PROCHILD
PROTECTION AND SUPPORT OF ABUSED CHILDREN THROUGH MULTIDISCIPLINARY INTERVENTION

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**WP3**
**Mapping of operators' needs and good practices for an early and integrated detection and treatment of abused minors**

# D3.7 Report on protective and risk factors after child abuse for the development of psychosis



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# Childhood Abuse and Adult mental health

## Introduction

The World Health Organization (WHO) defines Childhood Abuse (CA) as follows " *all forms of physical and/or emotional ill-treatment, sexual abuse, neglect or negligent treatment or commercial or other exploitation, resulting in actual or potential harm to the child's health, survival, development or dignity in the context of a relationship of responsibility, trust or power"*. According to the current literature, CA comprises neglect, emotional, sexual (CSA) and physical abuse (CPA) (see table n.1)[1].

It is estimated that about one third of the general population is exposed to traumatic events during childhood, which can have short and long-term consequences on mental and physical health (WHO, 2013). Traumatic life events in vulnerable children account for a wide range of disorders, ranging from mild psychiatric disorders such as anxiety to severe psychotic disorders like schizophrenia.

Trauma is associated with childhood and adolescence externalizing and internalizing psychiatric disorders. Externalizing pathology encompasses attention deficit/hyperactivity disorder (ADHD), conduct disorder (CD), oppositional defiant disorder (ODD; Cohen et al., 2001; Famularo et al.,1992), delinquency (Lansford et al., 2007; Staouthamer – Loeber et al., 2001; Widom 1989, Williams et al., 2010), antisocial behavior (Jaffe et al., 2004; Jonson – Reid et al., 2010; Lansford et al., 2002; Manly et al., 2001; Moylan et al., 2010) and substance use (Kaufman et al., 2007; Lansford et al., 2010; Rogosch et al., 2010). In adulthood, children who were diagnosed with externalizing disorders have higher rates of antisocial personality disorders and antisocial behaviors such as crime, criminal arrest and alcohol/drug use (Cohen et al., 2001; Noll et al., 2009, Scott et al., 2010; Thornberry et al., 2010). Internalizing disorders are also frequent in abused children, including major depressive disorder (Brown et al.,1999), anxiety disorders (Cohen et al., 2001), post-traumatic stress disorder (PTSD) and internalizing symptoms (Bolger &

Patterson, 2001; Lansford et al., 2002; Manly et al., 2001; Moylan et al., 2010). Their counterparts in adulthood are mood disorders (bipolar and unipolar depressive disorders; Brown et al., 1999; Noll et al., 2009; Scott et al., 2010; Widom et al., 2007) and anxiety disorders (Cohen et al., 2001; Scott et al., 2010). A recent metanalysis reported that childhood abuse was associated with depressive (OR= 2.03%, 95% CI 0 1.37-3.01) and anxiety disorders (OR=2.70, 95% CI = 2.10-3.47; Li et al. 2016). It was estimated that 59% of mood disorders may be attributable to child abuse and that a 10% reduction in child abuse could results in the prevention of 31.36 million cases of depression and anxiety disorders (Li et al., 2016).

Even though the most commonly reported forms of CA are CSA and CPA, there is growing evidence that emotional abuse and neglect are far more frequent among both clinical and general population samples and can also lead to deleterious effects on mental and/or physical health. Maltreatment is often recurrent rather than a single event and children are exposed to multiple types of CA (Gilbert et al., 2009). Neglect has the highest rate of recurrence and association with other types of abuse, followed by physical and sexual abuse (Sideli et al., 2012). Another aspect that may be particularly important to the clinician working with children and adolescents is the reported association between peer victimization and bullying, and the development of psychotic symptoms. Chronic or severe bullying is associated with even worse symptomatology. Peer victimization and bullying are increasing public health issues which worsen the developmental trajectories of abused/traumatized children, and so must be tackled as soon as possible. Bullying is a complex issue which often involves victims with certain features (children with mental or physical disability, ethnic minority, gender minority etc.). To improve the mental health of both children and the general public, it is compulsory to identify risk factors for child abuse, prevention strategies (primary and secondary prevention) and to sensitize general population and politicians about these issues.

*Tab. 1 Definitions of child maltreatment categories*

***Neglect***. Child lacked appropriate care: not provided enough to eat or drink, hygiene not attended to, lacked shelter, not provided routine or urgent medical care, left alone when too young to care for himself/herself, or left with inappropriate caregiver (e.g. sex offender, intoxicated individual).

***Emotional abuse***. A parent or other adult in the household told child that s/he is no good, yelled at child in a scary way, or threatened to harm, abandon, leave, or send child away.

***Physical abuse***. A parent or other adult in the household physically assaulted the child (e.g. hit, push, choke, shake, throw, bite, burn) causing bruises or physical injury. This may have occurred in the context of disciplining the child, or independent of discipline.

***Sexual abuse***. A parent, other adult, or peer five years or older than the child, made child see (e.g. watch pornography, watch other masturbate) or do something sexual (e.g. fondle, oral, anal, or vaginal intercourse).

*Adapted from J. Kaufman, S. Torbey, 2019*[1]

In the following paragraphs, we will examine the relationship between child maltreatment or child abuse and the development of mental disorders. Maltreated and abused children are vulnerable to experiencing dissociation, externalizing behaviors, auditory hallucinations and delusions (i.e. paranoia and psychotic experiences). The development of a psychiatric disorder in adult life after CA requires the interplay of genetic and environmental factors. Some of these environmental factors are well known risk factors for mental disorders, such as migration, urbanization and cannabis use in patients with a genetic vulnerability. Clinicians have a unique chance to detect any form of abuse, but often a history of CA is based only on patients' report, and the reliability of these self–reports (with its legal implications) is an important issue. In some studies, reports of abuse by psychiatric patients are surprisingly reliable. Despite this, concerns about abuse disclosure in this population are reasonable, particularly of child sexual abuse. Regardless, knowledge of a patient's history of CT /CA is a crucial point for both delivering targeted-preventive interventions for children/adolescent victims of CT, and offering individualized psychotherapies for adults with mental disorders and history of CT.

# Part 1, The Complex Post Traumatic Stress Disorder (PTSD)

**Agnese Cheli, Psychotherapist Psychologist**

Abuse and maltreatment, whose neglect - that is a severe emotional carelessness - is by far the most common form, when experienced during childhood, are the major risk factor for the development of physical and psychic illnesses in adulthood (Liotti e Farina, 2011).

Distinguishing among the various forms of child violence – sexual abuse, physical and mental violence, witnessed domestic violence, treatment disorders, physical and emotional negligence – is helpful for illustrative purposes; however, the clinical experience and research suggest that children are usually victims of various and multiple forms of violence that, apart from provoking the harmful and permanent consequences on child development, tend to transform into deficits during adolescence and to become chronic in adulthood, in cases lacking in reparative actions.

According to some broad and authoritative research, child trauma deriving from the exposition to obsessive and/or commissive interpersonal violence, or other forms of abuse, is the main risk factor for the development of at least one third of mental health disorders (Green et al., 2010; Teicher et al., 2012), as well as being linked to the development of highly common physical illnesses, early mortality, and the low life quality in the USA (Felitti, 2009).

The broad spread of abuse and maltreatment, and their consequences on physical and mental health, was denied until few years ago. Resultantly, it can be defined as a hidden epidemic (Lanius et al., 2010). Observing the difficult and complex clinical reality of these patients, notably those who were initially considered untreatable (like those with a borderline personality), produced a change of the theoretic paradigms of reference (Meares, 2012), suggesting the need to:

- Develop more clinical awareness on the consequences of complex traumatic experience during the child development;
- Adopt specific diagnostic instruments to evaluate the post-traumatic outcomes of patients;

- Have periodical screening to explore maltreatment stories of patients in charge of the mental health services.

**The Complex Post Traumatic Stress Disorder (PTSD)**

It was notably Bowlby's Attachment theory (Tondo, 2011), born from the observation of early separations caused by the second world war, which formed the theoretical paradigm that provided clinicians with important reference inputs to understand the complex role of trauma in developing attachment relationships (Farina e Simoncini, 2015).

More recently, the clinical paradigm of complex trauma, as development disorders, alongside neuroimaging techniques have provided studies with valuable insight on the short, medium and long-term consequences of interpersonal traumas caused by early exposition to violence in attachment relationships. These studies are now able to demonstrate the structural and functional effects of interpersonal forms of violence on a developing brain **(**Pagani, 2007).

Trauma has long been recognised to provoke diagnosable mental health disorders. For example, the possible clinical effects of singular traumatic events on individuals was described in the diagnosis of post-traumatic stress disorder in the DSM III in 1980. Repeated exposure to trauma and childhood trauma later began to be considered. Herman and Van Der Kolk (1989) drew attention to the role of repeated traumas, including physical abuse, sexual abuse, and witnessing serious domestic violence, in mental health. This study illuminated the complex clinical outcomes resulting from repeated trauma, namely interpersonal or development trauma. However, for a long time, only a singular diagnosis of the effects of trauma was agreed upon. A general definition of PTSD was inadequate to sufficiently describe the complex symptomatology resulting from all forms of exposure to trauma.

Since then, clinicians have acquired more awareness of this subject, and are becoming more competent in their knowledge of this subject. Unfortunately, there has been a large number of tragedies and traumatic events in the past few decades. This has generated a large quantity of

research on the psychopathological consequences of severe traumatic events. The literature has produced theoretical models, diagnostic tools and treatment protocols for PTSD. It has also enabled the development and acceptation of multiple forms of PTSD. For example, trauma experienced at a young age or for a long duration of time is commonly diagnosed under the term "complex post-traumatic stress disorder" (C-PTSD). The effects of repeated and long-term interpersonal traumas result in characteristics which distinguish this form of PTSD from others, including the onset of emotional disorders, somatization, disintegration and disassociation (Cheli, Gambuzza, 2017; Cheli e Al., 2012).

Herman was among the first to C-PTSD (1992), a diagnosis which revealed to be effective both on a theoretical and clinical levels for treating patients with early, chronic, repeated traumas with interpersonal nature (sexual abuse, violence, torture, segregations, severe neglect). It is appropriate to consider the interpersonal trauma (traumatic development) in a dimensional perspective, within which traumatic disorders are analysed along a spectrum of different clinical conditions.

Naturally, the gravity gradient of the clinical spectrum is determined by the variables which have a different impact on the child development dynamics. For example, age represents a determinant variable which is correlated to different clinical pictures. Traumatic experiences produce different outcomes depending on the developmental phase of the children. Indeed, numerous studies now affirm that both childhood and adolescence represent a period of important vulnerability. Regardless of age, cumulative trauma caused by a chronic exposition to traumatic experiences can disrupt developmental processes and produce negative outcomes for the child.

Risk factors which favour the emergence of maltreatment in childhood or worsen its conditions are well identified in research and are also variables which influence child growth (Di Blasio et al., 2015). Alongside risk factors, we should consider protective, subjective and environmental factors, which can influence the evolutionary course of a traumatic disorder, affecting its prognosis.

Today, it is agreed that the pathogenic potential of the trauma alongside the child's genetic composition and personal and environmental resources influence the diagnosis and the prognosis of a traumatic disorder in childhood. The impact of the trauma and the post-traumatic trajectory are highly varied, since they are influence by a number of factors. However, we can distinguish three “survival scenarios”:

1) Those who overcame successfully the traumatic experiences and whose life is now satisfying. These people experienced reparative relationships which contributed to the restoration of their well-being and to reactivate their personal resources (resiliency);
2) Those who periodically will present post-traumatic symptoms, in response to triggers of the original trauma and in absence of relational aid;
3) Those who continuously are in a “post-traumatic decline” or “spiral of loss of resources” conditions caused by severe impairment of their physical/mental health (Felitti, 2002).

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| Exploring the clinical profile of the complex post-traumatic stress disorder (C-PTSD) described by van der Kolk (2009) and by the National Child Traumatic Center Network (www.NCTSNet.org ), cases of impairments emerge in diverse and central aspects of the psychological functioning (Tab. 1, in Cheli e | Compromised sense of borders<br>Distrust and suspiciousness<br>Interpersonal difficulties<br>Difficulties in understanding and sharing other people’s moods<br>Difficulties in assuming other people’s perspective |

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| Gambuzza, 2017, adaptation) which can be identified later on by the mental health services for adults.<br><br>Affection | |
| Biological functions | Problems in sensory-motor development<br>Analgesia<br>Coordination, equilibrium and regulation of the body<br>Tone disorders<br>Somatization<br>Various medical problems, for example pelvic problems, asthma, dermatologic problems, autoimmune disorders, pseudo apoplectic fits |
| Emotional regulation | Difficulty in emotional regulation<br>Difficulty in identifying and expressing feelings<br>Inability to identify and describe one's own mood<br>Difficulty in communicating desires and needs |
| Dissociation | Alteration of the state of consciousness<br>Amnesia<br>De-personalisation and de-realisation<br>Two or more states of consciousness<br>Impairment of the episodic memory |
| Behaviour control | Inability to control impulses<br>Self-aggression or outward directed aggressivity<br>Pathologic ways of self-control<br>Sleep disorders<br>Food disorders<br>Substance abuse<br>Excessive complacency<br>Oppositional behaviours<br>Difficulty in understanding and respecting rules |

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| | Reiteration of emotional contents and aspects in the behaviour or play, linked to the traumatic events (violence, sexual abuse. etc.) |
| Cognitive area | Difficulty in regulating attention and executive functions<br>Curiosity temporal liability<br>Difficulty in processing new information<br>Difficulty in focusing on a goal and in delivering tasks<br>Deficit in the consistency of objectives<br>Difficulty in planning and making prediction for the future<br>Difficulty in understanding the sense of responsibility<br>Learning difficulty<br>Language development difficulty<br>Space-time orientation difficulty |
| Concept of self | Lack of a continuous and predictable self-perception<br>Lack of a separateness sense<br>Physical body disorders<br>Lack of self-esteem<br>Guilt and awkwardness |

**Neurobiology of traumatic developments in the perspective of developmental psychopathology**

The research, supported by the perspective of interpersonal neurobiology (Siegel, 2014) and increasingly sophisticated neuroimaging techniques, is now able to demonstrate that the most obvious consequence of traumatic development in children is the inability to regulate internal somatosensory and emotional states. This is due to:

1) The subcortical structures (limbic system) greatly influence the noradrenergic system and the hypothalamus-pituitary-adrenal axis (regulator of the production of the main stress hormones: cortisol, adrenaline, noradrenaline, serotonin, endogenous opioids, modulating the activation levels of the sympathetic and parasympathetic system, thus affecting the ability to regulate arousal activation levels in the individual);

2) There is a hierarchical functioning (bottom up) between the limbic system (seat of processing of emotions), the hypothalamus (deputy to the neuroendocrinological regulation of the hormones involved in stress responses), the hippocampus (which presides over the mechanisms of memory) and the prefrontal cortex (involved in cognitive processes and thought building) which determines the prevalence of mental functioning on needs centered on survival and defensiveness, rather than on mentalization;

3) Two areas of the brain are involved in the evaluation of the emotional significance of the stimuli: the amygdala and the insula, which work together to detect and respond to stimuli perceived as dangerous. These areas can be equated with a radar warning system. Some areas of the right hemisphere acquire a certain importance in the preconscious task of assessing environmental stimuli and the consequent levels of activation; a failure in the development of these areas leads to a deficit in the capacity for self-regulation and interactive regulation;

4) The perception of the sensation of danger or safety (concept of neuroception, Porges, 2016) are stored at the level of implicit procedural memory, and therefore unconscious, and is

located in the right hemisphere, unlike the explicit declarative memory that seems to be lateralized to left, in the "linguistic" and conscious hemisphere;

5) The adaptive ability to flexibly use regulatory models according to the social context derives from the quality of early attachment experiences, from a history of interactions of secure attachment of a maturing biological organism and a social environment early tuned. The experiences regulated and not regulated by the attachment figure are recorded and preserved in the procedural memory that is formed early in the orbitofrontal system and its cortical and subcortical connections as interactive representations (Schore, 2008).

The way in which affections are regulated within the parent-child dyad does not, therefore, only affect the attachment relationship and the ability to structure the self, but also on the underlying neural structures. The quality of primary relationships and their corresponding ability to regulate maladaptive states condition the mechanisms that promote brain development. The most recent scientific developments on the consequences of unfavourable childhood experiences have, in fact, led many researchers and clinicians to reconsider both the clinical centrality of trauma in developmental psychopathology, and the role of environmental determinants that stimulate and guide the neurobiological functioning of the mind;

6) Interpersonal trauma modifies neurophysiology: it is imprinted in the developing limbic system and in the autonomic nervous system. Stories of early abuse negatively impact the development of the right brain, which is dominant due to attachment, the regulation of affects, the modulation of stress (Schore, 2008), directing the child towards insecure or disorganized attachments;

7) The state of fear-terror produced by a serious disorder in attachment increases brain levels of adrenaline, noradrenaline and dopamine, creating a hypermetabolic state in the developing brain, which has deleterious effects on volume and hippocampal function, particularly pronounced in post-traumatic stress disorder. Research has shown that in conditions of chronic stress, the hippocampus is reduced in size by 10-20% (Courtois and Ford, 2009);

8) In 80% of children who have developed a disorganized attachment following the abuse suffered, contradictory behaviours and activations of both the sympathetic system and the parasympathetic (hyper or hypo arousal) coexist. This condition appears to be related to an inefficient regulation of the limbic system and of the frontal orbital cortex in the right hemisphere, produced by a lack of synaptogenesis, or a pathological synaptogenesis.

Authors such as Dawson, Panagiotides, Klinger and Hill (1992) have confirmed the widespread opinion on the role of the frontal lobes in the development of self-regulatory capacities. In fact, it seems that not only the frontal lobes manage the whole series of behaviours suitable for self-regulation, but that the orbital cortex are also involved, as they are vital in the development of functions useful for affection. This structure influences, and is in turn influenced by, the quality of the affection relationships. Thanks to its strategic position, as a meeting point between the cortical and subcortical structures, the orbital cortex acts as the main controller of the balance between the sympathetic and the parasympathetic systems.

This region is particularly expanded to the right, so it is particularly developed in the emotional brain, deputed to the recognition of facial expressions, of quick and unconscious evaluations, of mediation processes between pleasant and unpleasant sensations.

It could be hypothesized, therefore, that, within the attachment theory, considering it from Schore's perspective, as a theory of regulation, the "organ" that most seems to be involved in affective regulation is precisely the orbitofrontal cortex, which has all the anatomical and structural characteristics to carry out the tasks involved in attachment.

So this structure, so important in the first years of life for the structuring of the Self and for the regulation of internal states and behaviours, seems to take on a role of high importance for the health of relationships in the following ages, as well as in skills, or non-abilities, regulative of adulthood.

**C-PTSD and Mental Health**

From the point of view of mental health, the percentage of children exposed to violence and mistreatment who subsequently develop mental disorders is very high, ranging from 50% to 80% depending on the study. The consequences in adulthood are important: doubled or tripled suicide tendency compared to the general population, alongside a tripled risk of developing mental health disorders, such as major depression, traumatic chronic disorders, anxiety disorders and psychotic disorders compared to those who do not undergo maltreatment during development. Additionally, there is a greater predisposition to obesity, aggression, risky sexual behaviours, and alcohol and substances misuse, as well as higher incidences of chronic diseases. The effects of childhood maltreatment on mortality can also be direct: according to estimates by the World Health Organization (WHO), around 155,000 deaths are reported worldwide among children under the age of 15, following abuse and/or abandonment.

Abused women in the domestic environment become more ill, are four times more likely to suffer from depression and are 5 times more likely to attempt suicide (Straus and Gelles, 1990). The prevalence of PTSD in abused women varies from 45% to 84% (Herman, 1992), and they are more at risk of developing a peculiar maternal anxiety (Wolfe et al., 2003), and of being murdered (82% of crimes committed against women are feminicides).

In over 80% of abused children, insecure and disorganized attachment models are detected. These, in the absence of protective factors, are seen as important evolutionary risk factors for psychopathological disorders characterized by deficits in empathy, recognition and regulation of internal and syntonic emotional states. The possibility of building attachment bonds in adulthood on the basis of feelings of trust, security, reliability, self-availability and the investment of the other is commonly impaired due to these childhood experiences (Cheli, Ricciutello et al., 2012).

The various behavioural risks in adolescents commonly associated with a history of trauma, including self and other tendencies, eating disorders and sexual behaviour, deviance (Briere and Spinazzola, 2009), secondary victimization, the substance abuse, etc., place mental and adult-age

mental health services in the face of significant preventive, diagnostic, therapeutic and protective issues. Mood disorders are also a frequent consequence of childhood trauma, in its various expressions of depression, manic states and bipolar disorder (25.26).

Childhood trauma is associated with the development of both internalizing symptoms (inhibition, withdrawal, lowered self-esteem) and externalizing symptoms (impulsivity, aggression), as well as with hyper or hypo-controlling tendencies (Ford, 2000). One of the possible consequences, for example, is the emergence of a disruptive behaviour disorder in adolescence, characterized by self and other aggression associated with deficits in impulse control (Anda, Felitti and Bremner, 2006), social deviance, and dependence from substances for self-healing purposes.

Psychic dissociation, understood as a failure in the ability to integrate thoughts, emotions and events, is a peculiar feature of complex trauma as a developmental disorder (Putnam, 2003) and this underlies many psychiatric conditions. In the psychopathology of trauma, the dissociation is functional to the survival of the self, as an adaptive defence at the price of a discontinuity and fragmentation of the subjective psychological experience as well as memory processes. On the clinical level, it is characterized as a memory disorder (partial or total amnesia) which is associated with an alteration in the sensation and perception of self and the environment (depersonalization and derealization). In more severe forms it can result in a dissociative identity disorder or multiple personality disorder.

Steele (2016), in the framework of the indication of comorbidity between dissociative disorders and personality disorders, states that there is "a high overlap between borderline personality disorder and complex PTSD [...] sometimes it is very difficult to distinguish a DBP from a Complex PTSD [...] about 80% of DBP patients have an autobiographical history characterized by neglect, abuse and/or severe and early interruptions of attachment bonds".

**Transgenerational transmission of trauma**

Traumatic development has its origins in the quality of early attachment relationships. Neurobiological studies of attachment behaviours conducted with functional magnetic resonance imaging (fMRIs) seem to be a promising method of investigating possible traumatic developments in attachment, and their tendency to transmit from one generation to another.

"Safe" mothers show a greater response of oxytocin, an important neuromodulator hormone produced in the hypothalamus, involved in maternal behaviour (Strathearn, Fonagy, Amico, Montague, 2009). Oxytocin is released in response to stimuli such as breastfeeding, contact, sight, sound and smell of the new-born. Mothers with secure attachment patterns show higher levels of oxytocin than mothers with insecure/avoidant attachment and this activation directs them towards a more accurate interpretation of the child's signals. The mother's ability to tune into new-born signals, such as facial expressions, is a powerful regulator of the child's psychophysiological states. Mothers with an unresolved attachment style tend to react to the child's stimuli in frightening and frightened ways (Main, 2008), as demonstrated in the numerous studies conducted with the Strange Situation.

Of particular clinical importance is therefore the impairment of the development of emotional competence, which involves a series of linked functions fundamental for affective and social development. In children exposed to chronic traumatic stress, emotional competence represents the crucial clinical element, as disordered emotional competence can exert numerous negative effects on development.

Parents with traumatic experiences in the primary care setting report higher levels of anxiety and dissociation that compromise the ability to perceive and decode their own emotional states and those of others correctly and to detect the degree of dangerousness of the situations.

The studies of Yehuda et al. (2005) on the effect of PTSD in pregnant women have shown that infants, at birth, show lower levels of cortisol if the mother has undergone PTSD during pregnancy, and that the children of mothers with major depression already at 6 months, have high

levels of cortisol. These studies indicate that the level of physiological activation of the child varies systematically based on the interaction and the process of information processing in the interaction (Beebe and Lachmann, 2003).

The observation that oxytocin levels are higher in securely attached mothers, and lower in depressed mothers and in many children leaving early childhood (Fries et al., 2005) suggests the importance of this neuropeptide in mediating the attachment and social behaviour. In support of this perspective, important results have emerged from the Minnesota Longitudinal Study (Sroufe et al., 2005), which set itself the thirty-year objective to subject Bowlby's development model to empirical verification. This study found that 40% of parents who had been abused as children abused their own children and another 30% were neglectful. The 30% of parents who had been abused but were not abusers with their children had received emotional support from a non-abusive adult, had received psychotherapy or had developed a satisfying intimate relationship with their partner.

Numerous studies show that maternal dissociation leads to particular deficits in the reflexive function (the basis of a "sufficiently good" parenting), in the protective capacity towards the child, and in the ability to establish healthy boundaries and ask for help. These difficulties can easily turn into risk factors in parenting, and consequently perpetrate the transgenerational transmission chain. Dissociative mothers seem to present a deficit in the ability to process information properly, both internal and external (Freyd, 1994). Parents with a low reflexive function seem to be unaware of their own thoughts and feelings and deny the emotional experiences associated with parenting. Mothers with a history of unprocessed maltreatment, depression and PTSD show a deficit in reflexive function, i.e. a poor or absent awareness of the child's signals, and can be intrusive, withdrawn or emotionally unavailable. Depressed mothers generally have a low emotional sensitivity and do not reflect, or poorly reflect, the affective experience of their child (Martinez-Torteya et al., 2014). Unresolved trauma in primary caregivers can therefore interfere with their ability to appropriately respond to the child, thus influencing the

development of attachment and the network of neuronal networks in formation, potentially contributing to the intergenerational transmission of the trauma.

Interviews specifically aimed at parents with serious stories of chronic trauma reveal a dominant perception of the child as hostile and threatening in this population, a life of impotence in the parental role, seeing the self as non-valuable, inadequate, and "bad", and recurrent references to feelings of fear and empathic incapacity. These results also placed emphasis on the significant role of blindness to violence and its normalization frequently observed in parents c.d. "Non-protective", including mothers who are victims of domestic violence (for a review, see Chu and DePrince, 2006).

Epigenetic studies have also shown that the environment can activate or inhibit the genetic expression of certain genes, and that this mutation can be transmitted to subsequent generations. For example, increased methylation of DNA encoding the NR3C1 glucocorticoid receptor in the hypothalamus was detected in subjects experiencing adverse events (violence, abuse, strong emotional deprivation) in early childhood. This has been related to an increased production of glucocorticoids in these individuals, as well as in children of women who lived in violent and traumatizing contexts during pregnancy and so transmitted excess glucocorticoids to their children during foetal life. The more serious the negative events or contexts were, the higher the DNA methylation capacity level (McGowan et al., 2018). The reduced expression of the receptor following from methylation leads to an altered functioning of the hypothalamic axis, with a consequent reduced ability of the child to adapt.

Conversely, a particularly favourable context characterized by the high quality of maternal care reduces the production of glucocorticoids in baby animals, as well as in children, and is associated with a reduction in the methylation of the NR3C1 receptor gene. Consequently, more glucocorticoid receptors are expressed, which results in a less negative susceptibility to environmental stress and it’s short and long term negative consequences (Lester, 2018). The

importance of this research also derives from the fact that they indicate that the degree of methylation can be a marker of the severity of the maltreatment.

**Conclusions**

Cumulative psychological trauma, also known as complex trauma, has pathogenic effects that are significantly different from those of single trauma, and even more so when complex trauma is present in the life of an individual who is developing. The consequences of complex trauma during development remain indelibly impressed, like footprints left on the still fresh cement, not only in the mind, but also in the victim's body, as shown by the results of the ACE Study (https://www.cdc.gov/violenceprevention/childabuseandneglect/acestudy/about.html) which demonstrate a significant correlation between complex trauma in childhood and some medical conditions in adulthood (including diseases with suspected auto-immune genesis, recurrent infectious diseases, rheumatic diseases, heart disease and others). Time, data from the ACE Study suggest, cannot cure the wounds left by the trauma but only hide them. It is therefore the task of clinicians and researchers to reveal the effects of adverse experiences suffered during childhood, discover their pathogenetic mechanisms, study their multiform psychopathological consequences without stopping at symptomatic diagnosis, and finding the most appropriate treatments (Liotti and Farina, 2016).

# Part 2. Childhood Abuse and Psychosis

**Jatin Lal, MD & Ilaria Tarricone, MD, PhD**

Childhood Trauma (CT) has been extensively investigated as a potential risk factor of psychotic disorders and severe psychopathological symptoms in adulthood, including hallucinations and delusions, particularly paranoid delusions.

The term “psychosis” is used clinically as a generic term to refer to the positive symptoms of psychotic disorders, namely unusual beliefs (delusions) and anomalous experiences (hallucinations and other perceptual abnormalities), as well as disturbances of thought and language. Psychotic symptoms can occur in many psychotic disorders, i.e. non-affective psychoses (schizophrenia, schizophreniform disorder, schizoaffective disorder, brief psychotic disorder, delusional disorder) and affective psychoses (major depressive disorders, manic episodes of bipolar disorder). Schizophrenia is most likely the most investigated condition among the psychotic disorders. Schizophrenia is characterized by long duration of bizarre delusions, negative symptoms, and few affective symptoms (non-affective psychosis). The diagnostic statistical manual of mental disorders-fifth edition (DSM-5) and international classification of diseases - tenth edition (ICD–10) describes current diagnostic criteria of psychotic disorders (Tab.2).

Over the past few decades, clinical experiences and several studies have proven that positive psychotic symptoms may be present in many other syndromes, such as post-traumatic stress disorder (PTSD), dissociative disorders, personality disorders (borderline and schizotypal personality disorder).

***Table 2. Diagnostic categories of psychotic disorders***

**Based on current principles of diagnosis taking into account duration, dysfunction, associated substance use, bizarreness of delusions, co-presence of depression or mania, presence of a somatic disorder, and other criteria**

- **Non-affective psychotic disorders:**
  - **Schizophrenia**
  - **Schizoaffective disorder**
  - **Schizophreniform disorder**
  - **Delusional disorder**
  - **Brief psychotic disorder**
  - **Psychotic disorder not otherwise specified**
- **Affective psychoses:**
  - **Bipolar disorder with psychotic features**
  - **Major depressive disorder with psychotic features**
- **Substance-induced psychotic disorder:**
  - **Alcohol-induced**
  - **Other substance-induced**
- **Psychotic disorder due to a general medical condition**

***Adopted from Jim van Os, ShitijKapur, 2009***

The lifetime prevalence of schizophrenia is 0.30–0.66%; however, when the schizophrenic spectrum is considered, lifetime prevalence is 2.3% and reaches 3.5% if all psychotic disorders are considered as whole. Incidence of psychotic disorders preset a huge variation over place and time. The EU-GEI multinational study reported that after direct standardization for age, sex, and racial/ethnic minority status, the incidence of all psychotic disorders showed 8-fold variation between locations, from 6.0 (95% CI, 3.5-8.6) per 100 000 person-years in Santiago, Spain, to 46.1 (95% CI, 37.3-55.0) per 100 000 person-years in Paris, France (Jongsma et al., 2018)

Family studies have shown that schizophrenia is more common in the relatives of patients with psychosis that in the general population: vulnerability for schizophrenia is partly genetic. Twin studies suggest that the syndrome has heritability estimates of around 80% (compared with

~60% for osteoarthritis of the hip and 30–50% for hypertension; van Os & Kapur, 2009). There is evidence for gene X environment interactions for the pathogenesis of psychotic disorders. The environmental factors that showed stronger correlation with psychosis onset and course operate at area level (e.g. urbanization and ethnic density), as well as individual level (such as migration history and cannabis use; Anderson et al., 2014; Van der Ven et al., 2018; Di Forti et al., 2015; Volkow et al. 2016). Patients with psychosis report high rate of childhood adversities compared to healthy individuals (Varese et al., 2012).

Childhood/early adolescence seem to be the most vulnerable period for gene x environment interactions in the development of psychosis, which is consistent with the neurodevelopmental model. The final-common neurobiological outcome of the interplay between biological and environmental factors leading to psychosis is the excess release of dopamine in the dopaminergic circuits of the brain. Dopamine (DA) is a neurotransmitter that plays a central role in motivation, attention, reward motivational saliency (Shizgal, 1997; Berridge and Robinson, 1998; Berridge, 1999; Heinz,1999) and its reduced or excessive release is involved in the phenomenology of psychosis (Kapur S. et al., 2005). The ability of directing one's attention to a context related/rewarding activity and use it for future behavior is called "motivational saliency" (Berridge and Robinson, 1998; Berridge, 1999). In patients suffering from psychosis there is an abnormality in motivational saliency, underlying which is the loss of a context related DA release. An excessive release of DA in the limbic system, the "emotional part of the brain", is responsible for the novelty that patients perceive at the psychosis onset ("everything is new, something has changed"), and thus of the delusions and hallucinations development, the hallmark of psychosis (Kapur, 2003; Kapur et al 2005).

Cognitive–behavioral models have given a great contribution to the understanding of why the increase of DA release occurs in the brain of patients suffering from psychosis, and on the relationship between childhood trauma and psychosis development (Gibson et al, 2016):

1) **External locus of control (eLOC)**: this concept was developed by Julian B. Rotter in 1954 and it refers to an individual's tendency to attribute the cause of one's life events to his/herself or to external forces that are beyond one's control. The locus of control can be internal or external; early traumatizing experiences can lead to a development of an external locus of control. Some studies showed that an external locus of control and social cognition deficit are associated with psychotic experiences (PEs) in general population and PEs sometimes temporally precede psychotic disorders. Improving social cognition abilities and LOC (which is modifiable) can lead to improvement of psychotic or other mental illness in children and particularly in adolescents with PEs (Fischer et al., 2013; Sarah A. Sullivan et al., 2017).
2) **Behavioral sensitization:** patients with psychosis are more reactive to environmental stressful events and daily life stressors when compared to general population. This vulnerability to stress has a genetic base but can also be increased by over-activation of hypothalamus–pituitary–adrenal (HPA) axis, through exposure to traumatic events. The over-activity of this system, elicited by external stimuli, can lead to functional or structural alterations in emotional brain circuits that account for increased sensitivity and abnormal stress response. The interaction between HPA axis and DA is also involved in this process, demonstrated by findings of an increased cortisol secretion after administration of pro-dopaminergic drugs; this finding suggested a reciprocal influence between the two systems (Walker E et al., 2008). Advances in neuroimaging and neuropsychology have given an insight into human brain alteration in patients with stress related disorders, such as reductions of the hippocampus and alterations in the HPA axis.
3) **Dissociation:** this is one of the main sequelae of childhood adversities. There is a growing evidence of links existing between dissociation, reduced motivational saliency

and psychosis. In this regard, traumatic life events facilitate dissociation and dissociation promotes psychosis (Braeheler et al., 2013; Scharfer et al., 2012).

4) **Negative Schema:** Negative schemas about self and others are common among patients with psychosis who regularly experienced childhood experiences of vulnerability, humiliation and subordination, experiences which also sensitize individuals to psychotic experiences. It is worth noting that these attributional styles are associated with positive symptoms in clinical population, such as auditory commenting hallucination, and the phenomenology of these experiences align with traumatic events where exposed to; for example, bullying or CPS/CSA is associated with paranoia or persecutory delusion (Fowler et al., 2011; Gracie et al., 2007).

Patients suffering from psychoses often report abuse both in childhood and adulthood, but these self-reports have been poorly investigated. Varese and colleagues (2012) reviewed 18 cases – 10 perspective and quasi-prospective studies and 8 population based cross sectional studies, alongside control studies. The authors found that childhood trauma was associated with an odds ratio of 2.8 for the development of psychosis and patients with psychosis were 2.7 times more likely been exposed to childhood trauma than controls (Varese et al., 2012, Dvir et al., 2013). Nine of the ten prospective studies showed that there was a dose–response effect between trauma and severity of symptoms (Varese et al., 2012). The evaluation of trauma in patients with psychosis are frequently self–reported in clinical settings and questions are raised about the reliability of these self–reports. However, studies have clearly showed that patients report in hospital and outpatient facilities are reliable when compared with general population (Meyer et al., 1996; Goodman et al., 1999; Read et al., 2003). Schreier and colleagues (2012) found that acute or chronic bullying was associated with psychotic symptoms after controlling for confounding factors such as previous psychiatric disorders, family psychosocial stressors and child's I.Q. Another study by Fisher and colleagues (2013) showed a higher rate of psychotic symptomatology in

victimized children (bullying and domestic violence) after controlling for depressive or anxious symptoms; this could be evidence for trauma induced psychosis not mediated by affective disorders (Dvir et al., 2013). However, there are still some methodological issues that have limited the possibility of drawing conclusions about childhood trauma and psychosis: a major criticism is that the use of a retrospective study design does not facilitate drawing conclusions about the direction of effect and does not exclude alternative explanations (Sideli et al., 2012).

One important finding suggesting a strong association between trauma and psychosis is the rate of comorbidity between psychosis and PTSD. It is estimated that between 62-100% of combat veterans diagnosed with PTSD also experience at least one additional disorder (Boudewyns et al., 1991; Davidson et al., 1985; Kulka et al., 1988), and of these, between 15- 64% have been found to have co-morbid psychosis (Deering et al., 1996, Campbell et al., 2007). The relationship between PSTD and psychosis is complex: intrusive thoughts in traumatized patients bear resemblance to hallucination experienced by patients suffering from psychosis, and emotional numbing and social isolation in PTSD resemble negative symptoms in psychosis. Therefore, PTSD and psychosis confer vulnerability for each other as they are, to some extent, both related to traumatic life events.

Recent scientific evidence is validating the clinical hypothesis that PTSD and psychosis can co-occur. Patients suffering from PTSD have been shown to exhibit psychotic symptoms which occur episodically during the course of this disorder, such as delusions and auditory hallucinations (Bentall et al., 2014). Kilcommons and Morrison (2005) found an association between the severity and frequency of traumatic events and psychosis's course: patients with chronic and frequent traumatic life events had a worse outcome. An interesting finding is the relationship between the content of the traumatic event and the content of psychotic symptoms, particularly hallucinations (Hardy et al., 2005): child sexual abuse, especially rape, was associated with auditory verbal hallucination; physical abuse and bullying predicted paranoia as well as visual and auditory hallucinations; and institutional care placement and separation from caregivers was

associated with paranoia (Bentall et al., 2014). On the other hand, disorganized behavior and thinking is rarely observed (Kilcommons et al., 2005). Mood may be irritable, depressive, flattened, or anxious, and the level of personal is variable but generally modest. Alsawy and colleagues (2015) found that the odds of experiencing auditory hallucinations increased with the number of reliving trauma symptoms, suggesting a dose-response relationship.

Prevention is an essential intervention for vulnerable individuals who had experienced maltreatment in childhood or adulthood. Prevention aims to identify risk factors and then to intervene on multiple levels to reduce or delay the onset of event, in this case schizophrenia spectrum disorders or psychoses. Risk factors and prevention strategies for the development of mental disorders can be found in Table 3 and Table 4. As far as psychological therapy is concerned, the most effective interventions for trauma exposed individuals (children, adolescents, and adults) is a trauma cognitive–focused therapy. Cognitive behavioral therapy (CBT) seems to be the most effective form of treatment, especially when focused on the trauma (Silverman et al., 2008). This therapy should be available for any individual exposed to early traumatic life events, in addition to a high level of social support which has been demonstrated to reduce the burden of psychopathology in maltreated children or adolescents (Gangne & Melancon, 2013). CBT interventions include both exposure-based and non-exposure-based therapies. One example of exposure therapy is the PRACTICE approach, which stands for psychoeducation and parenting skills, relaxation skills, affect recognition and modulation, cognitive coping skills, trauma narrative, in-vivo exposure, conjoint parent–child sessions, cognitive restructuring, and enhancing future safety (Cohen et al., 2006; Dvir et al., 2013). Non-exposure therapies have also demonstrated efficacy in individuals with trauma and without psychosis. A randomized control trial conducted by Kredlow and colleagues (2017) demonstrated a statistically significant reduction in PTSD symptoms ($F(3, 43.7) = 5.28$, $p < .01$), depression (($F(3, 41.9) = 7.73$, $p < .001$), anxiety (($F(3, 42.7) = 2.72$, $p = .056$), quality of life ($F(3, 43.1) = 2.74$, $p = .055$) and overall

functioning (F(3, 42.4) = 6.13) following non-exposure-based CBT. Beyond psychological support, social supportive relations are also of great importance as they can reduce the risk of psychopathology in child victims of maltreatment or abuse. This hypothesis is confirmed by several studies and is even true for extreme cases of abuse such as rape (Schumm et al., 2006; Collishaw et al., 2007). For instance, women with childhood histories of abuse and rape during adulthood had fewer symptoms of PTSD if they had social support. These findings provide a significant evidence that patients with trauma and/or psychosis can benefit from social support as well as through CBT trauma–focused psychotherapy to improve their quality of life reducing psychological distress, suicidal ideation, and psychosis (Dvir et al., 2013).

**Conclusions**

Child abuse and maltreatment is one of the many environmental factors under investigation for the onset of psychosis, in addition in pre-established environmental risk factors for psychosis such as migration history, urbanization and cannabis use. In numerous studies, childhood trauma is associated with the development of several disorders in adolescence and adulthood, including depression, PTSD, suicidal behavior, alcohol abuse and dependence (Simpson et al., 2002; Enoch et al., 2011). Specificity of child abuse in psychotic disorders and particularly schizophrenia has not been fully demonstrated, in part due to methodological problems (most of the studies are retrospective and based on self–report). Research shows a higher prevalence of childhood abuse in patients with psychotic disorders. Studies from the general population and clinical samples have shown that there is a high rate of all types of abuse (CSA, CPA, CEA, CN) in patients with psychosis but none of them reported child abuse as sufficient or necessary to develop a psychotic disorder. There is evidence that early childhood adversities interact with genetic vulnerabilities in children and exert a moderating effect on other environmental risk factors for psychosis (Sideli et al., 2012). Thus, early interventions to care and support children who experienced childhood

trauma and abuse seem to be a generally recommended strategy to promote mental health and prevent the onset of mental health disorders, including psychoses.

## *Table 3*

### *The development of Mental Disorders after Child Abuse: mediating and risk factors* [1]

*Parental risk factors*

- Parents' inability to read child emotional cues
- Psychosis (both affective and non–affective) and maternal depression (including post–partum depression)
- Substance use, alcoholism
- Parental loss

*Family factors*

- Numerous families
- Young mothers
- Unwanted pregnancy
- Parental separation

*Child vulnerabilities*

- Younger age
- Child disabilities
- Prematurity and low neonatal weight
- Irritability and hyperactivity
- School difficulties
- Migration history[3]

*Socio – economic factors*

- Chronic poverty
- Low level of education
- Social inequality
- Lack of interpersonal relations
- Mono-parental family
- Cannabis use and its availability

*Environmental factors*

- Urbanicity: as it increases the risk of some mental disorders i.e. psychosis
  - Low social cohesion
  - Neighborhood deprivation
  - Crime victimization
  - Peer violence (i.e. bullying)
- Upbringing in institutional care

*Table 4*

## *The prevention of Mental Disorders after Child Abuse: General and targeted interventions*

### *Social and community*

- Human rights implementation: implementation of human and childhood laws at national level
- Social and cultural promotion: policies for social cohesion, cultural differences
- Economic interventions to reduce poverty:
  - Economic support for vulnerable individuals
  - Reduce unemployment
- Promote gender equality and appraisal/promotion and knowledge about ethnic diversities
- Improving general population mental/physical heath
  - Tackle racism and homophobia
  - Reducing use of alcohol and cannabis
  - Promotion of mental health and working on stigma about emotional/mental distress and psychiatric disorders

### *Parents and caregivers*

- Promotion of physical/mental health
- Training in parenting (especially in young parents) to support child victims of abuse
- Empowerment of access to family counselling

### *Children and schools*

- Promoting psychosocial support and psychological first aid for victims of abuse
- Training teachers and children to recognize early symptoms of mental disorders
- Promoting mental health particularly for vulnerable groups:
  - Peer violence, bullying and cyberbullying
  - Ethnic minorities
  - Gender
  - Children with disabilities

*Heath care workers*

- Awareness about child abuse and the different kind of abuse
- Training in the detection of child abuse
- Home visits
- Consider and investigate (in appropriate settings) childhood abuse when a psychological or a major psychiatric disorder is treated (potential benefits of trauma focused therapies)

## Bibliography

### Part I

Anda R.F., Felitti V.J., Bremner J.D., et al., The enduring effects of abuse and related adverse experiences in childhood. A convergence of evidence from neurobiology and epidemiology, European Archives of Psychiatry and Clinical Neuroscience, 256: 174-86, 2006.

Beebe B., Lachmann F. M., Infant Research e trattamento degli adulti, Raffaello Cortina, Milano, 2003.

Briere J., Spinazzola J., Assessment of the sequelae of complex trauma: evidence-based measures, in Courtis CA, Ford JD, Treating complex traumatic stress disorders. An evidence-based guide, The Guilford Press, New York, 2009.

Cheli M., Gambuzza C., (a cura di) Il Disturbo Post Traumatico Complesso. Dalla teoria alla pratica multidisciplinare, Franco Angeli, Milano, 2017.

Cheli M., Ricciutello C. et Al., Violenza intrafamiliare e salute mentale in adolescenza: il trauma complesso come disturbo dello sviluppo, Rivista di Psichiatria, 47, 5, 2012.

Chu A., DePrince A.P., Development of dissociation: Examining the relationship between parenting, maternal trauma, and child dissociation, Journal of Trauma and Dissociation, 7, 4, pp. 75-89, 2006. PubMedce, 2006.

Courtois C., Ford J., (a cura di), Treating Complex Traumatic Stress Disorders (Adults), Scientific Foundations and Therapeutic Models, Guilford Press, New York, 2009.

Dawson G., Panagiotides H., Grofer Klinger L., Hill D., The role of frontal lobe functioning in infant self-regulatory behavior, Brain and Cognition 20 (1):152-175. October 1992.

DOI: 10.1016/0278-2626(92)90066-U)

Di Blasio P. (a cura di), Tra rischio e protezione. La valutazione delle competenze genitoriali, Edizioni Unicopli, Milano, 2005.

Felitti V.J., Adverse childhood experiences and adult health, Academic Pediatrics, 9, 3, pp. 131-132, 2009.

Felitti V.J., "The Relation Between Adverse Childhood Experiences and Adult Health: Turning Gold into Lead", The Permanente Journal, 6, pp. 44 - 47, 2002.

Ford J.D., Child maltreatment, other trauma exposure, and posttraumatic symptomatology among children with oppositional defiant and attention deficit hyperactivity disorders, Child Maltreatment, 5: 205-17, 2000).

Freyd J., Betrayal Trauma: Traumatic Amnesia as an Adaptive Response to Childhood Abuse, Ethics & Behavior, 4(4):307-329, December 1994.

Fries A.B.W., Ziegler T.E., Kurian J.R., Jacoris S., Pollak S.D., Early experience in humans is associated with changes in neuropeptides critical for regulating social behavior, Proceedings of the National Academy of Sciences of the United States, November 22, 102 (47) 17237-17240, 2005.

Green J.G., McLaughlin K.A., Berglund P.A., Gruber M.J., Sampson N.A., Zaslavsky A.M,

Harris M., Fallot R.D., New directions for mental health services: Using trauma theory to design service systems, Jossey-Bass, San Francisco, CA, 2001.

Herman J.L., Trauma and Recovery: The Aftermath of Violence, New York: Basic Books, 1992. Trad. It. Guarire dal trauma. Affrontare le conseguenze della violenza, dall'abuso domestico al terrorismo, Magi Edizioni, Roma, 2005.

Kessler R.C., "Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication I: associations with first onset of DSM-IV disorders", Archives of General Psychiatry, 67, 2, pp. 113-123, 2010. PubMed

Lanius R.A., Vermetten E., Pain C., The impact of early relational trauma on health and disease. The hidden epidemic, Cambridge University Press, Cambridge, UK, 2010. Trad. It. L'impatto del trauma infantile sulla salute e sulla malattia. L'epidemia nascosta, Giovanni Fioritti, Roma, 2016.

Lester BM, et al. Epigenetic programming by maternal behaviour in the human infant, Pediatrics, 142:1890, 2018.

Liotti G., Farina B., Sviluppi Traumatici Eziopatogenesi, clinica e terapia della dimensione dissociativa, Raffaello Cortina, Milano, 2011.

Liotti G., Farina B., Prefazione, in Lanius R.A., Vermetten E., Pain C., L'impatto del trauma infantile sulla salute e sulla malattia. L'epidemia nascosta, Giovanni Fioritti, Roma, 2016.

Main M., L' attaccamento. Dal comportamento alla rappresentazione, Raffaello Cortina, Milano, 2008.

Martinez-Torteya C., Dayton C.J., Beeghly M., Seng J.S., McGinnis E., Broderick A., Rosenblum K., Muzik M., Maternal parenting predicts infant biobehavioral regulation among women with a history of childhood maltreatment, Development and Psychopathology, May; 26 (2):379-92, 2014. doi: 10.1017/S0954579414000017

McGowan P.O, Matthews S.G., Prenatal stress, glucocorticoids and developmental programming of stress response, Endocrinology, 159:69-82, 2018.

Meares R., A dissociation model of borderline personality disorder, Norton, New York, London, 2012.

Pagani M., "Ricerca sulle variazioni di volume dell'ippocampo dopo un trattamento con EMDR", Journal of Clinical Neuroscience, 19, pp. 475-476, novembre 2007.

Perroud N., Paoloni-Giacobino A., Prada P. e al., Increased methylation of glucocorticoid receptor gene (NR3C1) in adults with a history of childhood maltreatment: a link with the severity and type of trauma, Translational Psychiatry, Dec 13;1:59, 2011. PubMed

Porges S.W., The Polyvagal Theory: Neurophysiological Foundations of Emotions, Attachment, Communication, and Self-Regulation, Norton & Co Inc; NY, 2011. Trad. It., La teoria polivagale. Fondamenti neurofisiologici delle emozioni, dell'attaccamento, della comunicazione e dell'auto-regolazione, Giovanni Fioriti Editore, Roma, 2016.

Putnam F.W., Ten-year research update review: child sexual abuse, Journal of the American Academy of Child and Adolescent Psychiatry, 43: 269-78, 2003.

Schore A.N., La regolazione degli affetti e la riparazione del Sé, Astrolabio, Roma, 2008.

Siegel D., Mappe per la mente. Guida alla neurobiologia interpersonale, Raffaello Cortina editore, Milano, 2014.

Sroufe L.A., Egeland B., Carlson E., Collins W.A., The development of the person: The Minnesota study of risk and adaptation from birth to adulthood, Guilford Press, New York, 2005.

Steel K., "Training intensivo sul trattamento dei Disturbi Dissociativi", Istituto di Scienze Cognitive, 2-5 giugno, 3-6 novembre, Roma, 2016.

Strathearn L., Fonagy P., Amico J., Montague P.R., Adult attachment predicts maternal brain and oxytocin response to infant cues, Neuropsychopharmacology, 34(13): 2655-66, 2009. PubMed

Straus M.A., Gelles R.J., Reviewed Work: Physical Violence in 8.145 Families in American Families: Risk Factors and Adaptations to Violence, Family Relations, Vol. 39, No. 3, pp. 349-353, Jul., 1990.

Teicher M.H., Anderson C.M., Polcari A., "Childhood maltreatment is associated with reduced volume in the hippocampal subfields CA3, dentate gyrus, and subiculum", Proceedings of the National Academy of Sciences of the United States of America, 109 (9), pp. 563-572, 2012.

Tondo L., "John Bowlby interview January 1990", Clinical Neuropsychiatry, 8, pp. 159-171, 2011.

Tronick E., Regolazione emotiva. Nello sviluppo e nel processo terapeutico, Raffaello Cortina, Milano, 2008.

van der Kolk B.A., Il corpo tiene il conto. Introduzione alla psicobiologia del disturbo post-traumatico da stress, in (a cura di), Williams R., Trauma e relazioni, Raffaello Cortina, Milano, 2009.

Yehuda R., Engel S.M, Brand S.R, Seckl J., Marcus S.M., Berkowitz G.S., Transgenerational effects of posttraumatic stress disorder in babies of mothers exposed to the World Trade Center attacks during pregnancy, Journal of Clinical Endocrinology e Metabolism, 90 (7), 4115-8, 2005).

Wolfe D.A., Crooks C.V. et al., The Effects of Children's Exposure to Domestic Violence: A Meta-Analysis and Critique, Clinical Child and Family Psychology Review, 6 (3):171-87, October 2003.

**Part II**

Arseneault L, Cannon M, Witton J, Murray RM.sal association between cannabis and psychosis: examination of the evidence. Br J Psychiatry 2004; 184:110–117.

Burns T, Catty J, Dash M, Roberts C, Lockwood A, Marshall M. Use of intensive case management to reduce time in hospital in people with severe mental illness: systematic review and meta-regression. *BMJ* 2007; **335:** 336.

Cantor-Graae E, Selten JP. Schizophrenia and migration: ameta-analysis and review. *Am J Psychiatry* 2005; **162:** 12–24.

Crean RD, Crane NA, Mason BJ. An evidence- based review of acute and long-term effects of cannabis use on executive cognitive functions. J Addict Med. 2011;5(1):1-8

Dye C. Health and urban living. *Science*. 2008; 319:766–769

Di Forti M, Sallis H, Allegri F, et al. Daily use,especially of high-potency cannabis, drives theearlier onset of psychosis in cannabis users.*Schizophr Bull*. 2014;40(6):1509-1517.

Fearon, P, Kirkbride, J, Morgan, C, et al. Patterns of psychosis in black and white minority groups in urban UK: the ÆSOP study. Schizophr Bull 2005; 31(2): 222

Glaser JP, Van Os J, Portegijs PJ, Myin-Germeys I. Childhood trauma and emotional reactivity to daily life stress inadult frequent attenders of general practitioners. J Psychosom Res 2006; 61:229–236.

Jim van Os et al. Identifying Gene-Environment Interactions in Schizophrenia: Contemporary Challenges for Integrated, Large-scale Investigations (2014) European Network of National Networks studying Gene-Environment Interactions in Schizophrenia (EU-GEI). Schizophrenia Bulletin vol. 40 no. 4 pp. 729–736.

Kapur, S., 2003. Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. Am. J. Psychiatr. 160 (1), 13 – 23.

Kapur, S., Mizrahi, R., & Li, M. (2005). From dopamine to salience to psychosis—linking biology, pharmacology and phenomenology of psychosis. Schizophrenia Research, 79*(1), 59–68.*

Lataster T, Collip D, Lardinois M, Van Os J, Myin-Germeys I. Evidence for a familial correlation between increased reactivity to stress and positive psychotic symptoms. Acta PsychiatrScand 2010; 122:395–404

Lederbogen F, Kirsch P, Haddad L, et al. City living and urban upbringing affect neural social stress processing in humans. *Nature*. 2011; 474:498–501.

Li M, D'Arcy C, Meng X. 2016. Maltreatment in childhood substantially increases the risk of adult depression and anxiety in prospective cohort studies: systematic review, meta-analysis, and proportional attributable fractions. Psychol. Med. 46(4):717–30

Lieberman, J. A., & First, M. B. (2018). Psychotic Disorders. New England Journal of Medicine, 379(3), 270–280.

Marshall M, Lockwood A. Assertive community treatment for people with severe mental disorders. Cochrane Database Syst Rev 2000: CD001089.

McGrath J, Saha S, Chant D, Welham J. Schizophrenia: a concise overview of incidence, prevalence, and mortality. Epidemiol Rev 2008; 30: 67–76.

Mortensen PB, Pedersen CB, Westergaard T, et al. Effects of family history and place and season of birth on the risk of schizophrenia. N Engl J Med. 1999;340:603–608.

Phillips, P.E.M., Stuber, G.D., Heien, M.L.A.V., Wightman, R.M., Carelli, R.M., 2003. Subsecond dopamine release promotes cocaine seeking. Nature 422 (6932), 614 – 618

Pedersen CB, Mortensen PB. Evidence of a dose-response relationship between urbanicity during upbringing and schizophrenia risk. Arch Gen Psychiatry. 2001; 58:1039–1046.

Pinto R1, Ashworth M, Jones R. Schizophrenia in black Caribbeans living in the UK: an exploration of underlying causes of the high incidence rate. Br J Gen Pract. 2008 Jun;58(551):429-34.

Read, J., van Os, J., Morrison, A.P., Ross, C.A., 2005. Childhood trauma, psychosis and schizophrenia: a literature review with theoretical and clinical implications. Acta Psychiatr. Scand. 112 (5), 330.

Read J, Hammersley P, Rudegeair T. Why, when and how to ask about childhood abuse. Adv Psychiatr Treat 2007; 13:101–110.

Roger Hagen, Douglas Turkington, Torkil Berge, Rolf W. Gråwe - CBT for Psychosis. A Symptom-based Approach.

Romans, S., Belaise, C., Martin, J., Morris, E., Raffi, A., 2002. Childhood abuse and later medical disorders in women. An epidemiological study. Psychother. Psychosom. 71 (3), 141–150.

Silins E, Horwood LJ, Patton GC, et al; Cannabis Cohorts Research Consortium. Young adult sequelae of adolescent cannabis use: an integrative analysis. Lancet Psychiatry. 2014;1(4):286-293

Schultz, W., 2002. Getting formal with dopamine and reward. Neuron 36 (2), 241 – 263.

Sarah A. Sullivan, Andy Thompson, Daphne Kounali, Glyn Lewis, and Stan Zammit (2017). The longitudinal association between external locus of control, social cognition and adolescent psychopathology. Soc Psychiatry Psychiatr Epidemiol. 2017; 52(6): 643–655.

Swan, S., Keen, N., Reynolds, N., Onwumere, J., 2017. Psychological interventions for post-traumatic stress symptoms in psychosis: a systematic review of outcomes. Front. Psychol. 8, 341.

Trotta, A., Murray, R.M., Fisher, H.L., 2015. The impact of childhood adversity on the persistence of psychotic symptoms: a systematic review and meta-analysis. Psychol. Med. 45 (12), 2481–2498.

Tomassi, S., Tosato, S., Mondelli, V., et al., 2017. Influence of childhood trauma on diagnosis and substance use in first-episode psychosis. Br. J. Psychiatry 211 (3), 151.

Van Os, J., &Kapur, S. (2009). Schizophrenia. The Lancet, 374 (9690), 635–645

Varese, F., Smeets, F., Drukker, M., et al., 2012. Childhood adversities increase the risk of psychosis: a meta-analysis of patient-control, prospective- and cross-sectional cohort studies. Schizophr. Bull. 38 (4), 661.

Volkow ND, Swanson JM, Evins AE, DeLisi LE, Meier MH, Gonzalez R, Bloomfield MA, Curran HV, Baler R. Effects of Cannabis Use on Human Behavior, Including Cognition, Motivation, and Psychosis: A Review. JAMA Psychiatry. 2016 Mar;73(3):292-7.

Yung, A.R., &McGorry, P.D. (1996). The initial prodrome inpsychosis: Descriptive and qualitative aspects.Australianand New Zealand Journal of Psychiatry,30, 587–599.

Yung, A.R., McGorry, P., Francey, S., Nelson, B., Baker, K.,Phillips, L. &Amminger, G. (2007). PACE: A specialisedservice for young people at risk of psychotic disorders.Medical Journal of Australia,187, S43–S46.

Yung, A.R., Nelson, B., Stanford, C., Simmons, M.B., Cosgrave,E.M., Killackey, E.,...&McGorry, P.D. (2008). Validation of“prodromal” criteria to detect individuals at ultra-high risk ofpsychosis: 2 year follow-up. Schizophrenia Research,105,10–17.

WHO (1992), The ICD-10 Classification of Mental andBehavioural Disorders: Clinical descriptions and diagnostic guidelines. Geneva: World Health Organization

Wise, R.A., 2004. Dopamine, learning and motivation. Nat. Rev., Neurosci. 5 (6), 483 – 494.