Relational Psychosis Psychotherapy: A Neuropsychoanalytic Model

Brian Koehler PhD
New York University and the City University of New York

Science does not explain or describe nature, only nature as exposed to its methods of inquiry
Werner Heisenberg

Introduction

What we teach today is part biology and part history...but we don't always know where one ends and the other begins"
JT Bonner

Cichetti (2010), from a developmental psychopathology perspective, emphasized that the abnormalities in the broad domains of genetics, neurobiology, cognition, emotion and interpersonal relationships in severe mental disorders do not exist in isolation. He encouraged researchers to strive to comprehend the interrelationships between the biological, psychological and social in these disorders. I have conceptualized this as a non-reductionistic, translational, more three-dimensional approach which is integrative across the domains of brain, mind/self and culture. This model highly values interdisciplinary research such as exemplified in the study by Epel, Blackburn and colleagues (2004) which demonstrated that perceived helplessness is associated with premature cell aging. In this paper, I will attempt to demonstrate that looming threats of non-relatedness expressed in annihilation anxieties may be the core situation which helps to explain some of the neuroscience, epidemiological, sociocultural, and clinical findings in many persons diagnosed with a severe mental disorder. Although this model includes

both “bottom-up” neurobiological processes, such as the effects of various polymorphisms and neural alterations on psychological and psychosocial functions, and “top-down” processes, such as the effects of the environment on gene expression and neural morphology, it privileges the latter in its hierarchy of etiological factors. Relational psychosis psychotherapy, which will be broadly described, is one form of psychosocial therapy that seeks to address the terrifying threats of unrelatedness, the effects of relational trauma and social isolation. The author agrees with the proposals of Bowlby and Holmes (1993) that attachment may be the psychobiological basis of psychotherapy.

Neuroplasticity

The term “neuroplasticity” refers to the capacity of the nervous system to exhibit structural and functional adaptations to impinging stimuli. One important molecular biological basis for neuroplasticity is the transcriptional function of genes. The transcriptional function of genes, and therefore neuronal functioning, is responsive to social and environmental factors. Stress-induced neuroplastic changes may be observed in persons with schizophrenia. Hoffman (2007) suggested that social deafferentation-induced neuroplasticity plays a role in schizophrenia. He noted: “...it is at least plausible that severe social withdrawal in humans during critical developmental periods induces deafferentation-like reorganization in regions of association cortex underlying social cognition that consequently produce spurious experiences with social meaning [e.g., hallucinations, delusions]” (p. 1067). The subject of the effects of social isolation and loneliness on the brain and person will be discussed in more depth later in the paper.

The Social Brain and Schizophrenia

Brüne (2008), as well as Jonathan Burns (2007), emphasize that the human brain is very much a “social brain,”since to a large extent, the human brain evolved to deal with social

events and processes. Keyers and Gazzola (2009), in speaking of the role of mirror neurons in social cognition, proposed:

"Humans have an almost uncanny capacity: they can simply observe other conspecifics and get deep intuitive insights into their minds. Since the discovery of mirror neurons, this capacity seems a little less mysterious" (p. 3).

Over the years psychiatrists and psychologists have offered an evolutionary viewpoint in ithe search for meaning in psychosis (Burns, 2007; Brüne, 2008). Such evolutionary principles as 'rank-hierarchy' and 'dominance-submission' have been proposed as conceptual tools to understand depression, e.g., the concept of the 'social rank hypothesis of depression.' Since depression is very frequently observed in schizophrenia and other psychotic disorders (Birchwood et al., 2009), these concepts should be relevant to persons diagnosed with psychotic disorders. In fact, Birchwood and colleagues (2009) have made a strong case that such affective symptoms as depression and anxiety in schizophrenia are misleadingly referred to
as "co-morbidities," which tends to render them to a subordinate status in the symptom hierarchy in psychotic disorders. Brüne (2008) proposed that psychiatric disorders, particularly the schizophrenias, fall into the category of social brain disorders (Burns, 1997; Brüne, 2008). Burns (2007) presents evidence that the neuropathology and neurophysiology of schizophrenia overlaps with the anatomy and physiology of the social brain. Brüne (2003) presented evidence that emotion recognition and theory of mind (social cognition, mentalization) is impaired in persons diagnosed with schizophrenia. Hundert (1992) noted: "If the brain evolved to maximize our chances for survival through its many subtle adaptive mechanisms, we may well ask whether one such mechanism is the brain's capacity to form delusions" (p. 347).

Neurobiology of the Schizophrenias

Sullivan and colleagues (2006) emphasized that the "pathogenesis of schizophrenia is unknown, and no compelling biological markers of sufficient sensitivity and specificity exist" (p. 40). In reviewing recent research on structural brain imaging in schizophrenia, Lawrie & Pantellis (2011) noted: "It is beyond doubt that there are gross neuroanatomical changes in patients with schizophrenia, but these are probably non-specific, weakly related to the cardinal manifestations of the disorder, and of largely unknown cause" (p. 341). Harrison, Lewis and Kleinman (2011) pointed out that neuropathological studies examine the cellular and molecular correlates of the structural differences in schizophrenia identified in neuroimaging research. These researchers noted:

"There is a range of morphometric and cytoarchitectural findings, affecting the distribution, density, size, and phenotypic properties of various neuronal and glial populations. These are accompanied by alterations in the expression of various molecules indexing synaptic and oligodendrocyte functioning. The changes are prominent in, but not restricted to, the hippocampal formation, DLPFC [dorsolateral prefrontal cortex], and thalamus...Antipsychotic medication and other confounders cannot be excluded as contributing to some of the findings" (pp. 383-384).

Neurodevelopmental, (Weinberger & Levitt, 2011), dysconnectivity and dimensional models of schizophrenia are quite prominent. In regard to the latter, a dimensional model is represented in the viewpoint of Weinberger and Levitt (2011) who went so far as suggesting:

"Schizophrenia, of course, is not something someone has; it is a diagnosis someone is given. It is worth considering that the syndrome of schizophrenia is not a disease

at all, but a state of brain function based on an altered developmental trajectory from early programming with changing repercussions throughout life...That there appear to be numerous genetic and environmental factors that can contribute in various combinations to this recognizable state of altered brain function further suggests that what we call schizophrenia may represent 'not the result of a discrete event or illness process at all, but rather one end of the developmental spectrum that for genetic and other reasons approximately 0.5% of the population will fall into'" (p. 408).

White Matter (WM) and Dysconnectivity Models: Schizophrenia as a Disorder of Neural and Psychosocial Integration

White matter may be the new 'dark matter' in neurobiological research in severe mental disorders. Deficits in glial cell numbers and density have been observed in major depressive disorder, bipolar disorder and schizophrenia. White matter alterations in major depressive disorder have been observed by Kumar and Ajilore (2011) in normal-appearing white matter observed by diffusion tensor imaging (DTI) and magnetization transfer imaging (MT). White matter abnormalities, e.g., decreases in fractional anisotropy (FA), have been reported in bipolar disorder (Strakowski, 2011). Fractional anisotropy (FA), as measured by DTI, "is a measure of directionality of the axons forming the fiber bundles and is often used as an index of fiber integrity and, to a lesser extent, myelination" (de Weijer et al., 2011). Garver and Christensen (2005) observed that remission of psychosis was associated with partial recovery of white matter integrity. These researchers concluded that some patients with schizophrenia manifest an episodic functional-disconnect syndrome (FDS) during psychotic episodes which is associated

with inflammatory cytokine elevation, disruption of white matter integrity, and of information processing.

WM fiber bundles represent the "information highways of the brain." Some of the most prominent fiber bundles in the brain include the corpus callosum, the superior longitudinal fasciculus (connecting the parietal and temporal cortices with the prefrontal cortex), the inferior longitudinal fasciculus (connecting the temporal and occipital lobes), and the uncinate fasciculus (connecting the frontal and anterior temporal lobes). WM constitutes approximately 40% of the total mass of the brain.

Bartzokis (2002) offered a novel suggestion as to the underlying cause of the neural disintegration proposed to exist in the schizophrenias: it arises from abnormalities in the periadolescent process of myelination, a dysmyelination process (myelination of the association cortices are not complete until at least 30 years of age). Myelin increases the transmission velocity of neural signaling. This process could result in transmission delays causing a loss of the brain's ability to function normally by reducing its ability to maintain synchronous communication across functional neural networks. It should be noted at this point that stress interferes with the replication of glial cells, the cells that myelinate the CNS, and some antipsychotic agents not only can cause neural atrophy in gray matter, but also negatively impact on WM (Borgwardt et al., 2009). MRI studies have reported volumetric and/or morphometric WM abnormalities in schizophrenia as well as in first episode patients. Whitford, Kubicki and Shenton (2011) have reported that there have been over 50 studies investigating WM abnormalities in persons with schizophrenia. By far the most consistent finding is of fractional anisotropy (FA) reductions relative to healthy controls. Another consistent finding is the positive correlation between FA and severity of psychotic symptoms. Schneiderman and colleagues (2011), using the largest known sample to date to examine anisotropy in schizophrenia, confirmed a white matter deficit in these individuals.

The self-monitoring theory of Chris Frith (Frith, 2004) proposes that psychotic symptoms can arise when a person performs an act (physical or mental) without being aware of their intention to perform the action. This failure of awareness has been proposed to be caused by abnormalities in the "corollary discharges" (CDs) that are sent from the brain regions involved in initiating the action to the regions involved in processing the sensory consequences of that action. Specifically, if the FA reductions resulting from dysmyelination were present in WM fiber bundles connecting the sites of CD initiation and destination, then the consequently slowed transmission velocity of the CDs could result in the CDs and the primary discharges reaching their respective destinations asynchronously. Whitford and colleagues (2011) proposed that the nature of psychotic symptoms may depend upon whether primary discharges and CDs can be integrated if they arrive at their respective destinations within a critical time period, e.g., if CDs arrive outside of this critical window, negative symptoms may result. If the dysmyelination occurs in WM fiber bundles connecting the initiation and destination sites of certain CDs, then this may result in the CDs reaching their destinations subsequent to the termination of their corresponding primary discharge. This could lead to actions being performed in the absence of an intention to act, which in turn could lead to internally generated actions being perceived as externally generated, and subsequently certain types of psychotic symptoms like a delusion of external control. Ford and colleagues (2007) proposed that malfunction of the corollary discharge process, a neuronal circuit that suppresses the sensory effects of self-generated actions, such as the arcuate fasciculus, may be a basis for auditory verbal hallucinations. de Weijer and colleagues (2011) observed decreased FA and an increased magnetic transfer ratio (MTR) in the arcuate fasciculi (the most important fiber bundle between Broca's area and Wernicke's area). These researchers interpreted the disintegrated axonal fiber integrity in the connecting

pathways between frontal and temporo-parietal language areas as being associated with a liability for developing auditory verbal hallucinations.

The Genome and Epigenome in the Schizophrenias

Owen, Craddock and Jablensky (2010), in their recent review of genetic studies in schizophrenia, concluded: "There is an 'explanatory gap' between the findings of statistical association of a gene variant with the disorder and the demonstration of causality with regard to specific illness phenomena" (p. 78). Between the genome and phenome, resides the methylome, epigenome, proteome, connectome and envirome, and for human beings, the meanings given to experience (Fonagy, 2003). The role of genes in the schizophrenias is most likely polygenic and probabilistic as opposed to deterministic. Each of the genes thought to be involved in the schizophrenias (e. g., DISC 1 and 2, NRG1, DTNBP1, BDNF, COMT, RGS4, etc.) are of small effect and are thought to be in a dose-response relationship with multiple high risk environmental factors, e.g., urban birth/living, migration, social isolation, ethnic density factors, etc. (Morgan, Charalambides, Hutchinson & Murray, 2010). However, recent evidence on de novo protein-altering mutations and copy number variations (CNVs, e.g., microdeletions) with large effect sizes may be operative in some situations. Can environmental factors such as stress, social isolation, diet, exercise, substance misues and other lifestyle factors contribute to these mutations? Weinberger and Berger (2009) reminded us that "genes do not encode for psychopathology per se, and that the human genome did not evolve with the intention of reifying the DSM-IV criteria" (p. 41).

We must not ignore or minimize the significant role of the social-psychological environment on genetic and epigenetic function (Meaney, 2004). Social psychiatrist Leon Eisenberg (2004) concluded that "genes set the boundaries of the possible; environments parse out the actual" (p. 103). It is also not possible to reduce everything to the molecular

level or to physico-chemical processes without vital information being lost (Bolton & Hill, 1996). According to Bolton and Hill (1996), intentional-causal processes, e.g., subjective and sociocultural meanings, pervade biological systems to the level of DNA. Psychogenic/environmental stress has been shown to be genotoxic in various body cells ghth(Fischman & Kelly, 1999; Fischman, Pero & Kelly, 1996) and to contribute to premature cell aging (Epel et al, 2004, 2006).

It is the field of epigenetics that extends our understanding of genes from one to three dimensional processes (Francis, 2011). Petronis (2004) offered a succinct definition of epigenetics: "...epigenetics refers to regulation of gene expressions that are controlled by heritable but potentially reversible changes in DNA methylation and/or chromatin structure" (p. 175). A large number of genes demonstrate an inverse relationship between the degree of DNA methylation and gene expression. Social and psychological experience can epigenetically alter gene expression. Some epigenetic "marks," i.e., specific chemical attachments such as a methyl group, can be transgenerationally transmitted. This adds to the complexities of psychoanalytic models on the transgenerational transmission of trauma in psychosis (Davoine & Gaudilliere, 2004).

Petronis (2004) and Zorumski and Rubin (2011) proposed that epigenetic factors may help to explain the significant lack of full concordance for schizophrenia in monozygotic twins. Petronis (2004) suggested that because of its complexity, the brain is likely to be vulnerable to even mild epigenetic malfunction which might lead to a diversity of small morphological and functional changes. The neural morphological aberrations observed in schizophrenia, according to Petronis, "are more likely to be just reporters of mild deviation in the developmental program rather than factors causing or predisposing to schizophrenia" (p. 187). More recently, Petronis (2010) identified several dozen loci in

the genome where epigenetic differences between people diagnosed with schizophrenia and controls emerged.

Gene-Environment Interaction in the Schizophrenias

In Finland, Tienari and colleagues (2004) demonstrated that in the adopted-away children of a biological mother with schizophrenia, adoptive-family rearing behavior is predictive of the later development of a schizophrenia spectrum disorder. Tienari and colleagues (Wahlberg et al., 1997) also found a significant association between communication deviance in adoptive parents and thought disorder in those children thought to be at genetic risk for a schizophrenia spectrum disorder, but not in low genetic risk adoptees. These results are consistent with either genetic control of sensitivity to the environment or environmental control of gene expression. Importantly, there was no difference in the presence of communication deviance in the adoptive parents of high risk versus low risk adoptees, thus suggesting that the adoptees at high risk did not have a special impact of increasing the communication deviance in their adoptive parents. From the perspective of Tienari and colleagues (2004), diseases will tend to cluster in families not because of a direct genetic effect, but because relatives are more vulnerable to the risk-increasing effects of a particular environmental factor.

Developmental Traumatology: The Effects of Stress and Relational Trauma on the Brain and Person

In 1997, at an international ISPS conference on schizophrenia in London, I proposed that the neuroscience of the severe mental disorders significantly overlaps with the neuroscience of chronic and profound stress, trauma, social isolation, extreme loneliness and social defeat.

DeBellis (2010) defined developmental traumatology as:

"the systemic investigation of the neurobiological and psychological impact of early life adversity on the developing child. It is a relatively new field of study that synthesizes knowledge from developmental psychopathology, developmental neuroscience and stress and trauma research" (p. 124).

van der Kolk and d'Andrea (2010) observed that hundreds of research studies over the past three decades have documented the effects of "childhood interpersonal trauma on the development of affect regulation, attention, cognition, perception and interpersonal relationships" (p. 57). These researches noted that in the 1980s, Arthur Green and Dorothy Otnow Lewis documented that many relationally abused children, even when there were no reports of head injury, exhibited neurological damage. Subsequent research by such developmental traumatologists as Martin Teicher, Michael De Bellis, Ruth Lanius and others, demonstrated a constellation of neural abnormalities associated with childhood maltreatment, including neglect, bullying, etc. Based on the consistent results across studies, van der Kolk and d'Andrea concluded: "being in a persistent low-level fear state affects development of the primary information-processing areas of the brain" (p. 58).

Teicher and colleagues (2006) have conducted research on the effects of childhood maltreatment on the developing brain, with implications for the emergence of psychiatric disorder. Teicher and colleagues noted:

"We have proposed that early maltreatment produces a cascade of physiological and neurohumoral responses built on the following...fundamental premises: First, that exposure to stress early in life activates stress response systems, and fundamentally alters their molecular organization to modify their sensitivity and response bias. Second, that exposure of the developing brain to stress hormones [e. g., cortisol] exerts consequences

by affecting gene expression, myelination, neural morphology, neurogenesis [the birth of new neurons] and synaptogenesis [the creation of new synaptic connections].” (p. 180).

De Bellis (2010) has documented the neurobiological effects of child neglect and psychological unavailability. He noted: “Neglect, without social intervention, is a chronic stressor that may negatively influence the development of biological stress system responses and may lead to adverse brain, cognitive and psychological development” (p. 124). De Bellis pointed out that primates subjected to maternal and social deprivation demonstrate altered catecholamine, cortisol, and immune function.

Early life trauma such as physical/emotional/sexual abuse as well as neglect, bullying and social isolation, are correlated with pervasive neural alterations in both gray and white matter, e.g., atrophy and dysmyelination, respectively (Lanius, Vermetten & Pain, 2010). van der Kolk and d’Andrea (2010) noted that studies have documented associations between interpersonal trauma and structural/functional abnormalities in the following neural regions: prefrontal cortex, corpus callosum, amygdala, hippocampus, temporal lobe and the cerebellum. These researchers concluded: “Taken together, these areas of the brain represent key pathways for the regulation of consciousness, affect, impulse, sense of self and physical awareness” (p. 63). Numerous studies on the symptomatology arising from childhood relational trauma, have demonstrated the following: affect and impulse dysregulation; disturbances of attention, cognition and consciousness, e.g., dissociative symptoms; distortions in self-perception and systems of meaning, e.g., post-abuse shame and guilt; interpersonal difficulties including mistrust, poor boundaries and social skills, etc.; somatization and psychobiological dysregulation, e.g., chronic pain, migraines, cardiopulmonary symptoms, digestive distress, sensory integration difficulties, poor balance and proprioception, etc.; and co-occurring symptoms, e.g., substance misuse, depression, panic, etc.

Teicher and colleagues (2010), in reviewing the more recent research on the neurobiology of childhood trauma, noted:

"Exposure to early life trauma is associated with a host of structural abnormalities. There is consistent evidence for a reduction in the midsagittal area of the corpus callosum. Similarly, there is compelling evidence for reduction in hippocampal volume in adults but not children. There is also evidence from multiple laboratories for alterations in symmetry, GMV [gray matter volume], neuronal integrity, and EEG coherence in portions of the neocortex...It is particularly striking that exposure to repeated episodes of SA [sexual abuse] most significantly attenuated GMV in the occipital cortex and reduced GMV in the left fusiform and right lingual gyri. These regions appear to play an important role in recognition of familiar faces and dreaming. Witnessing domestic abuse was associated with reduced FA [again, fractional anisotropy is a measure of directionality of axons forming fiber bundles, used as an index of fiber integrtity, and to a lesser extent, myelination] in the inferior longitudinal fasciculus, which relays visual information to the limbic system. Exposure to VB [peer verbal bullying] was associated with reduced FA in the insula, where multisensory information is integrated, and with a reduction in the left lingual gyrus, which is involved in processing emotional response to visual or verbal stimuli. There was a substantial reduction in FA in subjects exposed to PVA [parental verbal abuse] along a portion of the arcuate fasciculus [an area identified in research to be associated with severity of auditory verbal hallucinations], which connects regions involved in the perception and expression of language...exposure to harsh corporal punishment was associated with alteration in FA and mean diffusivity throughout components of the cortical pain pathway. Hence, these findings suggest that exposure to various forms of maltreatment affect sensory systems or pathways through which the aversive stimulus is processed or interpreted. These findings are consistent

with the idea that sensory systems are malleable and strongly influenced by early experience" (pp. 119-120).

These findings by Teicher and colleagues raise the intriguing possibility that the neural alterations observed post-childhood maltreatment or social adversities, may be adaptive in that they are designed to reduce transmission and reception of specific pain and danger signals, perhaps involving the looming threat of unrelatedness and social isolation. This phenomena may be, along with excessive corticolimbic inhibition (Schmahl et al., 2010), a neurobiological form of dissociation.

Dissociation often "involves a disruption in the usually integrated function of consciousness, memory, identity, body awareness and/or perception of the environment" (Schmahl et al., 2010, p. 178). Schmahl and colleagues (2010) noted that in two prospective longitudinal studies (Bureau et al., 2010), parental emotional neglect and disorganized attachment in infancy, were the two strongest predictors of dissociation in young adulthood. Dissociation, as proposed by Moskowitz and colleagues (2009), may play a significant role in mediating psychotic symptoms. Lines from Shakespeare's King Lear appear to illustrate this link between dissociation and psychosis:

How stiff is my vile sense
that I stand up and have ingeneous feeling of my huge sorrows
better I distract [dissociate]
so should my thoughts be severed from my griefs and woes
by wrong imaginations [delusions]
loose knowledge of themselves
King Lear
Shakespeare

Shah, Mizrahi and McKenzie (2011) concluded that: “Genetic, biochemical and neurological evidence supports the link between stress and psychosis” (p. 11).An increased risk for psychosis is associated with cumulative exposure to traumatic life events as well as daily hassles (Shah, Mizrahi & McKenzie, 2011). Gene-environment interactions are being studied to identify the relevant polymorphisms which may partially account for these correlations.

Social-Survival Brain

The impact of early psychological trauma can derail normal psychobiological development, in particular, shifting a brain focused on learning and exploration to a brain (and body) focused on survival (Ford, 2009, 2010). The difference between them according to Ford (2009) is as follows:

> “...the learning brain is engaged in exploration (i. e., the acquisition of new knowledge and neuronal/synaptic connections) driven and reinforced by a search for an optimal balance between novelty and familiarity. The survival brain seeks to anticipate, prevent, or protect against the damage caused by potential or actual dangers, driven and reinforced by a search to identify threats, and an attempt to mobilize and conserve bodily resources in the service of this vigilance and defensive adjustments to maintain bodily functioning.... The survival brain relies on rapid automatic processes that involve primitive portions of the brain (e. g., brainstem, midbrain, parts of the limbic system, such as the amygdala), while largely bypassing areas of the brain involved in more complex adaptations to the environment (learning, e. g., anterior cingulate, insula, prefrontal cortex, other parts of the limbic system, such as the hippocampus...” (p. 32).

The Neurobiology of Stress Resilience: The Importance of Social Support

Meaney and colleagues (Meaney, 2004; Parent et al., 2010) have demonstrated that stable individual differences in maternal licking and grooming (LG) in rats are associated with individual differences in LHPAA (limbic-hypothalamic-pituitary-adrenal axis) responses to stress. Meaney noted:

"As adults, the offspring of mothers that undertake frequent licking and grooming and arched-back nursing (high-LG-ABN mothers) are behaviorally less fearful and show more modest HPA responses to stress than the offspring of mothers that do not (low-LG-ABN mothers). Cross-fostering studies show that the biological offspring of low-LG-ABN reared by high-LG-ABN dams resemble the normal offspring of high-LG-ABN (and vice-versa)" (p. 7).

Meaney (2004) reported: "The adult offspring of high-LG compared with low-LG mothers show increased hippocampal glucocorticoid receptor expression and enhanced glucocorticoid feedback sensitivity" (p. 7). Meaney suggested: "DNA methylation could serve as an intermediate process that imprints dynamic environmental experiences on the fixed genome resulting in stable alterations in phenotype" (p. 11).

Personally, I believe that a good human analogue of licking-grooming is maintaining psychotherapeutic empathy and containment despite, as Christian Müller (1972) pointed out, the therapist's fears of uncontrolled aggressivity in her- or himself arising from narcissistic injuries in the work with the patient.

Gumley and colleagues (2010), commenting on Paul Gilbert's affect regulation model, emphasized the importance of the attachment-based "soothing system, " linked biologically to endorphin and oxytocin systems, to serve as counterpoint to the threat detection system.

Ozbay and colleagues (2010) described the neurocircuitry and neurochemistry of stress resilience as follows:

"The neurocircuitry of stress resilience consists of a variety of brain structures intimately involved in mediating the stress response, including the amygdala, hypothalamus, hippocampus and prefrontal cortex...different forms of social support have been shown to play a role in the development of stress resilience and in reversing stress-related adverse changes" (p. 196).

Sociocultural Factors

The Role of the Social Environment

And now some god has flung me on this shore, no doubt to suffer more disasters here. For I have no hope that my troubles are coming to an end: Pity me my queen, you are the first person I have met after all I have been through, and I do not know a soul in this city or this land.

Odysseus

Homer: The Odyssey

Shah, Mizrahi and McKenzie (2011), in their review of a multidimensional model for the social etiology of psychosis, proposed that social factors play an etiological role in psychosis. From a sociocultural framework, the following factors have been demonstrated in epidemiological research to be associated with the initiation, course and outcome of severe mental disorders: urban birth/urban living, socio-economic status, migration, reduced social support and networks, social isolation, social defeat and marginalization, childhood adversity, expressed emotion (particularly hostile criticism) in caregivers, stigma and discrimination, ethnic density, marital status, relative inequality, etc. (Freeman & Stansfeld, 2008; Morgan, McKenzie & Fearon, 2008; Shah, Mizrahi &

McKenzie, 2011). Shah, Mizrahi and McKenzie (2011), in regard to the risk factor of urban birth/living, noted:

"Studies have demonstrated that the higher risk of psychotic illness for those living in cities is not the result of social drift but is associated with being born and growing up in an urban environment in childhood. Moreover, the bigger the city the bigger the risk" (p. 12).

Martti Siirala (1983) proposed a different perspective on the social factors involved in the initiation and course of the schizophrenias. Siirala focused on social pathologies and a common sickness that we all share: "...manifest schizophrenia is part of a common darkness" (p. 19). Schizophrenia, according to Siirala, emerges "out of a common soil of sickness" (p. 19).

Davoine and Gaudilliere (2004) emphasized the need to restore the disrupted link in psychosis between the family and the social fabric (Fromm, 2011), a link disrupted transgenerationally by dissociated experiences arising in the individual's "big history" such as social-familial catastrophes. Davoine and Gaudilliere (2009), in discussing their psychotherapeutic approach, noted: "...we aspire to continue along the lines opened by our predecessors, who considered transference in the psychodynamic treatment of psychosis as a process of co-research with the patient, exploring the 'death areas' that represent ruptures in the social fabric, in order to regenerate lost capacities for speech and history" (p. 143).

A viable and coherent model of the schizophrenias would have to be able to explain the neuroscience and clinical findings, as well as the epidemiological research on social factors, including recovery research and the findings of the WHO studies demonstrating

better recoveries in developing countries as opposed to the developed nations (Hopper et al., 2007). Hopper and colleagues (2007) challenged the premise that a deteriorating course is a significant feature of schizophrenia, a viewpoint which has accompanied us since the early taxonomic efforts of Kraepelin. Hopper and colleagues proposed:

"As the earlier WHO studies had suggested and others since have corroborated, the course of schizophrenia is not 'hard-wired' into the diagnosis itself; rather, it is a developmental product of continuing interaction of disease process, treatment, local environment, and the active agency of the person" (p. 277).

The Field of Neuropsychoanalysis

Over the past decade, psychoanalysts have accelerated their attempts to relate the third-person findings of neurobiology and cognitive (e.g., Reuter-Lorenz et al., 2010), affective (e.g., Panksepp, 1998), and social neuroscience (e.g., Cacioppo & Berntson, 2004) with the second- and first-person observations within the psychoanalytic setting. The emergent field of neuropsychoanalysis has inspired many in the field to articulate the relevance of neuroscience to the practicing psychoanalyst (Ansermet & Magistretti, 2007; Gedo, 2005; Green, 2003; Kandel, 2005; Leffert, 2010; Levin, 1991; Mancia, 2006; Mancia, 2007; Pally, 2000; Sasso, 2007; Schore, 2003a, 2003b). Neuropsychoanalysts are also researching the neural processes involved in the psychotherapeutic process as well as the successful effects of psychotherapy and psychoanalysis on the brain in functional imaging studies (Viamontes & Beitman, 2009). Parenthetically, CBTp (CBT for psychosis) researchers (Kumari et al., 2011) demonstrated that CBT with persons struggling with psychotic symptoms attenuated symptoms and brain responses to threatening stimuli as shown in decreased activation of the inferior frontal, insula, thalamus, putamen and occipital regions. The researchers suggested that CBTp may facilitate symptom reduction by promoting the processing of threats in a less distressing way.

An Early Neuropsychoanalytic Model of the Schizophrenias

One of the earliest and interesting attempts to articulate a neuropsychoanalytic model of the schizophrenias was that of Gerald Sarwer-Foner (1997). Sarwer-Foner understood schizophrenia to be a specifically human disease and its most significant clinical symptoms reflect how these individuals "...form symbols of themselves and of other human beings in their Psyche and how they respond to these" (p. 262). These individuals suffer from a defective and degraded sense of self, fluctuating body image and pathological ego defenses which are attempts to preserve and protect their damaged sense of self. Sarwer-Foner links these psychological processes to neurobiological events, particularly "neuronal-inhibiting processes" (p. 266). Neuronal circuitry alterations result from an inadequate sense of self and identity crises. Sarwer-Foner postulated:

"Thus inhibition, in the formation of an adequate sense of 'Me' correlates with identity crises and poor symbolic formation, accompanied by delays in or the absence of neuronal development, and in poor dendritic connections, producing an 'incomplete wiring.' This compromises functioning. The result is a reciprocal relationship between a poorly formed Psyche, which defensively inhibits the free use of the neuronal and dendritic association iiarea systems. This provides an impoverished neuronal network, giving its user a further impoverished Psyche" (p. 266).

Sarwer-Foner believed that psychotherapeutic efforts need to be directed towards character defenses, as well as at helping the person establish a viable sense of personal identity. Other people, especially their capacity for warmth and outgoingness, are experienced as frightening intrusions. These relational intrusions, Sarwer-Foner noted:

"...would demand responses too uncomfortable for the patient with stimulation of his/her poorly tolerated needs for closeness, love, aggression, hate, and aspects of their own sexuality. Lack of self-mastery, the sense of not belonging, low self-esteem, and not being a well loved 'Me,' is part of the poor tolerance for this sort of stimulation" (p. 267).

Sarwer-Foner theorized that the person diagnosed with schizophrenia, may unconsciously be terrified if she/he attempts to master with a defective, inadequate sense of self, such tasks as forming close relationships, seeking employment, etc. The defenses used to inhibit this terror and panic, may, over the years, result in an impoverishment of the capacity of the frontal lobes to engage in such executive functions as planning, judgment, working memory, etc., especially if these functions touch on the person's areas of terror. Sarwer-Foner believed that this inhibition of neuronal function extended to the parietal and temporal lobes as well.

Psychodynamic Understanding of Psychotic Symptoms

"I am an ameba into which everyone can enter"
(Benedetti, 1987, p. 103)

The emphasis on the role of emotions and affects in psychotic symptomatology has been noted by many clinicians and researchers (Garfield, 1995; Ciompi, 1998). Christian Müller (date?), in his paper "The Schizophrenic and His Family," reported:
"Once, in total despair, I cried out to a patient I had been treating for years: 'Wake up from your dream, look around you-the world is not a bit as you think it is!' And his answer...given in a tone of deep sadness, was: 'If I wake, I shall be dead.' It was then that I discovered for the first time the paradox of which Racamier spoke-the nonexisting in order to exist" (p. 183).

Barbro Sandin (1993) expressed a similar viewpoint, as have many other psychoanalysts:

"How can we understand the schizophrenic view of the schizophrenic? To be no one... Let us call this the schizophrenic's paradox. He or she who is no one. Someone is and expresses his or her being in words of non-being" (p. 23).

Swiss psychoanalyst Mireille Ellonen-Jequier (Quinodoz, 2008) also commented on the ego's attempt to save itself by disappearing in psychosis: Benedetti (1987) understood that the ego of the person diagnosed with a severe mental disorder is often dissolved by its own perceptions and conflicts. For example, if the person feels people are laughing at him, this not only reflects on projected self-contempt, but also on the fact that the latter as well as other chronic burdening emotions have weakened the person's ego structure to a point that such perceptions can no longer be organized within it. Thus, the person's ego becomes transformed by that which it cannot include safely within itself. Benedetti (1987) believed that the psychotic person hated her- or himself because their disintegrating ego is a source of death and destruction. This ongoing state of 'negative narcissism' and the disintegration of the psychotic individual's ego/self, is phenomenologically commented on by Benedetti:

"The schizophrenic patient fears us, in spite of our relatedness, and sometimes just because of it. He is dissolving, and the impact of the outer world dissolves him. Our mere presence, even our eyes, which look at him, 'hypnotize' him, disorganize him, push him into his nothingness. The fact of a 'presence,' which cannot be counteracted by the interior 'nothingness' of the patient, is a danger" (p. 58).

Psychoanalyst Paul Williams has written cogently about this experience of the invasive object in more disturbed individuals (Williams, 2010).

Barbro Sandin (1993) understood psychotic symptoms to be the direct result of a fracture of contact with others, a state lacking relationship, which makes the person strive for emotional self sufficiency: "...delusions which the patient express are attempts to organize a world instead of disintegrating or being annihilated into nothingness" (p. 17). Persecutory delusions can help fill the void of a deep and painful loneliness. This is similar to the Fairbairnian concept that a bad object is better than no object. Sandin, like so many other psychoanalysts that work with people experiencing psychotic symptoms, such as Martti Siirala (1983), recommend that therapists take into account the affective messages, the appeals, encoded in the symptoms, and regard the symptoms as containing possibilities for communication, thereby leading to increased human solidarity.

Mentzos (1993) proposed that the psychotic symptom is a substitute for an object relationship: "I propose that the psychotic symptom represents not only a defense and a protection against the danger of dissolution of the self, but at the same time is an attempt to fill the gap, to create a connection with the object, albeit in a roundabout way..." (p. 108). He also suggested that the person with psychotic symptoms is struggling with endangerment to the self through "an attractive, desirable but simultaneously dangerous object" (p. 131). The person is trying to maintain a viable balance between meeting her or his contact needs and protection of self-boundaries. Psychoanalyst Andre Green proposed a similar view, i.e., the person is caught between separation and intrusion anxieties (Fromm, 1989). Fromm (1989), in referring to the work of psychoanalyst Andre Green, noted:

"... the serious psychological disturbances of our day function between dual terrors: of intrusion, persecution, a flooding of the self by the object, on the one hand, and of separation, decathexis, and a draining of the self into unrelatedness, on the other. The object is either pure impingement, filling the self with reactions and thus owning, even annihilating it, or pure loss, permanently inaccessible and emptying the self toward deadness" (p. 493).

Psychoanalyst Otto Will (Sacksteder et al 1987) commented on the entire organisms response to the deathly threat of unrelatedness. In speaking of some of his patients diagnosed with psychotic disorders, Will noted their fear of isolation as well as fear of human relationship. Will pointed out that closeness to another implies anxiety, separation, and death. He understood the connection between the development of relatedness (i.e., secure attachment), the concept of the self and the reduction of anxiety (mitigation of affective dysregulation). Will noted that the psychotic patient "...fears nonbeing, and in the course of useful therapy forms a sense of self which can remain intact under the threats of nonrelatedness, panic, and death" (p. 288). Benedetti and Peciccia (Koehler, 2003) believe that schizophrenia is characterized by a de-integration of the separate and symbiotic selves. For these psychoanalysts, the danger the psychotic individual faces is one of self loss whether at the pole of separateness (separate self) or at the pole of relatedness (symbiotic self). If this is indeed the phenomenology and psychodynamics of many psychotic disorders, the patient would be confronted with a terrifying and painful loneliness.

Loneliness, Psychosis and Social Neuroscience

You think I'll weep, No, I'll not weep: I have full cause of weeping, but this heart shall break into a hundred thousand flaws Or ere I'll weep. O fool! I shall go mad. William Shakespeare
King Lear

I have come to believe that when patients often refer to deep feelings of depression, which some researchers claim is the most frequent symptom of schizophrenia (der Heiden & Häfner, 2011), they are often experiencing very painful states of loneliness. As pointed out by interpersonal psychiatrist Otto Will, the threat of unrelatedness can be fatal and is certainly pervasive in our more distressed and disturbed patients. Perhaps the terror of death itself involves an unthinkable loss of relatedness. Frieda Fromm-Reichmann (1990), towards the end of her life, wrote a very significant paper "On Loneliness." In describing the nature of profound loneliness, Fromm-Reichmann noted:

"The kind of loneliness I am discussing is nonconstructive if not disintegrative, and it shows in, or leads ultimately to, the development of psychotic states. It renders people who suffer it emotionally paralyzed and helpless" (p. 308).

Melanie Klein (1963) wrote on this subject also late in her life. Her last paper, "On the sense of loneliness," depicts the amelioration of this painful state: it is in the internalization of a good object that loneliness is abated and is the foundation of integration.

Berntson and Cacioppo (2004), architects of the field of social neuroscience, have noted that the impact of social factors on autonomic and neuroendocrine control has become apparent through their research on loneliness. They noted:

"Epidemiological research has found that social isolation is a major risk factor for morbidity and mortality from widely varying causes, including cardiovascular diseases, even after statistically controlling for other known risk factors....Although there are several routes by which social factors may impact health, one likely candidate is a unique pattern of autonomic and neuroendocrine control that appears to characterize loneliness" (p. 113).

Hofer (2003) and his colleagues demonstrated that the attachment system is comprised of multiple subsystems in which the early caregiver shapes and regulates the physiological, neurophysiological and psychological functions of the offspring. In maternal separation, all of these hidden regulators of the attachment bond (e.g., maternal warmth, feeding, licking, proximity, etc), are withdrawn at once thereby significantly disrupting the organism's psychobiological homeostasis. From a psychoanalytic perspective, separation and loneliness can occur even in the presence of the caregiver, e.g., during times of parental or the analyst's anxious preoccupation in the countertransference, i.e., a lack of containment.

Social neuroscience research (Lieberman & Eisenberger, 2006) has demonstrated that the same area of the brain, the dorsal anterior cingulate cortex (dACC), which is involved in the mediation of physical pain, also mediates psychic pain, e.g., the pain of social exclusion, social rejection, loneliness, etc. With implications for paranoia and psychosis, Cacioppo and Patrick (2008) saw the connection between social isolation and cognition: "The roots of our human impulse for social connection run so deep that feeling isolated can undermine our ability to think clearly..." (p. 11). Loneliness itself has been shown to predict the progression of Alzheimer's disease and has the power to alter DNA transcription in the cells of our immune system (Cacioppo & Patrick, 2008). Evolution

shaped us to feel bad when we are socially isolated as well as physically threatened. Cacioppo and Patrick (2008) noted:

"The person who starts out with a painful, even frightening sensation of being alone may begin to see dangers everywhere on the social landscape...When loneliness is protracted, impaired regulation, combined with distorted social cognition, makes us less likely to acknowledge someone else's perspective...The sad irony is that these poorly regulated behaviors, prompted by fearful sensations, often elicit the very rejection that we all dread the most [often observed in paranoid states]. Even more confounding, over time, the feeling of vulnerability that comes with loneliness can make us more likely to be...distrustful of, whatever social connections we have" (pp. 15-16).

Relational Psychosis Psychotherapy

Christian Müller and Gaetano Benedetti, co-founders of ISPS in 1956, as well as many colleagues in ISPS have been a source of inspiration for myself (Koehler, 2003) and many other clinicians. Müller (1978) emphasized the importance of making attempts to understand, make contact and dialogue with the person suffering from schizophrenia in contrast to the Jasperian legacy which claims the incomprehensibility of psychotic symptoms. Müller (1984) pointed out that the therapist's personal motivations in doing the work plays a key role in the unfolding "common adventure" and "common destiny." One must avoid, Müller noted, treating the patient as an object. In regard to the latter point, Fromm (2011) proposed that Freud reversed the usual position of doctor and patient:

"Within a traditional medical model, the patient was to make himself the object of the doctor's knowledge and ministrations. But Freud, though he sometimes struggled with

his startling new paradigm, set up a clinical situation in which he was to become the object of the patient's unconscious strivings" (p. 80).

Benedetti emphasized that psychosis psychotherapy is at root a positivization of the patient as person. Psychotic symptoms, in Benedetti's (1987) approach, become necessary channels through which we can contact the person. Symptoms are not interpreted for their resistance function, rather, Benedetti understands psychotic symptoms "to be an attempt at survival by means of organizing a last psychotic identity in the vacuum of... 'nonexistence'" (p. 85).The therapist seeks to be together with the patient within the symptoms, thereby creating a "dualized psychopathology." Benedetti proposed: "Our messages to the patient convey that we do not expect anything from him, that we only want to be with him in his dreams, fantasies, and terrifying experiences" (p. 83).

Part of this sharing, is the very painful experience of containing traumatic, terrifying, shame-inducing experiences which a traumatized patient communicates to the therapist, verbally and non-verbally, sometimes in very forceful ways. Interpreting these communications as attacks on the therapist's mind, especially as unjustified attacks, can lead to increased cycles of projective identification-counterprojection. Rosenfeld (1987) recommended that the analyst, in these situations, interprets the underlying anxieties correctly, and communicates that the patient has had to suffer these experiences for long periods of time alone, and that she or he needs to share these terrifying experiences with the analyst.

Benedetti (1987, 1993), in his existential, relational-dialogical psychotherapeutic approach, utilized such concepts as therapeutic transforming images, counteridentifications, transitional subjects, therapeutic symbiosis, duality, etc. (Koehler,

2003). Hoffman (2009) noted that for Benedetti, as for Harold Searles (1979), the "therapist's unconscious is an essential factor for the recovery of the patient" (p. 113). Benedetti and Searles' approach to psychosis psychotherapy is to help the person exchange the confusion and entanglement with others in the world of the patient with an unconscious therapeutic symbiosis with the therapist. Searles recommended that therapists do not offer transference interpretations outside of the phase of therapeutic symbiosis. He also believed that part of the reason why the work took so long was because both therapist and patient defended against the growing emotional closeness exemplified in the phase of therapeutic symbiosis. Benedetti advises the therapist against incorporating the patient through transference interpretations, but rather to enter into the terrifying images of the patient to make them her or his own. The therapeutic "mirror" gives back to the patient a coherent, positive image of her or his potential self.

One of the primary goals in this form of psychotherapeutic intervention, which is long-term in nature, is to facilitate the person's capacity for forming secure attachments, since the latter is correlated with better affect regulation (Bateman & Fonagy, 2004) as well as overall physical and emotional health (Carter et al., 2005 ; Carter, 2007; Cacioppo & Patrick, 2008). Attachment is from one perspective, an attempt at controlling annihilation anxieties. Cozolino (2002) noted: "Attachment is, at its primitive biological core, a means of survival and hence a means of controlling anxiety" (p. 182). Security of attachment brings about a cascade of molecular biological events impacting on epigenetic processes and gene expression, resulting in a greater capacity for affect and stress regulation. However, as Shakespeare's Hamlet laments "ay, there's the rub!"- emotional closeness for many individuals, particularly for those with psychotic disorders, brings with it significant threats of interpersonal entrapment, self-other boundary dissolution, shameful humiliation, fears of abandonment, social subordination and feelings of being victimized, colonized and controlled (Fowler et al., 2006; Birchwood et al., 2009; Williams, 2010).

The relational psychotherapist is closely attuned to the complexities of helping individuals achieve greater capacities for forming more secure attachments. It is hoped that the formation of secure attachments may be neuroprotective and potentially reverse some of the neurobiological and psychosocial consequences of chronic social fear and isolation, and indirectly reduce the intensity of such psychotic symptoms as hallucinations and delusions (Hoffman, 2007). This might be expressed neurobiologically as greater stress resilience (Ozbay et al., 2010), including, but not limited to: increased brain-derived neurotrophic factor and neurogenesis; a more optimal balance between CRF (corticotrophin-releasing factor) type 1 and type 2 receptors (the former is anxiogenic and the latter, anxiolytic); increased neuropeptide Y and galanin expression; increased DHEA (dehydroepiandrosterone) and allopregnanolone (a neuroactive steroid) serving to terminate excessive hypothalamic-pituitary-adrenal axis responses to stress thereby decreasing hypothalamic corticotrophin-releasing factor (CRF), pituitary adrenocorticotropic hormone (ACTH) and adrenal cortisol expression; increased glucocorticoid receptor expression in the hippocampus supporting a neuroendocrine-hippocampal negative feedback loop and homeostatic control of cortisol binding; increased synaptogenesis and dendritic branching, etc. In regard to the latter, acute and chronic stress can cause a remodeling (i.e., retraction for the most part) of synapses and dendrites in the amygdala, hippocampus and prefrontal cortex.

Hart (2011), in speaking about the role of attachment in psychotherapy from a neuropsychodynamic perspective, noted:

“In the psychotherapeutic relationship the therapist seeks to alter the microanatomy of the client’s brain. When an autonomic or limbic connection has been established as a neural pattern, it takes an autonomic or limbic connection [“limbic resonance”] to change it. The integration and reintegration of neural circuits require the nervous system to connect and

engage in a field of resonance with another nervous system. Successful limbic attunement enables the nervous system to develop flexibility and integrate neural patterns that spread hierarchically throughout the brain. Dyadic communication makes it possible to create resonance and coherence within the nervous system" (p. 290).

Relational psychosis psychotherapy is built primarily on contributions from such attachment-oriented psychoanalysts such as Christian Muller, Gaetano Benedetti (Benedetti, 1987; Koehler, 2003) and Otto Will (Sacksteder et al., 1987), contemporary relational psychoanalysis, attachment-based cognitive-interpersonal psychotherapies (e. g., Gumley & Schwannauer, 2006), compassion focused therapy (Gumley et al., 2010) as well as the current attempts being made by CBTp clinicians/researchers to link emotions, cognitions, trauma and the social world with the emergence and maintenance of psychotic experiences (Fowler et al., 2006; Bebbington et al., 2008). Gumley et al. (2010), in their description of Compassion Focused Therapy (CFT) for persons with serious mental disorders, noted: "Arguably...dysregulation of affect defines the core problems of schizophrenia and emotional recovery lies at the heart of functional and symptomatic recovery" (p. 186). The present author proposes that the psychobiological threats to unrelatedness which account for a large share of the neuroscience findings and suffering in the person with a severe mental disorder, can be ameliorated with psychotherapeutic approaches that place the capacity for relatedness and containment of the dual terrors of unrelatedness and emotional closeness, i.e., loss of a sense of self, at the center of their models of care. In this model, excessive hostility, envy, contemptuousness and other 'negative' emotions, are seen to arise from the more basic psychobiological threat of unrelatedness and loss of self. The relational psychotherapist attempts to not lose sight of the forest for the trees by keeping in close contact with the anxieties and terror of unrelatedness embedded in psychotic symptomatology.

References

Alanen, Y. O. (1997). Schizophrenia: Its Origins and Need-Adapted Treatment. London: Karnac Books.

Ansermet, F. & Magistretti, P. (2007). Biology of Freedom: Neural Plasticity, Experience, and the Unconscious.NY: Other Press.

Bartzokis, G. (2002). Schizophrenia: breakdown in the well-regulated lifelong process of brain development and maturation. Neuropsychopharmacology, 27: 672-683.

Bateman, A. W. & Fonagy, P. (2004). Psychotherapy for Borderline Personality Disorder: Mentalization-Based Treatment. Oxford, UK: Oxford University Press.

Bebbington, P. Fowler, D., Garety, P. Freeman, D. & Kuipers, E. (2008). Theories of cognition, emotion and the social world: missing links in psychosis. In C. Morgan, K. McKenzie & P. Fearon (Eds.), Society and Psychosis, pp. 219-237. Cambridge, UK: Cambridge University Press.

Benedetti, G. (1987). Psychotherapy of Schizophrenia. NY: New York University Press.

Benedetti, G. (1993). In G. Benedetti & P. M. Furlan (Eds.), The Psychotherapy of Schizophrenia: Effective Clinical Approaches-Controversies, Critiques and Recommendations, pp.. Seattle, WA: Hogrefe & Huber Publishers.

Bernston, G. C. & Cacioppo, J. T. (2004). Multilevel analyses and reductionism: why social psychologists should care about neuroscience and vice versa. In J. T. Cacioppo & G. C. Bernston (Eds.), Essays in Social Neuroscience, pp. 107-120. Cambridge, MA: The MIT Press.

Birchwood, M., Gleeson, J., Chanen, A., McCutcheon, L. K., et al. (2009). Emotional and personality dysfunctions in early psychosis. In H. J. Jackson & P. D. McGorry (Eds.), The Recognition and Management of Early Psychosis-A Preventive Approach: Second Edition, pp. 283-302. Cambridge, UK: Cambridge University Press.

Bolton, D. & Hill, J. (1996). Mind, Meaning, and Mental Disorder: The Nature of Causal Explanation in Psychology and Psychiatry. Oxford: Oxford University Press.

Borgwardt, S. J., Riecher-Rossler, A., Smieskova, R., McGuire, P. K. et al. (2009). Superior temporal gray and whit matter changes in schizophrenia or antipsychotic related effects? Schizophrenia Research, 113:109-110.

Brüne, M. (2003). Social cognition and behaviour in schizophrenia. In M. Brüne, H. Ribbert & W. Schiefenhövel (Eds.), The Social Brain: Evolution and Pathology, pp. 277-313. West Sussex, UK: John Wiley & Sons, Ltd.

Brüne, M. (2008). Textbook of Evolutionary Psychiatry: The Origins of Psychopathology. Oxford, UK: Oxford University Press.

Bureau, J.-F., Martin, J. & Lyons-Ruth, K. (2010). Attachment dysregulation as hidden trauma in infancy: early stress, maternal buffering and psychiatric morbidity in young

adulthood. In R. A. Lanius, E. Vermetten & C. Pain (Eds.), The Impact of Early Life Trauma on Health and Disease: The Hidden Epidemic, pp. 48-56. Cambridge, UK: Cambridge University Press.

Burns, J. (2007). The Descent of Madness: Evolutionary origins of Psychosis and the Social Brain. London: Routledge.

Cacioppo, J. T. & Bernsten, G. G. (EDs.) (2004). Essays in Social Neuroscience. Cambridge, MA: The MIT Press.

Cacioppo, J. T. & Patrick, W. (2008). Loneliness: Human Nature and the Need for Social Connection. New York: W. W. Norton & Company.

Carter, C. S., Ahnert, L., Grossmann, K. E., Hrdy, S. B., et al. (Eds.) (2005). Attachment and Bonding: A New Synthesis. Cambridge, MA: The MIT Press.

Carter, C. S. (2007). Neuropeptides and the positive effects of social bonds. In E. Harmon-Jones & P. Winkielman (Ed.), Social Neuroscience: Integrating Biological and Psychological Explanations of Social Behavior, pp. 425-438. New York: The Guilford Press.

Cicchetti, D. (2010). A developmental psychopathology perspective on bipolar disorder. In D. J. Miklowitz & D. Cicchetti (Eds.), Understanding Bipolar Disorder: A Developmental Psychopathology Perspective, pp. 1-32. New York: The Guilford Press.

Ciompi, L. (1988). The Psyche and Schizophrenia: The Bond between Affect and Logic. Cambridge, MA: Harvard University Press.

Cozolino, L. J. (2002). The Neuroscience of Psychotherapy: Building and Rebuilding the Human Brain. New York: W. W. Norton & Company.

Davoine, F. & Gaudilliere, J.-M. (2004). History Beyond Trauma: Whereof one cannot speak, thereof one cannot stay silent. New York: Other Press.

DeBellis, M. D. (2010). The neurobiology of child neglect. In R. Lanius, E. Vermetten & C. Pain (Eds.), The Impact of Early Life Trauma on Health and Disease: The Hidden Epidemic, pp. 123-132. Cambridge, UK: Cambridge University Press.

der Heiden, W. & Häfner, H. (2011). Course and outcome. In D. R. Weinberger & P. J. Harrison (Eds.), Schizophrenia: Third Edition, pp. 104-141. Oxford, UK: Wiley-Blackwell.

de Weijer, A. D., Mandl, R. C. W., Diederen, S. F. W., Neggers, R. S. et al. (2011). Microstructural alterations of the arcuate fasciculus in schizophrenia patients with frequent auditory verbal hallucinations. Schizophrenia Research, 130: 68-77.

Eisenberg, L. (2004). Social psychiatry and the human genome: contextualizing heritability. British Journal of Psychiatry, 184: 101-103.

Epel, E. S., Blackburn, E. H., Lin, J., Dhabarr, F., Adler, N. E., Morrow, J. D. & Cawthon, R. M. (2004). Accelerated telomere shortening in response to life stress. Proceedings of the National Academy of Sciences, 101: 17312-17315.

Fischman, H. K. & Kelly, D. D. (1999). Chromosomes and stress. International Journal of Neuroscience, 99: 201-219.

Fischman, H. K., Pero, R. W. & Kelly, D. D. (1996). Psychogenic stress induces chromosomal and DNA damage. International Journal of Neuroscience, 84: 219-227.

Fonagy, P. (2003). The interpersonal interpretive mechanism: The confluence of genetics and attachment theory in development. In V. Green (Ed.), Emotional Development in Psychoanalysis, Attachment Theory and Neuroscience: Creating Connections, 107-126. New York: Brunner-Routledge.

Ford, J. M., Roach, B. J., Faustman, W. O. & Mathalon, D. H. (2007). Synch before you speak: auditory hallucinations in schizophrenia. American Journal of Psychiatry, 164: 458-466.

Ford, J. D. (2009). Neurobiological and developmental research: Clinical implications. In C. A. Courtois & J. D. Ford (Eds.), Treating Complex Traumatic Stress Disorders: An Evidence-Based Guide, pp. 31-58. NY: The Guilford Press.

Ford, J. D. (2010). Complex adult sequelae of early life exposure to psychological trauma. In R. A. Lanius, E. Vermetten & C. Pain (Eds.), The Impact of Early Life Trauma on Health and Disease: The Hidden Epidemic, pp. 69-76. Cambridge, UK: Cambridge University Press.

Fowler, D., Freeman, D., Steel, C., Hardy, A. et al. (2006). The catastrophic interaction hypothesis: how do stress, trauma, emotion and information processing abnormalities lead to psychosis? In W. Larkin & A. P. Morrison (Eds.), Trauma and Psychosis: New Directions for Theory and Therapy, pp. 101-124. London: Routledge.

Francis, R. C. (2011). Epigenetics: The Ultimate Mystery of Inheritance. New York: W. W. Norton & Company.

Freeman, H. & Stansfeld (Eds.) (2008). The Impact of the Environment on Psychiatric Disorder. London: Routledge.

Frith, C. (2004). Schizophrenia is a disorder of consciousness. In C. McDonald et al. (Eds.), Schizophrenia: Challenging the Orthodox, pp. 145-152. London: Taylor & Francis.

Fromm, M. G. (1989). Disturbances of self in the psychoanalytic setting. In M. G. Fromm & B. L. Smith (Eds.) The Facilitating Environment: Clinical Applications of Winnicott's Theory, pp. 489-515. Madison, CT: International Universities Press, Inc.

Fromm, M. G. (2011). Transmission of trauma and treatment resistance. In E. M. Plakun (Ed.), Treatment Resistance and Patient Authority: The Austen Riggs Reader, pp. 80-96. New York: W. W. Norton & Company.

Fromm-Reichmann, F. (1990). Loneliness. Contemporary Psychoanalysis, 26:305-329.

Garfield, D. A. S. (1995). Unbearable Affect: A Guide to the Psychotherapy of Psychosis. New York: Wiley.

Garver and Christensen (2005) -GET REFERENCE

Gaudilliere, J.-M. & Davoine, F. (2009). The contributions of some French psychoanalysts to the clinical and theoretical approaches to transference in the psychodynamic treatment of psychosis. In Y. O. Alanene, M. Gonzalez de Chavez, A.-L. Silver & B. Martindale (Eds.), Psychotherapeutic Approaches to Schizophrenic Psychoses: Past, Present and Future, pp. 137-144. London: Routledge.

Gedo, J. E. (2005). Psychoanalysis as Biological Science: A Comprehensive Theory. Baltimore, MD: The Johns Hopkins University Press.

Gons, R. A. R., van Norden, A. G. W., de Laat, K. F., van Oudheusden, L. J. B. et al. (2011). Cigarette smoking is associated with reduced microstructural integrity of cerebral white matter. Brain, 134 (7): 2116-2124.

Green, V. (Ed.) (2003). Emotional Development in Psychoanalysis, Attachment Theory and Neuroscience: Creating Connections.NY: Brunner-Routledge.

Gumley, A. & Schwannauer, M. (2006). Staying Well After Psychosis: A Cognitive Interpersonal Approach to Recovery and Relapse Prevention. West Sussex, UK: John Wiley & Sons, Ltd.

Gumley, A., Braehler, C., Laithwaite, H., MacBeth, A. & Gilbert, P. (2010). A compassion focused model of recovery after psychosis. International Journal of Cognitive Therapy, 3 (2): 186-201.

Harrison, P. J., Lewis, D. A. & Kleinman, J. E. (2011). Neuropathology of schizophrenia. In D. R. Weinberger & P. J. Harrison (Eds.), Schizophrenia: Third Edition, pp. 372-392. Oxford, UK: Wiley-Blackwell.

Hart, S. (2011). The Impact of Attachment: Developmental Neuroaffective Psychology. New York: W. W. Norton & Company.

Hofer, M. A. (2003). The emerging neurobiology of attachment and separation: How parents shape their infant's brain and behavior. In S. W. Coates, J. L. Rosenthal & D. S. Schechter (Eds.), September 11: Trauma and Human Bonds, pp. 191-209. Hillsdale, NJ: The Analytic Press.

Hoffman, K. (2009). German-speaking Central Europe-Part 1: The development of psychosis psychotherapy in Switzerland. In Y. O. Alanene, M. Gonzalez de Chavez, A.-L.

Silver & B. Martindale (Eds.), Psychotherapeutic Approaches to Schizophrenic Psychoses: Past, Present and Future, pp. 108-123. London: Routledge.

Hoffman, R. E. (2007). A social deafferentation hypothesis for induction of active schizophrenia. Schizophrenia Bulletin, 33 (5): 1066-1070.

Holmes, J. (1993). Attachment theory: a biological basis for psychotherapy? The British Journal of Psychiatry. 163: 430-438.

Hopper, K., Harrison, G., Janca, A. & Sartorius, N. (Eds.) (2007). Recovery from Schizophrenia-An International Perspective: A Report from the WHO Collaborative Project, The International Study of Schizophrenia. Oxford, UK: Oxford University Press.

Hundert, E. M. (1992). The brain's capacity to form delusions as an evolutionary strategy for survival. In M. Spitzer et al. (Eds.), Phenomenology, Language & Schizophrenia, pp. 346-354. New York: Springer-Verlag.

Kandel, E. R. (2005). Psychiatry, Psychoanalysis, and the New Biology of Mind. Washington, DC: American Psychiatric Publishing, Inc.

Keysers, C. & Gazzola, V. (2009). Unifying social cognition. IN J. A. Paneda (Ed.), Mirror Neuron Systems: The Role of Mirroring Processes in Social Cognition, pp. 3-37. New York: Springer.

Klein, M. (1993). On the sense of loneliness (1963). In Envy and Gartitude and Other Works: 1946-1963, pp. 300-313. London: Karnac Books and the Institute of Psycho-Analysis.

Koehler, B. (2003). Interview with Gaetano Benedetti, M. D. The Journal of the American Academy of Psychoanalysis and Dynamic Psychiatry, 31 (1): 75-87.

Koehler, B. (1997). The Emergence and Evolution of the Psychobiological Self, Its Breakdown and Restoration in Schizophrenic Psychosis: Implications for Psychotherapy and the Crucial Role of the Social Environment. Paper presented at International Symposia for the Psychotherapy of Schizophrenia, London, UK.

Kumar, A. & Ajilore, O. (2011). Structural imaging of major depression. In M. E. Shenton & B. I. Turetsky (Eds.), Understanding Neuropsychiatric Disorders: Insights from Neuroimaging, pp. 139-150. Cambridge, UK: Cambridge University Press.

Kumari, V., Fannon, D., Peters, E. R., Ffytche, D. H. et al. (2011). Neural changes following cognitive behaviour therapy for psychosis: a longitudinal study. Brain, 134: 2396-2407.

Lanius, R. A., Vermetten, E. & Pain, C. (2010). The Impact of Early Life Trauma on Health and Disease: The Hidden Epidemic. Cambridge, UK: Cambridge University Press.

Lawrie, S. M. & Pantelis, C. (2011). Structural brain imaging in schizophrenia and related populations. In Weinberger & Harrison (Eds.), Schizophrenia: Third Edition, pp. 334-352. Oxford, UK: Wiley-Blackwell.

Leffert, M. (2010). Contemporary Psychoanalytic Foundations: Postmodernism, Complexity, and Neuroscience. NY: Routledge.

Levin, F. M. (1991). Mapping the Mind: The Intersection of Psychoanalysis and Neuroscience. Hillsdale, NJ: The Analytic Press.

Lieberman, M. D. & Eisenberger, N. I. (2006). A pain by any other name (rejection, exclusion, ostracism) still hurts the same: The role of dorsal anterior cingulate cortex in social and physical pain. In J. T. Cacioppo, P. S. Visser & C. L. Pickett (Eds.) Social Neuroscience: People Thinking about Thinking People, pp. 167-187. Cambridge, MA: The MIT Press.

Mancia, M. (Ed.) (2006). Psychoanalysis and Neuroscience. NY: Springer.

Mancia, M. (2007). Feeling the Words: Neuropsychoanalytic Understanding of Memory and the Unconscious. NY: Routledge.

Meaney. M. (2004). The nature of nurture: Maternal effects and chromatin remodeling. In J. T. Cacioppo & G. C. Berntson (Eds.), Essays in Social Neuroscience, pp. 1-14. Cambridge, MA: The MIT Press.

Mentzos, S. (1993). The psychotic symptom as a substitute for an object-relationship. Consequences for therapy and therapeutic technique. In G. Benedetti & P. M. Furlan (Eds.), The Psychotherapy of Schizophrenia: Effective Clinical Approaches-Controversies, Critiques and Recommendations, pp. 107-113. Seattle, WA: Hogrefe & Huber Publishers.

Morgan, C., Charalambides, M., Hutchison, G. & Murray, R. M. (2010). Migration, ethnicity, and psychosis: Toward a sociodevelopmental model. Schizophrenia Bulletin, 36 (4): 655-664.

Morgan, C., McKenzie, K. & Fearon, P. (Eds.) (2008). Society and Psychosis. Cambridge, UK: Cambridge University Press.

Moskowitz, A., Schafer, I. & Dorahy, M. J. (2009). Psychosis, Trauma and Dissociation: Emerging Perspectives on Severe Psychopathology. West Sussex, UK: Wiley-Blackwell.

Müller, C. (date?). The schizophrenic and his family. In (?).

Müller, C. (1972). The problem of resistance to psychotherapy of schizophrenic patients. In D. Rubinstein & Y. O. Alanen (Eds.), Psychotherapy of Schizophrenia. Amsterdam: Excerpta Medica.

Müller, C. (1978). The psychotherapy of schizophrenia. In H. B. Denber (Ed.), Schizophrenia: Theory, Diagnosis, and Treatment, pp. 93-103. Basel: Marcel Dekker, Inc.

Müller, C. (1984). Psychotherapy in schizophrenia: the end of the pioneers' period. Schizophrenia Bulletin, 10 (4): 618-620.

Owen, M. J., Craddock, N. & Jablensky, A. (2010). The genetic deconstruction of psychosis. In C. A. Tamminga, P. J. Sirovatka, D. A. Regier, & J. van Os (Eds.), Deconstructing Psychosis: Refining the Research Agenda for DSM-V, pp. 69-82. Arlington, VA: American Psychiatric Association.

Ozbay, F., Sharma, V., Kaufman, J., McEwen, Charney, D. & Southwick, S. (2010). Neurobiological factors underlying psychosocial moderators of childhood stress and trauma. In R. Lanius, E. Vermetten & C. Pain (Eds.), The Impact of Early Life Trauma on Health and Disease: The Hidden Epidemic, pp. 189-199. Cambridge, UK: Cambridge University Press.

Pally, R. (2000). The Mind-Brain Relationship. London: Karnac Books.

Panksepp, J. (1998). Affective Neuroscience:The Foundations of Human and Animal Emotions. NY: Oxford University Press.

Parent, C., Zhang, T.-Y., Caldji, C., Bagot, R., et al. (2010). Maternal care and individual differences in defensive responses. In K. A. Dodge (Ed.), Current Directions in Child Psychopathology, pp. 37-52. Boston: Allyn & Bacon.

Petronis, A. (2004). Schizophrenia, neurodevelopment, and epigenetics. In M. S. Keshavan, J. L. Kennedy & R. M. Murray (Eds.), Neurodevelopment and Schizophrenia, pp. 174-190. Cambridge, UK: Cambridge University Press.

Petronis, A. (2010). Epigenetic alterations of DNA may help explain the mystery of schizophrenia and other psychiatric illnesses. "Breakthroughs: How NARSAD Research Has Led to Results and Results Are Leading to Cures." Downloaded on 7.20.10 from NARSAD website: http://www.narsad.org/userFiles/breakthroughs_V1N1.pdf

Quinodoz, J.-M. (2008). Listening to Hanna Segal: Her Contributions to Psychoanalysis. London: Routledge.

Reuter-Lorenz, P. A., Baynes, K., Mangun, G. R. & Phelps, E. A. (Eds.) (2010). The Cognitive Neuroscience of Mind: A Tribute to Michael Gazzaniga. Cambridge, MA: The MIT Press.

Rosenfeld, H. (1987). Impasses and Interpretation: Therapeutic and Anti-Therapeutic Factors in the Psychoanalytic Treatment of Psychotic, Borderline, and Neurotic Patients. London: Tavistock/Routledge.

Sacksteder, J. L., Schwartz, D. P. & Akabane, Y. (Eds.) (1987). Attachment and the Therapeutic Process: Essays in Honor of Otto Allen Will, Jr., M. D. Madison, CT: International Universities Press, Inc.

Sandin, B. (1993). When being is not to be. In G. Benedetti & P. M. Furlan (Eds.), The Psychotherapy of Schizophrenia: Effective Clinical Approaches-Controversies, Critiques and Recommendations, pp. 23-27. Seattle, WA: Hogrefe & Huber Publishers.

Sarwer-Foner, G. J. (1997). The humanity of the schizophrenic patient. In H. D. Brenner, W. Böker & R. Genner (Eds.), Towards a Comprehensive Therapy for Schizophrenia, pp. 262-272. Bern, Switzerland: Hogrefe & Huber Publishers.

Sasso, G. (2007). The Development of Consciousness: An Integrative Model of Child Development, Neuroscience and Psychoanalysis. London: Karnac.

Searles, H. F. (1979). Countertransference and Related Subjects: Selected Papers. NY: International Universities Press, Inc.

Schneiderman, J. S., Hazlett, E. A., Chu, K.-W., Zhang, J. et al. (2011). Brodmann area analysis of white matter anisotropy and age in schizophrenia

Schore, A. N. (2003a). Affect Regulation and Disorders of the Self. NY: W. W. Norton & Company.

Schore, A. N. (2003b). Affect Regulation and the Repair of the Self. NY: W. W. Norton & Company.

Shah, J., Mizrahi, R. & McKenzie, K. (2011). The four dimensions: a model for the social aetiology of psychosis. British Journal of Psychiatry, 199: 11-14.

Siirala, M. (1983). From Transfer to Transference: Seven Essays on the Human Predicament. Helsinki, Finland: Therapeia Foundation.

Strakowski, S. M. (2011). Structural imaging of bipolar illness. In M. E. Shenton & B. I. Turetsky (Eds.), Understanding Neuropsychiatric Disorders: Insights from Neuroimaging, pp. 93-108. Cambridge, UK: Cambridge University Press.

Sullivan P. F., Owen, M. J., O'Donovan, M. C. & Freedman, R. (2006). Genetics. In A. Lieberman, T. S. Stroup & D. O. Perkins (eds.), Textbook of Psychiatry, pp. 39-53. Washington, DC: American Psychiatric Publishing, Inc.

Teicher, M. H., Rabi, K., Sheu, Y.-S, Seraphin, S. B. et al. (2010). Neurobiology of childhood trauma and adversity. In R. Lanius, E. Vermetten & C. Pain (Eds.), The Impact of Early Life Trauma on Health and Disease: The Hidden Epidemic, pp. 112-132. Cambridge, UK: Cambridge University Press.

Teicher, M. H., Samson, J. A., Tomoda, A., Ashy, M. & Andersen, S. L. (2006). Neurobiological and behavioral consequences of exposure to childhood traumatic stress. In B. B. Arnetz & R. Ekman (Eds.), Stress in Health and Disease, pp. 180-195. Weinheim: Wiley-VCH.

Tienari, P. , Wynne, L. C., Sorri, A., Lahti, I., et al. (2004). Genotype-environment interaction in schizophrenia-spectrum disorder. British Journal of Psychiatry, 184: 216-222.

van der Kolk, , B. A. & d'Andrea, W. (2010). Towards a developmental trauma disorder diagnosis for childhood interpersonal trauma. In R. A. Lanius, E. Vermetten & C. Pain (Eds.), The Impact of Early Life Trauma on Health and Disease: The Hidden Epidemic, pp. 57-68. Cambridge, UK: Cambridge University Press.

Viamontes, G. I. & Beitman, B. D. (2009). Brian processes informing psychotherapy. In G. O. Gabbard (Ed.), Textbook of Psychotherapeutic Treatments, pp. 781-808. Washington, DC: American Psychiatric Publishing, Inc.

Wahlberg, K. E., Wynne, L. C., Oja, H., Keskitalo, P. et al. (1997). Gene-environment interaction in vulnerability to schizophrenia: findings from the Finnish Adoptive Family Study of Schizophrenia. American Journal of Psychiatry, 154: 355-362.

Weinberger, D. & Berger, G. (2009). Genetic vulnerability. In H. J. Jackson & P. D. McGorry (Eds.), The Recognition and Management of Early psychosis-A Preventive Approach: Second Edition, pp. 31-46. Cambridge, UK: Cambridge University Press.

Weinberger, D. R. & Levitt, P. (2011). Neurodevelopmental origins of schizophrenia. In Weinberger & Harrison (Eds.), Schizophrenia: Third Edition, pp. 393-412. Oxford, UK: Wiley-Blackwell.

Weinberger, D. R. & Harrison, P. J. (Eds.) (2011). Schizophrenia: Third Edition. Oxford, UK: Wiley-Blackwell.

Whitford, T. J., Kubicki, M. & Shenton, M. E. (in press). Diffusion tensor imaging (DTI), schizophrenia and discrete brain regions. US Psychiatric Rev.

Will, O. A. (1987). Human relatedness and the schizophrenic reaction. In J. L. Sacksteder, D. P. Schwartz & Y. Akabane (Eds.), Attachment and the Therapeutic Process: essays in Honor of Otto Allen Will, Jr., M. D., pp. 263-297. Madison, CT: International Universities Press, Inc.

Williams, P. (2010). Invasive Objects: Minds Under Siege. New York: Routledge.

Zorumski, C. F. & Rubin, E. H. (2011). Psychiatry and Clinical Neuroscience: A Primer. Oxford, UK: Oxford University Press.