Social Adversity in the Etiology of Psychosis: A Review of the Evidence

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Despite increasing evidence for the role of psychosocial factors in the onset and continuance of psychosis, the experiences involved are still largely considered the result of a biogenetic anomaly for which medication is the first-line treatment response. This review summarizes the extensive literature demonstrating that adverse events involving trauma, loss, stress, and disempowerment have a central etiological role in psychosis. Evidence is further presented to show that many neurological changes traditionally considered indicative of a disease process can in fact be accounted for as secondary effects to the physiology of stress or the residual of long-term neuroleptic prescription. Particular emphasis is given to the traumagenic neurodevelopmental model of psychosis, which illustrates how many of the structural and functional cerebral anomalies observed in adult patients with psychosis (including dopamine dysregulation, atrophy, hippocampal damage, and overactivity of the hypothalamic–adrenal–pituitary axis) closely correspond to those in the brains of abused children. Finally, research is discussed that demonstrates how trauma may manifest in characteristic symptoms of psychosis, particularly hallucinations and delusions. It is suggested that if social adversities are of central importance in psychosis, then psychotherapy that addresses the long term sequelae of those adversities should be considered an essential aspect of treatment.

KEYWORDS: psychosis; schizophrenia; trauma; childhood abuse; traumagenic neurodevelopmental model

INTRODUCTION

Possibly more than any other psychiatric diagnoses, psychosis and "schizophrenia"[1] are saturated with the terminology of illness. Educational

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[1] It should be noted when discussing the etiology of schizophrenia that the construct has notoriously poor reliability and validity in that it fails to meet accepted scientific standards of

literature, pharmaceutical advertisements, and public information resources overwhelmingly emphasise biological factors that necessitate medical solutions. As of 2015, the National Institute of Mental Health (NIMH) website describes schizophrenia as "a chronic, severe, and disabling brain disorder," repeatedly referring in subsequent text to a "disease" and "illness" which is most effectively managed with pharmaceuticals (NIMH, 2015). Neither the NIMH nor the UK's National Health Service (NHS, 2014) websites cite the considerable research that implicates traumatic or adverse events as causes of psychosis.

This review will draw on a substantial literature to show how psychosocial understandings of psychosis are robustly evidence based and offer a compelling alternative to reductionist biomedical models. This is far from being a novel position. Indeed, in an early treatise on the nature of schizophrenia, the author of the concept, Eugene Bleuler (1911/1960) himself conceded that the new construct might be "the effect of a particularly powerful psychological trauma on a very sensitive person rather than . . . a disease in the narrow sense of the word" (p. 300). The political, historical, social, and economic contexts in which biomedical accounts have come to dominate so successfully are complex and numerous, and are beyond the scope of this article (see Kinderman, 2014; Read & Dillon, 2013). However, they have ultimately created a sclerotic and dominant framework that translates into a narrow model of biological treatment that offers only negligible success (Hutton, Weinmann, Bola & Read, 2013; Whitaker, 2010). Conversely, this review will demonstrate that psychological approaches are highly suitable for people experiencing psychosis on the grounds that distress, despair, and disorientation can often be traced to psychosocial causes. In addition to describing how life adversity can manifest in clinical presentation, it will also be argued that one of the biomedical model's major mainstays and justifications the concept of the "schizophrenic brain"—is not explicable in terms of a carnivorous disease process, but rather as a result of environmental insult; both adversity exposure and chronic medication use.

ADVERSITY AND PSYCHOSIS

After decades of doubt and denial, the claim that adverse life events (particularly, but not exclusively, childhood abuse) are inextricably linked

verification, and has limited usefulness for predicting and interpreting real-world outcomes (for review, see Read, 2013a). At the very least, this means a limited guarantee that studies reporting on schizophrenia are actually examining the same thing, the concept being "so diffuse . . . as to be unusable in a scientific context" (Bannister, 1968, p. 181).

to psychosis has moved "from heresy to certainty" (Read, 2013b, p. 249; see also Read & Bentall, 2012; Read, Dillon, & Lampshire, 2015). In the past 15 years a rapidly accruing literature, derived from a variety of sampling and assessment protocols, different patient and non-patient populations, and assorted cross-sectional, retrospective, and prospective research designs, has repeatedly shown that adversity exposure is linked with both psychotic symptoms, and schizophrenia itself. Indeed, for childhood sexual abuse (CSA) alone, this is a relationship which "is at least as strong as, and may be stronger than, that with other mental disorders" (Bebbington, 2009, p. 290). There are now numerous reviews summarising this evidence (e.g., Hammersley, Read, Woodall, & Dillon, 2008; Larkin & Read, 2012; Read, 2013b; Read, Bentall, & Fosse, 2009; Read, Fink, Rudegeair, Felitti, & Whitfield, 2008; Read, van Os, Morrison, & Ross, 2005; Skehan, Larkin, & Read, 2012). Two meta-analyses, which are more robust than narrative reviews owing to their rigorous inclusion criteria and analytical procedures, have also been published: one examining psychotic symptoms in general (Varese et al., 2012), and one with individuals diagnosed with schizophrenia (Matheson et al., 2013). The first screened 736 articles, retaining 41 of the best designed. When results were pooled, individuals with a history of childhood trauma (child sexual abuse, physical abuse, emotional abuse, neglect, bullying, parental death) were shown to be 2.8 times more likely to develop psychotic symptoms than those who had not. The second meta-analysis retained 25 studies from a search result of 1104, and found that rates of childhood adversity (including CSA, physical abuse, emotional abuse, neglect, witnessing domestic violence, and loss events) were 3.6 times greater in people diagnosed with schizophrenia relative to "healthy controls," at a high level of significance ($p<0.00001$), and comparable to that observed in samples of people diagnosed with affective psychosis, depression and personality disorders (although adversity in schizophrenia was lower compared to people diagnosed with dissociative disorders and posttraumatic stress disorder).

Large-scale population studies have shown that associations between adversity and psychotic experience remain significant when controlling for possible confounders, including: family history of psychosis and other mental health problems (which negates the notion that psychosis only occurs in those genetically predisposed), age, sex, ethnicity, marital status, exposure to discrimination, other psychiatric diagnoses, education level, neuroticism, and substance use (Janssen et al., 2004; see also Bentall, Wickham, Shevlin, & Varese, 2012; Morgan et al., 2014; Schreier et al., 2009; Shevlin, Dorahy, & Adamson, 2007; Shevlin, Houston, Dorahy, &

Adamson, 2008; Spauwen, Krabbendam, Lieb, Wittchen, & van Os, 2006; van Nierop et al., 2014). Furthermore, the association has repeatedly demonstrated a dose-response relationship; that is, the likelihood of psychosis increases relative to the extent of adversity exposure (see Read et al., 2008, 2009; Varese et al., 2012 for reviews). For example, a large-scale analysis of the United States National Comorbidity Survey ([NCS]; n= 5782) and the British Psychiatric Morbidity Survey ([BPMS]; n=8580) examined psychosis risk in response to five traumatic events: serious illness, injury or assault, bullying, violence at work, domestic violence, and sexual abuse (Shevlin et al., 2008). Experiencing two of these traumas was associated with a significantly heightened psychosis risk of 3.37 (NCS) and 4.31 times (BPMS) respectively, after adjusting for numerous demographic variables as well as depression and substance use. Individuals exposed to all five traumas were found to be 30.16 (NCS) and 192.97 (BPMS) times more likely to have become psychotic than those with no trauma history.

Despite much emphasis on childhood abuse, this is by no means the only environmental adversity associated with psychosis. Other cited factors (Larkin & Morrison, 2006; Read, 2013a; Scott, Chant, Andrews, Martin, & McGrath, 2007) include discrimination, witnessing domestic violence, prenatal stress, war trauma, torture, adulthood rape and physical assault, excessive marijuana use in adolescence (in some instances this may represent attempts to self-medicate posttraumatic symptoms, see Alemany et al., 2014), and disturbed attachment relationships with one's caregivers, including abandonment, being the result of an unwanted pregnancy, being raised in institutional care, dysfunctional parenting (often intergenerational), and parental death or separation. Another factor receiving significant attention is poverty and inequality (Longden, Sampson & Read, 2015. Read, Johnstone & Taitimu, 2013). Material deprivation is strongly associated with greater incidence of childhood maltreatment (Drake & Pandey, 1996; Gillham et al., 1998; Lee et al., 1999) and chronic stress dysregulation (Evans & Kim, 2007). In turn, complex interactions among inequality, deprivation, stress, discrimination, mistrust, and lack of social support, have been proposed as predictors of both affective and non-affective psychosis (Wickham, Taylor, Shevlin & Bentall, 2014).

Reliability of Abuse Disclosures

Although the veracity of research linking trauma and psychosis has been questioned on the grounds that abuse disclosures by patients with psychosis are unreliable (e.g., Susser & Widom, 2012), this is not an

evidence-based argument. On the contrary, accounts of adversity amongst groups with complex mental health problems have proven sufficiently valid to justify the use of self-report measures (e.g., Dill et al., 1991; Goodman et al., 1999; Herman & Schatzow, 1987; Meyer et al., 1996). One study found that erroneous reports of sexual victimization are no different between patients diagnosed with schizophrenia and the general population (Darves-Bornoz et al., 1995). Important evidence in this area has been provided by Fisher et al. (2011), who examined retrospective disclosures of childhood abuse (CSA, physical abuse, neglect) amongst 84 adult patients diagnosed with psychotic disorders. The accounts demonstrated high concurrent validity with a measure of parental bonding, good convergent validity with clinical case notes, and stability over a seven year period. There was no association between severity of psychotic symptoms and reports of abuse, thus negating the proposal that abuse disclosures in the context of psychosis should be discredited as a sign of mental disturbance.

Psychological Mechanisms

The increasing recognition that adversity and psychosis are causally related has led to increased research as to how this may be so. This review pays particular attention to literature on biological factors, as such research provides a powerful demonstration of how many structural and functional brain changes used to evidence a disease model can be accounted for in terms of psychosocial stress. However, considerable work has also been conducted using psychological frameworks. In this respect it is important that such endeavours are not perceived as offering competing accounts of the same phenomena. On the contrary, a genuine integration of biological, psychological, and social elements promises a much more sophisticated understanding of psychosis—and consequently, more promising avenues for intervention (Read et al., 2009).

An invited editorial in the *British Journal of Psychiatry* outlined a number of mechanisms shown to mediate between trauma and psychosis, including attachment, dissociation, psychodynamic defences, problematic coping responses, impaired social support, and re-victimization (Read & Bentall, 2012). Other candidate processes include behavioural sensitization and dysfunctional cognitive processes (Read 2013a). A discussion of this extensive literature is beyond the scope of the current article, although the reader is directed to existing reviews, such as those by Larkin and Morrison (2006), Moskowitz, Schäfer, and Dorahy (2008), Read (2013a), and Read et al. (2005, 2008). In isolation each process offers only a partial

account of the links between adversity and psychosis, and none will have equivalent relevance for all individuals diagnosed with psychosis. Furthermore, some models attempt to capture similar mechanisms with different terminology: an intrusive, de-contextualised memory of abuse, for example, might be deemed "projection" by a psychoanalyst, "impaired source monitoring" by a cognitive psychologist, or "depersonalisation" by a dissociative theorist (Read, 2013a). Nevertheless, a mutual theme is the conceptualisation of the psychological aftermath of adversity (including complex experiences like hearing voices, or extremely paranoid beliefs) as a meaningful way of responding to, or coping with, distressing and overwhelming events. This is a concept that reoccurs in survivor testimony (e.g., Bullimore, 2010; Coleman, 2011; Comans 2011; Longden, 2013) and is powerfully described by Jacqui Dillon, the chair of the English Hearing Voices Network (Dillon, 2011; p. 142):

> The survival strategies that I unconsciously developed as a child created an illusion of control, an illusion that I had some agency over what happened to me. Despite my abject helplessness, I utilized all the resources available to me at the time—my mind, my body, my spirit—and I fought for my life.

Genetic Factors

Both the NIMH and NHS websites emphasize a strong genetic component for schizophrenia. In fact there is no conclusive evidence for this hypothesis, and while genetic research dominates media coverage, academic publications, and funding awards, 30 years of predictions have met with a striking failure to identify (or, if identified, to replicate) relevant candidate genes. In a famous editorial, Tim Crow, fellow of the Royal Colleges of Physicians and Psychiatrists (and himself an early promoter of schizophrenia as a genetic anomaly), likened this search to emptying a pond—"one would 'drain the pond dry' and there would be the genes." (Crow, 2008, p. 1682) However, he concluded, "the pond is empty" (Crow, 2008, p. 1682). Accessible summaries of this literature are provided by Bentall (2009), Fosse, Joseph, and Jones (2016) and Joseph (2003, 2006, 2013). They delineate some major flaws and limitations in genetics research: for example, the considerable methodological problems in the schizophrenia twin studies, heritability coefficients that are often unreliable and become inflated with environmental effects, and associations between psychosis and common alleles that are fare weaker than associations between psychosis and trauma.

A particularly shocking demonstration of the limitations of the genetic argument is an epidemiological analysis of the prevalence and incidence of schizophrenia in Nazi Germany, wherein it is estimated between 220,000 and 269,500 citizens with the diagnosis were forcibly sterilized or murdered by the Nazi regime (Read & Masson, 2013; Torrey & Yolken, 2010). Contrary to everything that is known about genetic, heritable conditions, the rates of schizophrenia diagnoses in Germany did not diminish after the war but increased. The analysis showed this atrocity provided proof against the very reasoning used to instigate it.

This is not to imply that genetic factors have no relevance at all. However, genes encompass all human variation and experience, and are not the sole province of disease, disorder, and brain abnormality. Suggestions that an experience such as "voice hearing" is genetic say nothing about whether or not it is a symptom of a medical illness. Such complex interactions warrant more sophisticated attention, such as epigenetics, in which gene transcription is strongly influenced by environmental circumstances. The role of factors including poverty and abuse in altering genes during brain maturation—and the implications of this for subsequent psychosis—have already been expounded upon (Read et al., 2009), with epigenesis deemed "a plausible mechanism by which an adverse social environment gets 'into the mind' and results in poor mental health" (Toyokawa, Uddin, Koenen, & Galea, 2012, p. 67; see also van Os, Kenis, & Rutten, 2010; van Winkel et al., 2010). As with neurological research (discussed below), a more integrated bio-psycho-social approach to genetics can undoubtedly yield a richer understanding of how biology interacts with the environment to cause psychotic experience.

NEUROLOGICAL CHANGES IN PSYCHOSIS: EVIDENCE FOR THE ROLE OF ENVIRONMENTAL FACTORS

How might formative trauma exposure account for subsequent psychosis? A principle assumption of biomedical approaches is that the neurological and biochemical abnormalities observed in adult patients have a causal etiological status, with psychological and social conflict being either dismissed as irrelevant, or minimised to the role of catalyst for underlying genetic liability. However a major difficulty with this essentialist framework—what a President of the American Psychiatric Association deemed "a bio-bio-bio model" (Sharfstein, 2005, p. 3)— is that it ignores the fact that the brain's primary function is to respond to the environment (Read et al. 2009). A natural line of enquiry when brain anomalies are identified in any population should be "*What happened to that group to*

cause this pattern of functioning?" To assume that brain differences exist in a social vacuum, and are solely and causally responsible for schizophrenia, has the same logic as suggesting neural changes during bereavement are the causes of sadness rather than the loved one's loss. This lack of context—that external events in patients' lives are largely disregarded—is a serious logical flaw in much neuroimaging research. Indeed, given what is now known about the links between life stress and psychosis, the full extent to which ignoring such variables has jeopardised data integrity is only now becoming fully apparent.

The Traumagenic Neurodevelopmental Model of Psychosis

The traumagenic neurodevelopmental (TN) model of psychosis (Read, Perry, Moskowitz, & Connolly, 2001) synthesises biological and psychological research to emphasise the similarities between structural and functional abnormalities in the brains of abused children and those of adult patients with psychosis (which, correspondingly, reflect the differences between patients with psychosis and healthy adults, and traumatised and non-traumatised children). A major premise of the TN model is that the heightened stress sensitivity consistently found in patients with psychosis is not necessarily inherited, but caused by formative exposure to abuse and neglect. This is consistent with the original conception of the stress-vulnerability model of schizophrenia (Zubin & Spring, 1977), which contended that susceptibility to stress could be *acquired* "due to the influence of trauma, specific diseases, perinatal complications, family experiences, adolescent peer interactions, and other life events" (p. 109). Therefore, environmental stressors should not be relegated to "triggers" for those genetically predisposed to psychosis, but reconceptualised as causal events.

When the TN model was proposed in 2001, evidence emphasised that detectable neurological differences between individuals diagnosed with schizophrenia and healthy adults could be conceptualised as trauma-related. These included dopamine, serotonin and norepinephrine irregularities, overactivity of the hypothalamic–adrenal–pituitary (HPA) axis, and structural differences, such as cerebral atrophy, hippocampal damage, reversed cerebral asymmetry, and ventricular enlargements. All these features are typically cited to support the disease model of schizophrenia. At least 125 publications, using a range of methodologies, have subsequently provided either indirect support or confirmation of the central premises of the TN model (Read et al., 2014). The following sections present an abridged summary of this evidence.

HPA Dysregulation. A 2008 review of neurobiological mechanisms in psychosis conclude, a "heuristically useful framework . . . is the concept of 'behavioral sensitization that stipulates that exposure to psychosocial stress— such as life events, childhood trauma, or discriminatory experiences— may progressively increase the behavioral and biological response to subsequent exposures' " (van Winkel, Stefanis, & Myin-Germeys, 2008, p. 1095 It has long been recognised that adversity exposure can stimulate a cascade of chronic disturbances in the responsivity of the HPA axis (e.g., De Bellis et al., 1994; Heim et al., 2008; Tarullo & Gunnar, 2006). There is a growing corpus of data outlining associations between psychotic symptoms and hyperreactivity to stress, as evidenced by HPA dysregulation (see Read et al., 2014 for review). For example, people diagnosed with psychotic disorders who had a history of childhood adversity including emotional maltreatment (Braehler et al., 2005;CSA, (Mondelli et al., 2010a) and impaired parental bonding (Pruessner, Vracotas, Joober, Pruessner, & Malla, 2013) demonstrated greater dysregulation in the stress hormone cortisol, with associations additionally observed between irregularities in cortisol secretion and the severity of positive symptoms (Belvederi Murri et al., 2012; Walder, Walker, & Lewine, 2000), disorganized symptoms (Walder et al., 2000), and cognitive deficits (Aas et al., 2011; Halari et al., 2004; Walder et al., 2000) than those in comparison groups who were not abused. A one-year longitudinal examination of 56 adolescents found that at-risk individuals who transitioned to full psychosis exhibited significantly more elevated cortisol levels than those who did not convert (Walker et al., 2010).

Other evidence for HPA axis disturbances in psychosis include enlargement of the paraventricular hypothalamic nucleus (PHN), although these findings are currently less consistent. Tognin et al. (2012) and Goldstein et al. (2007) have reported increased hypothalamic volumes in people diagnosed with schizophrenia compared to controls, with hypothalamic abnormalities positively associated with anxiety in both studies. However, although some studies have found pituitary alterations in terms of enlargement prior to psychosis transition in high-risk groups (Garner et al., 2005; Pariante, 2008; Pariante et al., 2005), increased volume in chronic psychosis compared to non-patients (Takahashi et al., 2009), and associations between illness duration and pituitary size (Habets et al., 2012; Pariante et al., 2004), other research has not replicated the same morphological pituitary changes in psychosis (Klomp et al., 2012; Nicolo et al., 2010; Upadhyaya et al., 2007).

Structural Cerebral Changes. Other structural changes that may cause HPA axis dysregulation in psychosis include abnormalities in the hippocampus, a cortical region that is essential for consolidating information from short-term to long-term memory. Reduced hippocampal volume is a well-characterized sequala of childhood maltreatment (Bremner & Narayan, 1998; Frodl et al., 2010; Teicher, Anderson, & Polcari, 2012), with imaging studies revealing that early trauma is "associated with remarkable functional and structural changes even decades later in adulthood" (Dannlowski et al., 2012, p. 286). Hippocampal pathology is also an established and prevalent observation in people diagnosed with schizophrenia, and it has been reported from both post-mortem (neurochemical, genetic, histological, morphometrical) and *in vivo* (functional and structural imaging, neuropsychological) investigations (see Harrison, 2004). Specifically, hippocampal changes in the left cortex may progress after psychosis onset (Rosoklija et al., 2000; Shepherd, Laurens, Matheson, Carr, & Green, 2012), with reduced left hippocampal volume associated with hyper-secretion of cortisol (Mondelli et al., 2010b) and increased stress sensitivity in patients with psychosis (Collip et al., 2013). In addition, exposure to childhood trauma has been found to significantly predict left hippocampal volume in individuals with first-episode psychosis (Hoy et al., 2012). Abnormalities consistent with stress-induced pathology have also been detected in hippocampal formations of patients with psychosis (Rosoklija et al., 2000); there is evidence that this population exhibits abnormally heightened regional blood flow to the left hippocampus in response to cortisol infusion when compared to matched controls (Ganguli, Singh, Brar, Carter, & Mintun, 2002).

Other cerebral changes associated with childhood trauma are diminished gray-matter volume in the frontal lobes, particularly the anterior cingulate, and the dorsolateral, medial prefrontal, and orbitofrontal regions (Cohen et al., 2006; Hart & Rubia, 2012; Thomaes et al., 2012). In terms of subsequent stress-vulnerability, animal models have demonstrated that such morphological changes in the frontal lobes also have consequences for HPA axis regulation (Holmes & Wellman, 2009). This includes the potential for childhood stress to affect the expression of glucocorticoid receptors in the frontal cortex (Chiba et al., 2012; Mizoguchi, Ishige, Aburada, & Tabira, 2003; Patel, Katz, Karssen, & Lyons, 2008), receptors which mediate the direct effects of hormones secreted in response to stress, and in turn are linked with abnormal inhibitory HPA feedback regulation (Mizoguchi et al., 2003).

Similarly, loss of gray-matter volume in frontal and prefrontal cortical regions is widely observed in patients with psychosis (Ellison-Wright & Bullmore, 2010; Tian et al., 2011; Williams et al., 2013). This includes pathology consistent with stress-induced changes in the prefrontal cortex (Benes & Berretta, 2001; Glantz & Lewis, 2000; Harrison, 2004) as well as decreases in glucocorticoid receptor expression in the dorsolateral prefrontal cortex (Sinclair, Fullerton, Webster, & Weickert, 2012; Webster, Knable, O'Grady, Orthmann, & Weickert, 2002). A recent study directly comparing abuse exposure and brain volume in 60 patients and 26 matched controls (Sheffield, Williams, Woodward, & Heckers, 2013) has found that a significant amount of variance in gray-matter volume in psychotic disorders can be accounted for by a history of sexual trauma. The association was not significant for other types of childhood maltreatment, although rates of CSA, physical abuse, emotional abuse and physical neglect were all higher in the patients with psychosis than the healthy controls.

The Dopamine System. The notion of chemical imbalance as an explanation for a range of mental health difficulties has proven to be a popular theory for justifying expenditure on pharmaceuticals rather than expend resources towards psychosocial research and interventions. Correspondingly, the dopamine hypothesis (which posits that the positive symptoms of schizophrenia are partly attributable to disturbed, hyperactive signal transduction in the dopaminergic system), is probably one of the most widely cited theories of psychosis. In clinical terms the hypothesis underlies the widespread administration of neuroleptics (which are claimed to correct dopamine dysregulation), and has been deemed "one of the most enduring ideas in psychiatry" due to its ubiquity as an explanatory illness model (Howes & Kapur, 2009, p. 562). However, the dopamine hypothesis was crafted from indirect evidence—the seemingly beneficial sedative effects of neuroleptics. On discovering their main mode of action was blocking dopamine receptors, the argument developed that schizophrenia itself must therefore result from dopamine over-activity. Thus rather than designing a therapeutic agent to treat a disorder, a disorder was hypothesised to fit the drug; and, as pointed out by Jackson (1986), is as logically tenable as claiming headaches are induced by a lack of aspirin.

The role of antipsychotic medication in creating neurological changes will be discussed more fully below, although the drugs themselves have been linked with hyperactivity in the dopamine system (Snyder, 1974). However, as with the neuroanatomical, there is also evidence that abnor-

malities in the dopamine system can be explained in terms of psychosocial stress. For example, it is known that childhood adversity may increase sensitivity in the mesocorticolimbic dopamine system (Oswald et al., 2007; Trainor, 2011; Wand et al., 2007), and that chronic early-life stress is associated with dopamine overactivity in response to adulthood stress in both animals (Cabib, Puglisi-Allegra, & Ventura, 2002) and humans (Pruessner et al., 2010). In this respect, one of the most well-evidenced abnormalities relating to dopamine transmission in psychosis—hyperactivity of striatal dopamine systems, including elevated transmitter release, and heightened presynaptic and extracellular levels (Howes & Kapur, 2009)—is consistent with research findings in the stress literature. Similarly, the finding that dopamine function in the prefrontal cortex appears lower in individuals diagnosed with schizophrenia relative to controls (Abi-Dargham et al., 2002; Meyer-Lindenberg et al., 2002) would support a model based on the effects of chronic stress. An additional finding consistent with a stress-based account of psychotic symptoms is the contention that abnormal activity in the subiculum induces dopamine hyperactivity in the striatum and midbrain (Lodge & Grace, 2006, 2011). Subiculum function is believed to influence the kind of enhanced threat perception and "aberrant salience" underlying paranoid and delusion presentations (Roiser, Howes, Chaddock, Joyce, & McGuire, 2013) and is known to be affected by childhood adversity (Teicher et al., 2012). Bentall (2009) summarises this more sophisticated approach to understanding the role of dopamine in psychosis by emphasising that dysregulation can be clearly understood when considering one of dopamine's main functions: anticipation of threat. As such, "the dopamine system becomes sensitized as a consequence of adverse experiences that predate the onset of the illness" (Bentall, 2009, p. 175).

Trauma and the Therapeutic Alliance

It is important to note that the biological correlates of adversity, while grave, are not irreversible. For example, work with children with histories of severe attachment disruption and/or deprivation found that psychotherapeutic approaches are successful in both helping to regulate physiological reactivity and enhancing the capacity of the HPA axis to cope with stress (for review see Schuengel, Oosterman, & Sterkenburg, 2009). Similar results have also been found for adults with posttraumatic stress (Jones & Moller, 2011; Olff, de Vries, Güzelcan, Assies, & Gersons, 2007) and depression and anxiety (Church, Yount, & Brooks, 2012), in which psychotherapeutic work has a demonstrably beneficial impact on cortisol

secretion. In this respect a promising avenue for psychosis is compassion-focussed therapy (CFT), which is based on theories of emotional regulation derived from evolutionary psychology and neuroscience (Gilbert 2009a-b, 2014). Compassion-focused therapy posits that hypersensitive threat processing (including social-rank threats linked with shame and stigmatisation and/or that originating from traumatic experience) can severely impair emotional regulation and reduce affiliation capacities. In addition to enhancing mentalisation and affiliative relating, it aims to help patients develop the capacity for empathic, comforting, and compassionate responding to both self and others in regulating emotion and mitigating distressing threat appraisals. Although the evidence base for compassion-focussed approaches in psychosis is an emergent one, initial results are encouraging (e.g., Braehler et al., 2013; Heriot-Maitland, Vidal, Ball & Irons, 2014; Johnson et al., 2011; Laithwaite et al., 2009; Mayhew & Gilbert, 2008).

Neuroanatomy and Antipsychotic Medication

A final relevant factor for interpreting changes in brain morphology in people diagnosed with schizophrenia is the impact of neuroleptic medication. Although largely ignored as a clinical issue during the development of first-generation antipsychotics (Reveley, 1985), it has been known for several decades that the density of brain tissue decreases relative to medication dosage (Lyon et al., 1981). In recent years more controlled and technologically sophisticated work has reinforced the claim that the drugs are causally implicated in neurodegeneration; in effect, that long-term medication use may lead to some of the neurological anomalies traditionally ascribed to psychosis itself (Moncrieff & Leo, 2010; Smieskova et al., 2009).

It has been posited that antipsychotics can create dopamine over activity (which, in its simplest terms, can be understood as a compensatory effort to overcome the inhibitory effect of the medication: Snyder, 1974). Postmortem examinations, for example, do not support the dopamine theory of schizophrenia, in that while medicated patients demonstrated elevated levels, drug-free patients exhibited normal concentrations of dopamine (Haracz, 1982; Jackson, 1986). A similar lack of results has also been reported in examinations of dopamine metabolites amongst living patients (Haracz, 1982). A heightened sensitivity in dopamine receptors has been detected, although this in turn is acknowledged to be partly a result of antipsychotic use. For example, postmortem examinations found that increases in K_D dopamine receptors (but not B_{max} binding sites) were

attributable to neuroleptics (Mackay et al., 1982). Animal models likewise demonstrated that spontaneous hyperactivity of striatal dopaminergic mechanisms was the result of chronic neuroleptic administration (Murugaiah et al., 1982).

Numerous studies have demonstrated that antipsychotics lead to reductions in gray-matter volume and enlargements in lateral ventricle volumes (see Weinmann & Aderhold, 2010) and, more equivocally, in the thalamus and the cortex (see Navari & Dazzan, 2009). Critically (and contrary to the claims of some industry-sponsored studies; e.g., Lieberman et al., 2005) both animal models and research with patients with psychosis has also confirmed that this is not an issue limited to older, first-generation drugs. For example, placebo-controlled research with primates confirmed that 18 months of treatment with olanzapine and haloperidol, at equivalent dosages to human therapeutic use, resulted in reduced volumes of between 8% and 11% across all major brain regions (Dorph-Petersen et al., 2005). Later research, also administering olanzapine and haloperidol to macaque monkeys, likewise found that exposure to both drugs resulted in a 14.6% reduction of gray-matter volume in the left parietal lobe, a lower glial cell number, higher neuron density (Konopaske et al., 2007), and a significant 20.5% lower astrocyte number (Konopaske et al., 2008). Longitudinal research with human participants has confirmed that atypical antipsychotic medication contributes to the shrinkage of brain matter (Ho, Andreasen, Ziebell, Pierson, & Magnotta, 2011). A recent meta-analysis of 30 longitudinal MRI studies (representing 1046 people diagnosed with schizophrenia, 780 controls, and a median duration of 72.4 weeks follow-up) not only support this association, but report no effect for either symptom severity or psychosis duration on neuroanatomical abnormalities (Fusar-Poli et al., 2013). The latter distinction is an important one, as it refutes a model of psychosis as progressive and neurodegenerative; i.e., that underlying disease processes are causing brain shrinkage. A more recent longitudinal analysis also found strong evidence for medication-induced brain changes, but conversely claimed that the latter is linked to psychotic relapse (Andreasen, Liu, Ziebell, Vora, & Ho, 2013). However, this interpretation of psychosis as a malignant, progressive disease has been disputed (Zipursky, Reilly, & Murray, 2013), and it should additionally be noted that Andreasen et al. did not clearly distinguish clinical deterioration from drug-induced effects (i.e., as severity increases, dosage is likely to be raised, meaning the two variables are not necessarily independent, despite being treated as such in the paper's statistical analysis). In this regard, the associations between medication dosage and clinical severity is an impor-

tant consideration for future research, as while the severity of psychotic symptoms appear to be weakly associated with cerebral shrinkage, they are significantly correlated with medication exposure (Ho et al., 2011). The difficulty in finding comparison groups who have not been medicated compounds this problem.

Taken together there is strong evidence for inferring that chronic antipsychotic consumption causes serious neurological abnormalities, and that these alterations remain significant when controlling for substance use, and the duration and severity of psychotic symptoms (Fusar-Poli et al., 2013; Ho et al., 2011). While pharmaceutical companies claim that such changes are indicative of a disease process necessitating "medical correction" (see Read, 2013c), other researchers counter that "the effect [brain atrophy] is causal, and not some artefact of an underlying schizophrenia disease process" (Bentall & Morrison, 2011, p. 172). When revealing the results of the first large-scale longitudinal study (Ho et al., 2011) to the media, the eminent neuroscientist Nancy Andreasen (New York Times, 2008) stated that:

> The big finding is that people with schizophrenia are losing brain tissue at a more rapid rate than healthy people of comparable age. Some are losing as much as 1 percent per year. That's an awful lot over an 18-year period . . . Another thing we've discovered is that the more drugs you've been given, the more brain tissue you lose . . . The prefrontal cortex . . . is being shut down by the drugs. That reduces the psychotic symptoms. It also causes the prefrontal cortex to slowly atrophy.

TRAUMA AND CLINICAL PRESENTATION

Despite considerable conceptual and clinical overlaps between psychosis and diagnostically trauma-based conditions (e.g., dissociative and post-traumatic syndromes: see Longden, Madill, & Waterman, 2012; Moskowitz, Read, Farrelly, Rudegeair, & Williams, 2009; Moskowitz et al., 2008; Ross & Keyes, 2004), the treatment of patients with psychosis is markedly different. In general, this includes the recommendation of medication as a first-line treatment response (Sommer et al., 2012), poorer access to psychological therapies (Schizophrenia Commission, 2012), and greater reluctance on the part of clinicians to engage with the affective content and context of "characteristic symptoms," such as voice hearing (Romme, Escher, Dillon, Corstens, & Morris, 2009). Nevertheless, in addition to the emergence of psychosis, psychological trauma has also been repeatedly implicated in the content and maintenance of its main symptoms.

Hallucinations—a paradigmatic symptom of psychosis—have been characterised as "a symptom of brain disease just like blindness or hemiplegia" (Stephane et al., 2003, p. 186) and popularised as a bizarre and hazardous sign of mental disturbance (see Leudar & Thomas, 2000; Owen, 2012; Smith, 2007). Nevertheless, the claim that hallucinations are psychologically meaningful in relation to patients' lives (rather than arbitrary content induced by disease) has a long history in the disciplines of psychiatry, psychology, and philosophy, being argued by such theorists as Bleuler, Jaspers, Jung, Laing, and Pinel (McCarthy-Jones, 2012). Indeed, the association between CSA and non-auditory hallucinations was noted as early as 1886 in Freud's case history of "Frau P" (Freud, 1886/1950), with more contemporary work documenting a "predictive syndrome" for identifying a history of incest in female psychiatric patients (particularly chronic or sadistic abuse that commenced in early childhood) that included "intrusive recollections taking the form of sensory phenomena and usually involve shadowy figures, often moving rapidly in the peripheral vision. Psychosensorial auditory hallucinations are common, and psychic auditory hallucinations are sometimes quite elaborate" (Ellenson, 1986, p. 149; see also Ellenson 1985). In a study of 75 individuals with schizophrenia spectrum disorders, Hardy et al. (2005) reported that multi-modal hallucinations (auditory, n=49; somatic, n=5; visual, n=3; olfactory, n=1) had similar themes *and* content to previous traumas, particularly CSA and bullying, in 12.5% of cases, and similar themes in 45% of cases. Investigations with both maltreated children (Famularo, Kinscherff, & Fenton, 1992) and adolescents (Heins, Gray, & Tennant, 1990) have likewise found that hallucination content was often strongly reminiscent of previous traumatic victimization.

In a survey of 92 patients at "ultra-high risk" for psychosis, Thompson et al. (2010) report that sub-threshold psychotic symptoms with sexual content (delusions, auditory/visual/tactile hallucinations) were significantly related to a history of previous sexual trauma (OR=7.17, p=.01) after controlling for other traumatic experiences, PTSD symptoms, age, and gender. A further study with 45 individuals considered at clinical high risk for psychosis found significant positive associations between trauma exposure (psychological and/or physical bullying, emotional neglect, emotional abuse, physical abuse, CSA) and feelings of being watched or followed, as well as false beliefs about power or status. In turn, significant negative associations were found between trauma exposure and hearing benign voices, and reporting unusual negative beliefs about the self (Falukozi & Addington, 2012). Comparable work with 41 patients expe-

riencing a first episode of psychosis has found that attributes of stressful events in the year preceding psychosis onset were significantly associated with core themes of both delusions and hallucinations (Raune, Bebbington, Dunn, & Kuipers, 2006). Amongst other results, intrusive events were associated with persecutory delusions, threatening events with depressive delusions, and loss events negatively associated with grandiose delusions. Persecutory voices, in turn, were associated with humiliating events, intrusive events, and events impairing to self-esteem.

Research examining childhood events, as opposed to recent stressors, has also found associations between maltreatment and symptom content in adulthood (Reiff, Castille, Muenzenmaier, & Link, 2012). Of 30 patients with affective and non-affective psychosis, a nine-factor "trauma-relevant content score" for hallucinations and delusions (comprising: somatic/tactile, olfactory, or kinetic sensations; threat; real person involved; fear; malevolence; sexuality; and memories) was significantly higher amongst abused (n=22) than non-abused (n=8) respondents. In addition, parallels between interpersonal relationships in the context of psychotic symptoms, and those experienced during childhood abuse, were assessed using a multiple case study approach and the Core Conflictual Relationship Theme method of analysis. Numerous patterns were identified, including feelings of fear and helplessness; convictions of not being believed or taken seriously by medics (mirroring childhood experiences of abuse disclosures being disbelieved); hearing the voice of a past perpetrator; and hearing voices threatening rape. Examples from other studies include:

> Another's chart read *'Sexual abuse: Abused from an early age. . . . Raped several times by strangers and violent partners.' This person believes they are 'being tortured by people getting into body,' for example 'the Devil' and 'the Beast' and 'At one stage had bleeding secondary to inserting a bathroom hose into self, stating 'wanting to wash self as "people are trying to put aliens into my body'* (Read, Agar, Argyle, & Aderhold, 2003, p. 12)

And

> Another, who suffered *'ongoing sexual abuse by relative who is a violent person*', hears '*the voice of the relative telling to jump from the bridge and kill self. Has already tried to commit suicide several times'* (Read et al., 2003, p. 12; see also Heins et al., 1990; Read & Argyle, 1999; Romme et al., 2009).

Research around life events and symptom content has also been conducted using structured therapeutic interviews. A recent study of 100 persons who hear voices, 80% of whom had a diagnosis of psychotic

disorder, applied a method of psychological formulation known as "the construct" (Romme & Escher, 2000) to demonstrate that a broad range of acute, precipitating stressors in childhood and adulthood were associated with both voice hearing onset and content (Corstens & Longden, 2013). At least one childhood adversity was reported by 89% of the sample, including family conflict, neglect, physical/sexual/emotional maltreatment, and bullying. Representations for voice identity (e.g., disowned aspects of self, a family member, a past abuser) were formulated in 78% of cases. In 94% of cases, it was possible to formulate the underlying emotional conflicts embodied by the voices (e.g., low self-worth, anger, shame, and guilt).

CONCLUSIONS

The evidence summarized in this review reinforces a standpoint formed in the earliest days of psychiatry and that has gathered a striking momentum in the past two decades; that is no longer a scientifically or morally tenable position to view psychosis as a purely biogenetic disease. This is a position increasingly acknowledged within wider academic and clinical domains. For example, the British Psychological Society ([BPS] Division of Clinical Psychology) recently published a report emphasizing the utility of psychotherapeutic approaches to psychosis The executive summary opens with the observation that "Hearing voices or feeling paranoid are common experiences which can often be a reaction to trauma, abuse or deprivation. Calling them symptoms of . . . psychosis or schizophrenia is only one way of thinking about them, with advantages and disadvantages" (BPS, 2014, p. 6). In turn, a 2012 report in the *Proceedings of the National Academy of Sciences* published results of an extensive study demonstrating that childhood maltreatment has enduring neurological effects (Teicher et al., 2012). Although the findings were not novel, it is notable that psychosis was no longer excluded from the list of psychiatric disorders to which the findings were applicable.

As stated by British psychologist Lucy Johnstone (2012), there are no longer reasonable grounds to dispute the claim that people who hear voices or inhabit non-shared realities are "people with problems, not patients with illnesses" (p. 27). As such, mental health professionals have an ethical responsibility to engage with suffering and to bear witness to the experiences of loss, stress, adversity, abuse, and disempowerment that have shaped patients' lives (Thomas & Longden, 2013). This is not a formulation that prohibits the use of medication, but rather sees it as one of many possible elements of an integrated intervention; one that seeks to address an individual's psychological, social, and emotional wounds in

healing and restorative ways. There is now sufficient evidence that by deconstructing biological classifications like schizophrenia, professionals can utilize their existing therapeutic skills to shift the clinical emphasis towards personal, recovery-oriented goals and the alleviation of posttraumatic responses, emotional vulnerabilities, and psychosocial and interpersonal conflict.

Substantial survivor testimony attests to the value of psychological approaches to psychosis, including that from individuals diagnosed with schizophrenia (e.g., Coleman, 2011; Comans, 2011; Dillon, 2010, 2011; Longden, 2013; Romme et al., 2009). The first trial of its type has demonstrated that successful therapy (in this case CBT) can be conducted in unmedicated people experiencing psychosis (Morrison et al., 2014). Approaches which emphasize communal, social and dialogical processes with minimal medication use, such as Soteria (Calton, Ferriter, Huband, & Spandler, 2008; Mosher, 1999; Mosher, Hendrix, & Fort, 2004) and the Open Dialogue family and network approach (Seikkula & Alakare, 2012; Seikkula, Alakare & Aaltonen, 2011; Seikkula & Olson, 2003) have generated extremely positive outcomes (Bola, Lehtinen, Cullberg & Ciompi, 2009). The evidence for the impact of psychosocial stress in the onset and maintenance of psychosis is now beyond dispute. A failure to enact this evidence in a standardized way within clinical practice is an insurmountable barrier for developing genuinely humane and effective services. Excluding this at best risks complicity in maltreatment and injustice, and at worst it actively perpetrates it. In the words of psychiatrist Loren Mosher, when considering the evidence for the links between psychosis and overwhelming life events, "[the research] is a straightforward, unashamed wake-up call. Everyone involved should act, in whatever way your circumstances allow, to end this madness" (quoted in Read & Dillon, 2013, p. 406).

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