

Full title: Early life experiences and social cognition in major psychiatric disorders: a systematic review

Running title: Environment and social cognition

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Abstract

Objective: To present a systematic review of the literature on the associations between early social environment, early life adversity, and social cognition in major psychiatric disorders, including schizophrenia, bipolar disorder, borderline personality disorder, major depressive disorder and posttraumatic stress disorder.

Method: Relevant studies were identified via electronic and manual searches of the literature and included articles written in English and published in peer-reviewed journals up to May 2018. Quality assessment was performed using the quality evaluation scale employed in previous systematic reviews.

Results: A total of 25 studies were included in the systematic review with the quality assessment scores ranging from 3 to 6 (out of 6). The vast majority of the studies reviewed showed a significant association between early childhood social experience, including both insecure attachment and adversity relating to neglect or abuse, and poorer social cognitive performance.

Conclusion: We discuss these findings in the context of an attachment model, suggesting that childhood social adversity may result in poor internal working models, selective attention towards emotional stimuli and greater difficulties with emotional self-regulation. We outline some of the steps required to translate this understanding of social cognitive dysfunction in major psychiatric disorders into a target for interventions that mitigate the adverse effects of childhood maltreatment and poor parental attachment on social cognition.

1. Introduction

Childhood adversity is highly prevalent worldwide, affecting about one third of the general population [1, 2], and contributing to a number of negative outcomes in later life, including higher rates of criminal behaviour [3], alcohol and drug use [4], and lower academic achievement [5]. Adverse childhood experiences have been identified as major risk factors for the development of many psychiatric disorders, such as schizophrenia, bipolar disorder, borderline personality disorder, major depressive disorder and posttraumatic stress disorder [6-9]. Specifically, childhood trauma – often defined in terms of physical and emotional neglect, and physical, emotional, and sexual abuse – has been a particular focus of research because of their deleterious and long-lasting effects [10]. The types and frequencies of these traumatic experiences can have a negative impact on mental health in adulthood [11]. In fact, traumatic experiences in childhood are frequently reported to show increased prevalence in patients with psychiatric disorders, with rates as high as 85% in schizophrenia spectrum disorders [12], 82% in personality disorders [13], 77% in affective disorders including major depressive disorder and bipolar disorder [12], and 70% in patients with posttraumatic stress disorder [14]. Emotional abuse and neglect appear to represent the most common forms of childhood maltreatment [15, 16].

In addition to childhood maltreatment, a number of other types of adverse early life experiences, such as early loss of caregivers and insecure attachment styles (i.e. dismissive-avoidant, fearful-avoidant and anxious-pre-occupied [17]) have also been related to psychopathology in adulthood [18-20]. The link between childhood trauma and insecure attachment has been supported by a number of studies showing that a history of childhood trauma is significantly positively associated with attachment insecurities in later life [21-24], indicating significant overlap between these experiences. This suggests that adverse childhood experiences may provoke the development of insecure types of attachment. According to Fonagy [25], childhood trauma is the most destructive factor in the development of the attachment system.

The importance of attachment was emphasised by Bowlby [26], who argued that the relationships and bonds between parents and their offspring are critical for children's cognitive, emotional and social development. Specifically, he claimed that insensitive, maltreating and neglectful parenting negatively influences individuals' interpretations and expectations, and results in construction of an unworthy and inadequate internal working model of relationships [27]. This attachment structure not only integrates past experiences, but also provides the basis on which to form expectations for later relationships. Exposure to inconsistent and unreliable attachment figures, as well as the experience of childhood trauma, can negatively affect a child's sense of safety and security, essential to the development of secure attachment and positive mental representations of self and others [28]. Specifically, the first 3 years of life are a very sensitive period for the development of the attachment relationships and exposure to traumatic events during this time has irreversible effects on subsequent cognitive, social and emotional development [26, 27, 29]. Once an attachment pattern is formed in childhood, it tends to persist beyond youth [30].

Of relevance to social cognitive development, Bowlby's [31] 'defensive exclusion' hypothesis posits that insecurely attached individuals will filter out all information related to his/her attachment figure, as this is associated with emotional pain. Even positive attachment-related information will be prohibited from entering conscious awareness as it protects individuals from experiencing psychological pain associated with the notion that they have no or very little positive experiences with their attachment figure [32]. As a result of this selective or 'biased' information processing an individual also lacks integrated memories of negative states, which in turn may impact their Theory of Mind (ToM) development [33]. Without the proper use and reflection of positive and negative mental states within one's own mind, making correct inferences about another person's beliefs or intentions can also be impaired.

Also relevant to social cognitive development, children with the experience of abuse may also be more likely to develop an enhanced sensitivity to social cues that are reminiscent of the adults who

abused them [34]. Consequently, maltreated individuals may become more vigilant and distracted by threatening stimuli ('threat-related attention bias') [35], thus failing to adequately process peripheral cognitive and social information. There is also substantial evidence that maltreating parents provide less affective interactions as compared to non-abusive parents and tend to isolate themselves and their children from social interactions, providing no stable models for forming close relationships in later life [36-39]. Specifically, those children who develop an avoidant attachment pattern would be expected to show fearfulness and avoidance in social situations, so that they are less likely to develop adequate representations of the social environment and expressions needed to accurately recognise others' emotions.

Supporting these hypotheses, a number of studies in children have shown that exposure to adverse environments interferes with the development of social cognition [40-42], which refers to the set of mental operations underlying social interactions, and in psychiatric studies generally comprises the following domains: (1) emotion recognition and regulation, (2) ToM, (3) attributional style, and (4) social perception. Deficits in social cognitive function are a hallmark feature of major psychiatric disorders resulting in impaired social and occupational functioning [43, 44].

Despite the relevance of early life experience to understanding development of social cognition in those who go on to experience psychiatric disorders, the association between early life experiences and social cognition in psychiatric disorders remains poorly understood. To synthesise what is currently known, we undertook a systematic review of the existing literature on the relationships between childhood experiences of adversity, attachment (both secure and insecure) and social cognition in adults with major psychiatric disorders, including schizophrenia (SZ), bipolar disorder (BD), borderline personality disorder (BPD), major depressive disorder (MDD) and posttraumatic stress disorder (PTSD).

2. Methods

2.1. Search strategy

An electronic search was conducted using PubMed and PsycINFO to identify original articles addressing the relationship between adverse early life experiences, attachment and social cognitive measures in adults with major psychiatric disorders, published up to May 2018. The following terms were used as search terms ((emotion recognition OR self-regulation OR theory of mind OR attribution OR facial expression OR face perception OR social cognition OR social perception OR face discrimination OR emotion regulation OR emotion perception OR social inference) AND (parent death OR institutional care OR foster care OR physical abuse OR verbal abuse OR sexual abuse OR emotional abuse OR domestic violence OR parent divorce OR parental mental illness OR neglect OR parental alcoholism OR parental maltreatment OR adversities OR childhood trauma OR attachment OR early life stress OR parental bonding OR adverse childhood experience OR childhood adversity) AND (schizophrenia OR schizoaffective disorder OR psychosis OR bipolar disorder OR borderline personality disorder OR major depressive disorder OR posttraumatic stress disorder)). We included only studies that assessed the direct relationship between adverse early life experiences (e.g. childhood trauma) and/or attachment and social cognition (e.g. theory of mind, emotion recognition) in adult patients with schizophrenia spectrum disorders, bipolar disorder, borderline personality disorder, major depressive disorder and/or posttraumatic stress disorder. Searches were limited to original articles written in English and published in peer-reviewed journals up to May 2018. Neuroimaging studies were excluded.

2.2. Quality assessment

The quality assessment was based on the revised version of the quality evaluation scale employed in previous systematic reviews [45, 46], and comprised the following items: (1) The clinical sample was

representative of the target population (eligible cases were recruited in hospitals and/or mental health services settings with a diagnosis based on well-established clinical diagnostic manuals), (2) The clinical sample was appropriately matched to the control group (patients and controls matched for at least two confounding variables: age and/or sex and/or education level and/or body mass index), (3) The authors performed sample size calculations and/or power analysis, (4) The study used well-established measures of early life stress and attachment styles, (5) The study used well-established measures of social cognition, (6) The authors reported effect sizes and/or confidence intervals of their main findings. Each item scored one point if the criterion was met (i.e. present) and the overall quality score was calculated by adding up all the items.

2.3. Study characteristics

The literature search identified 2619 relevant publications of which 20 were found to meet criteria for inclusion after examining the titles and abstracts. Based on a review of the reference list of these papers a further five published studies met the inclusion criteria. In total 25 publications were included. These included nine studies conducted in patients with schizophrenia spectrum disorders, two studies included patients with bipolar disorder, six studies of patients with borderline personality disorder, three studies of patients with posttraumatic stress disorder, one study which included borderline personality disorder and bipolar disorder patients, one was performed on borderline personality disorder and major depressive disorder patients, two on patients with major depressive disorder and one was carried out in patients with borderline personality disorder plus additional personality disorders. Studies focused only on healthy participants were not included in this review; however, in patient studies in which a healthy comparison group was included, the data from these groups are reported. The PRISMA flow diagram is presented in **Fig. 1** [47] and the relevant studies are presented in **Table 1**.

Table 1. Characteristics of the studies included in the review.

Study	Participants N (male:female)	Age Mean (SD)	Environmental measures	Social cognitive measures	Main findings	Quality assessment total score
Schalinski <i>et al.</i>, (2017) [48]	Patients with psychosis= 168 (112:56) HC=50 (28:22)	Patients with psychosis = 27.9 (8.4) HC= 26.8 (7.9)	MACE	MCCB	Cumulative adverse childhood experiences and physical neglect at age 11 were significantly negatively associated with social cognition in patients.	5
Kilian <i>et al.</i>, (2017) [49]	FEP= 56 (42:14) HC= 52 (35:17)	FEP= 23.8 (6.2) HC=25.1 (6.8)	CTQ	MCCB	Childhood neglect was significantly correlated with social cognitive impairments in both patients and controls. These associations were stronger in the patient group.	5
Koelkebeck <i>et al.</i>, (2017) [50]	MDD= 38 (21:17) HC = 40 (23:17)	MDD= 40.3 (11.4) HC= 39.7 (10.9)	AAS	'animated triangles' task	Insecure attachment style (i.e. anxious, dependent) was significantly associated with ToM deficits in patients.	5
Jiménez <i>et al.</i>, (2017) [51]	LP BD= 10 (4:6)* AP BD= 74 (31:43)* HP BD= 29 (11:17)*	LP BD=52.0 (15.28)* AP BD= 48.23 (11.37)* HP BD= 45.24 (10.7)*	CTQ	MSCEIT-ME	No significant associations were reported between childhood trauma and social cognition.	4
Palmier-Claus <i>et al.</i>, 2016 [52]	SZ=20 (13:7) FEP=20 (16:4) UHR=14 (6:8) HC=120(35:85)	SZ = 39.6 (8.9) FEP = 24.6 (5.2) UHR = 22.6 (5.2) HC = 20.1 (2.5)	CTQ; PAM	Hinting Task; RMET	No significant effects of childhood trauma on either measure of ToM were reported.	4
Olbert <i>et al.</i>, 2016 [53]	SZ=138 (102: 36)	SZ = 41.3 (12.5)	PAM	SCAF paradigms; AIHQ (the blame bias subscale); Facial Affect Identification	No significant correlations between attachment and social cognitive measures were found.	3
Garcia <i>et al.</i>, 2016 [54]	Early psychosis patients=79 (48:31) HC= 58 (30:28)	Early psychosis patients (male) = 24.4 (4.5) Early psychosis patients (female)= 26.8 (5.9) HC (male)= 24.0 (4.8) HC (female) = 23.9 (4.2)	CTQ	MSCEIT-ME	A history of childhood trauma was associated with poorer social cognition in patients.	3
Brüne <i>et al.</i>, 2016 [55]	BPD=30 (all female) HC=30 (all female)	BPD=25.7 (6.3) HC= 25.3 (7.7)	CTQ; Parental Rearing Style Questionnaire (German version – FEE); RQ	Cartoon-based mentalization task	Significant correlations between childhood trauma, recalled parenting, attachment and performance on the mentalizing task were reported in the patient group. No CTQ or FEE data were recorded for the control group.	4
Petersen <i>et al.</i>, 2016 [56]	BPD= 19 (1:18) HC= 20 (1:19)	BPD=33.0 (14.27) HC=32.5 (13.57)	CAT	RMET; EAT; False-Belief Picture Sequencing Task – short version; Joke-Appreciation Task; Faux Pas Task	Childhood experiences of punishment were significantly associated with decreased mentalization ability in adulthood.	4
Beeney <i>et al.</i>, (2015) [57]	BPD= 150 (98: 52)	BPD= 44.9 (10.4)	ECR-R	PAI-BOR; DERS; IIP; clinician's assessment of mentalization	Anxious and avoidant attachment were significantly associated with mentalization difficulties.	4
Günther <i>et al.</i>, 2015 [58]	MDD=45 (15:30)	MDD= 34.04 (9.48)	CTQ	Dot-Probe task	A history of emotional abuse and physical neglect was significantly associated with attentional bias scores to sad faces.	3
Russo <i>et al.</i>, 2015 [59]	BD (type I: 52; type II: 22) = 75 (51:24)	BD=47.1 (10.2)	CTQ	ERT	A history of childhood trauma, specifically emotional neglect and physical abuse, was significantly associated with a decreased ability to recognise anger.	3

Nazarov et al., (2015) [60]	PTSD= 29 (all female) HC=21 (all female)	PTSD= 42.0 (12.3) HC=39.9 (14.7)	CTQ	Two computer-based tasks assessing affective prosody: recognition and discrimination	A history of childhood trauma was associated with emotion recognition and discrimination difficulties in patients.	4
Pos et al.,2015 [61]	SZ=111 (92:19) Siblings**= 106 (47:59) HC=63 (43:20)	SZ=31.1 (7.57) Siblings**= 30.81 (7.98) HC=30.65 (10.6)	CTQ – SF; PAM	CBE	Avoidant attachment (measured with the Psychosis Attachment Measure; PAM) showed a U-shaped association with affective ToM (first order and second order) as well as cognitive ToM (second order) indicating worse ToM performance at medium scores and better ToM performance at lower and higher scores on avoidant attachment in patients. Anxious attachment was significantly negatively associated with cognitive ToM (second order) in patients. No significant differences were found between attachment and ToM in siblings or controls.	3
Powers et al., (2015) [62]	PTSD*** = 67 (all female)	NR	TEI; CTQ	Emotional Conflict Regulation Behavioral Task	Higher levels of childhood trauma were significantly associated with emotion regulation difficulties.	5
Fletcher et al.,2014 [63]	BD II=24 (NR) BPD=24 (NR)	Both groups= 32.9 (11.3)	MOPS	CERQ; DERS	Dysfunctional parenting experiences were significantly associated with emotion regulation difficulties.	4
Nazarov et al., (2014) [64]	PTSD= 31 (all female) HC= 20 (all female)	PTSD= 42.1 (12.0) HC= 35.8(13.2)	CTQ; PBI	RMET; IPT-15	Childhood trauma was significantly associated with difficulties on the IPT-15 task in patients.	5
Nicol et al.,2014 [65]	BPD=20 (5:15) HC=21(5:16)	BPD= 34.3 (8.5) HC=34.5 (11.6)	CTQ	Ekman 60 faces test	In the patient group, a history of childhood trauma, specifically emotional and physical abuse, was significantly associated with deficits in recognising disgust.	4
Carvalho Fernando et al.,2014 [66]	BPD=49 (5:44) MDD=48 (22:26) HC=63 (22:41)	BPD= 28.63 (8.99) MDD= 33.15 (8.89) HC= 31.44 (9.98)	CTQ	ERQ; DERS	Childhood trauma experiences, specifically emotional abuse and neglect, were significantly associated with emotion regulation difficulties in both patients and controls.	4
Scott et al.,2013 [67]	BPD=100 (35:65)	BPD= 45.9 (10.6)	AAPR	EERI	Preoccupied (anxious) attachment was significantly associated with emotion regulation difficulties.	3
Zheng et al.,2011 [68]	Patients with personality disorders**** = 123 (61:62) HC=166 (82:84)	Patients with personality disorders**** = 24.42 (7.03) HC= 23.24 (3.86)	PBI	JACFEE	In patients and healthy controls, maternal care significantly predicted the accuracy of recognising sadness. Paternal care negatively predicted the accuracy of recognising anger in patients. In the control group, the maternal autonomy denial significantly predicted the accuracy of recognizing sadness.	4
MaBeth et al.,2011 [69]	FEP=34 (20:14)	NR	AAI	RF	Patients with secure and insecure/preoccupied attachment styles showed significantly higher RF than those with insecure/dismissing (avoidant) classifications.	3
Lysaker et al.,2011 [70]	SZ/SZD = 101 (86:15)	SZ= 46.26 (9.66)	TAA	MAS; BLERT	Patients with a history of childhood sexual abuse had lower awareness of other people's emotions than those without this history.	3
Preissler et al. (2010) [71]	BPD= 64 (all female) HC= 38 (all female)	BPD= 29.2 (8.9) HC=31.7 (10.3)	PDS	RMET; MASC	Experience of sexual trauma significantly negatively predicted social cognitive abilities on the MASC in patients.	6

Donohoe et al., 2008 [72]	SZ/SZD=73 (49:24) HC=78 (45:33)	SZ= 41.4 (11.5) HC=38.3 (13.5)	RQ	IPSAQ	Secure attachment was significantly associated with lower 'personalising bias' scores in the patient group only.	4
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*gender and mean age was reported for three different cluster groups

**non-affected siblings of patients

*** 67 participants with PTSD symptoms (30% of the sample met diagnostic criteria for PTSD)

****paranoid (n=13), schizoid (n=26), schizotypal (n=14), antisocial (n=8), borderline (n=7), histrionic (n=18), narcissistic (n=3), avoidant (n=14), dependent (n=8), or obsessive-compulsive (n=12) personality disorders

SZ: schizophrenia; SZD: schizoaffective disorder; BD: bipolar disorder; BPD: borderline personality disorder; MDD: major depressive disorder; PTSD: posttraumatic stress disorder; FEP: first-episode psychosis; LP: low performance; AP: average performance; HP: high performance; PAM: Psychosis Attachment Measure; CT: childhood trauma; MACE: Maltreatment and Abuse Chronology of Exposure Scale; MCCB: MATRICS Consensus Cognitive Battery; CTQ: Childhood Trauma Questionnaire; CTQ-SF: Childhood Trauma Questionnaire – Short Form; FEE: Fragebogen zum erinnerten elterlichen Erziehungsverhalten (German: questionnaire on recalled parental rearing behaviour); CBE: Conflicting Beliefs and Emotions; MAS: Metacognition Assessment Scale; MASC: Movie for the Assessment of Social Cognition; BLERT: Bell-Lysaker Emotion Recognition Task; ECR-R: Experience in Close Relationships Scale – Revised; CAT: Child Abuse and Trauma Scale; TAA: Trauma Assessment for Adults; AAS: Adult Attachment Scale; EAT: Expression Attribution Test; IPSAQ: Internal, Personal and Situational Attributions Questionnaire; SCAF: Social Cognition and Functioning; AIHQ: Ambiguous Intentions Hostility Questionnaire; MSCEIT-ME: Mayer–Salovey–Caruso Emotional Intelligence Test – Managing Emotions; IPT-15: Interpersonal Perception Task-15; PAI-BOR: Personality Assessment Inventory-Borderline Personality Disorder Identity Scale; IIP: Inventory of Interpersonal Problems; AAI: Adult Attachment Interview; RF: Reflective Functioning; TEI: Traumatic Events Inventory; RMET: Reading the Mind in the Eyes Task; ERT: Emotion Recognition Task; MOPS: Measure of Parental Style; CERQ: Cognitive Emotion Regulation Questionnaire; DERS: Difficulties in Emotion Regulation Scale; PBI: Parental Bonding Instrument; JACFEE: Matsumoto and Ekman Japanese and Caucasian Facial Expressions of Emotion; RQ: Relationship Questionnaire; AAPR: Adult Attachment Prototype Ratings; EERI: Emotion Experiencing and Regulation Interview; ERQ: Emotion Regulation Questionnaire; ToM; Theory of Mind; NR: not reported

3. Results

3.1. Quality evaluation

The quality of the 25 studies included in this systematic review was assessed by two independent reviewers and is presented in **Supplementary Table 1**. The scores ranged from 3 to 6 points (out of 6) in the quality assessment instrument. All of the studies recruited clinical populations in hospitals and mental health services, and their diagnosis was confirmed using well-established clinical diagnostic manuals (e.g. Structured Clinical Interview for DSM-IV (SCID) [73]). Only three studies reported performing sample size calculations and/or power analysis [50, 71, 74] and six studies used a sample size of less than 30 patients [52, 56, 60, 63-65], thus limiting the generalisability of findings. Other methodological flaws included either poorly matched control groups [52, 54, 61] or no control groups at all [51, 53, 57, 58, 63, 67, 69, 70, 74, 75]. The majority of the studies employed well-established measures of early life stress and attachment (e.g. Childhood Trauma Questionnaire (CTQ) [76], Relationship Questionnaire [77])) and social cognition (e.g. Reading the Mind in the Eyes Task [78], Emotion Recognition Task [79]) providing a valid description of the childhood experiences and social cognitive functioning. Less than half of the studies [48, 49, 51-53, 57, 60, 61, 63, 64, 71,

74] reported the effect sizes and/or the confidence intervals of the main statistical analyses affecting the interpretation of the findings.

3.2. Early social environment and social cognition in major psychiatric disorders

3.2.1. Schizophrenia Spectrum Disorders

We identified a total of nine studies that investigated the impact of early life environment on social cognition in patients with schizophrenia spectrum disorders.

In a study of 34 patients with first-episode psychosis (FEP) MaBeth et al. [69] showed that patients classified as having an insecure/dismissing (avoidant) attachment style had significantly lower scores on a measure of emotional ToM than patients with either a secure or an insecure/preoccupied (anxious) attachment style. However, the generalisability of these results was limited by the small sample size, particularly of patients with an insecure-preoccupied attachment style, and the absence of a healthy participant group. In terms of established illness, Donohoe et al. [72] examined the association between relationship style, an adult indicator of early childhood attachment, and attributional style in 73 patients with schizophrenia or schizoaffective disorder and 78 healthy controls. The authors found that lower 'personalising bias' (attributing negative events to others rather than to situational factors) was predicted by higher secure relationship style ratings in the patient group but not in healthy controls. Several studies since then have examined the link between (childhood) attachment/parental bonding styles and social cognitive outcomes in patients with an established psychotic disorder. Pos et al. [61] reported that avoidant attachment (measured with the Psychosis Attachment Measure; PAM [80]) was significantly associated with cognitive (second order) and affective (first and second order) ToM in patients with a diagnosis of schizophrenia spectrum disorder (n=111). Additionally, anxious attachment was linked to poorer performance in cognitive ToM (second order). Neither anxious nor avoidant attachment styles were associated with ToM measures in non-affected siblings (n=106) or healthy controls (n=63). By contrast, Olbert et al. [53],

who again used the PAM to assess the relationship between adult attachment style and social cognition in 138 patients with schizophrenia, found no correlations between these measures. The authors suggest that these findings may reflect construct validity issues with the PAM, the psychometric properties and construct validity in terms of measuring ToM.

In terms of association with early adversity, Lysaker et al. [70] investigated the relationship with social cognition in 67 patients with schizophrenia and 34 patients with schizoaffective disorder (a healthy participant group was not included in the study). Based on this analysis, the authors found that the group aware of their own emotions but not those of others had a significantly higher report of childhood sexual abuse. Significant associations were also reported in the study by Schalinski et al. [48] comprised of 168 patients with schizophrenia spectrum disorders and 50 healthy controls. The results highlighted a negative impact of adverse childhood experiences, specifically physical neglect at age 11, on social cognitive function in schizophrenia. Similarly, Garcia et al. [54] found a negative correlation between higher early life adversity total scores and ToM total scores in FEP patients and Kilian et al. [49] provided additional evidence for the association between adverse life events and social cognition as they found that childhood neglect was a significant predictor of social cognitive deficits in the same population of patients. By contrast, in an analysis of the relationship between childhood adversity and social functioning in small clinical groups (20 patients with chronic schizophrenia, 30 FEP patients and 14 ultra-high risk individuals) and a larger healthy control group, Palmier-Claus et al. [52] found that childhood adversity, as measured by the CTQ[76], did not significantly predict performance on either measure of ToM (Reading the Mind in the Eyes Task, Hinting Task) in any of the statistical models they tested.

3.2.2. Bipolar Disorder

Further, in a sample of 75 patients with bipolar disorder, Russo et al. [75] found that traumatic childhood experiences, specifically emotional neglect and physical abuse, resulted in impairments in

the recognition of angry faces in comparison to those with no such history. A trend level association was also observed for physical neglect. A healthy comparison group was not included in this study. By comparison, a similar study by Jiménez et al. [51] investigating the association between childhood trauma and cognitive performance in a sample of 113 bipolar patients did not fully replicate findings by Russo and colleagues [75] as they only observed a non-significant trend toward an association between physical neglect and social cognition (measured with the Managing Emotions branch of the MSCEIT [81]). However, as suggested by the authors, these findings may be due to the fact that the social cognitive tasks they used did not sufficiently measure this specific domain of social cognition.

3.2.3. Borderline Personality Disorder

In a sample of age and gender matched patients with bipolar disorder II (n=24) and borderline personality disorder (n=24), Fletcher et al. [43] investigated the relationship between perceived parental style and emotional self-regulation showing a significant association between dysfunctional parenting experiences and maladaptive emotion regulation strategies. Another study conducted by Zheng et al. [61] in 123 patients with various personality disorders and 166 healthy controls, found that parental care significantly predicted emotional accuracy in patients and controls. Specifically, better maternal care was associated with greater accuracy in recognising expressions of sadness, whereas worse quality of paternal care was significantly associated with better recognition of anger. Significant associations were also reported in the study by Scott et al. [51] comprised of 100 patients with borderline personality disorder (35 males and 65 females), with no comparison control group. The authors showed that preoccupied (anxious) attachment style and difficulties with emotion regulation were significantly positively associated. More recently, Beeney et al. [57] provided additional evidence for the relationship between attachment insecurities and social cognition as they reported a link between insecure attachments and deficits in mentalization in a sample of 150 patients with borderline personality disorder. Furthermore, Brüne et al. [61] found that ToM was

associated with parenting style, childhood trauma and attachment style in the patient group based on a study of 30 female borderline personality disorder patients and 30 female healthy controls. Specifically, poorer affective ToM performance was associated with lack of maternal emotional warmth, rejection and punishment, physical neglect and abuse, emotional neglect and preoccupied attachment style. Detrimental effects of childhood trauma, specifically sexual abuse and punishment, on ToM abilities were also reported by Preissler et al.[71] , and more recently by Petersen et al.[56] based on 64 and 19 patients with borderline personality disorder, respectively. Likewise, in the study comprised of 20 borderline personality disorder patients and 21 healthy controls, Nicol et al. [44] reported a significant association between a childhood history of emotional and physical abuse, and poorer emotional recognition – specifically, identification of disgust. Finally, another study on childhood adversity conducted by Carvalho Fernando [62] explored the association between self-reported childhood traumatic experiences and emotional self- regulation in a sample of 49 borderline personality disorder and 48 major depressive disorder patients and 63 healthy controls. They observed that maltreatment experiences, especially emotional neglect and abuse, were significantly associated with poorer emotional self-regulation in both patients and healthy controls, as measured with the Emotion Regulation Questionnaire [63] and the Difficulties in Emotion Regulation Scale [64].

3.2.4. Major Depressive Disorder

Evidence for the association between childhood adversity and social cognitive functioning was also provided by Günther et al. [58] in a sample of 45 patients with major depressive disorder; no healthy participants were included in the study. The authors reported that more severe maltreatment during childhood resulted in mood-congruent biases in emotion processing (i.e. sustained attention toward sad facial expressions). In terms of the association with attachment, Koelkebeck et al. [50] showed that dependent and anxious attachment styles were related to lower scores on the ToM task in 38

patients with major depressive disorder patients suggesting that trustful and less dependent attachment in relationships may result in better social cognitive abilities.

3.2.5. Posttraumatic Stress Disorder

Three further studies have examined the association between adverse early social environment and social cognition in patients with posttraumatic stress disorder. The first study by Powers et al. [74] conducted in 67 individuals with PTSD symptoms (19 of which met diagnostic criteria for PTSD) and comparing individuals with low and high childhood trauma reported that moderate-to-severe childhood abuse was significantly related to worse emotional regulation scores. This finding was independent of current PTSD symptoms, depressive symptoms, and adult trauma exposure.

Furthermore, Nazarov et al. [64] demonstrated, in a sample of female patients with PTSD (n=31) and matched healthy controls (n=20), that traumatic childhood experiences in individuals with PTSD were associated with difficulties interpreting scenes depicting kinship interactions, as measured with the Interpersonal Perception Task-15 [82]. Finally, in the subsequent and similarly sized study by Nazarov et al. [60] examining the ability to discriminate affective prosody in women with PTSD and healthy controls, the authors observed that childhood maltreatment (specifically emotional abuse, emotional and physical neglect) was related to less accurate discrimination and slower identification of emotions.

4. Discussion

The main aim of this review was to synthesise the literature exploring the association between early life environment (i.e. attachment, childhood trauma) and social cognition in individuals with a diagnosis of either schizophrenia, bipolar disorder, borderline personality disorder, major depressive disorder and/or posttraumatic stress disorder. Thus, we conducted a systematic search of the

literature, which identified 25 relevant studies. Of these studies, nine were conducted in patients with schizophrenia spectrum disorders, seven in patients with personality disorders, four in patients with affective disorders, three in patients with anxiety disorders and two in mixed groups of patients with either affective or personality disorders. This literature is relatively recent, with the first study being published ten years ago [72], with an apparent growth in the numbers of articles published, which indicates an increased interest in the topic.

The majority of the studies reviewed showed a significant association between early childhood experience, including both sub-optimal parenting and childhood adversity relating to neglect or abuse, and poorer social cognition. Together, these data suggest that these negative early social experiences deleteriously impact on later social cognitive function in patients, and to some extent in healthy participants also. Specifically, emotional and physical abuse, neglect, and avoidant attachment styles were found to be the strongest predictors of ToM, emotion recognition deficits, and emotional dysregulation. The only studies (n=3) that did not report this relationship were either based on small sample sizes (n<30)[52] which were likely to have been underpowered, employed a measure of attachment with unclear construct validity [53] or used a task that was not sufficient to measure a specific domain of social cognition [51].

Some limitations should be acknowledged regarding the generalisability of the data reviewed in this study. Firstly, a number of studies were based on small sample sizes, which may not have been sufficiently powered for detecting small effects regarding the relationship between adverse early life environment and social cognition. Secondly, the majority of the studies included either poorly matched control groups or no control groups at all, thus limiting the generalisability and reliability of findings. In particular, this made it difficult to determine whether there were differential effects of early social environment on social cognition according to status as patient or healthy controls, or between patient groups. Thirdly, these studies were conducted in patients of different age groups

and phases of the illness (e.g. FEP, chronic). While this has the advantage of reflecting the effects of social cognition on a broader population, the effects on different illness phases are unknown. Another limitation of the studies reviewed here is that the early childhood experiences were assessed through subjective retrospective measures affecting potentially the accuracy of these reports. A number of studies have previously provided strong support for the validity and reliability of the retrospective self-reports of childhood maltreatment [83-85]. However, an important factor that has yet to be addressed is whether and to what extent age of onset and frequency of traumatic experiences moderate their effects [9, 86]. Finally, social cognitive measures used in the studies were considerably heterogeneous, thus preventing us from conducting a meta-analysis. Notwithstanding these limitations, and as already noted, the vast majority of the studies provided firm evidence of the significant effects of early childhood environment on social cognitive functioning.

4.1. Early social environment and Social cognitive deficits in major psychiatric disorders: An attachment perspective

As noted in our introduction, Attachment theory [26] provides a framework for understanding the potential cognitive mechanisms behind this relationship between early social environment and social cognition. This theory proposes that typical social, cognitive and emotional development is formed on the basis of an attachment bond with the caregiver, which provides a child with the inputs from which internal representations of others and self are constructed. If the attachment process is disrupted, for instance by a traumatic event, the child may not develop the secure base essential to form and maintain relationships throughout life and acquire social cognitive skills.

The results of our review are complimentary to existing evidence of a strong link between adverse parental experience and childhood trauma and mental health problems in adulthood. In particular,

exposure to early life stress has been frequently shown to increase the risk for psychosis [87, 88], bipolar disorder [89, 90], borderline personality disorder [13, 91], major depressive disorder [92, 93] and posttraumatic stress disorder [94]. There is also consistent evidence that childhood adversity, specifically emotional abuse, is associated with clinical characteristics of these disorders, including an earlier onset of the illness [95, 96], an increased risk of at least one lifetime suicide attempt [97, 98], and higher symptom severity [86, 99, 100]. Because social cognitive abilities are likely to be acquired through interaction with primary caregivers and the broader environment, insecure attachment and traumatic experiences in early developmental stages may disrupt their development. Thus, social cognitive impairments may be a possible pathway through which childhood adversities increase the risk for developing psychiatric disorders and act as a mediator between negative early life experiences and later psychopathology. A direct link between social cognition and symptoms is suggested by the fact that many psychotic symptoms, such as auditory hallucinations or reasoning biases, referred to as 'jumping to conclusions', can be a result of attribution of one's actions, feelings and thoughts to external sources and impaired mentalising abilities, respectively [101].

4.2. Early social environment and Social cognitive development in major psychiatric disorders:

Biological factors

Since the era of candidate gene studies, the relationship between early life adversity, genetic risk and phenotypic variation has been a subject of great interest to the field of psychiatric genetics. Two genetic variants previously associated with psychiatric risk receiving particular attention have been the Serotonin transporter gene (5-HTT) and the BDNF Val66Met polymorphism. While the potential role for 5-HTT in mediating the effects of early adversity on later outcomes was first highlighted by Caspi et al. [102], the role of this variant has remained controversial, and unsupported in a meta-analysis by Risch et al. [103]. To our knowledge, no social cognition studies in humans have been carried out that test the interactive effects of 5-HTT and early adversity, although evidence from

animal studies point to cognitive effects [104]. Similarly, we found only one study of the interaction between early adversity and the Val66Met polymorphism at BDNF in relation to cognition [105], but a measure of social cognition was not included in this study.

Independent of early environment, variation at several genomic loci has been implicated in social cognition, both for specific disorders (e.g. in Schizophrenia with variants within *ZNF804A* [106] and *MIR137* [107]) and across disorders (e.g. Oxytocin; for a recent review see Kendrick et al. [108]). To date, however, and to our knowledge, no studies have tested the interaction between social cognition, early adversity, and genome wide associated risk loci for psychiatric disorders. This remains a priority for future research that seeks to model the relationship between early adversity and genetic risk in contribution to social cognitive development.

Patients with major psychiatric disorders reporting a history of early adversity have also been found to show increased hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis as compared to those with no prior experience of maltreatment [109, 110]. Furthermore, there is some evidence that this relationship may be conditional on genetic variation at the 5-HTT locus [111-113]. This hyperactivity of the HPA axis is thought to affect the neural growth in developmentally sensitive structures and function of brain regions with a high density of glucocorticoid receptors (e.g. hippocampus and prefrontal cortex [114]) as well as regions sensitive to repeated neuronal excitation (e.g. amygdala [115]). These structural and functional changes may result in disruption of cognitive processes, specifically memory, learning, and social information processing [116].

Chronically elevated corticosterone levels resulting from early life adversities have also been found to hinder the integrity of ventral and dorsal medial prefrontal cortex, which comprise the 'neural circuitry of self', leading to disruptions in self-referential and self-monitoring processes [117].

Furthermore, in major psychiatric disorders, a history of childhood abuse has been associated with decreased grey matter in brain areas involved in social cognitive processes, i.e. dorsolateral prefrontal cortex, ventromedial prefrontal cortex, and amygdala [118-122]. Although smaller gray matter volume is found in several brain regions associated with higher cognitive processes in all

patients with psychiatric disorders, the experience of childhood trauma appears to be an additional risk factor for gray matter loss [119]. Numerous studies have also shown that childhood adversities contribute to functional brain alterations that may lead result in social cognitive deficits. For instance, Quidé and colleagues [123] reported a positive association between early life trauma and activation of the dorsomedial prefrontal cortex in schizophrenia and an increased amygdala activation was reported by Hentze et al. [124] in trauma-exposed patients with chronic depression during an affective ToM task. Additionally, in a recent study involving patients with schizophrenia, Cancel et al. [125] has found that during an emotional valence task, childhood trauma was negatively associated with decreased connectivity between the amygdala and the precuneus, the posterior cingulate cortex and the calcarine sulcus, all of which are involved in theory of mind.

5. Conclusion

Deficits in social cognition are suggested to represent a core aspect of disability in psychiatric disorders such as Schizophrenia, and may be more predictive of psychosocial functioning than general cognitive ability [126]. The fact that these deficits are not generally improved by antipsychotic medication [127, 128] makes social cognition an important treatment target, and makes the development of a causal working model of social cognitive deficits of crucial importance.

This systematic review provides a comprehensive picture of current research on the relationship between early life environment and social cognition in patients with major psychiatric disorders. The studies reviewed suggest a crucial role of early childhood experiences in the development of social cognitive abilities, which may represent a mediator between early life adversities and later symptom severity. Studies to understand the mechanisms by which this occurs at neurocognitive and biological levels remain an important goal for the field. Alongside these research needs, the findings of this review underline the importance of addressing the various types of early childhood social experiences and adversity in clinical assessment and interventions, given the abundant evidence of

the later effects of these experiences. Finally, the studies reviewed are relevant from a public health perspective, highlighting the importance of early childhood interventions (e.g. parenting programs) that seek to minimise the occurrence and long term effects of adversity in early life.

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Conflict of interest

None to declare

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Vitae

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Prof. Gary Donohoe was appointed professor and chair of Psychology at NUI Galway in 2013. His research group (CogGene) studies how brain structure and function are affected by genetic risk factors. To do this, his work draws on neuropsychological, electrophysiological, and neuro-imaging techniques for investigating the role of gene function at the level of individual brain systems. This work has led to a number of important insights into newly discovered risk genes for psychosis.



Gary's research group is also actively involved in developing psychological therapies for major mental health disorders, including therapies that address cognitive deficits in schizophrenia.