Aims & Scope
The International Journal of Neuropsychotherapy (IJNPT) is an open access, online journal that considers manuscripts on all aspects of integrative, biopsychosocial issues related to psychotherapy. IJNPT aims to explore the neurological or other biological underpinnings of mental states and disorders to advance the therapeutic practice of psychotherapy.

Our mission is to provide researchers, educators and clinicians with the best research from around the world to raise awareness of the neuropsychotherapy perspective to mental health interventions.

Article Categories:
In agreement with the scope of the journal, papers submitted must be associated with the neurological or other biological underpinnings of mental states/disorders, or advances in any biological/psychological/social understanding of interrelatedness and impact on psychopathology or normative mental states and how these advances in knowledge impact therapeutic practice.

Empirical Studies: Original research with solid practical and theoretical advancements in neuropsychotherapy;
Case Studies: Case studies highlighting neuropsychotherapy theory and methodology in clinical application;
Articles: Theoretical articles using current research to advance theory, or a description of current theory (Theory). Methodological articles describing new approaches or changes to existing methods in neuropsychotherapy (Methodology), are welcome. Other articles include perspectives (brief accessible pieces covering a broad array of topics relevant to neuropsychotherapy); Applied NPT (brief accessible pieces describing the authors clinical application of neuropsychotherapy);
Review Articles (Literature Reviews): Meta-analytical papers and other such review research critically evaluating previously published research findings associated with, and important to, a biopsychosocial understanding of interrelatedness and impact on mental states/disorders, or advances in any biological/psychological/social understanding of psychopathology and therapeutic interventions.

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- A statement of financial or other relationships that might lead to a conflict of interest, if that information is not included in the manuscript itself.
- A statement that the manuscript has been read and approved by all the authors, and that each author believes that the manuscript represents honest work.
- The name, address, and telephone number of the corresponding author, who is responsible for communicating with the other authors about revisions and final approval of the proofs, if that information is not included in the manuscript itself.

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Table of Contents

Inaugural Editorial Statement .................................................. 1
  Pieter Rossouw, Ph.D.

Defining Bullying: The Role of Neurobiological Markers ................... 2
  Pieter Rossouw, Ph.D.

Epigenetics: The Dogma Defying Discovery That Genes Learn From Experience . 9
  Haley Peckham.

The Therapeutic Alliance: Exploring the Concept of ‘Safety’ from a
Neuropsychotherapeutic Perspective ........................................ 21
  Kobie Allison, & Pieter Rossouw, Ph.D.

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The International Journal of Neuropsychotherapy (IJNPT) is an open access online journal that considers manuscripts on all aspects of integrative, biopsychosocial issues related to psychotherapy. Papers of original and current research findings associated with the neurological or other biological underpinnings of mental states/disorders, or advances in any biological/psychological/social understanding of interrelatedness and impact on psychopathology or normative mental states and how these advances in knowledge impact therapeutic practice are welcomed.

IJNPT aims to explore the most recent neurological and other biological understandings of mental states and disorders in the hope that this understanding will advance the therapeutic practice of psychotherapy.

Our mission is to provide researchers, educators and clinicians with the best research from around the world to raise awareness of the neuropsychotherapy perspective to mental health interventions.

For further information about this journal and submission details please go to
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We are very excited to launch the first edition of the International Journal of Neuropsychotherapy (IJNPT). The aims and scope of this Journal is to be an open access, online journal, sharing quality research in the fields of Interpersonal Neurobiology, Neuroscience and Brain-based therapies.

Neuropsychotherapy is a relatively young science with strong roots in neurobiology and psychotherapy stretching back to the early twentieth century and the origins of modern neuroscience and psychotherapy. Neuropsychotherapy focuses on therapeutic processes developed specifically to address a range of mental health issues and thereby improve quality of life. Although a strong emphasis is placed on the neural correlates – the neuro-chemical, neuro-electrical and neuro-structural markers – of presentations, the focus is not reductionist but rather on the interconnectedness of neural systems and interpersonal neurobiology. New insights into the social brain, and the treatment of personal and interpersonal challenges, are now regularly being discovered in this innovative field. The International Journal of Neuropsychotherapy proudly embraces the dawn of this new paradigm in neuroscience and psychotherapy: the “Decade of the Brain” has evolved to the next phase – the focus on applied neuroscience.

The IJNPT has a strong Advisory Board where each member is a highly distinguished researcher in this field. We invite scholars to contribute to the Journal and submit papers for publication. All articles are peer reviewed and will be uniquely identified with a digital object identifier (DOI). Submissions should conform to the International Committee of Medical Journal Editors guidelines for biomedical journals available online at http://www.icmje.org/urm_main.html.

This first edition of IJNPT focuses on neuropsychotherapy and epigenetics as well as redefining bullying from a neuroscience perspective.

Pieter Rossouw

(Chief Editor)

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DEFINING BULLYING: THE ROLE OF NEUROBIOLOGICAL MARKERS.

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Summary

“Bullying” is a widely used term that is mostly linked to some form of harassment – be it emotional, verbal or physical. These definitions always refer to specific behaviours (the perpetrator perspective) and the emotional and physical harm they inflict (the victim perspective). Although some definitions of bullying refer to physical harm as one consequence, it is noteworthy that no definition specifically refers to neural changes, despite a large body of evidence that shows the detrimental effects on neurochemical production, changes in neural functioning, and neural damage.

This paper explores some core definitions of bullying and key neurobiological markers linked to bullying. These markers are:

- The neurodevelopmental indicators (genetic markers)
- Neurochemical markers
- Neuro-structural markers

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Introduction – bullying and neuroscience

Despite the common use of the term, many countries (such as the UK and some States in the USA) still do not have a legal definition for bullying. When bullying is conducted by a group, the term “mobbing” is used to describe the act/process. In the workplace, bullying is often referred to as “abuse” or “peer abuse” although some researchers (e.g., Fuller, 2006) call it “rankism”.

Sugden et al. (2010) define bullying as follows:

Bullying is the act of intentionally and repeatedly causing harm to someone who has difficulty defending him or herself, and is a relatively wide-spread school-age phenomenon. Being the victim of bullying is associated with a broad spectrum of emotional problems; however, not all children who are bullied go on to develop such problems.

However, this definition only refers to the perpetrator perspective and the emotional, but not the physical, consequence of bullying within the victim perspective.

Batsche and Knoff (1994) define bullying as a form of aggression in which one or more students physically and/or psychologically (and more recently, sexually) harass another student repeatedly over a period of time. This definition only focuses on the behaviour pattern from the perpetrator perspective, however. Similarly, the definition given by Olweus (1994) also focuses only on the behaviour/perpetrator perspective:

I define bullying or victimization in the following general way: A student is being bullied or victimized when he or she is exposed, repeatedly and over time, to negative actions on the part of one or more other students. It is a negative action when someone intentionally inflicts, or attempts to inflict, injury or discomfort upon another—basically what is implied in the definition of aggressive behavior. Negative actions can be carried out by physical contact, by words, or in other ways, such as making faces or obscene gestures, and intentional exclusion from a group. In order to use the term bullying, there should also be an imbalance in strength (an asymmetric power relationship): the student who is exposed to the negative actions has difficulty in defending him/herself and is somewhat helpless against the student or students who harass. Legal definitions invariably focus on the behaviour of the act of bullying. For example, the Queensland Government defines workplace harassment as a situation where a person is subjected to behaviour, other than sexual harassment, that:

- is repeated, unwelcome and unsolicited
- the person considers to be offensive, intimidating, humiliating or threatening
- a reasonable person would consider to be offensive, humiliating, intimidating or threatening.

Workplace harassment can be committed by:

- an employer
- a worker
- a co-worker
- a group of co-workers
- a client or customer, or
- a member of the public.

Workplace harassment covers a wide range of behaviours ranging from subtle intimidation to more obvious aggressive tactics, including:

- abusing a person loudly, usually when others are present
- repeated threats of dismissal or other severe punishment for no reason
- constant ridicule and being put down
- leaving offensive messages on email or the telephone
- sabotaging a person’s work, for example, by deliberately withholding or supplying incorrect information, hiding documents or equipment, not passing on messages and getting a person into trouble in other ways
- maliciously excluding and isolating a person from workplace activities
- persistent and unjustified criticisms, often about petty, irrelevant or insignificant matters
- humiliating a person through gestures, sarcasm, criticism and insults, often in front of customers, management or other workers
- spreading gossip or false, malicious rumors about a person with an intent to cause the person harm.

Management action may be considered as workplace harassment where it is used:

- primarily to offend, intimidate, humiliate or threaten workers
- to create an environment where workplace ha-
What is not workplace harassment?

- A single incident of harassing type behaviour
- Reasonable management action taken in a reasonable way
- Acts of unlawful discrimination, vilification or sexual harassment. (See Queensland Government, Department of Justice and Attorney-General, Code of Practice, 2004, for a full description of workplace harassment as used in Queensland.)

The Australian Human Rights Commission (2004) defines workplace bullying as:… the repeated less favourable treatment of a person by another or others in the workplace, which may be considered unreasonable and inappropriate workplace practice. It includes behaviour that intimidates, offends, degrades or humiliates a worker.

Workplace bullies tend to utilise the power that goes with their status, skills or position; both men and women can be the targets and/or the perpetrators. It can occur between a worker and a manager or supervisor, or between co-workers and the bullying behaviour can range from very obvious verbal abuse or physical assault to very subtle psychological abuse. Behaviours may include:

- physical or verbal abuse
- yelling, screaming or offensive language
- excluding or isolating employees
- psychological harassment
- intimidation
- assigning meaningless tasks unrelated to the job
- giving employees impossible jobs
- deliberately changed work rosters to inconvenience particular employees
- undermining work performance by deliberately withholding information vital for effective work performance.

Bullying is a complex phenomenon involving biological, psychological and social systems. For this reason, a clear understanding of bullying requires an interdisciplinary approach. Moreover, due to its complexity, any reductionist attempts to provide a comprehensive explanation of bullying will most likely not succeed. In this paper I focus on the neurobiological markers of bullying; at the same time, however, I am constantly mindful of the close interplay between neural development and the environment. The recent development of the field of epigenetics provides the scientific basis for the integrative model.

A phenomenological perspective on bullying underlines a question many researchers and therapists have asked, namely, “Why do some people who were exposed to bullying develop unhelpful emotional, behavioural and neural changes while others do not?”

The developing brain and bullying – genetics

Effective neural proliferation requires two key ingredients – a healthy genetic pool and an enriched environment. Both are vital to facilitate the development of a healthy brain that has the capacity to survive, problem solve, excel, establish interactions, and flourish. Traditionally, genetics and the environment were seen as unrelated, in line with the Darwinian theory of natural selection. In this view, natural selection is the result of the evolution of genetic make-up through the survival response – or what has been called “survival of the fittest”. Building on this analogy, bullying can be thought of as a form of natural selection where the weak will perish and the fittest survive. This process ensures a stronger genetic make-up that will enhance the superiority of the species. In 1809, Jean-Baptiste Lamarck suggested another theory whereby an organism acquires certain traits by adapting to the environment and the offspring subsequently inherit these traits. This theory is commonly seen as the birth of the study of epigenetics – the interdependent link between genetics and the environment. In his introduction to the study of epigenetics, Adrian Bird describes this process as: “The structural adaptation of chromosomal regions so as to register, signal or perpetuate altered activity states” (Bird, 2007, p. 397).

Studies on receptor and transporter genes, like serotonin and dopamine, show that there are different variables of the same gene that may increase wellness or increase risk. For example, the serotonin transporter gene (SERT) has two variables due to a polymorphism in the gene promoter of the gene (5-HTT). The specific region of the serotonin transporter has specific variants – a shorter (S) allele and a longer (L) allele. The (S) allele has less transcriptional efficiency and the (L) allele more effective transcriptional efficiency. The implications of this are that these genetic factors either enhance or reduce the risk of being
confronted by an adverse situation such as bullying. For example, fMRI studies indicate that the (S) allele is associated with enhanced amygdala activation due to environmental danger. The (S) carrier also picks up/learns fear quicker and retains fear for longer, and is therefore less likely to be extinct from the pre-frontal regions of the brain. On the other hand, people with the (L) variant have a stronger tendency to activate selective avoidance to threat. This response – which may also be attributed to more effective cortical connectivity – has been dubbed the “look at the bright side of life approach” (Sugden et al., 2010).

Avshalom Caspi and colleagues hypothesized that a polymorphism in the monoamine oxidase A (MAOA) gene could perhaps explain (at least in part) the reason why some people who are maltreated develop criminal behaviour patterns but others do not develop these patterns of behaviour. This hypothesis is based on analyses of a very large database compiled for the Dunedin Multidisciplinary Health and Developmental Study (Caspi et al., 2002). In another groundbreaking study, Kevin Beaver and colleagues linked two dopamine receptor genes, a dopamine transporter gene and the serotonin transporter gene, to genetic resilience factors to victimization (Beaver, Mancini, DeLisi, & Vaughn, 2011). The group analyzed data from the Add Health study – a longitudinal study of a representative sample of American youths enrolled in 7th grade (middle/junior high school) through to 12th grade (high school) during 1994–95. Of the more than 90,000 students who participated in the study, detailed in-home interviews were conducted with 20,745 youths and 17,700 primary carers, which formed the basis of in-depth analyses of the youth’s social relationships, family life, and involvement in risk-taking behaviours. All three genetic measures were found to be statistically significant predictors of resiliency (Beaver et al., 2011). A serious limitation of the study acknowledged by the authors is the failure to include an examination of the interaction between environments and genes in the prediction of resiliency, for example, the extent to which enriched environments shifted the genetic expression. In a timely article, Avshalom Caspi developed a powerful argument for a much closer interdisciplinary collaboration to study gene-environment interactions (Caspi et al., 2006).

The Darwinian perspective would view these differences as predispositions of the natural selection process. Traditionally, genetic predispositions were considered to be fixed, predetermined entities that are inherited and can predict the trajectory of wellness or risk (Ouellet-Morin et al., 2012). More recently, studies on genetic predisposition to risk point to the role of the environment in enhancing or reducing risk (genetic expressions). A significant proportion of these expressions are facilitated in the first 10 months after birth (Uher & McGuffin, 2010). A study by Shen and Battersby (2000) which indicated that genetic risk may not express when safe, enriched environments are provided during the early stages of development supports this view. In this study, a group of Macaque monkeys were bred with two strands of short (S) serotonin transporter alleles, however, they never expressed the risk because they were raised in a safe, enriched environment (Shen & Battersby, 2000). This finding indicates quite strongly that links between the genetic variables and the environment set the trajectory for neural development.

Human development and a higher code of survival (other than a mere physical baseline survival) are shaping our destiny. A threatened organism only survives by choosing one of two actions, that is, “avoid” (protective measures) or “approach” (expand measures). To illustrate this concept, consider that trees grow taller and other organisms in the environment with lesser capacity must find alternative solutions to adapt. Similarly, animals that cannot compete with more powerful competitors develop systems of protection to survive, for example, hunting in packs. Seen from this perspective, it can be said that the entire ecosystem operates in avoid or approach patterns.

From an epigenetic perspective, managing bullying is a moral choice. It is a choice we make to enhance certain neural developments and to inhibit other powerful neural mechanisms. In our society the moral, philosophical – even spiritual – choices we make are quite clear: we oppose a process of natural selection based on basic (primitive) neural patterns of survival. As humans, we prefer our species to be inclusive rather than exclusive, to maximize the neural development of all, rather than allow the aggressive survival response of some. Unfortunately, the moral choice is not always clear – the grey area presenting in our cultural environment (which we might see as survival of the fittest) has much to answer for in terms of favouritism at work or college, job (or research!) applications, promotions, professional and personal relationships, even human, animal and environmental rights. Opportunities for various forms of discrimination are endless.

Bullying and neurochemicals

The search to understand the predictors, risk factors and effects of bullying has inevitably led to a wide range of studies that link bullying with neurochemical changes. As a result, integrating biological markers in
research into bullying to maximize intervention outcomes has provided significant new insights. A major obstacle that has, up until now, restricted the study of the biological markers of social behaviours has been the difficulty of obtaining biological data, which is an intrusive process and often too far removed from real-life situations. More recently, however, saliva samples have been used to provide a non-invasive window to utilizing at least some biological markers. For example, saliva can be used to test hormones like testosterone, cortisol and dehydroepiandrosterone (DHEA) (Hazler, Carney, & Granger, 2006; Rossouw, 2012).

The role of testosterone as a biological marker in relation to social behavioural factors has been extensively studied. This hormone is directly linked to physical and sexual changes, such as increase in body mass as well as changes in appearance. The impact of “modifiers” is also important, where the environment seems to play a significant role in regulating the effect of testosterone. For example, Booth and colleagues found that testosterone-related behaviours were dependent on or “modified” (moderated) by the child-parent relationship, thus suggesting an indirect rather than direct relationship between testosterone and behaviour (Booth, Johnson, Granger, Crouler, & McHale, 2003). A major challenge in all testosterone studies is to establish a baseline, not least because there are significant differences between male and female production of this hormone.

For several reasons cortisol seems to be an attractive hormone to consider in studies of bullying. Unlike testosterone, cortisol is produced in the same quantities in both males and females. Furthermore, changes at puberty do not affect the production of this hormone. Finally, it should be noted that cortisol, as an end-product of the stress (fight/flight) response, is a stable chemical to study. In fact, the only major variation with cortisol is the change in production that occurs during the diurnal cycle. Cortisol levels shift rapidly and the efficacy of interventions can therefore be easily measured. When a person experiences a threatening situation, cortisol levels rise, the efficacy of the immune system slows down, and open (cortical) learning systems are compromised to maximize management of the threat. Stressful events also lead to increases in cortisol production. Cortisol is produced in the adrenal glands along with other stress chemicals like adrenalin. Its role is to push the body into hyper-alertness, hyper-activity, and increased physical responses such as increased heart rate to maximize the distribution of the stress chemical throughout the body. Cortisol also plays a role in the initial stress activation – it flows back into the initiator of the response, the hypothalamus, to regulate further stress responses, and “turn off” the stress signal. The implication is clear – the introduction of a stressful situation will result in an increase in cortisol. Overproduction of cortisol can lead to hypercortisolemia, which predominantly affects the pituitary and can lead to a variety of diseases like muscle weakening and wasting, high blood pressure, increased abdominal fat deposition, immune dysfunction, steroid-induced diabetes, and cardiovascular disease. Another serious consequence may be the eventual fatigue and failure of the adrenal glands.

Researchers have found significant differences between cortisol levels of students who experienced incidental bullying and those who experienced regular bullying. In line with their predictions, incidental bullying leads to increased cortisol levels (Booth, Granger & Shirtcliff 2008) whereas students who are bullied regularly have lower cortisol levels than their non-bullied peers (Vaillancourt et al., 2008). The authors of these studies hypothesise that chronic exposure to bullying leads to down regulation of cortisol production, due either to physical desensitization or “cortisol burnout”, or both (Carney, Hazler, Oh, Hibel, & Granger, 2013). The higher order presentation of this condition is anxiety and/or depression disorder. Richard Hazler and his colleagues have also suggested that biological markers like cortisol be included not only in studies that analyse intervention outcomes but in regular psychotherapy practice as well (Hazler, Carney & Granger, 2006).

The last of the saliva testable hormones is dehydroepiandrosterone (DHEA). This hormone acts as protector in the system of overexposure to cortisol and has a positive correlation with memory learning systems and facilitation of new behaviours (Wolf & Kirschbaum, 1999). The intercorrelation between cortisol and DHEA may provide helpful insights into bullying behaviour and its effects on victims of bullying. At The University of Queensland we are currently investigating this in terms of in-group and out-group experiences as well as in relation to bullying.

**Bullying and neural structures**

A number of neural structures have been found to be directly affected by bullying. These structures are the amygdala, hippocampus, corpus callosum, anterior or cingulate cortex and prefrontal cortex.

The role of the amygdala is (among others) to provide a first-line response to potentially harmful sensory triggers. Activation of down-regulation of unpleasant sensory stimuli and up-regulation of
shift in regional activation, therefore, the implication methodology used rather than . Despite the marginal that this difference could be the result of a shift in ti "tian et al 2010). The authors of this study speculated the orbito-frontal regions but not the dACC (Sebas Sebastian and colleagues found increased activity in be noted, however, that an fMRI study by Catherine (Eisenberger, Lieberman, & Williams, 2003). It should empathy is compromised when the dACC is affected regions such as the prefrontal regions. In addition, the corpus callosum provides a critical link between the deep brain structures and neural hemispheres. Martin Teicher and colleagues found a direct correlation between exposure to peer verbal abuse and abnormalities in the corpus callosum (Teicher, Samson, Sheu, Polcari, & McGreenery, 2010) while social rejection and social pain impaired the structural integrity of the anterior cingulate cortex—the dorsal anterior cingulate cortex (dACC) in particular. This means that bullying up-regulates the more primitive fear-based and survival systems and compromises activity in the frontal (especially right frontal) cortical systems due to the detrimental effect of bullying on the dACC. This also has significant implications for neural development of the higher order cortical regions such as the prefrontal regions. In addition, the ability to develop a moral code based on caring and empathy is compromised when the dACC is affected (Eisenberger, Lieberman, & Williams, 2003). It should be noted, however, that an fMRI study by Catherine Sebastian and colleagues found increased activity in the orbito-frontal regions but not the dACC (Sebast tian et al 2010). The authors of this study speculated that this difference could be the result of a shift in methodology used rather than . Despite the marginal shift in regional activation, therefore, the implication of both studies is the same – bullying and/or social exclusion changes the neural circuitry. In their study, noted previously, Viding and colleagues indicate that bullying behaviour has significant implications for the onset of anti-social behaviour patterns (Viding, Mc-Crory, Blakemore, & Frederickson, 2011) and others have noted an increased risk of major depressive disorder (Masten et al., 2011).

The prefrontal cortex, especially the right prefrontal cortex, plays a vital role in the development of the social brain. Lesions/damages to this part of the brain result in major changes in behaviour which directly affect social appropriateness and wellbeing. The story of Phineas Gage, a railroad worker who was severely injured by an iron rod that damaged his right frontal lobe, is frequently cited as a classic example of changes in behaviour as a result of damage to the prefrontal region of the brain. Although he survived the accident his personality changed dramatically (Adams 2009). A more recent example is patient “EVR” who, at age 35, underwent resection of a bilateral orbitofrontal meningoim involving excision of the orbital and mese cortices. After the operation his intellectual abilities were unchanged but his social conduct and de cision-making ability were significantly compromised (Saver & Damasio, 1991).

Summary

Bullying informs various aspects of the – it chang es neurochemical activation, inhibits neural prolif eration and causes neuro-structural changes. These changes set a new trajectory of neural functioning and provide the basis for changes in mood, cognition and behaviours. Recent developments in neurosci ence provide the platform for assessing bullying from a neural perspective. It also provides a platform for assessing the efficacy of interventions. In any definition of bullying, the neural impact on victims needs to be considered.

References


Batsche, G. M., & Knoff, H. M. (1994). Bullies and
their victims: Understanding a pervasive problem in the schools. School psychology review 23:165-165.


**PERSPECTIVE**

**EPIGENETICS:**

THE DOGMA-DEFYING DISCOVERY THAT GENES LEARN FROM EXPERIENCE.

Haley Peckham.

**Introduction**

Epigenetics challenges our acceptance of the dichotomy between nature and nurture. It is coming to be understood that nurture somehow writes its way into our genes; that experiences, or the effects of experiences on gene transcription, may continue throughout our own lives and into those of the next generation. For anyone engaged in the challenge of helping clients who have suffered traumatic, neglectful or abusive experiences, or for anyone offering clients a new experience through the psychotherapeutic relationship, an understanding of epigenetics is pertinent and illuminating. Here I introduce the concept of epigenetics, describe some epigenetic mechanisms, and review the findings of a number of recent studies that seek to understand why, what, and how our genes can learn from experience.

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The engaging debate of whether it is nature or nurture that has the most influence over who we are and what kind of lives we lead often illuminates the attitudes the debaters hold with regard to their own lives. In my early twenties, I tended to champion the influence of the environment, as although I felt affected by childhood adversity, I did not like to think of myself as passively, fatalistically accepting nature—my genetic inheritance—as my lot in life. Discoveries in biology have made this debate and my wrangling with it entirely passé with the enthralling field of epigenetics, which allows for degrees of gene expression or “shades of grey” that release us from the “black and white” dichotomy of genetic determinism. Epigenetics provides insights into how the environment dynamically impacts on our gene expression as humans, influencing, amongst other traits, our and our children’s health, ability to learn and remember, and responses to stress. The fabric of the lives led by our parents and grandparents, from their diet (Katada, Imhof, & Sassone-Corsi, 2012) to their education, the care they received, traumas they may have suffered, and perhaps many other experiences leave their legacy written alongside our DNA as “instructions for interpretation.” The purpose of this as yet inappreciably sophisticated and elegant code of epigenetic information, if it can be properly be called a “purpose,” is to record, use, and pass on information about the intricacies of the environment experienced in both our lives and those that have gone before us, so that we and our children can be as well prepared for survival in our particular environment as it possible to be. Life, over lives, continually perceives the environment, and the epigenetic instructions for interpreting the DNA are written, used, revised, and may be inherited, along with our genes.

Epigenetics is the contemporary study of how the environment influences gene expression both within and, through heritable changes in DNA, beyond the lifetime of an organism. The idea that organisms can inherit environmentally acquired characteristics is, however, the old idea of Lamarckian inheritance. In 1809, Jean-Baptiste Lamarck suggested that an organism would acquire traits through adapting to its environment, and that these traits would then be inherited by its offspring (Handel & Ramagopalan, 2010). Lamarck’s theory was overlooked in favor of Darwin’s natural selection theory of evolution, as the two explanations appeared at the time to be mutually exclusive, but the advent of epigenetics has made it possible for these theories to be reconciled. “Epigenetics” literally means “above the genes,” and is the means by which the environment “marks” the genes, dramatically or subtly, changing their level of expression either transiently or for our lifetime, or, through inheritability, throughout our children’s and grandchildren’s lifetimes. A formal definition of epigenetic events proposed by Adrian Bird is: “the structural adaption of chromosomal regions so as to register, signal or perpetuate altered activity states” (Bird, 2007, p. 398). This definition encompasses the broad remit of epigenetic marks from transient, where the epigenetic mark ascribed by the environmental adaption lasts only a few hours, to heritable, where the environmental effects last over a generation. The brain-derived neurotrophic factor (BDNF) gene, implicated in psychiatric disorders and learning and memory (Autry & Monteggia, 2012; Boulé et al., 2012; Lu, Christian, & Lu, 2008; Minichiello, 2009; Musumeci & Minichello, 2011), is subject to both short- and long-term epigenetic marking in rodents. For example, following the favorable social experience of being reared in a communal nest, mice challenged with one hour in a mildly stressful novel environment generate hippocampal BDNF faster than mice raised in a standard nest, as a result of an epigenetic mark on the BDNF gene (Branchi, Karpova, D’Andrea, Castren, & Alleva, 2011). However, rat pups subjected to a rat equivalent of childhood maltreatment are epigenetically marked by this experience, reducing the level of BDNF in their pre-frontal cortex throughout their adult life. The offspring of these rats also carry the same epigenetic mark on their BDNF gene even when they have been cross-fostered to non-maltreating mothers (Roth, Lubin, Funk, & Sweatt, 2009). Thus, epigenetics, the mechanisms by which our genes record or adapt to the environment, can shape gene expression over a few minutes, an hour, or a lifetime, and can even shape the gene expression pattern of the next generation. It is even possible for genes to “remember” an event and make a contingency plan for its recurrence, as in the case of the corticotropin-releasing hormone gene of rat pups. In response to maternal deprivation, the promoter region of this gene is epigenetically marked. Later, following a stressful experience in adulthood, the pre-recorded epigenetic mark leads to a hypersensitive stress response, observed as a more actively transcribed corticotropin-releasing hormone gene and increased levels of the stress hormone corticosterone (Chen et al., 2012).

There are three main types of epigenetic modification: DNA methylation and histone modification, outlined here together with examples of these mechanisms in action, and translational regulation by micro RNA (not pertinent to this review, but see (Haramati et al., 2011; Sato, Tsujiya, Meltzer, & Shimizu, 2011).
for useful introductions).

Types of epigenetic modification, Level I: DNA methylation

Methylation involves the addition of a methyl group to mammalian DNA, and can occur in response to environmental influence, making a stable, potentially heritable addition to the DNA that enhances or represses the transcription of a gene. Methylation is not a mutation, as the sequence of bases (adenine, guanine, cytosine, and thymine) remains the same. The methyl group is added to a cytosine nucleotide, usually followed by a guanine nucleotide (a CpG site), by enzymes known as DNA methyltransferases (DNMTs). The promoter regions or transcriptional start site of genes (the point at which RNA polymerase II begins transcription of the DNA into mRNA) are frequently rich in CpG sites, and methylation of these regions is associated with long-term silencing of genes. Methylation of CpG sites within the body of the gene is more ambiguous and context specific and can lead to either repression or activation (Jones, 2012). Methylation of DNA can also be bound by Methyl Binding Domain (MBD) proteins such as MeCP2 which recruit other protein complexes to re-model the local chromatin (DNA + histone packaging), leading either to repression or activation of specific genes. MeCP2 is an important point of integration between types of epigenetic modification, as MeCP2 binds methylated DNA but also can recruit chromatin re-modeling proteins which implement the other major type of epigenetic alteration, histone modification, described below (Cedar & Bergman, 2012). Methylation of DNA is reversible but instead of de-methylation occurring via the action of a single enzyme, it occurs through a multistep process. It is intriguing that almost half of the methylated DNA in the brain is 5-hydroxymethylcytosine, an intermediate formed during the multistep de-methylation of DNA (Szulwach et al., 2011), a process which is dependent on neuronal activity (Guo, Su, Zhong, Ming, & Song, 2011). The contemporary view of DNA methylation is that, in the brain especially, it is a highly dynamic process, responsive to neural activity (and therefore experience) and crucial for plasticity-related functions such as learning, memory and behavioral adaptation (Baker-Andresen, Ratnu, & Bredy, 2013).

Types of epigenetic modification, Level II: Histone modification

The DNA in the nucleus of each eukaryotic cell, including in the case of humans, contains all of the genetic material. So a human skin cell carries the same complete genetic code as a neuron or a parietal cell of the stomach. Each specialized cell need only be able to transcribe a small fraction of the total DNA it carries in order to perform its specific function. Since the rest of its DNA will never need to be accessed, it can be packed away as efficiently as possible. Histone proteins facilitate this efficient packaging of DNA, largely due to the electrostatic attraction between the negatively charged DNA and the positively charged histone proteins. DNA is coiled around a core octamer of histone proteins, like thread on a spool, forming a single nucleosome. Multiple nucleosomes together are known as chromatin, which has different conformations reflecting the accessibility of the genes for transcription. Euchromatin is open chromatin, conceiveable as separate beads on a string; here the genes are accessible, whereas in condensed chromatin or heterochromatin, the genes are inaccessible and un-transcribed, as they are so densely packed (Jenuwein & Allis, 2001).

Like most proteins, the histone proteins comprising the core around which the DNA winds itself can have chemical groups attached to them that may either subtly change their charge, and thus how tightly they are bound to the DNA, or change their affinity for other protein-binding partners. In this way, histone modifications alter the chromatin structure and hence the accessibility of genes, but can also affect the binding of other molecules including DNA methyltransferases—the enzymes that add methyl groups to DNA, not the histone proteins that the DNA coils around (Ooi et al., 2007). This interaction forms another point of integration between DNA-modifying and histone-modifying epigenetic mechanisms.
tones may be acetylated, methylated (including bi- or tri-methylated), phosphorylated or ubiquitinylated on specific residues, and each group or combination of groups may signal a precise outcome. For example, an epigenetic modification of a tri-methylated lysine4 residue on histone3 signals an actively transcribed gene, whereas a tri-methylation on lysine27 of histone3 signals a repressed gene state. If lysines 4 and 27 are both tri-methylated, the gene is thought to be “poised,” ready for activation (Bernstein et al., 2006). As there are four histones (two of each make up the octamer core), and at least four chemical groups that can attach to multiple residues, there are a large number of possible combinations of epigenetic marks that can be made on a histone octamer, giving rise to the concept of a “histone code” that can nuance gene expression (Jenuwein & Allis, 2001). There are enzymes that catalyze the addition and removal of each type of chemical group. Histone acetylases (HATs), for example, add acetyl groups to the histone, reducing the electrostatic charge difference and therefore the affinity between the histone and the DNA, thus loosening the coil. Accordingly, HATs tend to be associated with gene activation, whereas histone de-acetylases (HDACs) remove the acetyl group, increase the electrostatic attraction, tighten the coil, and are thus considered transcriptional repressors (Bannister & Kouzarides, 2011).

In contrast to the epigenetic modification of a methylation made to DNA, histone modifications are easily reversible and highly dynamic, although the enzymes that catalyze the addition and removal of various groups are themselves regulated. The histone code also has great flexibility in determining how long a gene’s activity may be enhanced or repressed, as epigenetic marks may record an experience on a gene without necessarily changing its level of transcription. They may transiently enhance or repress gene expression, or may recruit (or repel) DNA methylases that can administer de novo methylations on the DNA which result in the gene becoming stably repressed throughout the life of the organism and in the next generation (Ooi, et al., 2007). It is interesting to note that Valproic acid, a known teratogen used in the treatment of bipolar disorder, is a histone de-acetylase inhibitor but also leads to reduced levels of DNA methylation, demonstrating that a transient and easily reversible epigenetic histone acetylation is frequently followed by a more stable and less easily reversed DNA methylation, silencing the gene (Alonso-Aperte, Ubeda, Achon, Perez-Miguelsanz, & Varela-Moreiras, 1999; Gottlicher, 2004). Thus, histone modification and DNA methylation, whilst distinct epigenetic mechanisms, can act in synergy to produce permanent gene silencing.

The epigenetic impact of early maternal care

Many animal studies of epigenetics have looked at the impact of early maternal care on the hypothalamic-pituitary-adrenal (HPA) axis or, put more simply, the stress axis. This axis co-ordinates the response to stress from the brain, which perceives the stress, to the adrenal gland, which releases glucocorticoids such as cortisol (corticosterone in rodents) in response to the stressor. The hypothalamus receives neural input—our perception of the stress—and releases corticotropin-releasing hormone (CRH) that acts on the anterior pituitary gland to release adrenocorticotropic hormone (ACTH). This in turn acts on the cortex of the adrenal gland to release cortisol. The multiple steps in this process allow multiple opportunities for the glucocorticoids to negatively feed back at several levels of the HPA axis, including the hippocampus and the hypothalamus, limiting CRH release, and at the pituitary, limiting ACTH release (Anacker, Zunszain, Carvalho, & Pariante, 2011; Pariante & Lightman, 2008). Glucocorticoids feed back via glucocorticoid receptors. More receptors means a swifter, more efficient negative feedback
mechanism resulting in lower levels of circulating CRH, ACTH and cortisol, and consequently an HPA axis that readily returns to homeostasis. However, in response to chronically high levels of circulating glucocorticoids, glucocorticoid receptors are down-regulated; as a result, the negative feedback mechanism is less efficient, and the HPA axis is slower to return to homeostasis or may become dysregulated (Anacker, et al., 2011; Sapolsky, Meaney, & McEwen, 1985). The HPA axis is an adaptive system subject to early-life epigenetic programming both prenatally and postnatally through variations in maternal care, separation and abuse.

Early pre-natal stress in mice has been epigenetically linked to enduring changes in HPA axis reactivity and a depressive phenotype in male offspring. Male adult mice whose mothers had been mildly stressed early in utero had higher levels of CRH and fewer glucocorticoid receptors in their hippocampus, the former increasing the activation of the HPA axis and the latter reducing the ability to regulate the HPA axis. These mice exhibited behaviors associated with depression and, following exposure to restraint stress, had increased levels of corticosterone compared to mice whose mothers had not been subjected to early pre-natal stress. When the promoter regions of relevant genes were examined, it was discovered that the promoter for corticotropin-releasing hormone was hypo-methylated, increasing the expression of CRH, the hormonal activator of the HPA axis. The glucocorticoid receptor promoter was also hyper-methylated, reducing its level of expression and thereby the mouse’s ability to negatively regulate its HPA axis after activation by CRF. This would at least contribute to, if not cause, the observed depressed behavior (Mueller & Bale, 2008).

Early post-natal stress has also been linked to enduring epigenetic changes that alter the reactivity of the HPA axis. Rat pups that receive enhanced licking and grooming by their mothers in the first ten days of life acquire a permanent increase in their number of glucocorticoid receptors, meaning that their HPA axis is more readily negatively regulated. Thus, when these pups become adults and are exposed to an acute stressor, they release corticosterone, which negatively feeds back through a greater number of glucocorticoid receptors, quickly reducing the levels of CRH, circulating ACTH, and corticosterone (Liu et al., 1997). If this effect was correlated with measurable changes to the epigenome, i.e., DNA methylation or histone code changes at the site of a relevant gene, it would support the hypothesis that maternal care leads to epigenetic changes that moderate the activity of the stress axis. In support of this hypothesis, a landmark study by Weaver’s group (Weaver, Diorio, Seckl, Szyf, & Meaney, 2004) compared rat pups that had either high or low levels of licking and grooming from mothers with whom they were cross-fostered, and found epigenetic differences in the promoter region of the glucocorticoid receptor gene. Pups that had received high levels of licking and grooming had hypo-methylated DNA and hyper-acetylated histone3 at the promoter region of the glucocorticoid receptor gene where a transcription factor binds, leading to enhanced transcriptional activity of the glucocorticoid receptor gene and therefore to more glucocorticoid

![Figure 3. Combinations of histone marks corresponding to active, permissive, repressed or inactive (silenced) genes. From “Epigenetic Regulation in Psychiatric Disorders,” by N. Tsankova, W. Renthal, A. Kumar, and E. J. Nestler, 2007, Nature Reviews Neuroscience, 8, p. 356. Copyright 2007 by Nature Publishing Group. Reproduced with permission.](image-url)
receptors. As adults, pups that had received low levels of licking and grooming had fewer glucocorticoid receptors and correspondingly higher levels of circulating corticosterone following restraint stress. Taking the study a step further towards identifying maternal care as a cause of epigenetic changes that modify the reactivity of the HPA axis, a histone de-acetylase (HDAC) inhibitor was administered to the rats which not only enhanced acetylation of the glucocorticoid promoter in the low licking and grooming group, it also removed all of the other observed differences in this group: the glucocorticoid promoter became hypo-methylated, more glucocorticoid receptors were expressed, and the corticosterone response following restraint stress was normalized to the same level as the high licking and grooming group. Essentially, the epigenetic differences brought about by lower levels of maternal care were reversed by the HDAC inhibitor (Weaver et al., 2004). In a follow-up study by the same group (Weaver et al., 2005), rats were infused with a methyl group donator. Even if the rats had received high levels of licking and grooming by their mothers when they were pups, leading to hypo-methylation of the glucocorticoid promoters, if they received the methylating drug as adults, all of the beneficial effects of this extra licking and grooming were reversed; the glucocorticoid promoter became hyper-methylated and fewer glucocorticoid receptors were expressed, leading to higher levels of corticosterone following a stressful experience and higher scores in a test of behavioral responses to stress (Weaver et al., 2005). From their combined studies, the authors primarily concluded that maternal behavior programs the stress response through epigenetic modification of the glucocorticoid promoter, and secondarily concluded that although maternal care makes stable changes to the epigenome, these are pharmacologically modifiable even in adults (Weaver, et al., 2005). Since then, in the case of studies showing that differences in estrogen receptor levels correlated with the level of maternal care received as a pup and the level of maternal care given in turn to offspring (Champagne, Weaver, Diorio, Sharma, & Meaney, 2003), the relationship has also been found to be mediated through epigenetic changes to the estrogen receptor promoter. Thus, receiving a high level of maternal care leads to reduced methylation of the CpG region within the promoter of the estrogen receptor, correspondingly increased levels of expressed estrogen receptors, and the capacity to give a high level of maternal care to the following generation of pups (Champagne et al., 2006).

Separation from mother in infancy has long been known to have emotionally and psychologically detrimental sequela, and the work of two brilliant and influential researchers, Harry Harlow and John Bowlby, is eloquently discussed in van der Horst and van der Veer’s review (van der Horst & van der Veer, 2008). In the field of epigenetics, the effects of maternal separation on the reactivity of the HPA axis are beginning to be discovered. In the HPA axis, stressful stimuli perceived at the level of the hypothalamus lead to secretion of CRH-stimulating ACTH. Arginine vasopresin (AVP) is also secreted by the hypothalamus, and potentiates the effect of CRH at the anterior pituitary, stimulating more ACTH release and increased HPA activity. Mice that were separated from their mothers for three hours a day for the first ten days of their lives had higher basal levels of corticosterone as well as higher levels following a stressful experience, and also scored higher on behavioral measures of stress and lower on memory tasks. Higher levels of expressed AVP correlated with hypo-methylated DNA in the regulatory region of the AVP gene (Murgatroyd et al., 2009). The methyl-binding protein MeCP2, which binds methylated DNA, ordinarily represses AVP transcription. But in mice that have been separated from their mothers, MeCP2 cannot bind as readily to the AVP promoter, as it is hypo-methylated even when the mouse reaches adulthood, leading to reduced repression by MeCP2 and consequent higher levels of AVP transcription. This results in a persistent hormonal activation of the HPA axis throughout the life of the mouse (Murgatroyd, et al., 2009).

As well as enduringly activating the HPA axis, early life stress induced by maternal separation has been shown to enhance performance in stress-related memory tasks in young rats (Suri et al., 2012). The rats’ improved performance correlated with increased neurogenesis, reduced repressive histone methylation of a BDNF gene promoter, and corresponding-
ly higher levels of BDNF in the hippocampus, compared to controls. Interestingly, once the maternally separated rats reached middle age, all these beneficial effects were lost, although this could be ameliorated by long-term antidepressant treatment. The authors of this study suggested that maternal separation stress induces biologically adaptive responses including epigenetic changes that increase the rat pups’ chances of having to survive alone, without the mother’s help and protection, but that these adaptive changes exact a heavy toll when the rat reaches middle age (Suri et al., 2012). From an evolutionary point of view, as long as the adaptive response to maternal separation allows the rat to survive on its own long enough to be able to reproduce, the exacted toll is worthwhile.

Paradigms that mimic abusive behavior in humans have also been used to examine the epigenomic effects of maternal abuse in rodents, demonstrating that abuse leads to significant hypo-methylation of the BDNF promoter in the pre-frontal cortex. Notably, rats that had suffered maltreatment in infancy also maltreated their own (or cross-fostered) pups, and the effect of their own maltreatment could be seen in their biological offspring as a hypo-methylated BDNF promoter region even when the pups were fostered to a caring mother (Roth et al., 2009). Maltreatment, or abuse, appears to be such a profound environmental influence that its effects linger in the generation following that which experienced the maltreatment firsthand. A similar observation of the trans-generational transmittance of a profound experience has been made by Rachel Yehuda, a researcher into post-traumatic stress disorder (PTSD) who found a higher than normal prevalence of PTSD in the children of mothers who had PTSD as a result of the Holocaust, suggesting a mechanism other than traditional genetic contribution in play, with epigenetics being the obvious candidate (Yehuda, Bell, Bierer, & Schmeidler, 2008). Although specific epigenetic modifications have not yet been linked to experiences that lead to the development of PTSD in humans, a recent study has identified patterns of genes that are differentially methylated in human sufferers of PTSD (Uddin et al., 2010). Additionally, in the rat model of PTSD, where the animals are exposed on two occasions to a cat, as well as having a new rat cage mate daily for 31 days, dramatic epigenetic changes have been observed in the promoter region of the BDNF gene in the hippocampus (Roth, Zoladz, Sweatt, & Diamond, 2011). Taken together, these results suggest that the development of human PTSD may occur through traumatic events causing epigenetic changes to specific genes, which, as well as leading to PTSD in the trauma victim, could confer an increased risk of the same in the victim’s children, as the epigenetic signatures on the genes caused by the trauma could be inherited (Yehuda & Bierer, 2009).

Although speculative, it seems likely that the inheritance of genes that have been epigenetically marked by trauma could be biologically adaptive and enhance the chance of survival if the environment remains life-threatening for the next generation. Hyper-vigilance and extreme alertness following trauma, whilst profoundly exhausting and distressing, may be life-saving in a dangerous environment.

**Human studies looking at the epigenetic impact of the environment**

Gathering data for human studies tends to involve the use of postmortem tissue and detailed retrospective analyses of significant life events or trauma. A recent study using these methodologies compared the differences in DNA methylation across the whole genome of 25 men with a history of severe child abuse compared to 16 controls, and found that fewer genes are actively transcribed in men who suffered abusive childhoods. The methylation profiles of the men showed 248 genes were hyper-methylated and 114 genes were hypo-methylated in the group with a history of abuse compared to the control group (Labonte et al., 2012). Of these, the top five most hyper-methylated genes were neuronal, and many of the genes that were differently methylated in the group who had experienced childhood abuse were related to plasticity, i.e., genes that are known to have a role in learning or adaptive mechanisms. A similar study using blood samples found that children raised in institutions had more methylated, and thus fewer expressed, genes than children raised by their biological parents (Naumova et al., 2012). It is tempting to speculate that perhaps lower levels of care restrict the variety of genes that can be expressed, whereas higher levels of care are the epigenetic gateway to our available genome. We speak of wanting to give our children “every opportunity”, but the reality of what epigenetic opportunities are available to our children could largely depend on the care we give them very early in life. Access to the widest potential of their genome could be profoundly influenced by their experience of our care, and if the genes that are accessed by enhanced care perform plasticity-related functions, the effect of that care is compounded for good or ill. Poor care may mean that fewer plasticity-related genes are expressed, thus restricting a child (and the adult’s) potential to learn, remember or adapt within their environment, manifesting in less flexibility and perhaps more stereotyped or rigid responses.
Studies that identify the epigenetic effects of levels of care or experiences on specific genes have been undertaken in humans. In a striking human parallel to Weaver's (2004) rodent study showing that low levels of maternal care epigenetically modified the glucocorticoid receptor promoter by hyper-methylation, reducing the transcription of the glucocorticoid receptor gene, McGowan et al. (2009) found that suicide victims who had a history of childhood abuse had hyper-methylated glucocorticoid promoters and fewer HPA axis-regulating hippocampal glucocorticoid receptors than controls. Both prenatal stress and even the birth experience have also been linked to epigenetic changes. The depressive mood of mothers in the third trimester of pregnancy has been linked to hyper-methylated glucocorticoid receptor promoters and higher cortisol responses in three-month-old babies (Oberlander et al., 2008), while infants born by Caesarean section have significantly higher levels of DNA methylation in their leucocytes compared to vaginal births at the time of delivery, although this normalizes after 3–5 days (Schlinzig, Johansson, Gunnar, Ekstrom, & Norman, 2009).

**Pharmacotherapeutics, enriching environments, and reversible epigenetic change**

Pharmacological treatments can reverse epigenetic marks caused by environmental experiences on both the BDNF gene (Roth, et al., 2009; Suri, et al., 2012) and the glucocorticoid receptor gene (Weaver, et al., 2005; Weaver, Meaney, & Szyf, 2006). Antidepressant treatment has frequently been shown to restore levels of BDNF in animal models of depression (Balaratnasingam & Janca, 2012), and in the social defeat, mouse model of depression, imipramine has been demonstrated to act through epigenetic mechanisms, reversing the down-regulating effect that social defeat has on BDNF transcription levels, although it does so by a compensatory HDAC-inhibiting mechanism rather than direct reversal of repressive histone methylations (N. M. Tsankova et al., 2006). The HDAC inhibitor, valproic acid, a treatment in certain psychiatric disorders, also epigenetically enhances BDNF transcription, facilitating the forgetting (or extinction) of fear-conditioned learning (Bredy et al., 2007; Whittle et al., 2013). Other histone-modifying agents may become useful psychoactive medications. It has recently been demonstrated that the acetylating agent L-acetyl-carnitine, already available as a dietary supplement, enhances transcription of the type II metabotropic glutamate receptor, which has a swift and enduring anti-depressant effect in rodents (Nasca et al., 2013). As epigenetic mechanisms mediate the effects of environment, the involvement of epigenetic mechanisms in psychiatric disorders that have an environmental component is axiomatic. Whilst pharmacotherapeutics holds promise for the treatment of psychiatric disorders (Grayson, Kundakovic, & Sharma, 2010; N. Tsankova, Renthal, Kumar, & Nestler, 2007), for the many people who fall below the threshold of a psychiatric diagnosis or who prefer non-medicating treatments, the very nature of the epigenetic mechanism suggests an alternative to drug treatment in the form of new, desirable environmental experiences to overwrite previous negative or undesirable experiences written on the epigenome. Environmental enrichment is proof of the principle that new environmental experiences can reverse or ameliorate the epigenetic effects of a previously impoverished or stressful environment.

Enriching environments provide opportunities for enhanced sensory, motor, cognitive, and social stimulation, and have a multitude of beneficial effects, from enhancing neural plasticity and learning and memory, to conferring resilience to depression and ameliorating the effects of many brain disorders including Alzheimer’s and Huntington’s diseases and stroke (Bekinschtein, Oomen, Saksida, & Bussey, 2011; D’Andrea, Gracci, Alleva, & Branchi, 2010; Nithianantharajah & Hannan, 2006). The effects of an enriched environment in rodents are profound, and can even mitigate the effects of prenatal stress or maternal separation on the HPA axis (Francis, Diorio, Plotsky, & Meaney, 2002; Morley-Fletcher, Rea, Maccari, & Laviole, 2003). Analogously to the effects of trauma, the effects of enrichment can be seen in the next generation, improving learning and memory (Arai, Li, Hartley, & Feig, 2009) and, following the socially enriching experience of being reared in a communal nest, enhancing levels of maternal care in the next generation, reducing anxiety behavior, and increasing litter sizes (Curley, Davidson, Bateson, & Champagne, 2009). It is likely that epigenetic mechanisms mediate the benefits of enrichment in terms of both the generation experiencing the enrichment and the trans-generational effects of enrichment that are observed. Recent work shows that rats whose parents had enriching experiences have less methylated DNA than rats whose parents experienced standard housing (Mychasiuk et al., 2012), suggesting that enrichment (such as high levels of care) increases the number of genes that will be actively transcribed. This perhaps reflects a need for greater biological complexity in order to be able to thrive in a more complex (enriched) environment. One gene that is extremely responsive to the environment is BDNF, which is epigenetically modified by the
experience of abuse (see above) as well as by the experience of an enriched environment. A recent study demonstrated increased levels of permissive histone methylations, enhancing transcription of the gene and raising levels of hippocampal BDNF in mice that experienced a month in an enriched environment (Kuzumaki et al., 2011). The role of BDNF in learning and memory behaviors, combined with its epigenetically regulated transcription, suggests this gene is a critical transducer of the experienced environment. Environmental enrichment is a powerful tool to effect epigenomic changes, which subsequently affect the levels of BDNF and modulate HPA axis activity, which, in turn, builds resilience to, or delays the onset of, various psychiatric or neurodegenerative disorders.

The relevance of epigenetics for psychotherapy

When I learned that real-life subjective experiences could regulate gene transcription, it changed the way I understood myself. I was not just an immutable collection of transcribed genes. My genes had my experiences of early care, my traumas and dramas and education written onto them in the tiniest molecular inscription of the histone code and DNA methylations. Furthermore, even as I was born, the most salient facts of my parents’ and even their parents’ lives—the kinds of care they had received, their education, their sense of safety or fear—was etched into my genes too, to help me adapt to what was biologically anticipated to be a similar environment. I did not know about epigenetics when I underwent psychotherapy, but if I had, it may have inspired my curiosity about my parents’ lives and informed my developing narrative that who they were, who I was, was a more intricate and elegantly entwined interplay between our genes and our environments than I could ever have imagined. Neither they nor I was responsible or to blame; instead, we were, who I was, a more intricate and elegantly entwined interplay between our genes and our environments than I could ever have imagined. Neither they nor I was responsible or to blame; instead, we

In writing this article I wanted to share the concept of epigenetics and to review the most relevant findings in contemporary epigenetics research with psychotherapists or anyone who seeks to understand and alleviate emotional and psychological distress. Epigenetics is an astounding and revolutionary discovery that brings compassionate understanding and great hope for the future to anyone who suffers distress, as well as those who work so intimately with distressed clients. An appreciation of epigenetics inspires compassion for those of us who come into the world vigilant and defensive, our epigenetic legacy anticipating a harsh world, a dangerous place to live; yet it also inspires hope, for even the most epigenetically determined aggressive, defensive stance is, by its very nature, responsive to the novelty of benign and benevolent environments. Fundamentally, epigenetics translates experience in the world into a gene expression profile that shapes who we are. If we are to develop or change ourselves, we must actively seek the experiences that will help us develop along the trajectory we desire. Psychotherapy can be seen as a form of emotional, environmental enrichment. It is perfectly placed to offer an enriched experience of a caring relationship, albeit an asymmetrical one, where one can received empathic, attuned attention that may be wholly novel and life changing. By offering a new, benevolent experience of relationship, psychotherapy can be reasonably assumed to change gene expression, calming a hyper-reactive stress axis and ameliorating the effects of an epigenetically scarred BDNF promoter, and in so doing, changing our responses to stress and perhaps our capacity to learn and flexibly respond to emotionally challenging situations. For the client in psychotherapy, as in many situations in life, it really is the experience that counts.

References


Jones, P. A. (2012). Functions of DNA methylation:
islands, start sites, gene bodies and beyond. Nat Rev Genet, 13(7), 484-492. doi: 10.1038/nrg3230

hav Brain Res, 228(2), 294-298. doi: 10.1016/j.bbr.2011.11.036


Weaver, I. C., Diorio, J., Seckl, J. R., Szyf, M., & Meaney, M. J. (2004). Early environmental regu-


THE THERAPEUTIC ALLIANCE: EXPLORING THE CONCEPT OF “SAFETY” FROM A NEUROPSYCHOTHERAPEUTIC PERSPECTIVE

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The role of the therapeutic relationship in the counseling process has been extensively demonstrated in the literature; however, the neurobiology of this relationship and the critical role of safety in enhancing therapeutic outcomes, and to ensure compliance and prevent relapse, are less well understood. The need for a safe space has deeply rooted neurobiological markers that have been well described by Seymour Epstein's cognitive-experiential self-theory and Klaus Grawe's neuropsychotherapeutic model. Epstein showed how attachment and control are two of the basic human needs that must be fulfilled to facilitate change—indeed, these mental conditions must be obtained in order for the human species to flourish—and Grawe subsequently demonstrated how these needs play a vital role in the therapeutic relationship.

Recent research by Allan Schore, Richard Davidson and Eric Kandel indicates that the right hemisphere of the brain is generally responsible for assessing safety or danger from others and in organizing a sense of the emotional self. Importantly, it is this appraisal of events that may lead to the development of motivational avoidance or approach schemas during the course of one's life in order to satisfy basic needs.

This paper explores the fundamental neurobiological markers that need to be considered in the therapy process as without effective regulation of these primitive neurobiological markers, the process may be jeopardized. Crucially, the therapeutic relationship captures these key indicators. Clients who seek counseling not only have difficulties with the presenting problem itself but also need a safe space to effectively address the issues. For people in distress their experience of safety is an area of critical importance yet, to date, little research has investigated this factor. The focus of this paper is the need for attachment and control, which are discussed in relation to their dual function in facilitating safety within the therapeutic alliance.
Current research in psychotherapy has shown unequivocally that what clinicians do in psychotherapy is effective on a neurobiological level (Furmark et al., 2002; Goldapple et al., 2004; Kandel, Schwartz, Jessell, Siegelbaum, & Hudspeth, 2013). Contemporary neuroscience and psychotherapy have identified neural correlates not only with mental disorders but also with therapeutic changes (Fuchs, 2004). Furthermore, recent research has demonstrated that the formation of the brain is inseparably connected to a person’s environment and life history (Cacioppo, Bernstein, & Adolphs, 2002; Fuchs, 2004). The growing field of neuropsychotherapy integrates analyses of the biological, psychological and social elements of mental disorders into a coherent framework that will further stimulate effective psychotherapeutic theory and practice (Cacioppo et al., 2002). Neuropsychotherapy thus provides the necessary framework for therapists to direct their attention to their patients’ brains whilst providing them with a safe enriched environment.

Safety and its Neuropsychotherapeutic Implications

Research has progressed beyond viewing the human brain as hardwired and static to an understanding that brains have the capacity to change through a process called synaptic and neural plasticity (Davidson & Begley, 2012; Kandel et al., 2013; Sporns, 2011). In 1998, Eric Kandel outlined the beginnings of a new intellectual framework for psychiatry that linked psychiatric thinking and training to biology, arguing that the biological components of behavior might best be studied by analyzing the interaction between the biological and the social determinants of behaviour (Kandel, 1998). He suggested that psychotherapy might induce both alterations in gene expression and structural changes in the brain, whereby the neuronal machinery in the therapist’s brain has an indirect effect upon the neuronal machinery of the client’s brain. He posited that client care is the therapist’s most important responsibility and thus that therapists ought never let client care become secondary (Kandel, 2006). Indeed, he maintained that client welfare is the ultimate goal of biological science; consequently therapists must develop an understanding of the neuropsychological principles governing their own behavior—and their client’s behavior—or otherwise risk violating these basic principles and being ineffective with their clients.

Contemporary research has also progressed from seeing the brain as a chemical system to perceiving it as a network of neural connections (Cozolino, 2010; Davidson & Begley, 2012; Kandel, 2006; Kandel et al., 2013; LeDoux, 2005; Rossouw, 2010; Schore, 2012; Sporns, 2011). This recent shift includes the way in which safe environments through talking therapy can facilitate the establishment of new and more effective patterns of neural firing. The research currently maintains that on a molecular level neural connections form the essence of memory (Kandel et al., 2013). Indeed, memory is more than the connection of a single axon with a dendrite, rather it is a sequence of neurons in a network that forms the basis of neural functioning (Kandel et al., 2013). In other words, one neuron in isolation is not effective but when a network of neurons forms a memory sequence, thoughts, feelings, and perceptions may be generated (Kandel et al., 2013). Whilst there is a genetic element to these connections, the environment enables the unique expression of genetic predispositions that permit the creation of emotions and cognitions—one’s sense of self and the mind. Ultimately, this is a higher order function, as networks are constantly changing in association with the environment, and new pathways of firing are facilitated (Kandel et al., 2013). As Feinberg (2009) suggested, the self is defined by thoughts and memories that influence our emotions. Neural responses of protection and avoidance may form as a result of trauma, whereas positive experiences are more likely to induce responses of approach and growth (Wilkinson, 2004; Feinberg, 2009). Thus, the role of therapy is to engender new pathways of firing via the creation of a safe environment and a corrective emotional experience.

Studies of learning and memory suggest that synapses are modified by experience and that they form a crucial aspect of brain plasticity (Ekstrom, 2004).
While LeDoux (2005) posited that genes shape the broadest outline of mental and behavioral functions, he further argued that the essence of the individual is in fact determined by the patterns of synaptic connections in the brain.

Neuroplasticity extends the existing paradigm for understanding the capacity of the brain to change by enhancing our understanding of neural activation (Ekstrom, 2004). As noted above, the early neuroscientists adopted a deterministic approach, likening the brain to an electrochemical system (Ekstrom, 2004). This approach is often referred to as the “medical model” because it was primarily concerned with the individual achieving a neurochemical balance amongst the chemical agents involved in communication between neurons (LeDoux, 2005; Rossouw, 2013; Valenstein, 1998). Whilst this approach resulted in the development of a number of drug treatments for various mental disorders, it has proved inadequate in terms of understanding the pathogenesis of illnesses such as depression, schizophrenia and anxiety (Rossouw, 2013; Valenstein, 1998). The study of brain circuits has proved to be a more constructive approach (LeDoux, 2005).

Recent studies have shown that talking therapies affect neural activation through chemical balance, neural firing, neural structure and neural networks (Furmark et al., 2002; Grawe, 2007; LeDoux, 2007; Sporns, 2011). However, in contrast to the earlier chemical theory, in network theory the provision of safe environments is now seen as a vital additional factor to understanding the brain (Rossouw, 2013). The implications are both profound and clear—that a safe environment for talking therapy, which would include mechanisms to manage stress and affect regulation, can address unhelpful patterns of neural activation and enable more functional outcomes (Rossouw, 2013). Research has shown that a safe enriched environment actually facilitates the development of new neural patterns, which, in turn, leads to enhanced attachment and control, and stress reduction (Rossouw, 2013). Psychotherapeutic approaches that provide safe environments will thus enhance the positive social interaction that is an essential element of healthy neural proliferation (Rossouw, 2013). This process can be attributed to the neuroplasticity of the brain, which is instrumental in re-writing neural pathways (Rossouw, 2012b). It is only at this point, when down-regulation of unhelpful neural patterns of avoidance and stress is facilitated, that an individual feels safe. At this point also the individual may be able to open up and reveal why they have presented to therapy, because so often the stated reason why a person presents is not at the core of what is happening for them.

Grawe (2007) states that organisms are biologically driven to patterns of approach oriented to what is life-sustaining, and to avoid danger. Such approach and avoidance decisions influence whether or not an organism survives and it appears that the fight or flight circuitry in the brain evolved in association with areas of the cerebral cortex used to consciously identify danger (Grawe, 2007).

Internal homeostatic processes—such as balancing approach and avoidance, excitation and inhibition, and fight and flight responses—are actively involved in the body’s regulatory systems (Kandel et al., 2013). These systems regulate an individual’s biological and emotional states—for example, the body’s response to stress and threat is regulated through the secretion of stress hormones (cortisol and adrenalin) from the hypothalamic-pituitary-adrenal axis (Kandel et al., 2013). While short-term survival is governed by the immediate response to stress, a rapid return to homeostasis is necessary for long-term survival (Kandel et al., 2013). The implications of prolonged stress, therefore—such as that which occurs in attachment breakdown, parental deprivation or prolonged traumatic stress—may result in long-term damage (Kandel et al., 2013). Prolonged stress results in elevated levels of stress hormones and the hypothalamic-pituitary-adrenal axis system acts as a mediator to reduce the long-term consequences of cortical arousal (Kandel et al., 2013).

However, the release of such hormones from the amygdala initiates a fight-flight response to fear, pain and discomfort in what has been described as a first-line protective survival mechanism that activates a sympathetic branch of the autonomic nervous system, producing symptoms of anxiety, agitation or panic (Cozolino, 2006). Thus, the primary function of the amygdala is to protect us by pairing stimuli with a fear response (Cozolino, 2006). It has a reciprocal relationship with the orbital medial prefrontal cortex, which functions to constrain the amygdala through conscious awareness (Beer, Heerey, Keltner, Scabini, & Knight, 2003). However, when an individual experiences high levels of distress, the orbital medial prefrontal cortex becomes inhibited, and its capacity to control thoughts and to be rational and logical is reduced (Beer et al., 2003). The networks linking the orbital medial prefrontal cortex and the amygdala are molded by experience, thus an individual’s understanding of safety and danger (Beer et al., 2003; Sibberschatz, 2005).

The implications of this for neuropsychotherapy
are, first and foremost, the importance of establishing a good therapeutic alliance with the client at the outset, which can promote the safety needed to allow for the down-regulation of distress responses (Rossov, 2012a). This emphasizes the need for therapists to work from a bottom-up approach rather than a top-down approach—specifically because the establishment of a safe environment allows physiological symptoms to down-regulate unhelpful neurotransmitter firing of the stress hormones norepinephrine, corticotrophin releasing factor, corticotrophin hormone, adrenaline and cortisol (Rossov, 2012a). It also allows for the up-regulation of serotonin flow, dopamine release, and activation of the parasympathetic nervous system, as well as addressing the scanning for novelty (danger) by the amygdala (Blackford, Buckholtz, Avery, & Zald, 2010).

As stated previously, a therapeutic environment facilitates an enriched safe environment where psychotherapy has the potential to facilitate neural change and proliferation. Safety is essential for people in distress because it down-regulates the hypothalamus-pituitary-adrenal system (Rossov, 2013). When the fear response, which is triggered from the pons, amygdala, basal ganglia, hypothalamus, pituitary and adrenal glands, is activated, the distress activates the release of the corticotrophin releasing factor, adrenocorticotrophic hormone, adrenaline and cortisol (Rossov, 2013). If these patterns are activated frequently, the patterns of firing will become well established resulting in a default neural activation when a trigger is received (Rossov, 2013). Through psychotherapy it is possible to facilitate down-regulation of the stress response system and encourage the development of new patterns of neural activation (Rossov, 2013). Hence it is vital to enable change through the provision of a safe environment in which the individual can experience controlled incongruence, or stress, to prevent activation of the default distress response (Rossov, 2013). A controlled environment is essential; however, if change is facilitated too quickly, the stress signal may be activated and the habitual pathological patterns facilitated (Rossov, 2013).

By understanding the role of neural activation in brain activity, the need for safe environments to facilitate effective neural pathways becomes clear (Rossov, 2013). It is also clear that the basic human needs of safety and nurturing provide the basis for the development of strong open neural networks—and for the brain to maximize development, open neural activation is vital (Rudy, 2008). The contemporary understanding of neurobiology has revealed the profound impact of the lack of safety on the functioning of the brain, and emotional wellness. This demonstrates the critical role of safety within the therapeutic alliance.

A Neuropsychotherapeutic Model of Safety

Epstein (1990, 1993, 1995) developed cognitive-experiential self-theory as a means of understanding the basic human needs of the individual. Grawe (2004) extended Epstein’s theory using a consistency-theoretical model to provide a more sophisticated meta-theory to examine the basic needs. The fundamental needs for attachment and control seen within the context of neuropsychotherapy influence safety within the therapeutic alliance.

Grawe (2004) also referred to consistency regulation as a basic principle of mental functioning; however, this need for coherence cannot be subsumed as one of the basic needs but rather it is foundational by way of the consistency principle. He described consistency regulation as a state of emotional wellness that can be understood in relation to goal-orientated activity, which is largely orientated toward the fulfillment of the basic needs. In this context the term consistency refers to the state of the organism—that is, the consistency of mental processes (Grawe, 2004). The consistency principle supersedes all other needs as without consistency among the neural processes a violation of the fulfillment of needs can occur. In contrast to the consistency principle, basic needs relate to the experiences of the individual that are determined by their environment (Grawe, 2004). These experiences result in perceptions with positive or negative associations with regard to the respective need (Grawe, 2004). Thus, consistency regulation and need satisfaction are intrinsically linked. The link connecting the two can be explained by the construct of congruence, that is, the compatibility of current motivational goals and actual perceptions.

Motivational schemas are developed in the course of one’s life in order to satisfy basic needs and to protect them from violation (Grawe, 2004). Although it is not a mainstream psychological perspective—that a person’s goals during their life ultimately serve the satisfaction of basic needs—examples of such conceptualizations are provided by the cognitive-experiential self-theory of Epstein (1990, 1993, 1995) and the self-determination theory of Deci and Ryan (2000). In addition, the consistency-theoretical model described in Grawe (2007) further states that if a person is raised in an environment that is oriented to fulfilling their needs, the person will develop primarily approach motivational goals and will gain great experience in
achieving such goals. In contrast, if a person is raised in an environment where their basic needs are repeatedly violated, threatened, or disappointed, the individual will develop avoidance motivational goals, to protect him- or herself from further harm (Grawe, 2007).

Grawe (2007) stated that there are two “levers” of mental functioning—the striving for congruence and the striving for consistency—and that mental functioning is oriented toward enabling perceptions which are consistent with activated motivational goals that develop around them. While people differ in terms of the absolute and relative constitution of their basic needs, inconsistency leads to the impairment of the effectiveness of an individual’s engagement with their environment—in particular, over a long period of time inconsistency can lead to a state of incongruence and impairment in the attainment of the individual’s needs (Grawe, 2007).

When incongruence emerges, the goals, means, plans and behaviors that have been effective in the down-regulation of incongruence under the specific conditions are activated (Grawe, 2007). Given that inconsistency is detrimental to need fulfillment, mental systems form mechanisms to avoid states of strong inconsistency, or to down-regulate them if they occur (Grawe, 2007). In fact, various schools of psychology have provided labels for consistency-securing mechanisms—defense mechanisms, coping mechanisms and emotional regulation, for instance—that emerge automatically from the unconscious (Grawe, 2007). In accordance with this meta-theory, mental illness arises from the process of consistency regulation. For example, avoidance motivational schemas may be dominant in individuals who have experienced trauma (Grawe, 2007). Such schemas impair an individual’s positive need fulfillment and lead to a permanently elevated level of incongruence. These experiences consequently result in decreased well-being and poor mental health, limiting a person’s ability to cope with difficulties (Grawe, 2007). Thus, physical and emotional safety is a prerequisite for effective development of the young brain (Rossouw, 2013). This leads to congruence and consistency, emerging from a secure attachment to a primary caregiver.

The basic human needs of attachment and control are briefly described below.

**The need for attachment.** Epstein (1990, 1993, 1995) referred to the need for attachment as human reliance on other people. Whilst the need for attachment is fundamental, its critical importance for human well-being has only been given credence in recent decades (Grawe, 2007). For instance, Sullivan (1953) was among the first to explicitly regard interpersonal aspects as the central causes of mental disorders, but he failed to provide empirical evidence for his views. With regard to the etiology of mental disorders in contemporary psychology, the need for attachment is now considered the most empirically substantiated basic need (Grawe, 2007).

In terms of Grawe’s (2007) consistency theory, this inner-working model corresponds with the motivational schemas that develop around the need for attachment. For instance, childhood trauma may lead to the child internalizing the perceptual, behavioral and emotional experience of the event, such that the event has been encoded in implicit memory.

According to Grawe (2007), the availability and empathy of the primary attachment figure in early childhood will determine whether an individual develops approach or avoidance motivational schemas. Young (1994) posited that a good attachment figure is one that provides a safe haven, which affords physical closeness, protection, security and support. An avoidance motivational schema develops when a child has limited or impaired access to a primary attachment figure or when such an attachment figure is not consistently accessible (Grawe, 2007).

A helpful framework for understanding the developing brain in relation to attachment is the circle of security model proposed by Cooper, Hoggman, Powell, & Marvin (2005), which shows how a child develops a sense of safety and security that will lead to normal development. The circle of security model is based on supporting parents to create an environment through which secure attachment is facilitated (Cooper et al., 2005). The basic premise of this model is that if a child has an adverse experience, they may traverse back to a secure base in order to be taken care of. For instance, the therapeutic relationship may be an opportunity for individuals who have experienced childhood trauma to experience safety and stability in their environment (Cooper et al., 2005). Through the provision of a safe environment, therefore, the circle of security fosters secure attachment relationships that in turn create neural pathways. Importantly, these new neural patterns facilitate approach rather than avoidance motivational schemas.

**The need for control.** According to Epstein (2003), the most fundamental of human needs is the need for control, whereby an individual assimilates real experiences into their model of reality. The inner working model proposed by Bowlby (1973) is a similar such model in the domain of relationship experiences. This
is an important part of what Epstein terms “conception of reality.” He suggested that people form conceptions of reality, based on their life experiences, which they attempt to maintain through their interactions with the environment (Epstein, 2003).

An individual’s experience of real-life events is based on their motivational schemas and this influences how the individual interacts with their environment (Powers, 1973). Accordingly, a person will continuously aim to achieve control over their perceptions, if their behavior is oriented towards the attainment of perceptions that fit with their activated motivational goals. Thus, based on their life experiences, an individual develops a fundamental belief about whether predictability and control are possible (Powers, 1973). Mental functioning is largely dependent upon control, such that one needs control in order to fulfill the other basic needs (Epstein, 2003).

Grawe (2007) derived his understanding of control from the construct of self-efficacy beliefs proposed by Rotter (1966) and Bandura (1977). In particular, Bandura (1977) suggested that individuals with high self-efficacy—that is, those who believe that their performance is within their control—are most likely to view difficult tasks as goals to be mastered, rather than goals to be avoided. According to Powers (1973), all behavior is motivated toward the attainment of perceptions that are congruent with specific goals—therefore, if successful, the need for control may be satisfied, whereas non-satisfaction or violation of this need may lead to a state of incongruence. Furthermore, the need for control is permanently activated when important goals are involved. Thus, events that satisfy the need for control will almost always lead to an improved mental health state through the creation of neural pathways that facilitate approach rather than avoid patterns (Powers, 1973).

On the other hand, events that frustrate or violate the need for control will lead to impoverished mental health functioning (Powers, 1973). A violation of the need for control exists when a client experiences mental disorders, as these experiences are beyond the client’s locus of control (Powers, 1973; Rotter, 1954). In this view, the goal of psychotherapy is thus to provide the opportunity for the client to learn to better cope with their problems and regain a sense of control (Powers, 1973). A positive control experience that facilitates a person’s sense of safety may ultimately restore the violation of the person’s need for control (Powers, 1973); therefore, when an individual regains belief in their ability to exercise control over events a sense of safety may be restored.

In undertaking psychotherapy with a new patient, the therapist has a responsibility to endeavor to create an atmosphere of safety (Grawe, 2007). This can be achieved by the therapist providing a predictable, respectful relationship—for example, when a therapist is curious about an individual’s life, including the history of their control experiences, they are in a better position to then understand how the client developed their present disorder (Grawe, 2007). Crucially, the fulfillment of an individual’s need for attachment and control in the therapeutic setting may lead to improved emotional wellness (Grawe, 2007). In addition, with a secure attachment environment leading to a greater locus of control, individuals are likely to experience enhanced well-being and mental health (Grawe, 2007; Rotter, 1954).

Safety and the Therapeutic Alliance

The therapeutic alliance has emerged as an important variable for psychotherapy process and change (Orlinsky, Grawe, & Parks, 1994). In this comprehensive review of the literature, Orlinsky and colleagues (1994) demonstrated links between aspects of the therapeutic relationship and a range of treatment outcomes in a wide variety of psychotherapies (see, e.g., DeRubeis & Feely, 1991; Eaton, Abeles, & Gutfriend, 1988; Greenberg & Webster, 1982; Safran & Wallner, 1991; Salvio, Beutler, Wood, & Engle, 1992).

Researchers have argued that improved therapeutic outcomes may be the result of the therapist being more able to consistently form stronger alliances with their clients (Del Re, Fluckiger, Horvath, Symonds, & Wampold, 2012). Indeed, several recent studies have found evidence suggesting that the therapist contribution is more critical than the patient contribution to the therapeutic alliance and resulting outcomes (Baldwin, Wampold, & Imel, 2007; Dinger, Strack, Leichsenring, Wilmers, & Schaufenburg, 2008; Marcus, Kashy, Wintersteen, & Diamond, 2011; Zuroff, Kelly, Leybman, Blatt, & Wampold, 2010).

Therapists who practice from psychodynamic, humanistic and cognitive behavioral orientations have all advocated that the quality of the therapeutic relationship is dependent upon the therapist being able to provide a safe enriched therapeutic environment (Basch, 1980; Rogers, 1961; Sampson, 1990; Shay, 1996; Yalom & Bugental, 1997). In neurobiological terms the therapeutic relationship is comprised of right-brain to right-brain interaction (Rossouw, 2013). This includes mirror neuron activity, down-regulation of limbic responses, and the establishment of safety by creating a
safe, empathic, and supportive environment (Schore, 2012). In addition, the therapeutic relationship facilitates the up-regulation of safety and control that are linked closely to the primary need for attachment. Thus, through engaging in therapy, the therapeutic process which involves controlled incongruence (rather than uncontrolled incongruence), open neural firing (rather than up-regulation of the stress response), and enhanced cortical activity (rather than a reduction of cortical blood flow due to the stress response), are vital aspects of the overall therapeutic relationship (Rossouw, 2013). New neural patterns can be activated by down regulating the stress response and enhancing the basic needs of attachment and control. Safety is thereby facilitated through the development of new neural pathways that shift unhelpful patterns of thinking, feeling and behaving (Rossouw, 2013). Facilitating safety is essential in activating open neural patterns rather than closed, protective, neural activation, which reflects psychopathology (Rossouw, 2012b). It is important to be aware that building rapport takes time, and to be mindful that imposing techniques too soon may activate the client's stress response, inhibiting the therapeutic process (Rothschild, 2000).

These implicit right brain operations are activated in the therapeutic alliance and are essential for adaptive interpersonal functioning (Schore, 2012). The right hemisphere is dominant for aspects of communication and subjective emotional experiences (Schore, 2012). The implicit communication of affective states between the right brains of the patient and therapist may be referred to as intersubjectivity (Schore, 2012). In the therapeutic relationship, the neurobiological correlate of this is expressed through the self-organization of the developing brain, which occurs in the context of an inter-personal relationship (Schore, 2003). Engaging in therapy is a deeply personal experience. Essentially the human brain is a social entity which flourishes through its connections to other brains (Schore, 2012; Siegel, 2012). However, in the absence of an environment in which to flourish, pathology may develop (Rossouw, 2013). The therapeutic process may therefore provide an environment in which the basic needs of safety and control are met—specifically, in a safe therapeutic environment a gradual shift may take place, from patterns of protection to patterns of approach. Neural integration may also lead to cognitive, emotional and behavioral integration (Siegel, 2010). Ultimately, neuroscience clearly indicates that who we are as therapists is far more significant than our body of knowledge (Kandel, 2006).

Summary and Concluding Discussion

This paper contends that the preferred approach to facilitate safety within the therapeutic alliance is from a bottom-up approach rather than a top-down approach. Due to the up-regulation of distress in the primitive regions of the brain, which result in deep brain activity, and shifts in cortical blood flow away from left pre-frontal cortical areas, cognitive interventions that are introduced at the beginning of therapy may not be effective. The capacity of the brain to activate new neural connections and ultimately new pathways is facilitated only when a safe therapeutic relationship is established and down-regulation of the fear response is effectively addressed (Rossouw, 2011). It is in this safe enriched environment that cognitive, emotional and behavioral interventions can be successfully introduced.

In this paper we propose a meta-theoretical model within the context of neuropsychotherapy in which the fundamental needs of attachment and control work together to facilitate safety within a therapeutic alliance. The implications of this research for service delivery are significant—first, effective delivery of early interventions is required to assess, identify and address violations of the needs for attachment and control; and, second, effective service delivery to enhance neural development has to be a collaborative activity between mental health services and parental systems (Rossouw, 2013). Future research will extend this model, utilizing a neurobiological experiential study to provide specific therapeutic guidelines for the ways in which clinicians can maximize wellness from a neurobiological perspective. Exploring the concept of safety from a neuropsychotherapeutic perspective demonstrates that facilitating safety should not be assumed but incorporated as an essential part of the therapeutic process.

References


Siegel, D. J. (2012). The developing mind (2nd ed.). How relationships and the brain interact to shape who we are. New York, NY: Guilford Press.


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