet searches via search engines such as Google. Once the evidence had been located, each study was carefully appraised for its rigour and relevancy. Since some of these studies contain medical and neuroanatomical references, I felt that, in order to have a sound understanding of the material, additional study was necessary. I read numerous medical and neuroscience books and articles to educate myself in this arena to be in an appropriate position to synthesise the research material accurately. The following section describes the search process undertaken for each chapter.

Chapter 2 – Neuroplasticity (an overview)

As mentioned previously, an overview is not necessarily focussed on a single concept with specific search criteria and for this reason, it is an applicable method for this chapter. Since a number of important neural concepts are presented in this particular chapter, the overview provides a good framework for the illustration of these concepts.

In preparation for this overview, an enormous amount of medical and neuroscience literature pertinent to the brain's remarkable plasticity was reviewed. Due to recent technological advances (such as neuroimaging techniques), medical researchers are now exploring how best to harness the brain's plasticity in the treatment of neurological and medical conditions such as traumatic brain injury, strokes and aphasia (Cherney, Patterson, & Raymer, 2011; Dombovy, 2004; Hancock, Shepstone, Rowe, Myint, & Pomeroy, 2011). Pharmacotherapy studies for psychiatric disorders are also being carried out for the purpose of designing new psychotropic medication that can enhance the brain's plasticity bringing about more significant change when treating patients (Krystal, 2007). In addition, neuroimaging research on neuroplasticity and learning, and how change comes about through these intensive learning processes, has also been reviewed. The selection of articles for this overview is based on relevance to psychotherapy, for example, since psychotherapy is considered to be an emotional learning process, articles relating to intensive learning are used to demonstrate the effects that this has on the brain. In addition, articles have also been chosen for their accessibility while, at the same time, providing a comprehensive explanation of the concept of neuroplasticity.

This chapter, therefore, provides an overview of this neuroscience literature pertaining to neuroplasticity and also includes basic anatomy of neurons and neural networks to give the reader an understanding of the neuroscience concepts used in this study. Neuroimaging studies on how intensive learning alters the neural networks in the brain have been included to illustrate the concept of neuroplasticity.

Since this is a relatively new field of study, a limited number of studies using imaging fMRI imaging techniques, specifically pertaining to intensive learning, are available and these studies were selected based on their ability to illustrate the concept

of neuroplasticity. Without this concept of neuroplasticity, in response to learning, this study would not have been possible.

Chapter 3 – Neuroimaging (a systematic literature review)

In accordance with the EBM model, systematic reviews are necessary to obtain available evidence related to the research question to formulate recommendations for clinical practice and to eliminate bias. For this reason, it was paramount to review all possible literature to answer the question "does psychotherapy actually alter neural structures within the brain?" This in an important step of this research, as it is creates a framework for making sense of the relationship between session frequency and neuroplasticity. Once the literature was located (process described below), it was scrutinised and appraised for its relevancy in that, only articles relating to the actual impact of psychotherapy on the brain were chosen. There were a few papers where the psychotherapy treatment groups were also being treated with psychotropic medication thus the neural changes could not be directly attributed to the therapy itself – these were excluded (see inclusion and exclusion criteria below). In addition to this, the relevant literature (24 studies) has been synthesised into groups according to the psychotherapy treatment for ease of accessibility, for example, the CBT studies have been grouped together with the heading 'Cognitive Behavioural Therapy' followed by 'Psychodynamic Psychotherapy and so on. In addition to this, a table (see table 5) has been created that summarises all 24 studies and includes an overview of the neural changes associated with each study. It also includes a summary of the type number of important factors such as the modality of therapy administered, session length and treatment duration.

Inclusion / Exclusion Criteria

This study reviews research that examines the effects that psychotherapy has on the adult brain by means of neuroimaging technology. As previously mentioned, there are a number of studies evident in the research that review the efficacy of pharmacotherapy for psychiatric disorders where patients had also been receiving psychotherapy. However, these articles were excluded as there is no delineation between changes associated with psychopharmacotherapy (treatment of mental illness with psychotropic medication) and psychotherapy. In addition, criteria for this review are limited to studies that examine the efficacy of psychotherapy where the treatment group are free from psychotrophic medication while undergoing psychotherapy.

The Literature Search

According to Gray (2004), research carried out in evidence-based psychiatry is best done according to the "4s" approach to searching for answers, as this method provides the most efficient and comprehensive searches. This "4s" hierarchical strategy involves systems, synopses, syntheses, and studies (see Table 1 below) where priority is given to sources of top-quality, pre-appraised information. Databases, such as MEDLINE can also be researched if necessary. This study included additional searches in MEDLINE via AUT and PsychINFO and also Internet searches using Google Scholar as well as reviewing reference lists in the relevant literature. Search terms included: "neuroimaging", "fMRI", "PET", "SPECT" and "psychotherapy".

TABLE 1: The Comprehensive EBM 4S Approach for Reviewing Literature Systematically.			
Type of Information resource	**Examples**	**Website**	**Search results** **Total / relevant**
Systems (comprehensive sources)	*Clinical Evidence* National electronic Library for Mental Health APA practice guidelines	www.clinicalevidence.com psychiatryonline.org/guidelines.aspx	7 / 0 38 / 2
Synopses (structures abstracts)	*Evidence-Based Mental Health ACP Journal Clu*	www.ebmh.bmjjournals.com www.acpjc.org	10/0 3/0
Syntheses (systematic reviews)	*Cochrane Database of Systematic Reviews Database of Abstracts of Effectiveness (DARE)*	www.update-software.com/abstracts/mainindex.htm www.crd.york.ac.uk/CRDWeb/AboutDare.asp	0/0 40/0
Studies (original articles)	*MEDLINE (EBSCO)*	www.ncbi.hlm.nih.gov:80/entrez/query/static/clinical.html	46/24
AUT University	*PsychINFO database (via OVID)*	http://ovidsp.tx.ovid.com.ezproxy.aut.ac.nz/sp-3.7.1b/ovidweb.cgi	143 / 24
Source: Adapted from Gray (2004).			

Table 1. Neuroimaging. The comprehensive 4s approach for reviewing literature systematically.

Chapter 4 – Session frequency (a systematic literature review)

Since there is no literature linking the concept of neuroplasticity and psychotherapy, another way of exploring the relationship between intensive learning / harnessing of neuroplasticity and psychotherapy as a learning experience has been to systematically review the psychology, psychoanalytic and psychotherapy literature to find evidence suggesting that session frequency (learning frequency) or psychotherapy dosage have an impact on patient outcome. This systematic review of the literature produced a small amount of studies (10 studies) which illustrate a relationship between session frequency and therapeutic outcome. The studies were reviewed and synthesised into two groups namely 'Session Frequency' and 'Psychotherapy Dosage' which refer to the same concept albeit with different terminology; therefore, these terms are used interchangeably. All ten studies have been included in this dissertation.

Inclusion / Exclusion Criteria

Studies pertaining to both psychotherapy dosage and psychotherapy session frequency have been included in this review. Studies relating to dosage of psychotropic medication have been excluded.

The literature search

The "4s" approach, as described earlier (Gray, 2004), has been used to guide a comprehensive search using the same process as above (including Internet searches and reference list reviews). The keywords included in this search are "session frequency", "frequency of sessions", "dosage" and "psychotherapy dosage". The table below outlines the search results – a few of the relevant results were replicated in the various searches. The 10 studies identified in this search will be discussed in depth in the following chapters.

TABLE 2: The Comprehensive EBM 4S Approach for Reviewing Literature Systematically.

Type of Information resource	**Examples**	**Website**	**Search results** **Total / relevant**
Systems (comprehensive sources)	*Clinical Evidence* National electronic Library for Mental Health APA practice guidelines	www.clinicalevidence.com psychiatryonline.org/guidelines.aspx	4/1 0/0
Synopses (structures abstracts)	*Evidence-Based Mental Health ACP Journal Club*	www.ebmh.bmjjournals.com www.acpjc.org	22/0 11/0
Syntheses (systematic reviews)	*Cochrane Database of Systematic Reviews* *Database of Abstracts of Effectiveness (DARE)*	www.update-software.com/abstracts/mainindex.htm www.crd.york.ac.uk/CRDWeb/AboutDare.asp	0/0 7/0
Studies (original articles)	*MEDLINE (EBSCO)*	www.ncbi.hlm.nih.gov:80/entrez/query/static/clinical.html	8/6
AUT University	*PsychINFO database (via OVID)*	http://ovidsp.tx.ovid.com.ezproxy.aut.ac.nz/sp-3.7.1b/ovidweb.cgi	27/10

Source: Adapted from Gray (2004).

Table 2. Session Frequency. The comprehensive 4s approach for reviewing literature systematically.

Explanation of Terms and Definitions

The following terms are used interchangeably in this study: neuroplasticity, neural plasticity, synaptic plasticity and brain plasticity. In addition, neuronets, neuronetworks, and neural networks are also used interchangeably and refer to networks of neurons.

As previously pointed out, session frequency and psychotherapy dosage are used interchangeably as they refer to the same concept. Lastly, the phrase "intensive therapy" means high frequency psychotherapy or frequent psychotherapy sessions and refers to more than two sessions per week.

Chapter 2 Neuroplasticity

> We now know that all areas of the brain are "plastic"—capable of reorganizing themselves, growing new cells and neural networks, and making other areas obsolete in response to experience (Ogden, 2011, p. 57).

This chapter is an overview of the neuroscience literature and includes the introduction of a few basic neurological concepts such as neuroplasticity, synaptic plasticity, neural networks, neurons, long term potentiation (LTP) and long term depression (LTD) with a specific focus on learning and repetition. These concepts, as well as other important concepts such as the mirror neuron system, neurogenesis and also inhibiting factors of neurogenesis and neuroplasticity are discussed and will be illustrated with both imagery and studies. The concepts are then linked to psychotherapy practice that will be developed in later chapters.

Overview

The brain is a dynamic ecosystem made up of neurons, the basic units of the nervous system, that organise themselves into neural networks (Arden, 2010; Cozolino, 2010; Doidge, 2010; Kandel, 2006; Peled, 2008; Ratey & Ivey, 2008; Siegel, 2012; Wilkinson, 2010) that respond to incoming stimuli to accomplish the complex tasks for behaviour. Research, as evident below, confirms that the brain changes and adjusts itself according to its experience and this concept is known is plasticity. As described by William James, "plasticity, then, in the wide sense of the word, means the possession of a structure weak enough to yield to an influence, but strong enough not to yield all at once" (cited in Cozolino, 2010, p. 17). In the past, adult neural pathways were believed to be hardwired into the brain's circuitry and therefore could not be altered (Andreasen, 2005; Arden, 2010; Cozolino, 2010; Fisher & Ogden, 2011; Kandel, 2006; Schore, 2012; Wilkinson, 2010). However, in contrast, modern scientific research has shown that the brain is actually "soft wired" and changes physically in response to learning

(Koehl & Abrous, 2011) - a fundamental rule of neuroscience is that nerve cells that fire together, wire together (Hebb, 1949). These changes also occur in reverse: nerve cells that do not fire (or become excited) together, no longer wire together; they lose their long term relationship. Solms (2002) notes that, "in short, the fine organization of the brain is literally sculpted by the environment in which it finds itself - far more so than any other organ in the body, and over much longer periods of time" (p. 11).

Basic Anatomy

To make sense of the meaning of neural plasticity and the studies that illustrate this plasticity, the following basic anatomical overview of the brain and its cells (or neurons) is included to represent these structures. The brain is an organ like other organs (Solms & Turnbull, 2002), such as the liver and spleen, and is made up of billions of microscopic cells called neurons[3] which are connected together to form the tissue of the brain which has certain characteristics and shapes such as gray and white brain matter.

Each individual neuron within the brain (Cozolino, 2006) is made up of a cell body, dendrites (like tree branches) and an axon (as pictured in Figure 1 below) – the axon is covered in a fatty sheath (myelin sheath) which gives it a white appearance (white brain matter). The cell bodies of neurons tend to clump together and this appears as the gray matter in the brain.

[3] Although neuroscience usually focuses on neurons, they only account for half of the cerebral cortex. The other half of the brain is made up of around one trillion cells known as glia. One reason why so much more is known about neurons is that they are roughly 10 times larger than glial cells. Glia play a significant supportive role in the creation, organisation and continual maintenance of neuronal systems and it has been recently discovered that they are also implicated in neuronet communication and plasticity (Cozolino, 2010).

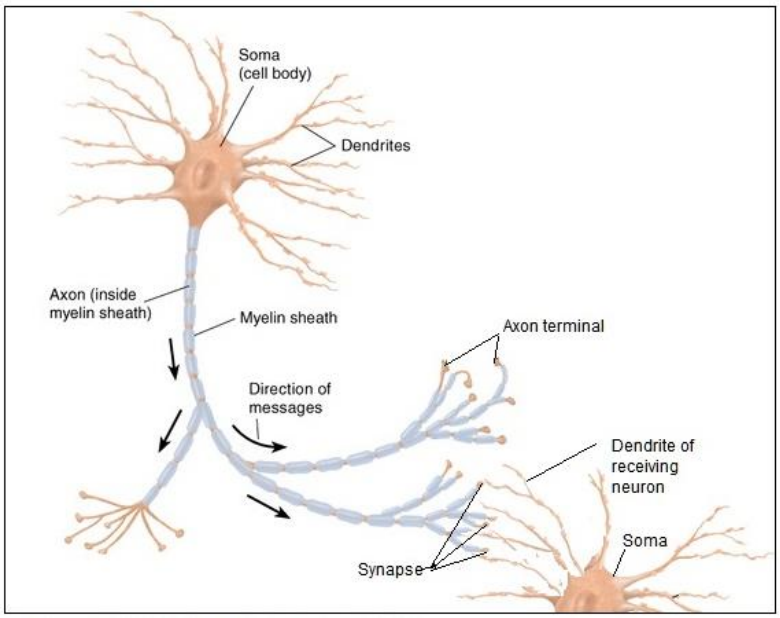

Figure 1. Neuron connecting with dendrites of receiving neuron.

The ends of the axon (axon terminals) of each neuron connect to the dendrites (branches) of other neurons and they "fire" or transmit signals to each other through this connection which is called a "synapse" as pictured above by means of chemical messengers called neurotransmitters.

The two images (Figure 2) immediately below are actual (digitally colourised) images of brain tissue (neural networks) that have been photographed under a powerful electron microscope. The first image on the left depicts a neuron that has grown dendrites branching out to connect into a network. The second image captures the complexity but also the intricacies of these networks and their relationships with one another.

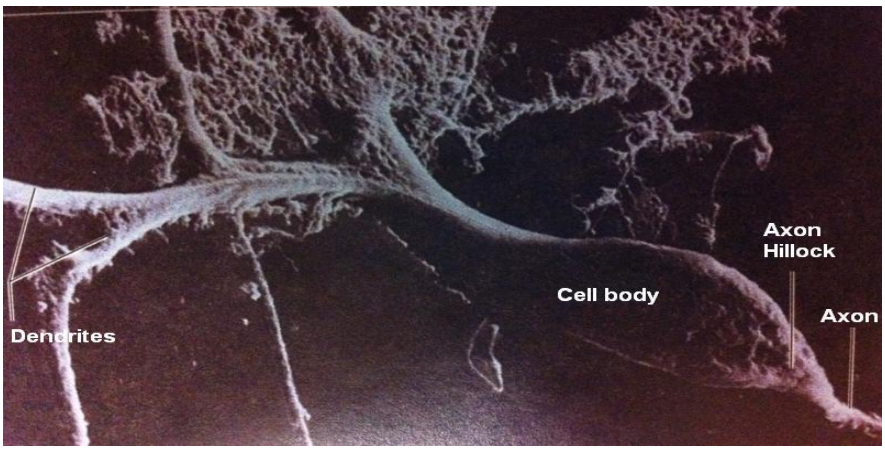

Figure 2 - Actual images of a neuron from a scanning electron microscope magnified x 15 000 (Adapted from Thibodeau & Patton, 2009).

Long Term Potentiation and Long Term Depression (LTP & LTD)

Neurons are either firing in response to some stimulus or not firing. When firing, they stimulate the firing of surrounding neurons and when fired repeatedly, metabolic (Arden & Linford, 2009; Cozolino, 2006, 2010) and electrochemical changes occur in both cells; joint activation increases their efficiency[4]. If firing is repetitive, prolonged and long-lasting, the connectivity between the cells and their dendritic spines is strengthened otherwise the activated pattern soon fades (Ratey & Ivey, 2008). This process, that was originally discovered in 1966 (Teyler & Cavus, 2007) is known as long term potentiation (LTP) and is now recognised a fundamental principle and cellular (physiological) mechanism of neuroplastic learning (LeDoux, 2003; Zoladz, Park, & Diamond, 2011). The counterpart of LTP is long term depression (LTD) which firing together ceases in adjacent cells causing brain map shrinkage through disconnection, dendritic spine weakening resulting in breakages and unlearning in the neuronal associations (Butz, Worgotter, & van Ooyen, 2009; Pearson, 2009; Wolpaw,

[4] It is interesting to note that the body and brain follow the natural laws of physics and the particular law that applies to this process is the first law of thermodynamics in physics called the Law of Conservation of Energy (Arden, 2011; Franklin, Muir, Scott & Wilcox, 2010). When learning a new skill, the brain uses more glucose and oxygen to process the new information, however, it becomes more energy efficient when the new skill becomes automatic as it no longer requires intense cognitive thought.

2010).[5] Cozolino (2006) notes that "neurons are, by their nature, social; they shun isolation and depend on their neighbours for survival. If they aren't sending and receiving messages from other neurons on a constant basis, they literally shrink and die" (p. 39).

Brain Matter

As pictured in Figure 3 below, the neuron cell bodies forming the gray matter are grouped either as nuclei or in layers when the cell bodies line up in rows. These "cellular sheets" are typically located on the brain's cortex which means the outer layer. The nuclei lie underneath these layers of cortex, deeper within the brain, and the white matter appears between the two. Solms (2002) notes that "the white matter-principally axons-thereby connects the cell bodies of the nuclei and cortical layers with one another. The precise anatomy of the resultant systems is enormously complex, but these basic principles are easier to understand" (p. 12).

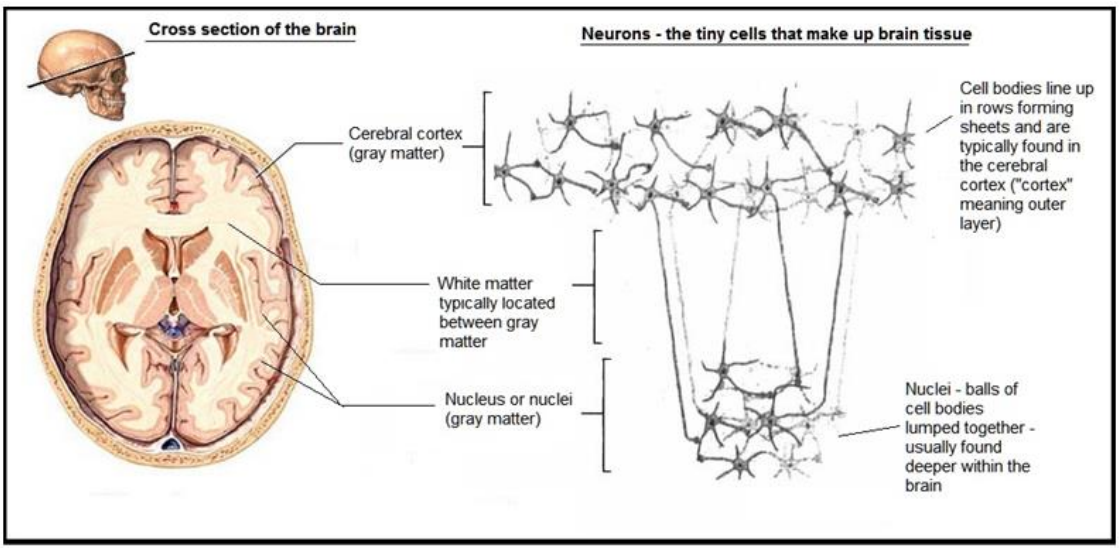

Figure 3. Gray and white matter : collections of cell bodies are gray; the fibre connections between them are white (adapted from Solms, 2002).

[5] Studies documenting altered synaptic plasticity in a number of animal models of disease, including major depressive disorder (MDD), schizophrenia, addictive disorders, and Alzheimer's disease (Teyler & Cavus, 2007), demonstrate the pertinence of LTP and LTD to both behaviour and memory. These researchers note that, "in parallel, the theory that psychiatric disorders are in part disorders of network connectivity and plasticity also has gained attention" (p. 371).

When we learn, or undergo training, or even experience psychotherapy (Arden, 2010; Kandel, 2006; LeDoux, 2003; Peled, 2011) the gray matter in the associated areas of the brain increases, in other words, plasticity is induced. Pajonk et al. (2010) mention that "several studies indicate plasticity of gray matter volume in humans to be associated with learning and other types of training" (p.133). Some psychiatric neuroimaging studies have found correlations between reduced white brain matter with psychopathology (Nakamuraa et al., 2012; Wanga et al., 2012). The following studies, by means of technologically advanced equipment such as fMRI (Functional Magnetic Resonance Imaging), examine neural gray matter changes in response to repetitive training producing exciting "observable" results as they illustrate the brain's enormous plastic ability.

Neuroimaging Studies of Neural Plasticity - White and Gray Matter Changes

A number of neuroimaging studies have revealed that plastic changes (gray matter volume and growth) are more elaborate in response to intense activities and prolonged training (Altenmüller, 2008; Altenmüller, Jäncke, Münte, 2002; Draganski et al., 2006; Kuhn et al., 2011b). Draganski et al. (2006) carried out an MRI (Magnetic Resonance Imaging) study that examines neurological structural changes in response to, and associated with intensive, repetitive learning. The sample group were a group of thirty-eight medical students who were studying intensively (over a period of three months) for their final end of year oral and written examinations and the control group were medical students not engaging in active study.

The researchers obtained three sets of data in the form of MRI brains to contrast neurological changes between the images taken before, during and after study. In the medical student group, the first brain scan was imaged three months prior to their medical exam, the second scan was obtained at the commencement of the exam and the

last was performed three months later. As illustrated in Figure 4 and Figure 5 below (the results have been superimposed into one subject's brain scan), it was observed there was a significant gray matter increase between the medical students' first and second scans – specifically in the posterior (rear) parietal cortex (as highlighted in Figure 4 below) - and an insignificant decrease in the third scan.

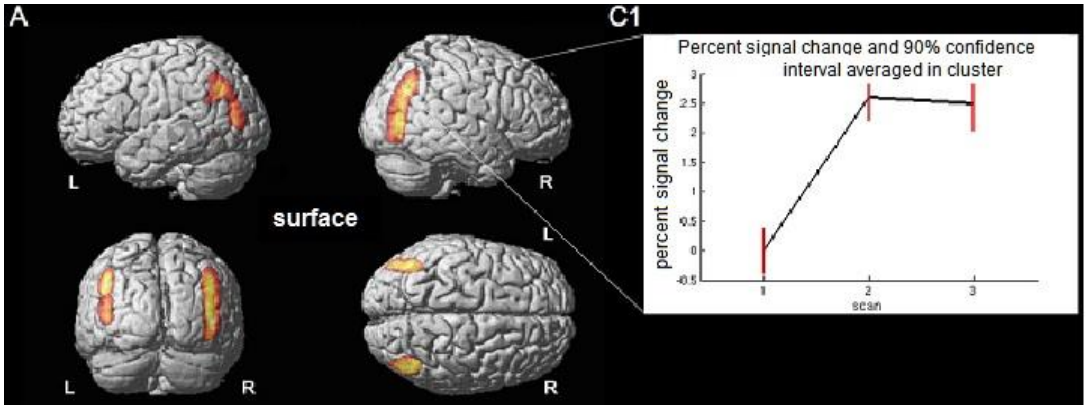

Figure 4. A - Gray matter increase related to learning. Statistical parametric maps demonstrating the structural difference in gray matter during the learning period in med students. The left side of the picture is the left side of the brain (L, left; R, right) (Draganski et al., p. 6415)

In addition to this, Figure 5 below (cross section brain scan slices) also demonstrates that, while a significant increase in gray matter was observed between the first and second scans in the posterior (rear) hippocampus, the gray matter continued to increase three months post examination. There was no change detected in the control group.

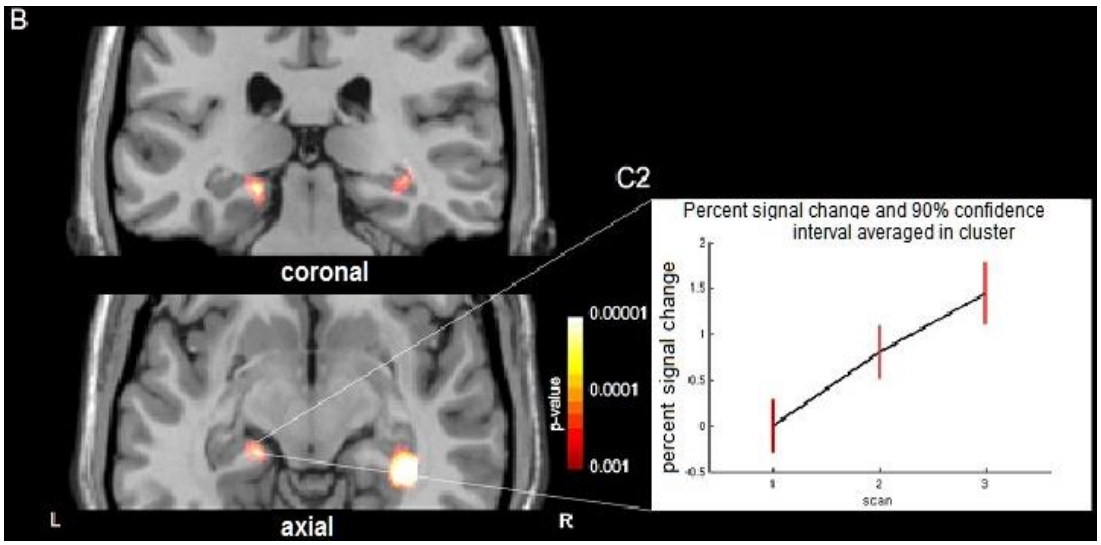

Figure 5. B - Gray matter increase related to learning. Statistical parametric maps demonstrating the structural difference in gray matter during the learning period in medical students. Coronial and axial slices (Draganski et al., p. 6415).

This paper concludes that intensive study alters the shape of the brain and it was noted that it continued to do so in the hippocampus even after the exams during the semester break. This phenomenon seems to parallel with the psychotherapy studies, in that patients that had had more intensive psychotherapy had a better internalised therapist and were able to make use of this long after their therapy termination (Blomberg et al., 2001; Fonagy & Target, 2002; Frosch, 2011; Leuzinger-Bohleber, Stuhr, Rüger, & Beutel, 2003).

Another study that reported similar findings in terms of significant increases in gray matter in response to intensive learning is as follows. Kuhn et al.'s (2011) fMRI (functional Magnetic Resonance Imaging) research investigates how high frequency video gaming alters reward processing centres in the brain. The researchers studied 154 healthy 14 year olds and divided them into two groups; high frequency players (9 hours or more per week) and infrequent players (less than 9 hours per week). The study reports that structural neural changes (i.e. changes in gray matter volume) were associated with the high frequency video gamers as opposed to their control group of infrequent video gamers. It was noted that there was higher left striatal grey matter

volume in the frequent gamers compared to the infrequent video gamers group. Interestingly enough this concept of change associated with high frequency is in accordance with the psychoanalytic research (Fonagy & Target, 2002; Frosch, Freedman, Vorus, & Hoffenberg, 1999; Hansen, Lambert, & Forman, 2002; Howard, Kopta, Krause, & Orlinsky, 1986; Kopta, 2003; Seong-Hyeon, 2011) that suggests that intense, high frequency therapy produces more significant results and better therapeutic outcomes (discussed in a later chapter).

The findings reported in Khun's study above are consistent with Altenmüller et al.'s (2008) study who report that extensive music practice (learning) not only enhances gray matter growth but also augments the formation of fibres in the brain that is associated with the specific musical task. The research team recruited a group of non-musicians who had never played an instrument before and studied the changes in their brains after they were trained to play the piano twice a week over a period of five weeks. An fMRI (see Figure 6 below) was taken prior to practice, after 20 minutes of practice and again after 20 days. The images were compared with fMRI's of experienced musicians (top image in figure below). It was noted that "after 20 minutes of training, first signs of increased neuronal coupling between auditory and motor brain regions were observable. After five weeks, listening to piano tunes produced additional activity in the central and left sensorimotor regions" (p. 411). As pictured in Figure 6 below, training for 20 minutes and 20 days resulted in the topographic distributions becoming increasingly similar between both states as well as similar to the experienced musicians. Professional musicians (Altenmüller, Jäncke, & Münte, 2002) with 20 years of experience have maps that are virtually identical in both listening and playing and provide a good model for neuroplasticity.

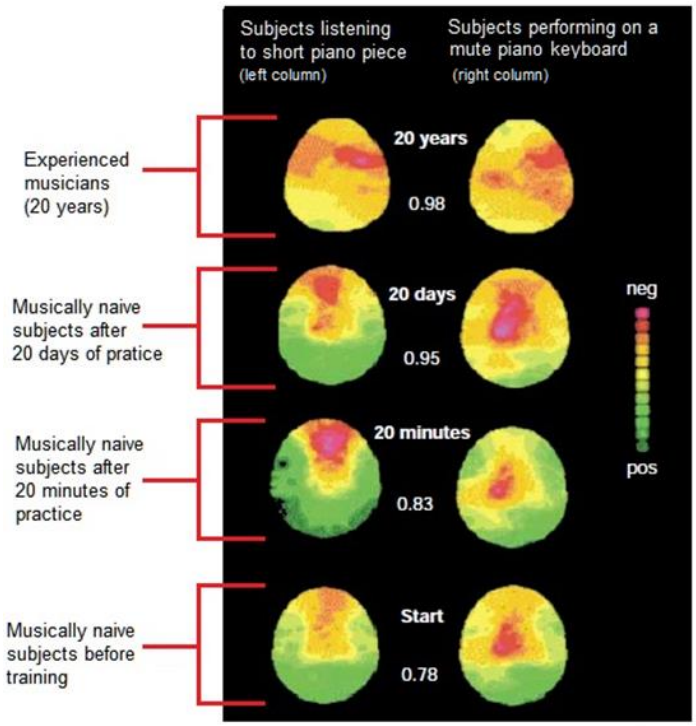

Figure 6. Shown are spline-interpolated isovoltage maps of averaged electro-encephalographic (EEG) recordings (Adapted from Altenmüller, Jäncke, & Münte, 2002).

The activation of motor co-representations occurs not only when these musicians perform, but when they observe a pianists fingers moving on a keyboard. This phenomenon of learning by observation is thought to be facilitated by of a complex neural system called the mirror neuron system.

Mirror Neuron System

In recent years, the neural mechanisms of learning through observation have been studied and this is mode of learning is thought to occur through the activation of the mirror neuron system (Arden, 2010; Cozolino, 2010; Gallese, Eagle, & Migone, 2007; Iacoboni, 2009; Schore, 2012; Siegel, 2012). The mirror neuron system was accidentally discovered in the 1980's when a group of neurophysiologists were studying the neurons specialised for movement, specifically hand and mouth movements in marquee monkeys, by means of capturing data from electrodes attached to the monkeys' heads (Gallese et al., 2007; Olds, 2006). During these experiments, the researches were

astounded to notice that these same neurons fired when the monkeys observed the scientists performing a similar action. This ground breaking discovery has had numerous implications for making sense of how learning occurs – not only in animals but in human beings too. Ramachandran (Ramachandran, 2005; Ramachandran & Blakeslee, 1999), a medical professor of psychology and neuroscience, has noted the importance of this discovery and goes on to say that he predicts "that mirror neurons will do for psychology what DNA did for biology: they will provide a unifying framework and help explain a host of mental abilities that have hitherto remained mysterious and inaccessible to experiments" (p. 5).

Since the initial study on the marquee monkeys, there has been extensive neuroscience research carried out in this field to decipher this complex mirror neuron system in humans - it is thought that the mirror neuron system is the neural basis for empathy (Cozolino, 2010; Flores, 2010; Gallese et al., 2007; Siegel, 2012; Yuan & Hoff, 2008). Within the context of a therapeutic relationship, Siegel (2010) notes that by perceiving another person's expression, the brain creates an internal state that is thought to "resonate" with that of the other. The neural firing within each individual becomes more coherent when two minds feel connected or become integrated. In Gallese, Eagle & Migone's (2007) research on the Neural Underpinnings of Interpersonal Relations, mention that, with reference to the mirror neuron system, there is also a functional mechanism of "embodied simulation" that consists of the automatic, unconscious, and noninferential simulation in the observer of actions, emotions, and sensations carried out and experienced by the observed" (p. 131). Siegel goes on to say that "literally, this may mean that the corresponding activations between the body proper, limbic areas and

even cortical representations of intentional states between two individuals enter a state of "resonance" in which one matches the profiles of the other" (p. 255).[6]

However, for the mirror neuron system to be activated during the observation of an action, it must be a recognised action with both a beginning and end and even possibly a purpose (Olds, 2006). The researchers in the marquee monkey study noticed that, for example, when a person uses a pair of pliers to retrieve a nut for this first time, this action will not initially be recognised by the monkeys. Therefore, a mirror neuron response in the monkey will only occur after several repetitions of observing this action. This notion is consistent with the psychoanalytic research that links higher session frequency with an increased ability to "internalise the therapist" – it is as if these patients are developing / exercising their mirror neuron systems through the therapeutic experience (which causes activations of the patients' mirror neuron system) and are, therefore, able to have a broader emotional resonance in other relationships outside of the therapeutic relationship.

In addition to the above, the same scientists (Arturo Alvarez-Buylla, Joseph Altman & Giacomo Rizzolatti), renowned as "worldwide leaders in neurology" (Asturias, 2011), who discovered this mirror neuron system, have also been internationally recognised for their research that produced solid proof of the regeneration of neurons in adult brains (neurogenesis). This concept is discussed in detail in the next section.

Neurogenesis

Cajal (1852-1934), a neuroanatomist and neuroscientist (Kandel, 2006) who discovered the structure and theory of nerve cells within the brain, which he called

[6] The malfunction of these shared states has been linked to forms of psychopathology, including schizophrenia. In addition to this, recent research indicates that impairment in the mirror neuron system is a proposed characteristic of autism (Ramachandran, 2004).

neurons, also postulated that since (Koehl & Abrous, 2011) nerve cells do not multiply, new neurons could not be produced in the brain. However, in the 1960s (Altman, 1962), it was discovered by Altman, through his animal models, that neurogenesis does occur.

Unfortunately, these findings were largely ignored by the scientific community for over twenty years and only began to reach mainstream research in the 1990s. Koehl & Abrous's article published in 2011 notes that "until the last decade reports of neurogenesis in the adult brain rested on only a few studies and it was only with new technical advances in cellular and molecular biology that adult neurogenesis became widely accepted" (p. 1102). It took 40 years of research to overturn the traditional stance that (Schoenfeld & Gould, 2011) neurogenesis does not occur in the adult brain.

The concept of neurogenesis is an essential component of synaptic plasticity – the researchers Butz, Wörgötter & van Ooyen (Butz et al., 2009) have hypothesised a causal relationship between synaptic rewiring and adult neurogenesis in that adult neurogenesis is a substantial drive for neural network rewiring and structural plasticity. Much like the concept of synaptic plasticity, new nerve cell growth also increases with "intensive training within stimuli-rich environment" (Peled, 2010, p. 91). However, there are factors that can have a profoundly negative effect on neurogenesis and neuroplasticity which will be discussed below.

Stress, Neuroplasticity and Neurogenesis

As evident in the research, experience and learning has lasting effects on (Wolpaw, 2010) neural plasticity and neurogenesis. However, it has been reported that if the learning or experience is too difficult or stressful, or if the environment is not conducive to growth, the resultant inhibitory effect on adult neurogenesis is apparent

(Schoenfeld & Gould, 2011). [7] Rosenzweig's (1960) animal study (cited in Arrowsmith-Young, 2012) illustrates this notion of the inhibitory impact of stress on the brain. This study found that rat subjects that were raised in a social (with other rats) and "enriched environment" (i.e. exercise wheels, ladders, tunnels and tubes) in contrast with those that were raised in an isolated environment, with little stimuli, showed significant neural and behavioural differences. The rats in the enriched environment not only performed better on mazes, they also had heavier brains i.e. they had more extensive neural connections. This is accordance with other studies (Johansson, 2006) that expanded on this finding and also reported that "enriched environment" rats also had more gray matter, increased blood flow, and subsequently larger neural capillaries, and that their neurons had more dendrites and branches to other neurons as depicted in Figure 7 below.

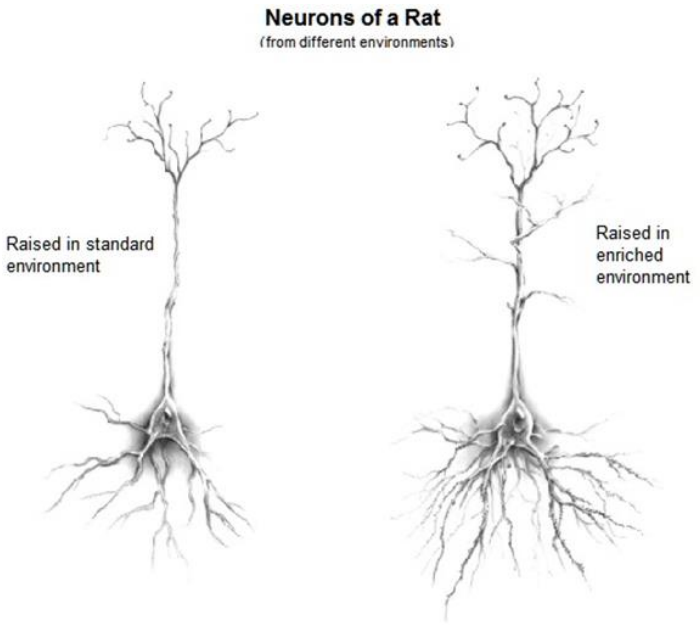

Figure 7. Neuronal plasticity. Note more dendrites and dendrite spines on the neuron of the rat raised in the enriched environment (Adapted from Arrowsmith-Young, 2012).

[7] Recent neuroscience research also indicates that neurogenesis and synaptic plasticity are associated with aerobic exercise (Cramer et al., 2011) while stressful experiences not only alter neurogenesis in certain areas of the brain, they also disrupt many other neuronal processes including blood flow (Schoenfeld & Gould, 2011).

The researchers have concluded that, rats that have experienced the enriched and stimulating environment have better brains and greater learning capacities and abilities to problem solve than those raised in the standard environment. This concept is also not only applicable in the developing human brain, but also in the adult brain as it also adapts with its experience. Therefore, given this concept, it makes sense that a more stimulating and enriched therapeutic relationship with a good therapeutic alliance that is experienced more frequently will enhance the patient's ability to transform, which is consistent with the notion of Winnicott's (1960) "holding environment".

Summary

This chapter has provided an overview of basic neural anatomy as well as reviewed neural concepts such as neural plasticity, gray matter, long term potentiation (LTP) & long term depression (LTD), the mirror neuron system and neurogenesis.

The studies in this chapter have demonstrated how intensive practice and learning, that can even occur by observation (the mirror neuron system), increases gray matter within the brain as well as promote neural plasticity. The research in this chapter not only reports the enormous plasticity of the brain in response to its environment, it also reports that repetitive and focussed practice or experience has more significant effect on neural changes. This is in accordance with medical research studying ground breaking findings in utilising the brain's enormous plasticity to enhance treatment for traumatic brain injury and stroke.

The studies revealed that the act of focussed observation also brings about plastic changes through a system called the mirror neuron system. When others' actions are observed the same associated neural networks in the observer's brain are activated as the person performing the action. This mirror neuron system is thought to be the basis of empathy and is considered to play a significant role within the therapeutic

relationship (Arden, 2010; Cozolino, 2010; Gallese, Eagle, & Migone, 2007; Iacoboni, 2009; Siegel, 2012). However, the findings state that, for the mirror neuron system to be activated during the observation of an action, it must be a recognised action with both a beginning and end and even possibly a purpose (Olds, 2006).

In addition, it was noted that excess stress and a harmful environment can have significant negative impacts on the brain's plasticity and its ability to form new neurons while an enriched environment has the opposite effect and promotes neuroplasticity and neurogenesis. This research has important implications for the practice of psychotherapy considering the impact that the 'holding environment' may have on the patient and the frequency at which this is experienced could enhance [or inhibit] neuroplasticity.

Substantiated through research (Arden, 2010; Cozolino, 2010; Doidge, 2010; Peled, 2011; Schore, 2012; Siegel, 2012; Wilkinson, 2010), it is now accepted that psychotherapy alters the way neuronets are wired by providing the client with a new relational experience. Lewis, Amini and Lannon (2000) write that "psychotherapy alters the living brain" (p. 168) when the therapist is able to listen and attune to the patient. Siegel (2012) agrees with these notations and notes that "to put it simply, human connections shape neural connections, and each contributes to mind. Relationships and neural linkages together shape the mind. It is more than the sum of its parts; this is the essence of emergence" (p. 25).

Although this psychotherapy / psychoanalytic literature reports that psychotherapy alters brain structure (Lewis et al., 2000; Siegel, 2012), the question then emerges, what neuroimaging studies have been published that demonstrate the effect of psychotherapy on the brain. The following chapter seeks to explore this in in detail.

Chapter 3 Neuroimaging Studies and Psychotherapy

> Questions pertaining to the neurobiological effects of psychotherapy are now considered among the most topical in psychiatry (Paquette, 2003, p. 401).

The previous chapter introduced a number of neural concepts including neuroplasticity and how the brain changes in response to intensive learning. Questions that arose from the research led me to query whether there were any neuroimaging studies that examine how psychotherapy changes the brain. Are there any particular aspects of the practice of psychotherapy that enhance neural changes? This chapter is a systematic review of the literature that seeks to demonstrate, through the 24 studies extant, the effects that psychotherapy has on the brain.

Due to the numerous clinical trials that have been run associated with pharmacotherapy for psychiatric disorders, it is common knowledge (Roffman et al., 2010) that psychotropic medication affects neural structure and the neurotransmitters in the brain. However, the neural impact of psychotherapy in the absence of pharmacotherapy is a relatively recent and emerging field of study. Recent advances in neuroimaging techniques and the increasing accessibility of this technology[8] has made these neuroimaging studies an exciting new field of study.

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[8] The studies examined in this research (chapter 2 and chapter 3) use the following neuroimaging technologies: PET (positron emission tomography), SPECT (single photon emission computed tomography), fMRI (functional magnetic resonance imaging) and one study used CT (computed tomography) scans. Unlike traditional static brain images, these modern techniques provide a measure of the brain by detecting activation through blood flow – activated neural areas are associated with higher blood flow. Both PET & SPECT, which are nuclear (Weight & Bigler, 1998) metabolic imaging techniques, rely on radioactive (isotope) tracers that are injected into the bloodstream prior to imaging on a biologically active molecule, for example FDG (in PET), which is an analogue of glucose – hence the name FDG-PET. These traces enter the cerebral blood supply and are detectable with a camera placed near the patient's head through the signal emitted. As activity fluctuates in brain regions, blood flow to these regions rises or falls accordingly (Dougherty, Rauch, & Rosenbaum, 2004; Roffman, Marci, Glick, Dougherty, & Rauch, 2005). Due to the radioactive nature of the tracers, there are limitations in scan length and frequency - 2 PET per year (Roffman, Gerber & Glick, 2012).

PET & SPECT provide a reliable but indirect measure of neuronal firing. fMRI scans, on the other hand, do not use radiation but rather strong magnetic fields to measure brain activity. Unfortunately, the fMRI physical tubular environment is more restrictive than the other forms of scanning but it has better temporal resolution and the scan duration / yearly frequency limit is not as restrictive as the methods using radioactive materials. Like PET & SPECT, fMRI signals also estimates cerebral blood flow and activated parts of the brain are highlighted at any given time. The signal is generated by measuring relative concentrations of deoxygenated versus oxygenated blood.

Overview

As detailed in Chapter One (the methods chapter), my systematic search has identified 24 studies on neural changes in response to psychotherapy which is consistent with earlier meta-analyses of the literature (Karlsson, 2011; Porto et al., 2009; Roffman, Marci, Glick, Dougherty, & Rauch, 2005). Table 3 below provides the distribution of the disorders studied and Table 4 provides the distribution of the therapies employed.

Disorder according to DSM3 & 4	% of studies	Therapeutic Treatment Modality
Major depressive disorder (MDD)	29%	Psychodynamic psychotherapy (PDT) Interpersonal Psychotherapy (IPT), Cognitive Behavioural Therapy (CBT)
Obsessive compulsive disorder (OCD)	25%	Behavioural Therapy (BT) Cognitive Behavioural Therapy (CBT)
Panic Disorder (PD)	13%	Cognitive Behavioural Therapy (CBT) Psychodynamic psychotherapy (PDT)
Post-traumatic stress disorder (PTSD)	13%	Cognitive Behavioural Therapy (CBT) Brief Eclectic Psychotherapy (BEP)
Spider phobia	8%	Group Cognitive Behavioural Therapy Cognitive Behavioural Therapy (CBT)
Borderline personality disorder (BPD)	8%	Dialectical Behavioural Therapy (DBT) Psychodynamic psychotherapy (PDT)
Social phobia	4%	Cognitive Behavioural Therapy (CBT)

Table 3. Percentage of studies associated with DSM disorder and therapeutic treatment modality.

Therapeutic Treatment Modality	Abbreviation	% of studies
Cognitive behavioural therapy including Group CBT	CBT	50%
Psychodynamic Psychotherapy 1-2 yrs	PDT	17%
Short term psychodynamic psychotherapy	ST PDT	5%
Interpersonal psychotherapy	IPT	9%
Behavioural psychotherapy	BT	9%
Dialectical behavioural therapy	DBT	5%
Brief Eclectic Therapy	BEP	5%

Table 4. Percentage of studies associated with therapeutic treatment modality.

A number of particular brain regions have been implicated in these neuroimaging studies and, for ease of reference, have been identified in Figures 8, 9 and 10 below. Figure 8 outlines a basic anatomical overview of the brain's cortex (outer structure) and shows the medical terms for front (anterior), back (posterior), upper side

(dorsal) and lower side (lateral). Rostral typically means towards the nose or front end of the body and caudal, toward the back or tail end. Figure 9 shows the location of the various lobes in the brain and Figure 10 details the specific brain regions referenced in the neuroimaging studies.

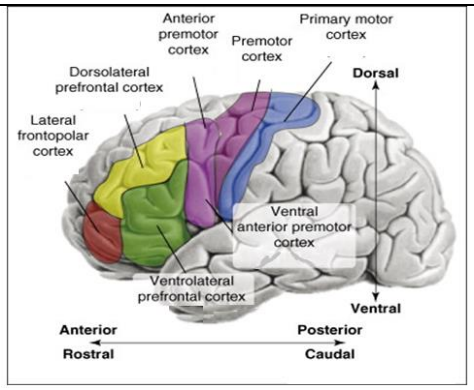

Figure 8. Various regions of the cortex of the brain.

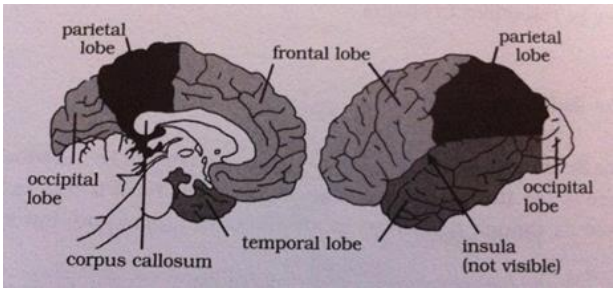

Figure 9. The lobes in the forebrain.

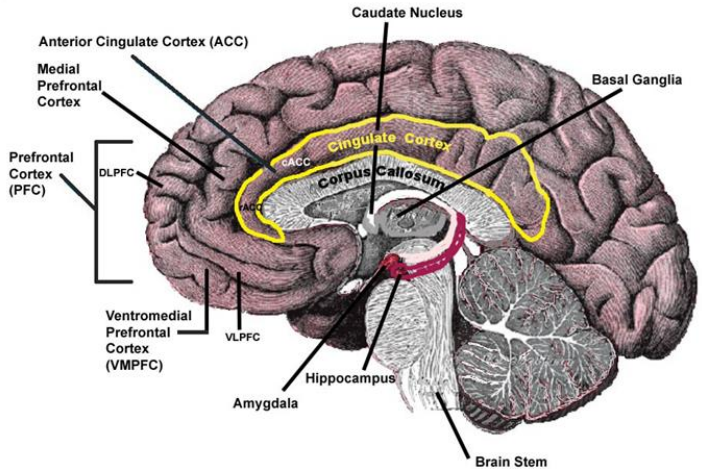

Figure 10. Cross section of the brain identifying areas that are examined in the neuroimaging studies.

Neuroimaging Studies

In addition to the above, a comprehensive review of the neuroimaging studies follows. However, an easy reference table (see Table 5 below) outlining each of the 24 studies and the neural changes in observed in the studies has been included below.

Author	Diagnosis	Medication	Therapy	Study	Healthy Controls	Waiting List / Med Group	Psychotherapy patients	Therapy Duration	Total therapy sessions	Session length	Session frequency	Number of Therapists	Outcome
Baxter (1992)	OCD	Fluoxetine	BT	BT vs. medication	4	9	9	10 wks - some patients grp therapy	8 - 24	-	1 or 2 p/w	3	1. Both Groups - decreased metabolism in right caudate.
Schwartz (1996)	OCD	-	CBT	-	4	-	9	10 wks - some patients grp therapy	8 - 24	-	2 / varying	3	1. Decreased metabolism in right caudate. 2. Uncoupling of cortico-striato-thalamic circuit.
Brody (1998)	OCD	Fluoxetine	BT	BT vs. medication	-	9	18	8-12 weeks	-	-	-	-	1. BT group - left orbitofrontal cortex metabolism positively correlated with treatment response. 2. Fluoxetine patients exhibited a negative correlation.
Martin (2001)	MDD	Venlafaxine	IPT	IPT vs. medication	-	15	13	6 wks (2nd scan after 6 wks)	16	1 hr	1 p/w	1	1. Both groups - increased CBF in right basal ganglia. 2. IPT group, increased CBF in right posterior cingulate.
Brody (2001)	MDD	Paroxetine	IPT	IPT vs. medication	16	10	14	12 (3 sessions in the first 2 weeks)	12		Varying	2	1. Both MDD groups - decreased metabolism in PFC, increased in inferior temporal cortex & insula.
Furmark (2002)	Social Phobia	Citalopram	Group CBT	CBT vs. medication	6 WL	6	6	8 weeks	8	3 hrs	1 p/w	2	1. Both groups - decreased limbic metabolism. 2. CBT group - decreased periaqueductal gray metabolism. 3. Med group - decreased thalamic metabolism.
Nakatani (2002)	OCD	-	BT	-	31	-	31	Varying BT duration	-	-	-	-	1. Decreased regional cerebral blood flow in head of right caudate nucleus.
Paquette (2003)	Spider Phobia	-	Group CBT	-	13	-	12	4 (3 hour sessions) group sessions once a week	4	3 hrs	4 p/w	2	1. Abnormal activation in the dorsolateral prefrontal cortex or the parahippocampal gyrus normalised after CBT.
Goldapple (2004)	MDD	Paroxetine	CBT	CBT vs. Paroxetine	-	13	11	-	15-20	-	-	2	1. CBT group - decreased metabolism in frontal regions, increased in limbic regions. 2. Med group - changes in opposite direction.
Prasko (2004)	PD	Antidepressants	CBT	CBT vs. medication	-	6	6	20 (3 grp sessions p/w - 1.5 hrs & 2 individual)	20	1.5 hrs	3 + 2	> 1	1. Both groups - decreases in right frontal and temporal regions.
Nakao (2005)	OCD	Fluvaxamine	CBT	CBT vs. medication	-	4	6	12 wks (+ homework)	12	45 mins	1	> 1	1. Both groups - decrease in hyper-activation of the frontal lobe. 2. Both groups - increase in posterior brain activity.
Farrow (2005)	PTSD	-	CBT	-	-	-	13	-	4 - 10	-	-	1	1. Significant activation in left middle temporal gyrus in response to empathy judgments 2. Activation in posterior cingulate gyrus in response to forgivability judgments.
Ramon (2005)	PTSD	-	BEP	BEP	18	9	9	4 months	16	45-60	-	> 1	1. Smaller hippocampal volumes in PTSD patients did not change after effective psychotherapy.
Sakai (2006)	PD	-	CBT	-	-	-	11	6 months Fortnightly for 4 months & monthly afterward	10	50 mins	Varying	1	1. Decreased glucose utilization in the right hippocampus, left AC, left cerebellum, and pons. 2. Increased glucose utilization was seen in the bilateral medial prefrontal cortices.
Straube (2006)	Spider Phobia	-	CBT	-	14	12	13	2 wks & grp therapy 2/3 in grp	2	5 hrs		> 1	1. Decreases in bilateral insula, thalamus, ACC in treatment group.
Schnell (2007)	BPD	-	DBT	-	6	-	6	12 wk inpatient group & individual sessions	-	-	Varying	1	1. Reduced activation in bilateral dorsolateral & dorsomedial frontal areas (including the AC) and in the left superior temporal gyrus & caudal ACC.
Lai (2007)	BPD	-	PDT	-	5	-	2	16 months	-	-	1 p/w	1	1. Post treatment neural pattern presented a strong frontal activation, absent in pre-treatment, suggesting a more efficacious cortical modulation on subcortical areas.
Felmingham (2007)	PTSD	-	CBT	-	-	-	8	8 weeks	8	-	1 p/w		1. Increased rACC and reduced amygdala activation during fear processing which is consistent with evidence of vmPFC involvement in fear extinction.
Lehto (2008)	MDD	-	PDT	PDT vs. Wait List	-	9	13	1 year	80	45 mins	2 p/w	> 1	1. Midbrain serotonin reuptake transporter (SERT) density significantly increased during psychotherapy in atypicals but not in nonatypicals.
Fu (2008)	MDD	-	CBT	-	16	-	16	16 weeks	16	-	-	3	1. Normalization of amygdala-hippocampal activity. 2. Increase in activity from dorsal anterior cingulate extending to the parietal cortex.
Beutel (2010)	PD	-	PDT	-	18	-	9	4 weeks (intensive inpatient)		-	-	> 1	1. Fronto-limbic (lateral prefrontal areas) activation patterns were normalised.
Apostolova (2010)	OCD	Paroxetine	CBT	CBT vs. med	-	7	9	7 - 20 weeks	40	-	Varying	-	1. Both group - scaled local metabolic rate of glucose (SLMRGlc) increased in the right caudate.
Karlsson (2010)	MDD	Fluoxetine	ST PDT	ST PDT vs. medication	-	15	8	16 weeks	16	-	1 pw	> 1	1. PDT group -Increase in 5-HT1A receptor bindings in a number of cortical regions. 2. No change in 5-HT1A in medication group although symptoms improved.
Buchheim (2012)	MDD	-	PDT	-	17	-	16	15 months	-	1 hr	2-4pw	1 6	1. Significant changes noted in subgenual cingular and medial prefrontal cortex.

Table 5. Table of 24 neuroimaging studies.

Three of these studies (Buchheim et al., 2012; Karlsson et al., 2010; Straube, Glauer, Dilger, Mentzel, & Miltner, 2006) will be discussed in detail to illustrate how these neuroimaging studies are typically carried out and show the associated neural changes (depicted in fMRI images) in response to the intervention. The remainder of the studies will be grouped together by means of the therapeutic intervention (for example, cognitive behavioural therapy, interpersonal therapy and psychodynamic psychotherapy).

Behavioural therapy (BT)

Behavioural therapy is considered an effective form of therapy particularly for social phobias and obsessive compulsive disorder (OCD) and abnormalities in metabolism in certain areas of the brain have been associated with OCD (Baxter et al., 1992; Brody et al., 2001; Nakatani et al., 2002). Three neuroimaging studies exploring this have been published to date; Nakatani et al.'s (2002) study examines the neural changes in response to behavioural therapy while the other two studies (Baxter et al., 1992, Brody et al., 2001) compare their results to a medication group (fluoxetine in both studies). Baxter et al.'s study was the first ever neuroimaging study of psychotherapy to be conducted and it was found that elevated metabolism decreased in the caudate nucleus area of the brain, in response to behavioural therapy (BT) – similar changes were reported in the medication group. Building on Baxter's study of abnormalities in brain regions associated with OCD, Brody et al.'s (1998) study sought to find pre-treatment metabolic predictors of response to behavioural therapy vs. pharmacotherapy. They observed that higher metabolism in the left orbitofrontal cortex (OFC) positively correlated with response to behavioural therapy but had worse outcomes in the medication group. Therefore, patients with higher left metabolism in the left OFC are best treated with BT rather than fluoxetine.

Nakatani et al.'s (2003) large scale study (31 patients) of treating OCD with BT produced results that were consistent with the findings of the previous two studies even although the scanning technology was different (Xe-CT) – the study measured regional cerebral blood flow. The researchers reported that a significant decrease was observed in the regional cerebral blood flow (rCBF) in the right head of the caudate nucleus after successful treatment - this tended to correlate with clinical improvement.

While BT treatment for OCD is associated with decreased metabolic rate changes in the caudate nucleus, the BT was not standardised across all three studies; there are inconsistencies in the overall length of the therapy and the frequency of the sessions per week with some patients receiving additional group therapy. Therefore, it cannot be maintained that it was necessarily the specific form of the BT that was the curative factor especially since other forms of therapy for OCD have also observed similar results, discussed in section below.

Cognitive behavioural therapy (CBT)

A large proportion (50%) of the studies identified in this review used the psychotherapy treatment modality of cognitive behavioural therapy. According to these 12 studies, CBT can be used to successfully treat a number of different conditions although is particularly effective for treating phobias and panic disorders where cognitive distortions are observed. While there seems to be a certain detachment associated with treating "disorders" rather than suffering patients, as perhaps more evident in psychodynamic psychotherapy, I have grouped these studies according to the presenting issue for ease of reference.

- CBT for obsessive compulsive disorder (OCD)

There are a total of three neuroimaging studies that examine neural changes associated with cognitive behavioural therapy (CBT) for OCD patients. Consistent with the findings in the behavioural therapy studies for OCD, Schwartz et al's (1996) study also reported decreased metabolism in the caudate nucleus in response to CBT. In accordance with the BT studies for OCD, it was also observed that the OCD patients also display abnormalities in metabolism in specific brain regions. In addition to this, Nakao et al.'s (2005) of OCD patients found that OCD patients also demonstrate hyperactivity in the frontal cortex and that after successful treatment with either medication or therapy, this activation decreases. While these areas identified are slightly different, the findings are congruent with the studies of OCD patients (Baxter et al, 1992; Schwartz et al., 1996) treated with the behavioural therapy.

In contrast to the above two studies, the last of the three studies (Apostolova's et al., 2010), interestingly enough, produced opposite findings in OCD patients being treated with either CBT or paroxetine. The researchers report that successful therapy of OCD in both the medication and the CBT group resulted in an increase of scaled local metabolic rate of glucose (SLMRGIc) in the right caudate nucleus rather than a decrease as reported in other studies. This raises questions about what was different in this study. Was the treatment group different? Did the patients have other diagnoses? Unlike the previous studies, this particular study did not exclude patients with comorbid diagnoses of major depressive disorder (MDD), affective and anxiety disorders therefore the sample group cannot be accurately compared with the other studies.

- CBT for panic disorder (PD)

Prasko et al. (2004) conducted the first neuroimaging study on panic disordered (PD) patients who were treated with either CBT or medication. The researchers found

similar metabolic rate decreases in the right frontal and temporal regions after either treatment and concluded that CBT is as effective as medication in the treatment of PD. Other areas of the brain have also been implicated in response to CBT treatment for PD - Sakai et al.'s (2006) study reported a decrease in the metabolism at the right hippocampus, left ventral (frontward) anterior cingulate cortex, uvula, and pyramid of the left cerebellum and pons, and an increase in metabolism was found in the bilateral medial prefrontal region. While these two studies observe CBT treatment for panic disorder, there are enormous differences between the treatment methods in each study for example the frequency of sessions and the utilisation of additional group therapy.

- CBT for post-traumatic stress disorder (PTSD)

CBT is also thought to be an effective treatment for PTSD (Farrow et al., 2005; Linden, 2006) as it is thought to have an effect on the way that the brain processes fear (Felmingham et al., 2007) and empathy judgments. Abnormalities in activation in particular areas of the brain (the anterior cingulate context and amygdala) have been observed in patients suffering PTSD; CBT treatment has brought about changes in these areas - for example, Furmark et al.'s (2002)'s study reported that abnormal activation of the amygdala and hippocampus was reduced after successful treatment with either CBT or citalopram. This finding is consistent with Felmingham et al.'s study (2007) of PTSD patients treated with CBT. The researchers observed a significant association between efficacious exposure therapy for PTSD and an increased activation in the rACC (rostral anterior cingulate cortex) and a reduction in amygdala activation during the processing of fear. The researchers note that this finding is consistent with evidence of vmPFC (ventromedial prefrontal cortex) involvement in the extinction of fear. In addition, activations of other areas of the brain (activation in the left middle temporal gyrus and posterior cingulate gyrus) have also been observed in response to successful treatment of PTSD (Farrow et al. 2005). However, Farrow's

study has some major limitations; although these patients were recruited from an emergency department following a trauma (such as a car accident), head trauma was not considered an exclusion criterion which may have contributed significantly to outcome measurements.

- CBT for major depressive disorder (MDD)

Goldapple and colleagues (2004) note that "like other antidepressant treatments, CBT seems to affect clinical recovery by modulating the functioning of specific sites in limbic and cortical regions" (p. 34). These researchers examined the underlying neural correlates of symptom reduction of major depression (MDD) in response to a course of CBT in comparison with a pharmocotherapy group taking paroxetine. While both groups experienced clinically significant symptom reductions, the neural changes reported were opposite in both groups. This finding contrasts with Brody et al.'s study (2001) where the paroxetine group exhibited the same neural changes (decrease in metabolism in prefrontal cortex, increase in inferior temporal cortex and insula) as the therapy group.

In addition to the above, elevation of activity in the amygdala-hippocampal has been associated with depression - in Fu et al.'s study (2008) of how patients with MDD process sad faces following CBT, the researchers found elevated amygdala-hippocampal activity in depression and interestingly enough found significant associations between anterior cingulate activity and treatment response to both pharmacotherapy and CBT – it could be considered a treatment predictor for treatment response. However, in contrast, Goldapple et al.'s (2004) study found no correlations between brain regions (at the pre-treatment) scan and clinical response.

- CBT for phobia

Research demonstrates that CBT, especially with a component of gradual exposure, is found to be particularly efficacious for treating phobias. The following neuroimaging study, researched by Straube and colleagues (2006), examines neural changes in response to CBT for spider phobia.[9] The therapy was based on the "rapid gradual exposure to the feared animals" technique associated with CBT. A group of 28 spider phobic females and also a group of 14 healthy female control subjects were recruited for this study – although all subjects (who were diagnosed as spider phobic prior to this study) were free from additional neurological or psychopathological disorders, the authors do not explicitly indicate whether or not patients were free from psychotropic medication.

The patients were divided into two groups; a treatment group (TG) and a waiting-list group (WLG). All patients were scanned twice in an fMRI (functional magnetic resonance imaging) scanner separated by a two week interval; the control group were only scanned once. While being scanned, participants were presented with spider video clips and control clips (moving objects) projected into a screen - the video presented in both scans contained different movement sequences – and after the scan, participants rated fear-induction, valence and arousal during the video clips. Scan results will be discussed in the section below.

The TG patients were treated with CBT in groups of two to three people with two sessions of four to five hours each. Patients were educated around misconceptions of the danger of spiders and were given the following therapeutic goals: "1) to hold a living tarantula for about 10 min; (2) to catch moving and non-moving spiders at least 10 times with a glass at different locations within the therapy room; (3) to catch any

[9] Karlsson (2011) notes that Straube's study used DBT as the therapy intervention, this is incorrect as CBT was the treatment modality

species of spiders at least 3 times in the basement of the institute; (4) to touch a rapid moving house spider" (p. 127) and these were to be performed without overwhelming feelings of anxiety. Outside of the therapeutic environment, participants were encouraged to ‘‘avoid’’ avoidance behaviour and capture as many spiders as possible. Gradual exposure started with spider photographs, followed by video clips and lastly, live spiders. Remarkably, the therapeutic aims were reached by all of the TG and they all responded successfully to the therapy. Essentially, these patients were encouraged to harness their brain's plasticity through extensive experience [exposure] using multiple forms of learning [e.g. tactile, visual, cognitive] causing the brain to rewire itself in response to the phobia.

The first fMRI scan analysis for the contrast of the spider vs. baseline images revealed increased activity in a number of areas in both control subjects and phobics. However, while amygdala activation (specifically the left amygdala and bilaterally in the parahippocampal gyrus) was only seen in control subjects, the phobics showed activation in the (left & right) insula & ACC (anterior cingulate cortex). However, in contrast, Paquette et al.'s (2003) neuroimaging study of CBT treatment for spider phobics, detected significant bilateral activation of the parahippocampal gyrus and associative visual cortex in the phobic group as well as activation of the right dorsolateral prefrontal cortex (inferior frontal gyrus).

Figure 11 below shows this activation (in red) in the ACC in image A on the left and in the insula in image B on the right. The plots in Figure 11 graphically represent the differences in brain activation between the phobic subjects and the control subjects where no activation in these areas was observed.

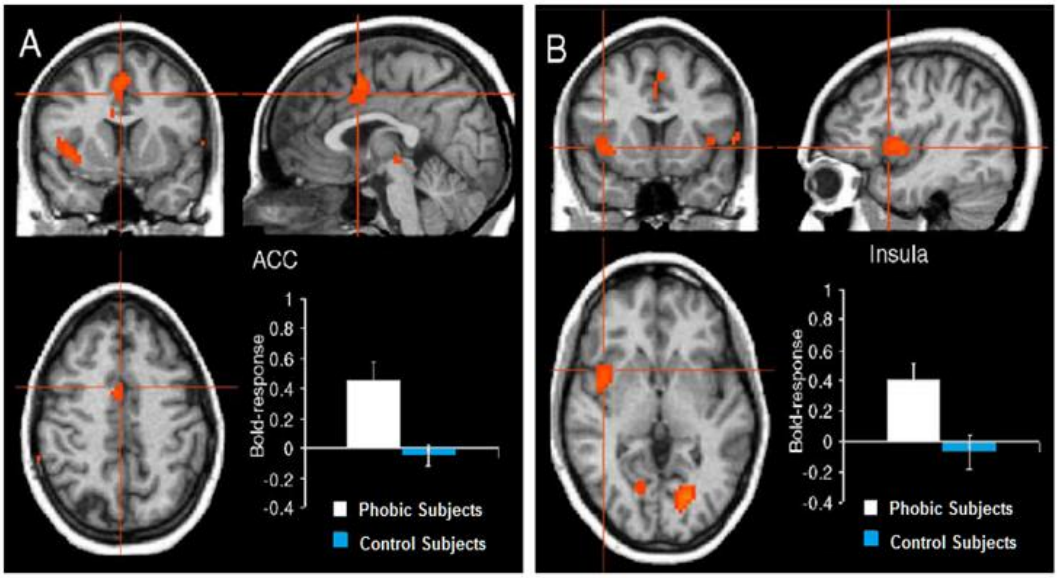

Figure 11. Increased activation of ACC and Insula to spider vs. control videos in phobic subjects compared to control subjects during the first scanning session. The plots show the contrasts of parameter estimates (Straube et al., 2006).

In sharp contrast to the initial scan where the phobics in the wait list group (WG) & therapy group (TG) displayed no differences in the brain activation regions of interest (ROI), significant changes were observable between the two groups in the second scanning session. There was no activation of the ACC in the TG in response to the spider videos and only slight activation in the ventral anterior insula in comparison to the WG group who exhibited notable responses bilaterally in the insula and the ACC.

In comparison to Figure 11 above, Figure 12 below shows no activation in the ACC (image A) and only slight activation in the insula (image B). The plots in Figure 12 below compare the differences in this brain activation after the first and second scan. The activation observed in scan one (see also Figure 11) in the therapy group subjects

was absent in the second scan while there was no change in the waiting list group.

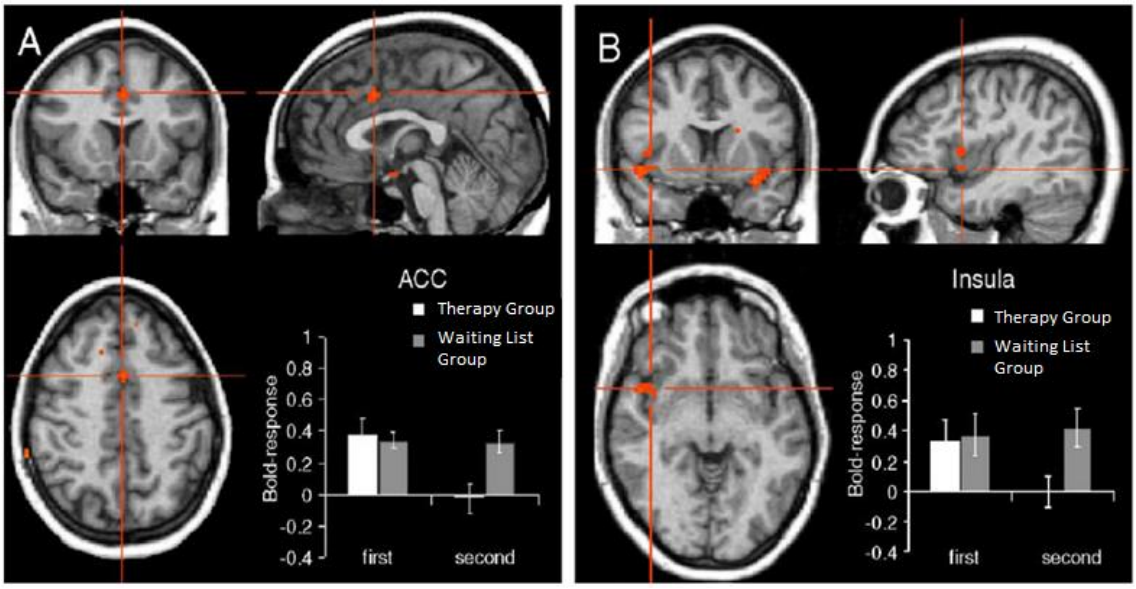

Figure 12. Increased activation of ACC and insula to spider vs. control videos in the waiting-list group compared to the therapy group during second scan. The plots show contrasts of parameter estimates for both scanning sessions (Straube et al., 2000).

After the treatment, there was no difference in brain activation between the healthy control group and the CBT group where an absence of activation of the anterior ventral insula was displayed. Although this study produced statistically significant results, there was no long term follow up on patients to confirm the long term efficacy of this treatment for a specific phobia.

Interpersonal psychotherapy (IPT)

There are two studies that examine the efficacy of IPT for the treatment of MDD compared to a medication group (venlafaxine in one study and paroxetine in the other). After six weeks of IPT, Martin et al.'s (2001) study reported increases in the resting activity in the posterior (back) cingulate and basal ganglia while Brody et al. (2001) observed decreased activation levels in the both anterior (front) cingulate and right prefrontal cortices, and increases in the insula and temporal regions were observed after 12 weeks of IPT for MDD. In addition the IPT structure was different for each study in

terms of amount of therapy sessions and the frequency of the sessions (Baxter et al., 1992; Brody et al., 2001; Nakao et al., 2005; Prasko et al., 2004).

In Brody et al.'s study of IPT vs. fluoxetine, both treatments reduced symptoms; changes in the ventrolateral prefrontal cortex (VLPFC) were only observed in the Paraxotine group. However, Fu et al. (2008) notes that there are few consistencies evident in these data but this may be due to substantial differences in patient clinical response rates and time-frames associated with scans and follow-up scans.

Psychodynamic Psychotherapy (PDT)

The first neuroimaging study of the efficacy of psychodynamic psychotherapy for BPD patients was carried out by Lai et al. (2007) which reported a strong frontal activation neural pattern that was absent prior to 16 months of treatment. The authors note that "this neural pattern could be the correlate of an increased capacity of the two patients to manage the emotional stimuli and the stressful events" (p. 405). A major drawback of this study is its sample size – two patients completed the therapy. In addition, only one therapist conducted the treatment - there was no waiting list or control group and, since the treatment lasted 16 months, time could have been a curative factor although the authors note that BPD is considered a chronic condition.

Up until now, there have only been six neuroimaging studies (including the one above) examining the neural changes associated with psychodynamic psychotherapy (PDT); three studies of long term (1–2 years) psychotherapy and three of short term psychotherapy (1-3 months) although the number of weekly sessions varies for each of these studies. Some of these studies have examined brain regions while others have reported molecular brain changes. Lehto and colleagues (2008) explored the neural effects of psychodynamic psychotherapy (1 year) for MDD including the atypical depression (ATD) subtype by means of a molecular study. The authors note that

previous studies report variations in serotonergic systems in MDD sufferers in that there is a decreased midbrain serotonin reuptake transporter (SERT) density. Serotonin transporters (SERT) regulate the transmission of the neurotransmitter serotonin through reuptake and removal of 5-HT from the synaptic cleft both in the brain and in peripheral serotonergic systems. The study compared results between the wait listed group (WL) and the psychotherapy group. Although there were no differences in SERT levels in both groups prior to therapy, patients with ATD responded to psychotherapy showing a significant elevation of midbrain SERT which contrasted with the non atypicals where there was no change recorded. However, all patients improved after one year of psychotherapy at a frequency of 2 x 45 minute sessions per week.

While there are neuronal structural changes that occur in response to psychodynamic psychotherapy, as demonstrated in the previous studies, the molecular mechanisms mediating the effects of psychotherapy are unknown (Karlsson et al., 2010). According to Karlsson et al., other molecular imaging studies have implicated the serotonin 5-HT1A receptor system in the pathophysiology of major depressive disorder (MDD). It has been discovered that there is a prevalence associated with the density of serotonin 5-HT1A receptors (decreased in MDD) and therefore serotonergic medications are extensively prescribed in the treatment of this disorder. Karlsson notes Kandel's hypothesis that it is possible that, through learning, psychotherapy can lead to changes in gene expression inducing morphological neuronal changes by altering the strength of synaptic connections between these neurons – this particular neuroimaging study supports this hypothesis.

Karlsson and colleagues (2008) ran a randomised comparative study comparing and testing the effects of brief psychodynamic therapy and fluoxetine medication through examining imaging results of 5-HT1A receptor density in patients suffering MDD. Twenty-three patients, participated in the study - they were recruited from

occupational health care services providing primary health care and received brief psychodynamic psychotherapy (n=8) or fluoxetine (n=15) for 16 weeks. Although all patients were anti-depressant free for at least five years prior to the study, and severe somatic illness was an exclusion criterion, the study does not mention whether histories of physical illness, neurological disease or head trauma were taken into account.

Patients were randomly assigned to either the psychotherapy treatment group or the pharmacotherapy group; the psychotherapy group received 16 weekly psychodynamic therapy sessions with experienced psychiatrists or psychologists. This particular neuroimaging study is based on a previous study (2008) that the researchers published which compared the efficacy of short term psychodynamic psychotherapy in contrast to fluoxetine treatment. However, it is unclear when the neuroimaging took place since the initial study, which makes no mention of neuroimaging, was carried out in 2008 but the latest study was published in 2011. It would, however, seem that the neuroimaging sample group was taken from the recruited psychotherapy (PSY) & fluoxetine (FLU) groups in the initial study. Unfortunately it was not mentioned how the neuroimaging patients were selected from the main treatment group which creates implications for the general design of the study. Subjects who participated in the neuroimaging study (2011) underwent two whole body 3D PET scans before and after therapy and four healthy volunteers were also scanned twice over the period to confirm the stability of the PET measurements.

Response to the treatment was defined as a 50% reduction in symptoms. Both groups displayed similar clinical outcome in that 59% of the patients reached remission by the end of the treatment, and 77% reached the criteria for response after four months. The 5-HT1A receptor density was analysed after treatment and the researchers found an increase in receptor binding in a number of cortical regions in the PSY group. No changes were observed in the patients in the fluoxetine medication group, although

symptom ratings associated with clinical outcomes were similar in both groups. There is a suggestion that possible risk of future depression is associated with reduced 5-HT1A receptor binding which is consistent with the finding that the relapse rate of MDD is higher in those treated with pharmacotherapy in comparison with those treated with psychotherapy – Karlsson et al.'s study is consistent with this hypothesis although the sample group for the study was small with only four patients reaching remission in the psychotherapy group.

The first neuroimaging study using fMRI technology and assessing the efficacy of long term psychodynamic psychotherapy was carried out in 2012 by Buchheim et al. on patients suffering severe depression previously unresponsive to psychopharmacotherapy and / or psychotherapy. Patients suffering from MDD were recruited for this study from two outpatient departments of two psychoanalytic institutes. Eight patients were diagnosed with double depression (dysthymia and previous MDD episodes), the rest of the patients were suffering severe depression and ten patients had a comorbid anxiety disorder. This particular study had good exclusion criteria such as the absence of other main psychopathologies, substance abuse, significant medical or neurological conditions including organic psychiatric conditions, and all patients were free from psychotropic medication throughout the entire 15 months. A healthy control group were recruited and were matched for age / sex and education but there was no untreated depressed group given the researchers' ethical considerations due to the length of treatment. Patients in this study were treated by 16 experienced psychotherapists and underwent 2-4 hours of psychodynamic psychotherapy per week.

At the onset of the treatment, all patients and the control group underwent an fMRI scan of approximately 25 minutes. In the scanner, patients' attachment systems were assessed by presenting them with imagery designed to evoke their attachment

systems – these images and personally relevant sentences associated with the images, which were acquired at interviews prior to the fMRI scanning, were of personal significance to each patient. Activation in the emotional regulation processing areas of the brain was observed namely the anterior cingulate cortex (associated with both mood dysregulation and its resolution) amygdala-anterior hippocampus region and medial prefrontal cortex.

Figure 13 below shows the following: the red circle (image A) highlights the activation in the amygdala / anterior hippocampus; in image B, the blue circle highlights the subgenual cingulate and the yellow circle, the anterior medial prefrontal cortex.

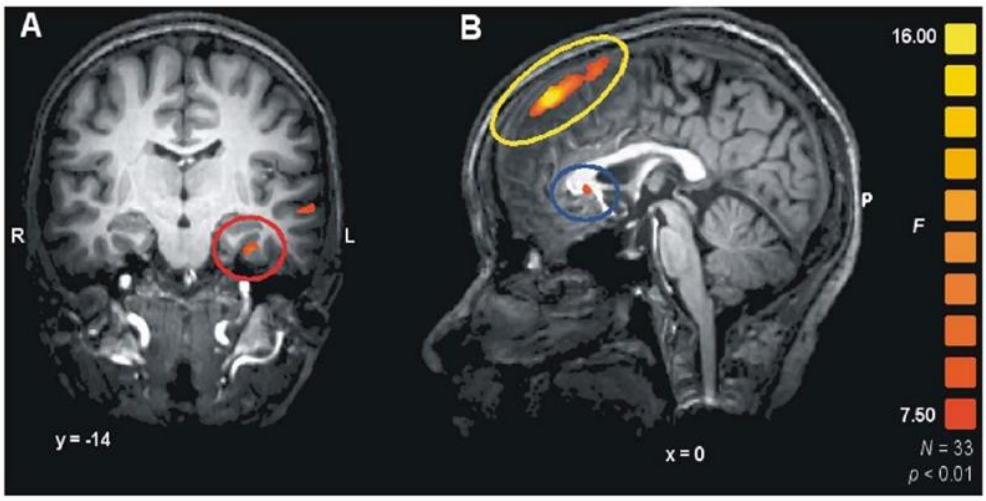

Figure 13. Neuroimaging results. Statistical maps of the interaction between contrast 'relevant' vs. 'neutral', group and time. A: frontal slice showing the interaction in the amygdala/anterior hippocampus (red circle), and B: in the subgenual cingulate (blue) and the anterior medial prefrontal cortex (yellow) (Karlsson et al., 2008).

Patients' progress was assessed using BDI & GDI scores where BDI scores refer to the level of depressive symptoms and GSI scores reflect general symptomatic distress. The researchers found correlations between brain activity and BDI & GDI scores in patients but there were no changes detected in the control group. It was noted that "the significant association of the changes in the subgenual cingulate and medial prefrontal cortex with symptom improvement supported the hypothesis of their relevance to the changes intervened during therapy" (p. 5).

The researchers report that although there were no significant changes detected in the hippocampal /amygdala cluster part of the brain, a significant association between imaging signal contrast and BDI changes and general improvement (GSI) were of significance in the ventral ACC.

Figure 14 below plots the BDI & GDI scores and captures these changes / improvements in the two specific implicated areas of the brain namely the ventral ACC (image A) and the medial PFC (image B). Changes in the contrast signal were more strongly affiliated with the GSI (in red) scores (general improvement) than with recovery from depression as shown by the BDI scores (in blue).

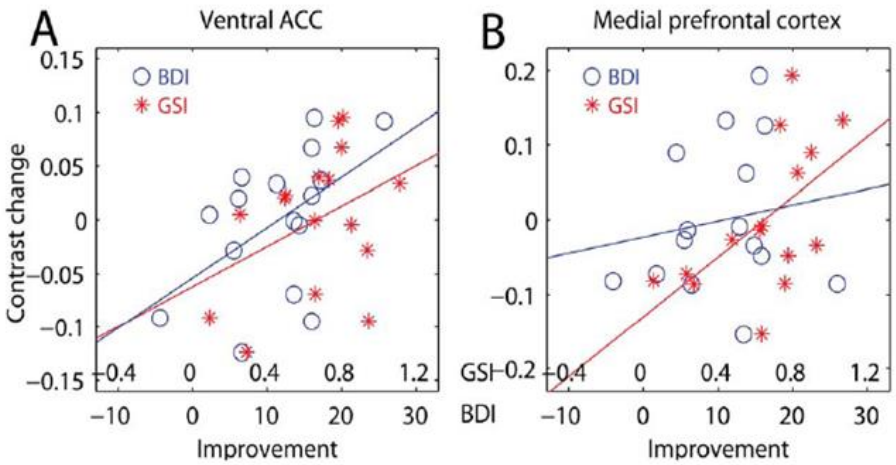

Figure 14. Association between neuroimaging data and improvement. The regression of the interaction of effect on BDI (blue circles) and GSI (red stars) improvement is shown for the subgenual cingulus (A) and the medial prefrontal cortex cluster (B) (Karlsson et al., 2008).

The conclusion of this study is that "long-term psychodynamic psychotherapy is indicated for the treatment of chronic depression, and may be expected to address a wide range of issues that may complicate the depressive illness and contribute to chronicity" (p. 5). As mentioned previously, this study did not have an untreated patient group as the researchers found it unethical. However, an untreated group could have had support sessions with a primary health care professional or another non-therapy professional and this would have controlled for the efficacy of the actual model of treatment rather than the relational experience of being supported for 2-4 hours per

week. In terms of receiving supportive advice, the medication group in Baxter et al.'s study (1992) examining the neural changes associated with BT vs. fluoxetine, received supportive advice twice a week.

Another critique of this study is that although the study considers the efficacy of "psychodynamic psychotherapy", the description of the method of treatment matches psychoanalytic treatment or psychoanalysis – patients were treated using the couch at a frequency of up to four sessions a week – which is a misleading methodological inconsistency. According to Stern (2009) psychoanalysis is generally defined by the amount of sessions and the use of the couch, therefore it seems that perhaps these patients were receiving psychoanalysis rather than psychotherapy which is carried out typically once or twice a week.

In accordance with the findings above, related to frequent weekly psychotherapy, Beutel et al.'s study (2010) on the efficacy of psychodynamic therapy for panic disorder demonstrates an impressive outcome after four weeks of intensive psychodynamic psychotherapy. Nine patients were treated in an inpatient treatment programme and results were compared with a healthy control group. Differences previously observed between patients and controls in the prefrontal-limbic circuit were no longer found post treatment. Limbic function normalisation was supported by a substantial reduction of activity in the hippocampus in the second scan in contrast with the first. The authors conclude that their results indicate that short-term psychodynamic treatment demonstrates changes in fronto-limbic circuitry which is in accordance with findings on cognitive–behavioural treatments.

Summary

In summary of the above studies, the majority of the studies in this chapter reveal that various forms of psychotherapy (CBT, DBT, Psychodynamic Psychotherapy) for depression, anxiety and some other disorders (PTSD, PD) reported surprisingly similar neural changes compared with medication treatment. In addition, it was noted that there is a correlation between treatment outcome / success and the observed neural changes (Doidge, 2010) – better outcomes produced more significant neural changes while other studies revealed that certain abnormalities in the brain were good predictors of outcome in either psychopharmacotherapy or psychotherapy treatment.

A number of the studies have suggested that the neural changes in response to psychotherapy have a regulatory effect on the brain, perhaps restoring its natural homeostasis. CBT, for example, is thought to be an effective treatment for phobias, panic disorders and OCD (Porto et al., 2009) in that it reduces phobic avoidance by eliminating the contextual fear stored in the hippocampal region while, at the same time, normalises dysfunctional thought processes / neural activity in the prefrontal cortex.

In addition to the above, the neuroimaging studies that have examined brain changes in response to psychodynamic therapy have had statistically significant results especially those associated with high frequency (4x per week) long term psychodynamic psychotherapy. It was also reported that while other forms of therapy, for example CBT and BT, were efficacious in treating single disorders such as phobias or OCD, long term psychodynamic therapy is more effective in treating "complex" cases. This finding of the efficacy of long-term high frequency psychotherapy is consistent with the psychoanalytic literature (Sandell, 2001; Frosch, Fonagy, & Target, 2002).

Limitations of the Neuroimaging Studies

According to the literature to date, Carrig, Kolden & Strauman (2009) note that study reviews "suggest that neuroimaging can elucidate the effects of psychotherapy on both mental processes implicated in a range of disorders and on brain functions associated with those processes" (p. 410). However, it is clear from these studies that neuroimaging research of psychotherapy is still in its infancy due to the number of design and methodological limitations in these studies. For example, the modality of psychotherapies that are being compared in the various studies are not always similar, and in some instances the same form of therapy advocated in one study, for example, CBT, is enormously different from the CBT in another study. There have also been significant inconsistencies in session length and session frequency as well as differences between the use of single vs. multiple therapists. The question is, how do we know that it is the modality of therapy that is being delivered that is the curative factor in contrast with perhaps, a supportive relationship? Cozolino (2006) notes that "from both animal and human research we have learned that positive social interactions result in increased metabolic activity, mRNA synthesis, and neural growth; in other words, relationships can create an internal biological environment supportive on neural plasticity" (p. 299).

In addition, while neuroimaging in psychotherapy is an exciting new method of research, the imaging modalities vary greatly between studies and each modality has different mechanisms which influence image resolutions and also have patient-related limitations. Roffman et al. (2005) note that by measuring cerebral blood flow (CBF) or glucose metabolism, these techniques provide an indication of brain activity and go on to say that "although the relationship between glucose metabolism or CBF and neuronal activity remains controversial it is commonplace to use the term 'brain activity' essentially interchangeably with 'metabolic activity' or 'hemodynamic activity'" (p. 1389). In terms of fMRI, which is a flexible and powerful technique, there are

questions around the precise form and latency of the BOLD (blood oxygenation level dependent) response signals (used to measure brain activity in some of the studies). In addition, Dichter et al. (2012) note that other factors can have serious implications for BOLD responses and goes on to say that "variables such as caffeine, nicotine, pharmacologic agents, and varying severity of disease states can drastically impact resting brain perfusion and thus the hemodynamic properties and BOLD response in the brain" (p. 485).

Lastly, and probably the most striking critique for all of the studies, is the absence of consideration for the substantial response associated with placebo effect which is present in many psychopharmacological studies. The implications associated with the power of placebo and its effects on the brain are nothing short of profound. Cozolino (2010) examines the effect of placebo in psychotherapy treatment and notes the following findings associated with the impact of positive expectancy on major depression: "increased activity in prefrontal, anterior cingulate, premotor, parietal, posterior insula, and posterior cingulate. Decreased activity in subgenual cingulate, parahippocampus and thalamus" (p. 338).

Conclusion

Despite the various limitations of the neuroimaging studies, this systematic literature review demonstrates that every study of psychotherapy has shown changes in neurological processing. We can therefore conclude with some certainty that psychotherapy changes the brain. Now that we have evidence that psychotherapy changes the brain, the question of how session-frequency affects psychotherapy outcome can be addressed. Does intensive psychotherapy bring about more change? Is intensive psychotherapy a way of harnessing the brain's plasticity? Although there is no neuroscience literature addressing these questions, a systematic review of the

psychotherapy / psychoanalytic literature on session-frequency and psychotherapy dosage seeks to answer these important questions.

Chapter 4 Session frequency / psychotherapy dosage

> Because therapy itself is a learning experience, it, too, involves changes in synaptic connections (Le Doux, 2003, p. 278).

Chapter Three demonstrated that structural neural changes are the result of psychotherapy and is evidence of neuroplasticity which was discussed in Chapter Two. This chapter begins with the famous words of Donald Hebb: "Synaptic efficiency arises from the cell's repeated and persistent stimulation of the postsynaptic cell" (1949, p. 70). The chapter is a systematic review of the literature to ask what "repeated and persistent" might mean in relation to psychotherapy.

In the neuroimaging studies of psychotherapy, intensive psychotherapy produced excellent results as did intensive learning in the studies on neuroplasticity. Evident in the medical literature, repetition, iteration and frequent practice harness the brain's plasticity in terms of treatment technique for sustained neurological or traumatic brain injury or stroke patients (Dombovy, 2004; Dobkin; 2006; Hancock et al., 2011; Lang et al., 2009). Perhaps the neuroplastic result of psychotherapy / change can be harnessed with an increase in session frequency[10]? If the brain is as plastic as the neuroscience research has found, surely therapeutic outcome increases incrementally or is proportionate to the amount of sessions a patient has in a week.

However, unlike assessing outcomes in medicine, evaluating success in psychotherapy is not as straightforward since desired outcomes of treatments may be diverse. For example behavioural therapy may assess changes in behaviour while the psychoanalyst may focus on more subtle psychic changes (Freeman & Tyrer, 2006). Allot (2005) mentions that, according the New Zealand Blueprint for Mental Services, the definition for recovery is: "the ability to live well in the presence of absence of one's mental illness (or whatever people choose to name their experience). Each person with

[10] The terms "session frequency" and "dosage" are used interchangeably as they refer to the same concept

mental illness needs to define for themselves what 'living well' means to them" (p. 324). It is important to hold this in mind while reviewing the research presented in the following psychotherapy outcome studies on session-frequency or psychotherapy dosage.

The medical and psychological literature was systematically reviewed to find associations between neural plasticity and psychotherapy session frequency and psychotherapy dosage. Since there was no psychological literature linking these two concepts, I wondered if considering a psychological correlate of this medical research (on repetition, iteration and frequency in terms of neuroplasticity) was a viable line of enquiry. As previously mentioned, I consulted with the experts in this research field (psychiatry, neuroscience and psychoanalysis) who expressed the following: Eric Kandel (Personal Communication, 2011) noted that he felt that this research was exactly what was needed while Norman Doidge (Personal Communication, 2011) advised that he had recently reviewed research that found that psychotherapy session frequency directly related to the speed at which a patient recovered. Louis Cozolino (Personal Communication, 2011) found the idea most interesting and offered few free associations including questions such as, "What maximizes persistent dendritic modelling?" In terms of plasticity, Mark Solms (Personal Communication, 2011) felt in agreement with my assumption that more psychotherapy sessions would facilitate neural plasticity although he felt that were also other factors that influenced therapeutic outcome. After these most helpful responses I wondered: had Freud published any recommendations on session frequency since psychoanalysis is renowned for its high session frequency?

This question will be answered in the second part of the following section which reviews the literature on both psychotherapy dosage and session frequency. We begin by looking at the dosage literature.

Psychotherapy Dosage

The search word which rendered results around session frequency, was the term "dosage" where psychotherapy, like psychophamacotherapy, is administered as a dosage. In much the same way that certain dosages of psychotropic medication are required to adjust the neurotransmitters in the brain to achieve a desired results, this research examines the relationship between the amount of psychotherapy administered and change, or neuroplastic and molecular changes in the brain (in neuroscience terms).

Dose-response

The theoretical framework associated with dose-response which originated from the biological sciences (Hansen, Lambert & Forman, 2002) is widely used in medical / pharmacological research and has also been adapted for psychotherapy research. Considering the terms "dose" and "response" in the psychotherapy research below, one session (Hansen et al. 2002; Howard, 1986) of therapy is generally defined as a "dose" and the "response" would be whether a particular outcome or measurable level of change (such as sick days taken off from work) has occurred.

Although using this biological framework from the dose-response research seems to be an apt method, Reese, Toland & Hopkins (2011) point out that there are two caveats when it comes to defining psychotherapy dosage making it substantially different from doses of medication which are typically administered either when needed (such as pain relief) or at regular intervals to sustain a certain desired effect. Firstly, since there are numerous types of "therapeutic treatments employed by different clinicians with complex individuals who present with a myriad of issues that may respond to any one session differently" (Reese et al., p. 609), equal therapy dosage per session cannot be assumed. Secondly, noting when psychotherapy dosage is administered should be as important as it is with medication. Sometimes the

psychotherapy outcome literature assumes (Reese et al., 2011) that psychotherapy adopts the traditional 50-minute session at a once a week frequency and is therefore suggesting an equal interval between sessions. However, from the neuroimaging research we have observed that session length and frequency can be enormously different even between the administration of the same type of therapy, such as CBT or even PDT (psychodynamic psychotherapy).

The studies

A large-scale meta-analysis (Howard, Kopta, Krause, & Orlinsky, 1986) found correlations between the dosage of psychotherapy and recovery and notes that patients' ratings of overall wellbeing increases with more therapy (Hanson, et al., 2006; Howard, et al., 1986; Kopta, 2003; Seong-Hyeon, 2011). This meta-analysis consists of extensive data that "were based on over 2,400 patients, covering a period of over 30 years of research" (p. 159) and these notable findings are detailed in Figure 15 below.

The authors used the probit analytical model (usually used in bioassay research for evaluating dosage) to evaluate the data and this method proved to be satisfactory; the data analysis produced consistent results across the various studies. Although the meta-analysis found that better outcome was associated with more psychotherapy, the frequency of these sessions was at a rate of once a week sessions and therefore this study does not take into consideration the rate of improvement associated with frequency but rather with the length of therapy. In addition to this, the outcome of each treatment was only measured at the termination of therapy and improvement can often rapidly decline in the weeks, months and years that follow treatment – improvement results vary depending on when the follow-up is carried out (Freedman, 2002; Frosch, et al., 1999; Frosch, 2011; Leuzinger-Bohleber, et al., 2003; Sebek, 2001; Sandell, et al., 2001).

Figure 15 represents the analysis of two data sets taken from the psychiatric outpatient clinic based in Chicago – the researchers explored the relationship between the percentage of patient improvement and number of psychotherapy sessions: the first set (represented by the solid line) includes 151 patients who, following treatment termination, had their "closed charts" evaluated by researchers; the second set (represented by the broken line) includes 148 patients who completed "emotional well-being" reports while they were still in therapy (2,448 session-by-session subjective reports).

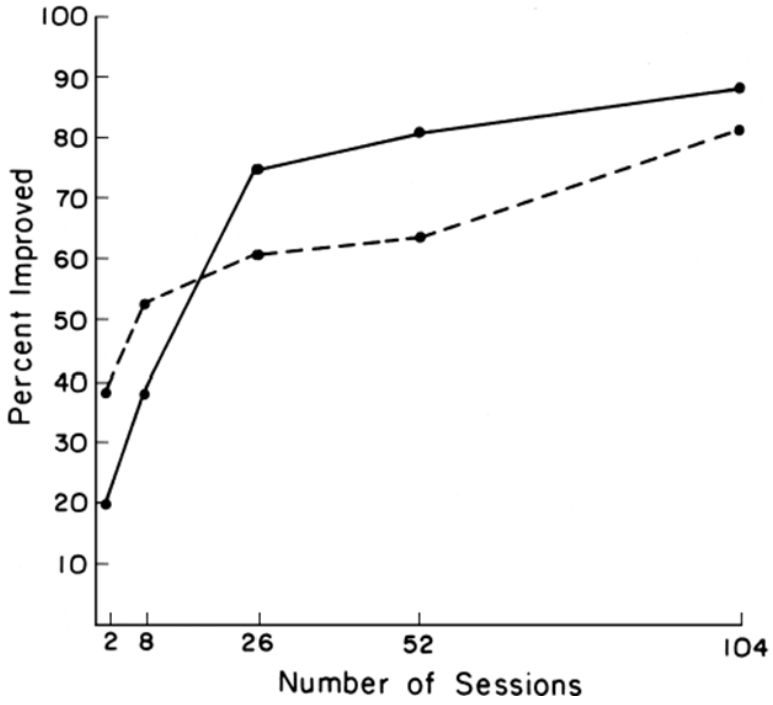

Figure 15. Relation of number of sessions of psychotherapy and percentage of patients improved. Objective ratings at termination are shown by the solid line; subjective ratings during therapy are shown by the broken line (Howard, Kopta, Krause & Orlinsky, 1986).

Howard, et al. (p. 160) note that (as seen in Figure15) "the plots of the actual percentage of patients improved as a function of number of sessions resulted in negatively accelerated curves" and goes on to say that higher rates of improvement occurred earlier rather than later in the therapy. This phenomenon has been considered in other literature as is referred to as "sudden gains". Drymalski & Washburn's (2011) research on sudden gains or rapid improvements carried out in a partial hospitalisation

program for depression found that there is a relationship between sudden gains and the dose of treatment received rather than the treatment duration – the sudden gains appeared early in the treatment rather than later and the authors suggest that this is likely to be due to the intensity of the treatment. It is also interesting to note that the group that experienced sudden gains had significantly better treatment outcomes than the group without sudden gains which has also been found to be consistent with prior research (Hardy et al., 2005; Tang et al., 2007 cited in Drymalski & Washburn). This makes sense from a neurobiological point of view, where initial sudden gains can be thought of as significant neural plastic changes. However, the researchers do cite another study, Vittengl et al. (2005), where sudden gains were associated with worse long-term outcomes.

Further to the above, Howard et al.'s study created three diagnostic groups (Figure 16 below) namely; depression, anxiety, and borderline-psychotic to review the dose-effect model for differences among patients and trends in outcome – the results of these probit analyses are shown in the graphs below adapted from "Table 4" (p. 163). The graphs display percentages of improvement in three different patient groups (depression, anxiety and borderline / psychotic) which are associated with the number of psychotherapy sessions undertaken. It can be clearly seen that a higher dose of psychotherapy produces better improvement. Different rates of improvement between

the patient groups are also compared.

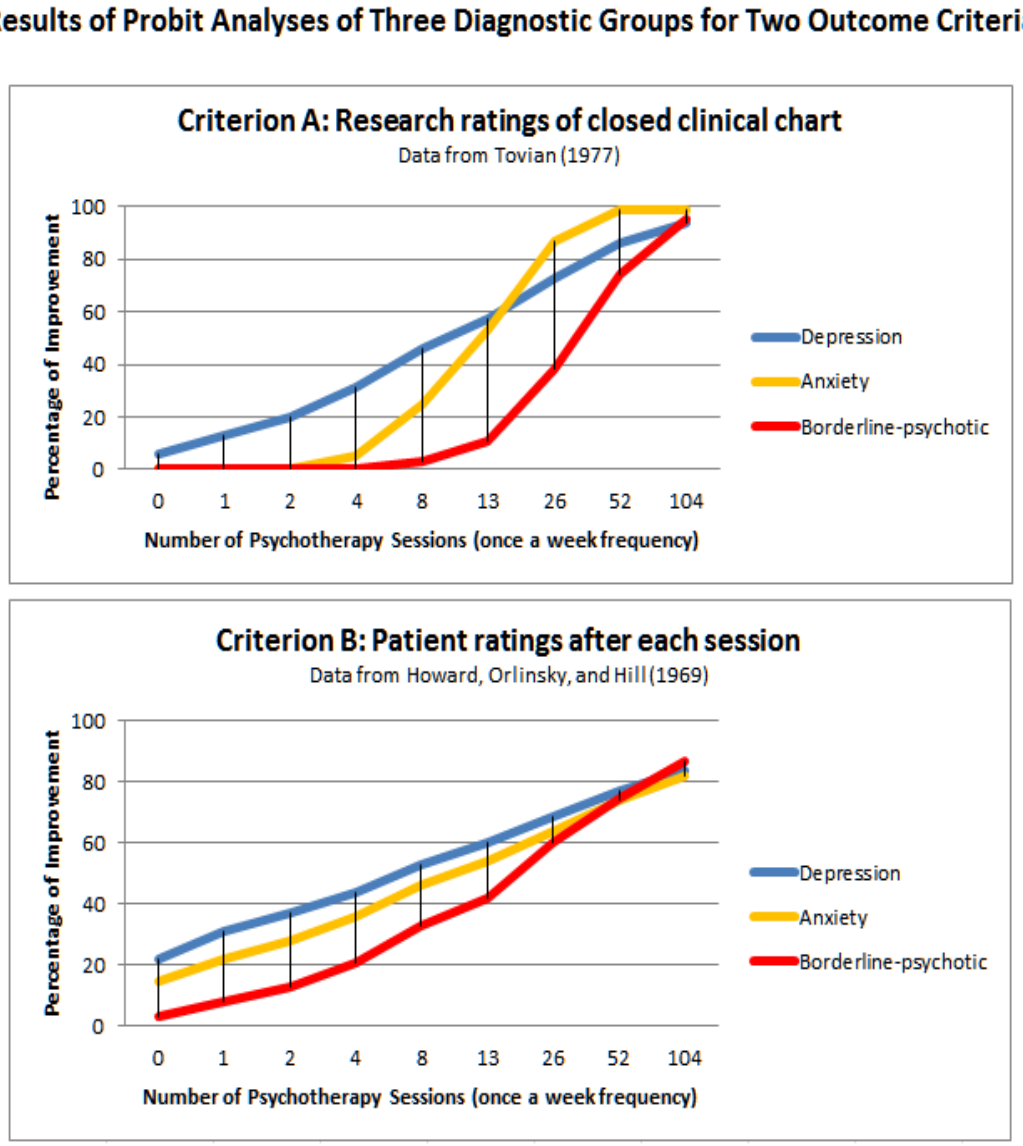

Figure 16. Outcome Criterion A & B depict percentage of improvement in relation to amount of sessions for three particular diagnoses from both patient and researcher's perspectives.

Overall it was found that 50% of the patients treated for anxiety and depression improved within 8 – 13 sessions while, with borderline patients, improvement at this level occurred later at 13 – 26 sessions. Therefore, as observed by Howard et al., "depressive patients began responding at the lowest dosages of psychotherapy, anxiety neurotics at a somewhat higher dosage, and borderline-psychotics at a still higher dosage" (p. 162).

These findings are consistent with a later study carried out by Howard & colleagues (Kopta, Howard, Lowry & Beutler, 1994) where they explored the relationship between symptom relief and psychotherapy dosage. In this particular study, 854 patients were given symptom checklists to complete at the beginning and completion of treatment. In a review of this study, Hansen, Lambert & Forman (2006) report that "results showed that different symptoms improved at different rates, with "acute" symptoms requiring five sessions, "chronic" symptoms requiring 14 sessions, and "characterological" symptoms requiring 104 sessions for a 50% response" (p. 332). This raises the question that perhaps different dosages of therapy need to be applied to different presenting issues – consistent with the neuroimaging studies where two weeks of intensive therapy (including 2 x 5 hour therapy sessions) cured spider phobics but patients suffering severe depression with other co-morbid diagnoses (and who had previous unsuccessful therapy – psychopharmacotherapy / psychotherapy) all recovered with an intensive 15 month four times a week psychodynamic psychotherapy (Buchheim et al., 2012).

Lastly, Figure 17 (adapted from the Howard, et al. meta-analysis) demonstrates trends captured in the data across a number of different studies using the prohibit analysis tool. The data were aggregated from 15 samples reporting data for 2,431 patients spanning a period of more than 30 years and incorporated a number of different outcome criteria: patient groups, treatment settings, therapists and treatment orientations which were generally either interpersonal or psychodynamic. Howard et al. note that "none of the therapies were primarily behavioural or psychopharmacological" (p. 161). The patients in these samples were generally "neurotic" (depression or anxiety) with a small proportion being diagnosed as psychotic or having a personality disorder and were being treated in individual outpatient psychotherapy once weekly.

The results shown in Figure 17 below are estimates rather than the numerical results of each study "in that they are extrapolated or interpolated values of the expected percentage improved for the selected number of sessions. These estimates are based on the best-fit lines produced by the probit analysis of each set of raw data" (p. 162). The graph (Figure 17) indicates that 10% - 18% of patients are likely to have shown some improvement before the first session. Howard et al. (1986) mentions that sometimes the process of initiating contact with the psychotherapist or clinic can result in an improvement prior to the first session. This phenomenon has been observed in the neuroimaging studies and is associated with the term 'spontaneous recovery', or perhaps the placebo effect.

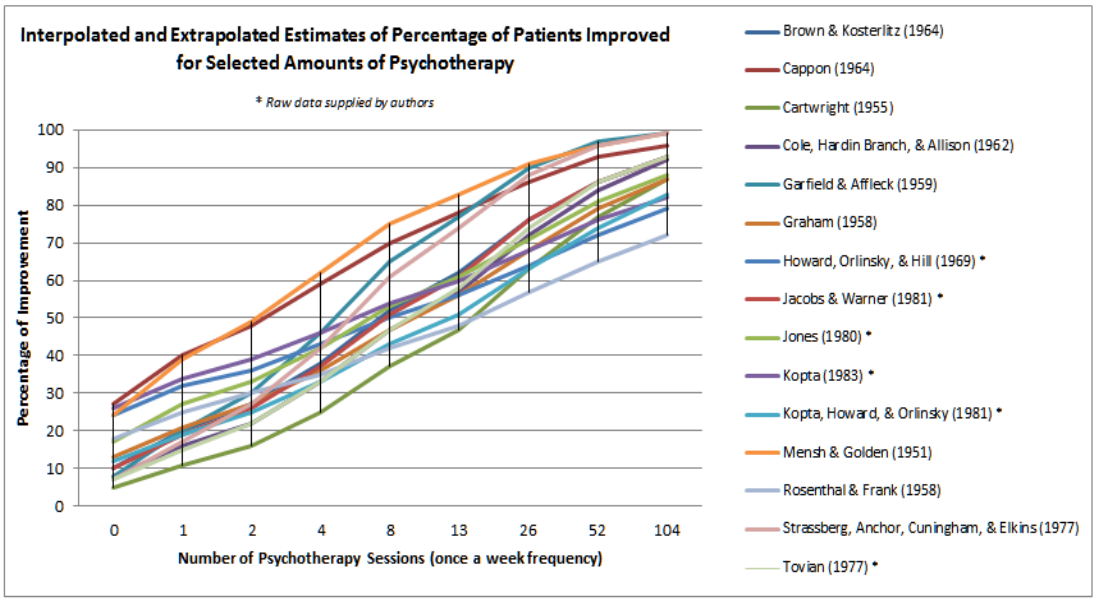

Figure 17. Overlaid data from a number of different outcome studies (see key on the right) in relation to amount of psychotherapy sessions.

In addition, the graph also displays that by the 8th session, 48% - 58% of patients would be expected to show a measureable improvement, and after 6 months, about 75% (26 sessions) and by the end of the year, 85% are expected to show a measurable improvement. Therefore this study demonstrates clear correlations between session dosage and recovery although it does not take into account session frequency. What would the treatment outcome be if compared to high frequency therapy? The session

frequency studies indicate better long term outcome with higher frequency and according to neuroplasticity research on learning, focussed intensive learning produces significant brain changes (see neuroplasticity Chapter Two).

Kopta (2003), who reviewed the late Dr Howard's work, noted that "over a period of ten years, Dr. Howard's research moved from the dose–effect relationship to the phase model to patient profiling. This impressive progression produced the methodology to answer an expanded version of Gordon Paul's (1967, p. 111) "ultimate" question, "How much of which psychotherapy by whom is most effective for which patient with what type of problem?" (Kopta, 2003) This is a poignant question as it has implications for how best to harness the brain's enormous plastic capability to bring about significant change. While these studies conclude that more psychotherapy produces better results through an accumulative effect, there was no comparison between higher weekly dosages of psychotherapy with a single weekly dose. The following large scale dose-response study reviews outcomes associated with more frequent therapy. Page and Hooke (2009) note that "research has shown that the more outpatient psychotherapy sessions people attend, the better the outcomes" (p. 426) and their study sought to examine whether this would translate to inpatient contexts.

This research, conducted at a private psychiatric facility in Australia, examines psychotherapy outcomes for a total of 2,782 patients – the researchers implemented a strategy that was run over the course of two years where inpatients (n=1274) received an additional group psychotherapy session (1.5 – 3 hours) per day. Their outcomes were then compared with a comparison group (n=1508) who had been treated previously at the clinic and who had undergone single daily group sessions. The frequency of the group psychotherapy was doubled. This study found that the additional psychotherapy produced superior outcomes and that patient re-admittance was halved. These findings are consistent with the dose-response model of

psychotherapy and although notable especially given the large sample size, no information was provided on the therapists that had conducted the group therapy. Since the comparison group had been treated two years prior to the implementation of the initiative, there may have been a different therapists conducting therapy at the time, or the political climate of the organisation may have been different at the time which may have contributed to differences in outcome.

Overall, these dosage studies show that there is a definite relationship between the accumulative effect psychotherapy and better outcomes. The first few studies do not review the effects of multiple or additional therapy sessions per week but rather report the impact of the total number of sessions where the finding consistently is, more therapy produces better results. However, this does not answer the question of the impact of more frequent sessions per week - the last study (Page & Hooke, 2009) above examines this relationship and finds that additional therapy sessions produce statistically significant improvements. This particular study, which reviewed daily psychotherapy, reminded me of the initial tradition of psychoanalysis which was typically conducted daily. The following section is a systematic review of the literature using the keyword "session frequency" in response to my question in the beginning of the chapter wondering what Freud's rational was for high session frequency since psychoanalysis is renowned for its high session frequency.

Session Frequency

Freud and Session Frequency

> I work with my patients every day except on Sundays and public holidays—that is, as a rule, six days a week (1913, p. 127).

Although Freud worked with his patients daily, he never provided explicit reasoning for this rationale other than that he felt it helped the flow of the psychoanalytic process

(Harticollis, 2003; Schwartz, 2003; Zusman, Cheniaux & de FreIitas, 2007). However, in Freud's overview of the "rules of psychoanalytic technique", he preferred (Rose, 2010) to refer to these rules as "recommendations" or "advice" which negated the impression that these were unconditional. Although Freud outlines recommendations for the analytic frame (in terms of session frequency), Frank (2011) makes an important observation when he points out that, within Freud's extensive writing collection, he [Freud] only addresses the matter of frequency of sessions once. This is referenced in Freud's work (1913) "On beginning the treatment" and further on Freud noted that he also treated patients at lesser frequencies. By the 1920's, Freud was offering psychoanalysis at a frequency of 5-6 times a week but with a total duration of six months. Freud did not elaborate on his reasons for proving such a therapeutic frame. When I read this, I wondered whether a higher frequency of sessions with shorter duration (6 months) was more effective especially given the brain's ability to change. Is this stance, albeit indirectly, harnessing that brain's plasticity to change? What does research indicate about the effectiveness / efficacy of session frequency?

While session frequency pertains mostly to field of psychoanalysis as it is traditionally practiced at high frequencies (BJP, 1999; Psychoanalytic Institute, 1997; Brafman, 2008; Conrotto, 2011; Frank, 2011; Heinicke, 1969; Rose, 2010; Schwartz, 2003; Zusman, Cheniaux, & de FreIitas, 2007), the literature is not particularly forthcoming around the discussion of session frequency. This is likely to be due to the political implications this topic has for the practice of psychoanalysis and its discussion has raised much heated debate within the psychoanalytic circles (Conrotto, 2011). Barrett (1996) mentions that he has "observed that this issue seems to possess a power to generate passionate emotions in most therapists and often leads to heated controversy" (p. 443). Although the literature is almost silent on the topic, the following studies that directly relate to the impact of session frequency on efficacy /

outcome of psychotherapy (located using the "session frequency" search term) will be discussed below.

The studies

One of the earliest studies evident in this review is Christof Heinicke's (1969) study that compares therapeutic outcome of either low intensity or high intensity psychotherapy. The participants were boys, aged between eight and ten years, who were referred to the clinic due to learning disturbances associated with psychological difficulties which posed issues at school. They were assessed by a child psychiatrist both before the treatment and after the treatment and in addition to the boys' therapy (which lasted between 1.5 to 2.5 years) the mothers of the children were also treated weekly and the fathers were in contact with the therapists.

The participants were then divided into two groups; the first group underwent once a week treatment (n=4) whilst the other was seen four times a week (n=4) by two psychoanalytic child therapists with similar experience and training. The researchers note that the results from the study indicate that there is a correlation between high session frequency and long term post therapy improvements. The graph depicted in Figure 18 below, adapted from Heinicke, represents the outcome of this study – the dark colour represents the group treated four times a week, while the other represents the once-a-week treatment group. The last two sets of values are based on post treatment follow up and report that the high frequency group continued to improve after therapy while the low frequency group's progress relapsed to levels prior to and below the initial treatment a year post treatment. The differences in outcome between these two groups are significant in that, while the graph displays better initial therapy results in the once a week group during treatment, it displays that the four times per week frequency is associated with better long term outcome.

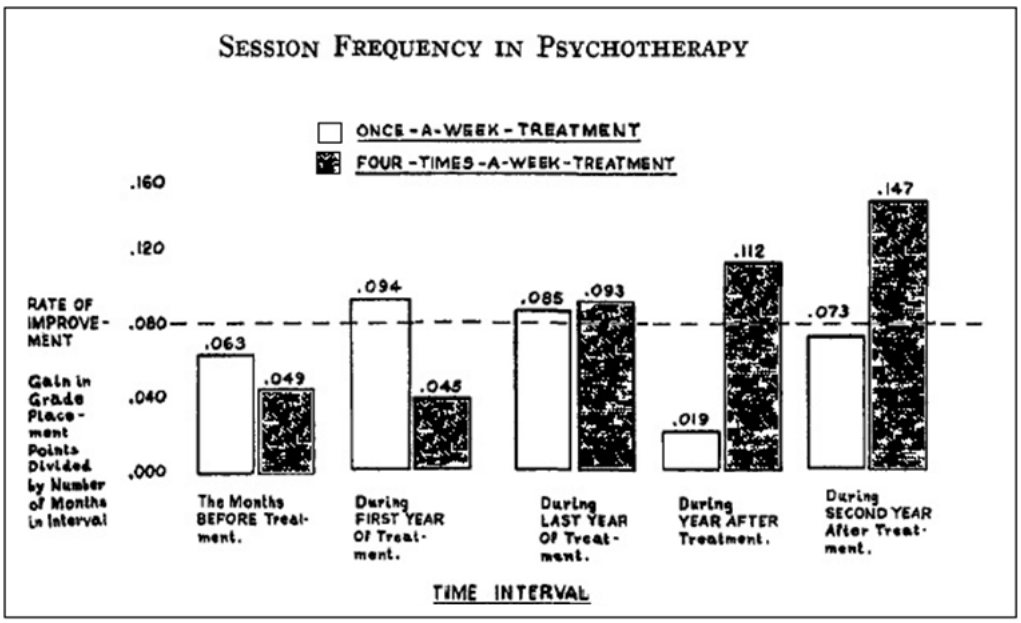

Figure 18. Rate of improvement: once-a-week treatment compared to four-times-a-week treatment (Adapted from Heincke, 1969).

Heinicke notes that although the outcome differences between the two groups are striking, it is possible that factors other than those associated with session frequency could account for this such as therapist attitude and sample size. In addition to this, if larger sample sizes for each group were available (four boys in each group), a variation in the results may have been observed. The lower frequency group presented issues of a more immediate nature while the high intensity group were able to work through intrapsychic and environmental conflicts which are not always in favour of initial symptom improvement. However, this more in-depth and extensive process provided the patients with a level of ego integration that facilitated further improvement not only by the end of the treatment but in the follow-up period following the treatment. This is finding is consistent with other research (Beutel, Stark, Pan, Silbersweig, & Dietrich, 2010; Fonagy & Target, 2002; Frosch, Freedman, Vorus, & Hoffenberg, 1999; Leuzinger-Bohleber, Stuhr, Rüger, & Beutel, 2003; Sandell, 2001) that observed a similar phenomenon of continued improvement beyond the treatment - these authors consider the concept of "internalisation" [of the therapist] facilitated by session frequency to be a strong predictor of outcome consistent with a number of theorists

(Freedman, 2002; Frosch, 2011). Falkenström et al.'s (2011) follow-up study of 20 patients treated with either psychoanalysis (high frequency) or psychotherapy (low frequency), found that it was the patients' ability, as a result of the high frequency treatment rather than the psychotherapy treatment itself, to sustain long term self-supporting strategies two years post therapy – this included the notion of the 'internalised therapist'.

Henicke, along with Ramsey-Klee, conducted another study in 1986 that evaluated three frequencies of psychoanalytic treatment over two years for children who were having reading difficulties due to emotional disturbances. Group 1 received once a week therapy, Group 2 received once a week for the first year and four times a week for the second year and Group 3 had four times a week therapy for two years. The findings from this study report that the gains for both high intensity groups were significantly better especially relative to self-esteem, adaptation and the capacity for relationships. However, the design of this study was flawed by current standards (Fonagy and Target, 2002) in that there was no definition of disorders or treatment procedures and the assessment method of outcomes had not been validated.

While the last two studies have been of children rather than adults, and children are more likely to adapt than adults, the following study is a large scale study of adult patients examining the role of session-frequency in therapeutic outcome. Freedman, Hoffenberg & Frosch (1999) examined a sample group of outpatients who had undergone psychotherapy at the IPTAR Clinical Centre – all previous patients of the centre were contacted to participate in the study and 99 responded. The respondents had had variable lengths of treatment - between a month and over two years and had been treated at a frequency of one, two or three sessions per week.

In order for the researchers to measure outcomes, an adapted Effectiveness Questionnaire (EQ) created by Consumer Reports was used to measure patients' scores. Figure 19 shows the relationship between these effectiveness scores and the amount of sessions that the patients received per week. The researchers note that one of the findings indicated an "incremental gain with greater session frequency from one to two or three weekly sessions" (p. 741). As can be distinctly seen in Figure 19 below, the more sessions per week, the greater the effectiveness of the therapy.

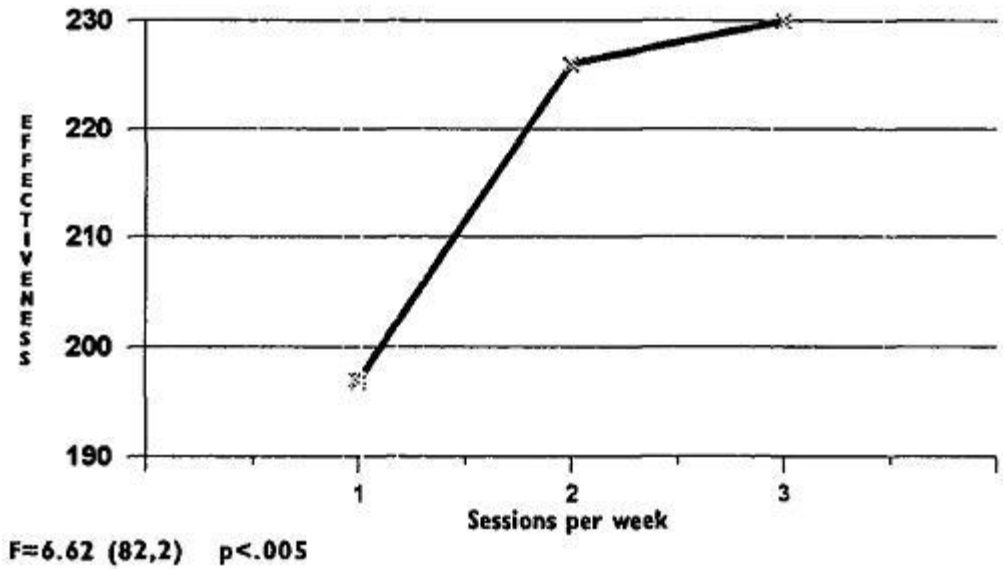

Figure 19. Gains on the effectiveness scale (left) increase in relation to number of weekly sessions (Freedman, Hoffenberg & Frosch, 1999).

In a later publication Freedman (2002) notes that, with reference to this study, "mean EQ (effectiveness questionnaire) scores among patients with varying levels of session frequency increased in steady increments from one to three times per week" (p. 267). Freedman, Hoffenberg & Frosch (1999) concluded that "increased sessions made a difference, a finding with specific relevance to psychoanalytic psychotherapy" (p. 756).

The results of the above study are consistent with the findings published from the large scale study called The Stockholm Outcome of Psychotherapy and Psychoanalysis Project - STOPPP (Sandell et al, 2000; Sandell, Blomberg, Lazar, 2001). This outstanding contemporary study followed-up 400 patients (over a period of three years) of which 74 patients were in private psychoanalysis (3-5 times weekly) and 331 in psychoanalytic psychotherapy (1-2 times weekly) for a period of 3 years (Sebek, 2001). The psychoanalysis patients had had a total of 642 sessions while the psychotherapy patients had a total of 233 sessions over approximately the same period of time. All patients had roughly the same DSM IV axis 1 & 2 diagnoses. The findings from this well designed study clearly demonstrate that intensive psychoanalyses are superior to low-frequency treatment and that this gap increases beyond termination. Figure 20 below captures this relationship between different outcome points and compares low-frequency treatment with high-frequency treatment.

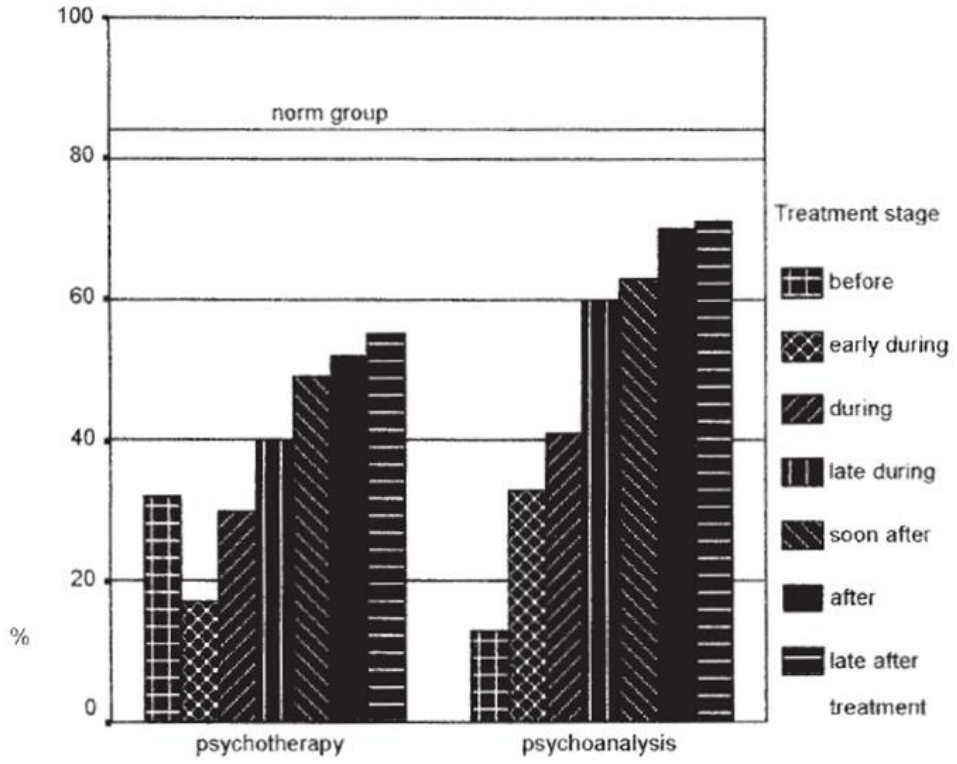

Figure 20. Percentages of patients in psychotherapy (n=331) and psychoanalysis (n=74) with clinically significant outcomes. Key on the right represents various stages during therapy and stages after therapy (Sandell et al, 2000; Sandell, Blomberg, Lazar, 2001).

As graphically represented (Figure 20), the large outcome differences between the two groups are striking. This finding is consistent with the notions of internalisation (from an analytic perspective) or the neuroplastic changes in response to intensive learning.

The researchers have taken a number of other factors into consideration such as design structure, measurement scales and sample groups that could have accounted for the notable outcome differences between to the two groups but conclude that this surprising result seems to relate to session frequency rather than therapy duration. However, Blomberg, Lazar & Sandell (2001) do agree that the effect of the session frequency is complex in nature. They go on to say that "we can only infer that something is occurring during the more frequent sessions that prompts a post treatment process that has to be qualitatively different, because there are no quantitative differences between the treatment regimens after termination" (p. 377).

While the study above is a large scale analysis of outcomes extrapolated from completed therapy data, Gerber, Fonagy, Higgitt & Bateman (2004) designed and ran a clinical trial to compare outcomes between high (five times weekly) and low frequency (once weekly) treatments at the Anna Freud Centre. The 25 participants in each group were matched in terms of age, socio-economic status and were treated by experienced psychoanalysts in either the five times weekly (n=14) or the once weekly group (n=11). Progress analysis, carried out by independent raters, was undertaken before therapy and at 18 month intervals by running a battery of tests to measure progress such as the "Spielberger State and Trait Anxiety Inventory, the Social Adjustment Scale", the "Adult Attachment Interview, the SADS-L and the SCID II" (p. 96). Improvement was measured by significant increases on at least three of the scales.

Gerber et al. note that the results of this clinical trial "indicate that analytic treatment is superior in achieving clinically significant symptomatic changes" (2004, p. 96). Figure 21 shows that significant improvement is seen in the intensive therapy group in sharp contrast with the non-intensive therapy group.

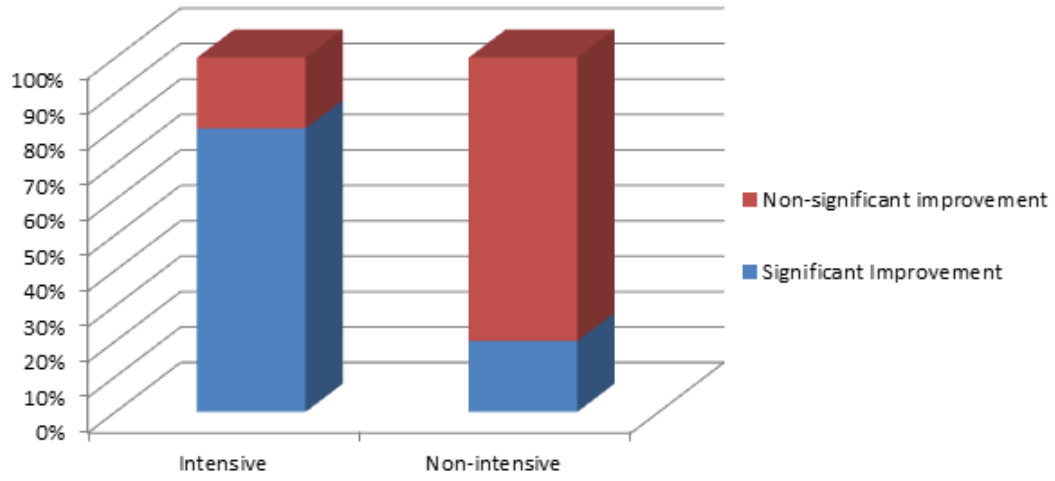

Figure 21. Significant and non-significant improvement in patients completing intensive and non-intensive treatment (Adapted from Gerber, Fonagy, Higgitt & Bateman, 2004).

Although this study produced notable results, the sample group was small and little detail is provided on how many therapists carried out the treatment and whether the psychodynamic group were being treated by a different group of therapists.

Summary

In summary of the above research, although there were few studies published around this topic, the studies revealed that psychotherapy at a higher frequency did, indeed, lead to better long term outcomes (Frosch, Fonagy, & Target, 2002; Leuzinger-Bohleber, Stuhrast, Rüger & Beutel, 2003; Sandell, 2001). Some authors noted that therapeutic outcome is a process rather than a fixed point at the termination of the therapy (Sandell, Blomberg & Lazar, 2001) and outcomes were assessed at various points post therapy termination. It was found that patients who underwent intensive

therapy had a better 'internalised therapist' and this led to sustained and also increased improvement beyond the termination point of the therapy.

In accordance with the above, the dose-response literature reports similar findings that are consistent with the notion that more therapy sessions produce better outcome. While the first few dosage studies review an accumulative effect of psychotherapy (total number of sessions) rather than the impact of additional sessions per week, the last study examines the outcome as a result of having more therapy sessions per week compared to fewer sessions. Consistent with the 'session frequency' studies' findings, this study reports that additional therapy sessions per week produce more significant improvements.

Overall, it is evident that psychotherapy conducted at a higher frequency produces better clinical outcomes and that these favourable outcomes are long lasting in contrast to less frequent sessions. If we apply a neuroscientific lens to interpret these outcomes, it appears that, these findings are consistent with Hebb's cellular notion: "synaptic efficiency arises from the cell's repeated and persistent stimulation of the postsynaptic cell" that this persistence or repetition that induces lasting cellular changes adds to its stability (1949, p. 70). Hebb's theory is the key concept underpinning the concept of neuroplasticity.

Chapter 5 Discussion

> Brain circuits and psychological experiences are not different things, but rather, different ways of describing the same thing (Le Doux, 2003, p. 278).

The findings of this dissertation are based on three studies, one overview and two systematic literature reviews. Although all contribute towards providing an answer for my research question, these will be discussed separately and the relationship between the studies will be elaborated on at the end. In addition, this chapter will also include the overall limitations of this study and suggestions for further research.

Summaries

Chapter 2 – Neuroplasticity

This chapter provides an overview of basic neural anatomy as well as reviews neural concepts such as neural plasticity, long term potentiation (LTP) & long term depression (LTD), brain matter, the mirror neuron system and neurogenesis. The research in this chapter not only reports the enormous plasticity of the brain in response to its environment, it also reports that repetitive and focussed practice or experience has more significant effect on neural changes.

Long term potentiation (LTP) is the concept that describes the relationship formed between neurons in response to repetitive activation (stimulated by iterative practice or experience). If the neuronal firing is repetitive, prolonged and long-lasting, the connectivity between the cells and their dendritic spines is strengthened, otherwise the activated pattern soon fades. Therefore practice is needed to activate LTP. The counterpart of LTP is long term depression (LTP), where the opposite occurs. When neuronal pathways are no longer used, the neurons within the network begin to lose their relationship each other and the connections begin to fade.

The neuroimaging studies included in the chapter report that repetitive practice (through the concept of LTP), increases gray matter within the brain to enhance processing efficiency. The observed neural changes in response to vigorous focussed learning are in accordance with medical research studying ground breaking findings in utilising the brain's enormous plasticity to enhance treatment for traumatic brain injury and stroke.

The studies reviewed in the chapter found that, not only does focussed learning bring about change in the brain, but the act of focussed observation also brings about plastic changes through a system called the mirror neuron system. For example, it was reported that musicians' brains were not only changed in response to extensive music practice but that the act of observing others practicing also brought about neural changes (Altenmüller et al., 2002). When others' actions are observed the same associated neural networks in the observer's brain is activated as the person performing the action. However, the findings state that, for the mirror neuron system to be activated during the observation of an action, it must be a recognised action with both a beginning and end and even possibly a purpose (Olds, 2006). This mirror neuron system is thought to be the basis of empathy and is considered to play a significant role within the therapeutic relationship (Arden, 2010; Cozolino, 2010; Gallese, Eagle, & Migone, 2007; Iacoboni, 2009; Siegel, 2012). This notion is consistent with the psychoanalytic research that links higher session frequency with an increased ability to "internalise the therapist" – it is as if these patients are developing / exercising their mirror neuron systems through the therapeutic experience (which causes activations of the patients' mirror neuron system) and are, therefore, able to have a broader emotional resonance in other relationships outside of the therapeutic relationship.

Another pertinent finding in this chapter is the concept of neurogenesis - while it was previously thought that the brain could not generate new brain cells, this has been

found to be incorrect in that the brain does produce new brain cells. Neurogenesis is an important part of neuroplasticity as it promotes neural change and enhances the plasticity of the brain. In addition to this, it was also found that significant stress can have profound effects on the brain, inhibiting neurogenesis and neuroplasticity. This finding extends to the environment too where a stressful environment has a negative impact on the brain, its neural networks, and plasticity. While conversely, it was found that an enriching environment promotes neurogenesis and neural plasticity – this notion has implications for the practice of psychotherapy; a more stimulating and enriched therapeutic relationship with a good therapeutic alliance that is experienced more frequently is likely to enhance the patient's ability to transform.

This important research about repetitive and focussed learning lead me to think about the role of more intensive psychotherapy consistent with [the intensity of] Freud's original practice of psychoanalysis. Was more sessions per week away of harnessing the brain's enormous plasticity? There was no literature linking these two concepts – neural plasticity and session frequency. While this learning research led to emerging parallels between neural changes in learning and in psychotherapy as a learning experience, was there any neuroimaging evidence that reported actual neural changes in response to psychotherapy? The findings from the following section outline that the brain is, indeed, altered by psychotherapy.

Chapter 3

One of the questions that arose in my research namely, "does psychotherapy actually change the brain and if so are there particular areas of the brain that are altered with psychotherapy?" has been answered by the data presented in this chapter. New computerised imaging technologies have enabled the possibility of studying brain changes in humans (by measuring alterations in metabolism and blood flow) in response

to psychotherapy and medication through these imaging technologies namely fMRI, PET, SPECT.; with the advent of this technology, an exciting new dimension for measuring therapeutic outcome (Roffman, Gerber & Glick, 2012) can now be included in research.

The majority of the studies in this chapter reveal that various forms of psychotherapy (CBT, DBT, Psychodynamic Psychotherapy) for depression, anxiety and some other disorders (PTSD, PD) reported surprisingly similar neural changes compared with medication treatment. In addition, it was noted that there is a correlation between treatment outcome / success and the observed neural changes (Doidge, 2010) – better outcomes produced more significant neural changes while other studies revealed that certain abnormalities in the brain were good predictors of outcome in either psychopharmacotherapy or psychotherapy treatment. These findings are extraordinary since although I think that it is relatively logical that one would expect alterations in neurochemistry from the ingestion of chemical compounds (psychopharmacotherapy), finding similar changes in response to a talking cure is remarkable.

Many types of psychotherapies aim to build a patient's ability to solve problems, enhance their capacity for emotional regulation and strengthen their core sense of self. According to the research, the areas of the brain that are associated with these functions, include the dorsolateral prefrontal cortex, ventral anterior cingulate cortex, dorsal anterior cingulate cortex, ventral and dorsal subregions of the medial prefrontal cortex, posterior cingulate cortex, precuneus, insular cortex, amygdala, and ventrolateral prefrontal cortex. A number of the studies have suggested that the neural changes in response to psychotherapy have a regulatory effect on the brain, perhaps restoring its natural homeostasis.

A large proportion of these neuroimaging studies focussed on CBT and although the study of psychodynamic therapy does not often fit well within the current constraints of some research methodologies that are commonplace in medicine and psychiatry (Roffman, Gerber & Glick, 2012), the recent neuroimaging studies that have examined brain changes in response to psychodynamic therapy have had statistically significant results, especially those associated with high frequency (4x per week) long term psychodynamic psychotherapy. It was also reported that while other forms of therapy, for example CBT and BT, were efficacious in treating single disorders such as phobias or OCD, long term psychodynamic therapy is more effective in treating "complex" cases. This finding of the efficacy of long-term high frequency psychotherapy is consistent with not only the psychoanalytic literature, but other psychotherapy research for example, Rabung &Leichsenring (2012) noted in the following:

> Evidence suggests that many patients suffering from complex mental disorders (e.g. personality disorders) do not sufficiently benefit from short-term psychotherapy. Long-term psychotherapy may be helpful for these groups of patients….If compared to other methods of psychotherapy, which were predominantly less intensive or shorter term, LTPP proved to be significantly superior with regard to overall outcome, target problems, and personality functioning (p. 43).

However, although the findings from the neuroimaging studies are significant, none of the studies had a control group where a placebo therapy was administered. It is assumed that it is the form of therapy that is practiced that is the curative factor rather than the relationship between two people where one is particularly empathic. It is now widely accepted that the relationship between therapist and client plays a pivotal role in terms of successful therapy and can even alter the neurobiological state of the patient. Adler (2002, as cited in Schore, 2009) notes that the therapeutic relationship can serve as "the antithesis of the fight-flight response" and goes on to say that "the experience of

feeling cared about in a relationship reduces the secretion of stress hormones and shifts the neuroendocrine system toward homeostasis" (p. 883). Therefore, had each study employed an empathic teacher, for example, to meet for chats with the control group at the same frequency as the therapy group, it may have been clearer whether it was the type of therapy practiced (or the therapy itself) that was indeed the curative factor.

Similarly, although CBT is thought to be an effective form of treatment for a number of disorders (as demonstrated in the neuroimaging studies), and is generally offered in a limited number of sessions, it is important to note that typically patients are given homework that is followed up at subsequent sessions. It is highly likely that this act of practicing homework stimulates the patient's experience with the therapist and therefore the therapist is held in mind during those practice sessions perhaps strengthening the new synaptic connections formed in the actual therapy session which is consistent with the neuroplasticity research (Bangert, Haeusler & Altenmüller, 2006; Münte, Altenmüller & Jäncke, 2002). Frosch (2011) notes that it is the internalisation of the therapeutic relationship that is associated with better clinical outcome which, in the session frequency literature, is consistent with high-frequency therapy.

The answer to my question of "does psychotherapy actually change neural structures?" lead me back to examining the relationship between intensive learning and intensive psychotherapy as an emotional learning experience (Le Doux, 2003).

Chapter 4

The questions that prompted this chapter's exploration were, does more intensive psychotherapy produce better outcome? Is high frequency therapy an example of harnessing the brain's plasticity? According to a number of well-known authors (see session frequency chapter for personal communications), these were important questions and a worthwhile field of study. The psychoanalytic/psychotherapy literature

was systematically reviewed for studies around the role of high frequency psychotherapy and psychotherapy dosage. Although there were few studies published around this topic, the studies revealed that psychotherapy at a higher frequency did, indeed, lead to better long term outcomes (Frosch, Fonagy, & Target, 2002; Leuzinger-Bohleber, Stuhrast, Rüger & Beutel, 2003; Sandell, 2001).

In accordance with the above, the dose-response literature reports similar findings that is consistent with the notion that more therapy sessions produce better outcome. While the first few dosage studies review an accumulative effect of psychotherapy (total number of sessions) rather than the impact of additional sessions per week, the last study examines the outcome as a result of having more therapy sessions per week compared to fewer sessions. Consistent with the 'session frequency' studies' findings, this study reports that additional therapy sessions per week produce more significant improvements.

In addition to the above, some authors noted that therapeutic outcome is a process rather than a fixed point at the termination of the therapy (Sandell, Blomberg & Lazar, 2001). This delineation contrasts with the neuroimaging studies that measure outcome at the termination point of therapy. The studies found that patients who experienced intensive therapy continued to improve post termination and were able to stay healthy for longer periods of time.

Although overall these findings suggest that high-frequency therapy produces better long term outcomes, this type of treatment is exorbitantly expensive and I imagine that the group of people associated with undergoing high frequency treatment have better financial resources and are perhaps a remarkably different population group from those examined in other studies. In addition to this, on the one hand, a large proportion of the studies were related to psychoanalysis rather than psychotherapy as

typically psychoanalysis is associated with numerous sessions per week therefore it may be the modality of treatment rather than the frequency that brings about statistically significant long term outcome. On the other hand, although not mentioned in these particular studies, it is well known that intensive in-patient psychotherapy programmes are more effective in treating personality disorders or addiction rather than non-intensive psychotherapy.

Conclusion

> Therapists often lament the fact that parents don't do a better job during their children's early development, when relationships have such a powerful impact on their brains. But if we approach the brain from the perspective of ongoing plasticity, what are we capable of in our consulting rooms? How plastic is the brain? Can plasticity be enhanced, and how much of an effect and the therapeutic relationship have on the brain? These questions are central to psychotherapy, because we rely on the brain's ability to change well after traditional sensitive periods have passes (Cozolino, 2010, p. 323).

Overall, the literature reviewed in this study provides convincing evidence that suggests that there is, indeed, a relationship between psychotherapy session frequency and the brain's remarkable plasticity. It may be that intensive psychotherapy harnesses the brain's natural plasticity towards change and is, therefore, more effective than less intensive psychotherapy.

Limitations of the study

This research has employed the methodology of two systematic literature reviews and an overview, and while systematic literature reviews are considered to be an important method of research in the EBP model, they are not independent of the quality of contributing studies for their results. Crowther & Cook (2007) note that "in areas with limited data, or when the quality of primary studies is poor, systematic reviews of these primary studies will be flawed" (p. 493). It is important to hold this

limitation in mind especially in relation to the systematic literature review of the psychotherapy/psychoanalytic research where a limited amount of studies were identified.

In the systematic review of this body of literature, while it appears that more therapy sessions produce better long term outcome, we cannot be certain that it is the frequency per se of face to face therapy sessions that enhances successful outcome as there are many other factors that may contribute to successful therapy. Although this study focussed neuroplasticity; the brain, the mind and body are extremely complex and there are other processes that occur simultaneously; for example the role that both short and long term memory plays in learning new experiences. Memory is a very important part of psychotherapy, and without it, clients would not be able to change. Solms (2003) notes that "the physiology of short-term memory is not very well understood, but neuroscientists agree that it differs radically from that of long-term memory" (p. 57).

In addition to this, it is also important to note that not all neuroplasticity has a positive impact on clinical status – my study is limited as it only focusses on positive neural plasticity. In the medical literature relating to strokes and neural trauma, there are reported negative consequences due to plasticity. For example, according to Cramer et al. (2011), "new onset epilepsy is a common complication of cerebral trauma, often arising months to years after the insult" (p. 1593). They go on to say that the neural changes in terms of the brain sprouting new connections alters neural signalling which can result in seizures. "Thus, recovery from trauma or disease may reflect both adaptive and maladaptive neuroplasticity, which can occur simultaneously" (p. 1593). Therefore, it is possible that perhaps neuroplasticity in response to psychotherapy treatment (bad therapy) may produce long lasting negative results.

While psychological symptoms can be thought of being the product of negative plasticity, from a neural point of view, psychological symptoms can often be the result of an imbalance in physiological homeostasis reported in the field of organic psychiatry. For example diseases of the endocrine system (such as diabetes and thyroid disorders) as well as various severe vitamin / mineral deficiencies (B12, D and low Iron count) can often present as depression or anxiety (Lishman & David, 2009). Therefore, in clinical practice, while holding concepts of neuroplasticity in mind, it may be useful to consider the patient's physiological homeostasis if they have not been referred via primary health care professionals.

Another limitation of this study is that this research did not take into account the mind and body as a complex dynamic ecosystem as it only focussed on the brain. A number of authors have written about the mind and body using systems theory suggesting that the body is a dynamic complex system and that psychotherapy session frequency plays a role in maintaining the system (Rose, 2010). According to Hyman:

> A system is an entity which maintains its existence through the mutual interaction of its parts…what we see as the symptoms of depression are reflections of a few common interconnected imbalances in the body that have nothing to do with the medical specialties as we know them. Depression is not a psychiatric illness, but a systemic disease. To treat it we need to address the whole system – the ecosystem of your body (2010, p. 59).

I suggest that this field of dynamic systems theory it would be an interesting and worthwhile field of enquiry for making sense how the body systems impact the mind and the brain in the context of psychotherapy.

In today's modern age especially with the advent of EBM and managed health care, the demands for outcome research can lead to a reductionist approach to practice. While the temptations are great to find the answers within the MRI machine, it is also useful to hold the art of psychotherapy in mind. Freud notes that; "I shall entirely

disregard the fact that the mental apparatus with which we are here concerned is also known to us in the form of an anatomical preparation, and I shall carefully avoid the temptation to determine psychical locality in any anatomical fashion. I shall remain on psychological ground" (1900, p. 541).

Suggestions for further research

In addition to further exploration around dynamic systems theory (as mentioned above), another important avenue of enquiry for further research would be the study of memory and its implications for the practice of psychotherapy as a learning experience. This would include the role that dreams play within the therapy relationship as, in the field of neuroscience, dreams are thought to play a role in memory consolidation.

Another import suggestion for further research is as follows. As outlined in the five-step EBM model for psychiatry research, this study carried out steps 1-3 (Formulate the question, the systematic literature review, and appraising the evidence). Steps four and five of this model concern applying the results and assessing the outcome. Therefore, I suggest that a clinical trial for testing the findings from this study is necessary in order to implement best practice.

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