Family Environment in Early Psychosis.
In search of the psychological mechanisms underlying the manifestation of Expressed Emotion in at-risk and onset stages of psychosis

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Doctoral Thesis

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Prof. Neus Vidal Barrantes

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Als meus pares,
per un tot immesurable.

A tu, Roger,
per fer sempre fàcil el
que resulta difícil.

"Understanding is a two-way street"

Eleanor Roosevelt

"Normality is a paved road:

It's comfortable to walk,

but no flowers grow"

Vincent van Gogh

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CONTENTS

1. INTRODUCTION

Schizophrenia and other schizophrenia-spectrum disorders are among the most impairing mental conditions, commonly associated with substantial personal suffering as well as with significant costs and burden to the individual, the family, but even for the larger social system (Andlin-Sobocki & Rössler, 2005; Rössler, Salize, van Os, & Riercher-Rössler, 2005; Shah, Mizrahi, & Mckenzie, 2011; van Os & Kapur, 2009). Their estimated lifetime prevalence is around 3% in the population (Perälä et al., 2007) and their onset usually first appears in late adolescence or early adulthood, provoking significant levels of disability, loss of psychosocial functioning and negatively affecting the quality of life of both the individual and their family (Miller, Dworkin, Ward, & Barone, 1990; Caqueo & Lemos, 2008; Lua & Bakar, 2011). Despite intensive research, their etiology remains insufficiently understood; however, there is a growing body of research suggesting that some factors (e.g., genetic, biological, psychosocial) may be involved in its pathogenesis and most probably interact in complex ways to create vulnerability (Shah, Tandon, & Keshavan, 2013; van Os, Krabbendam, Myin-Germeys, & Delespaul, 2005; van Os, Kenis, & Rutten, 2010). Comprehending how these discouraging disorders develop is especially important for identifying effective prophylactic and therapeutic interventions.

Traditional medical models have proposed a categorial view of disorders represented by diagnostic classifications systems of mental disorders such as the Diagnostic and Statistical Manual of Mental Disorder (DSM; APA, 2002) and the International Classification of Disease (ICD; WHO, 1992). Based on this, the spectrum of psychotic disorders, which includes both affective and non-affective psychoses (i.e., schizophrenia-spectrum) has been defined by the presence of abnormalities in one or more of the following five domains: delusions, hallucinations, disorganized thinking, abnormal motor behavior and negative symptoms. In contrast to categorical approach, increasing evidence from multiple lines of

research has indicated that schizophrenia-related phenotypes are better conceptualized as continuous rather than categorical – with vulnerability extending well beyond the diagnostic thresholds (Johns et al., 2004; Kwapil, Chapman, & Chapman, 1999; Myin-Germeys, Krabbendam, & van Os, 2003). According to this, schizophrenia-related phenotypes might be better represented across a broad continuum of nonclinical (schizotypy traits, psychotic-like experiences), subclinical ("prodrome" or at-risk mental states), and clinical (psychotic-spectrum disorders) manifestations with discontinuous degree of disability and need for care (Kwapil & Barrantes-Vidal, 2015). Therefore, dimensional or continuum models consider the existence of continuity between health and pathology (Kerr & McClelland, 1991) and offer a great opportunity for understanding the processes and mechanisms involved in symptom formation and for identifying fruitful targets for both prevention and intervention (Claridge, 1997).

Increasing interest has been raised on the prognostic potential of early identification and intervention in the prodromal and first-episode psychotic phases, thus allowing to improve the course of the disorder and decreasing its long-term impact (Correll, Hauser, Auther, & Cornblatt, 2010; Csillag et al., 2016; Larson, Walker & Compton, 2010). Early detection and intervention strategies facilitate the prevention of progression to full-blown manifestation of psychosis, with all its associated risk, stigma and morbidity, as well as the opportunity to examine risk factors and developmental processes around the onset phase of schizophrenia spectrum disorders (Fusar-Poli, McGorry, & Kane, 2017; McGorry, Killackey & Yung, 2008; McGorry, Nelson, Goldstone & Yung, 2010; McGorry, 2015). Additionally, assessing individuals at their first episode of any psychosis diminishes the effects of potential confounding factors such as illness severity, illness progression, or long-term pharmacological treatment (Addington, McKenzie, Norman, Wang, & Bond, 2013) and allows multicomponent interventions aimed at symptomatic and functional recovery and the prevention of relapse (Breitborde, Moe, Ered, Ellman, & Bell, 2017).

The role of family support in the early stages of psychosis is highly relevant given that relatives are the main informal caregivers of individuals with mental health difficulties, and therefore play an invaluable role in the process of recovery (Domínguez-Martínez et al., 2011; McFarlane, 2016a). Unfortunately, they often experience grief, shock and high levels of distress, including depression, anxiety and subjective experience of burden (Addington & Burnett, 2004; Jansen et al., 2015; Jansen, Gleeson, & Cotton, 2015). This is particularly important since most of early psychosis individuals live at home (50-70%) with their families at the early stages of illness (Addington, Addington, Jones, & Ko, 2001). An early understanding and assessment of these factors, accompanied by an adequate therapeutic support, is a significant component of a comprehensive early intervention programme to prevent long-term distress in the whole family following psychosis onset (McGorry, Killackey, & Yung, 2008).

The work presented in this thesis has been developed within the framework of the new paradigm of early detection and intervention in psychosis, focusing primarily on the study of early psychosis family environment. Importantly, the way that a family has of reacting to and organizing itself around a psychotic condition has been found to have considerable influence on illness course and outcome (Miklowitz, 2004; Hooley, 2007). Consequently, family environment has been extensively studied as an influential psychosocial factor that impacts on psychosis prognosis (Schlosser, Pearson, Perez, & Loewy, 2012).

In this regard, family members' attitudes toward the patient, as measured by the level of Expressed Emotion (EE), have received most of the psychosocial research attention (Leff & Vaughn, 1985). In fact, high-EE attitudes, characterized by the presence of elevated levels of criticism, hostility, and/or Emotional Over-Involvement (EOI), have been considered the strongest psychosocial predictor of relapse in schizophrenia (Butzlaff & Hooley, 1998; Cechnicki, Bielańska, Hanuszkiewicz, & Daren, 2013; Marom, Munitz, Jones, Weizman, &

Hermesh, 2005; Wearden, Tarrier, Barrowclough, Zastowny, & Rahill, 2000). Just recently, research has begun to study EE in the early stages of the psychosis continuum (Domínguez-Martínez, Medina-Pradas, Kwapil, & Barrantes-Vidal, 2017; Koutra, Vgontzas, Lionis, & Triliva, 2014; Meneghelli et al., 2011; Schlosser et al., 2010) in order to prevent the entrenchment of high-EE and its associated poor prognosis. Part of the work carried out in the present thesis had the goal of examining relatives' EE in early psychosis stages, which should contribute to our understanding of the relevant mechanisms underlying the ontogenesis of EE without the bias created by the chronic course of psychosis and relatives' long-term burden.

To date, research on the etiological factors of EE is limited by the fact that most of the studies have been conducted have focused on families with individuals diagnosed with chronic forms of psychosis (Hooley, 2007; Kavanagh, 1992). Hence, speculations on the developmental precursors and initial expression of EE during the early stages of the illness await empirical evaluation. Notwithstanding, some previous studies in the field of early psychosis have suggested that relatives' attributions of patients' illness and symptoms contribute to the manifestation of high EE levels (Domínguez-Martínez et al., 2017; McNab, Haslam, & Burnett, 2007; Vasconcelos, Wearden, & Barrowclough, 2013). On the other hand, it has also been proposed that EE could be conceived as a coping strategy that reduces the perceived stress and relatives' burden of care (Álvarez-Jiménez et al., 2010; Kuipers et al., 2006) and has also been interpreted as an adaptative reaction to grief and perceived loss (Patterson, 2013; Patterson, Birchwood, & Cochrane, 2000, 2005). However, despite the large number of previous research efforts, little is known about the factors accounting for the nature of EE in the early course of the illness and further research is required. This work may contribute to expand and improve the early recognition of family environmental risk factors for psychosis that act in the early stages of the illness, and the findings may ultimately have clinical implications in terms of reducing, postponing or event preventing the

expression of full-blown clinical psychosis or reducing the possibility of relapse in those experiencing the recent onset of psychosis.

The present thesis is embedded in a larger longitudinal research (PSI2011-30321-C02-01; PSI 2014-54009-R; PSI2017-87512-C2-00) linked to the Sant Pere Claver Early Psychosis Program (SPC-EPP) currently being carried out in two Community Health Centers for Adults (CSMA-Sants and CSMA-Montjuic), a Community Health Center for Children and Adolescents (CSMIJ), and a Day Hospital (HD) for adolescents belonging to the Sant Pere Claver Clinical Foundation in Barcelona, Spain. The sample of informal caregivers of early psychosis patients has been recruited in the context of these projects in the centers mentioned above.

The investigation conducted in this current thesis consists of two main parts: a theoretical investigation that deepens into the state of the art in this field of endeavor and an empirical investigation. In the theoretical investigation section, one review of the current state of family research in At-Risk Mental State (ARMS) stages is included.

The empirical investigation section contains three empirical studies conducted with relatives of At-Risk Mental State (ARMS) and First-Episode of Psychosis (FEP) patients who receive treatment and belong to the SPC-EPP. Both groups of patients represent two different stages of the psychosis continuum: the "prodromal" or clinical high-risk stage (ARMS), and the onset of full-blown psychosis characterizing the first psychotic episode (FEP).

All the studies included in the empirical investigation section are focused on the study of family factors that have been found to have considerable influence on the course and outcome of psychotic disorders.

It should be noted that each of the four studies were presented in an article format and therefore include their own abstract, introduction, methods, results and discussion, since they will be submitted for publication in scientific journals in the near future. Reference style

of articles are according to the Journal's requirements where they are going to be submitted for publication.

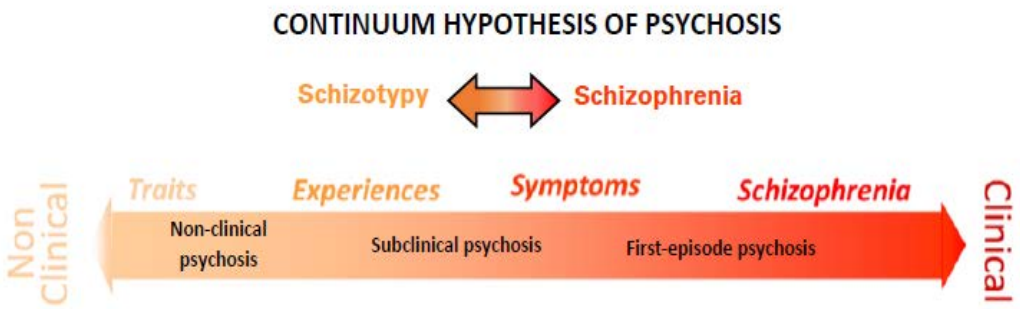
2. THEORETICAL FRAMEWORK

2.1. The Extended Psychosis Phenotype and the Continuum Hypothesis

A substantial amount of research has consistently shown that the psychosis phenotype is expressed along a severity continuum that encompasses a wide spectrum of psychotic symptom expressions, ranging from the nonclinical (e.g., schizotypy, psychotic-like experiences), subclinical (e.g., at risk mental states for psychosis) to a wide range of full-blown clinical manifestations (e.g., schizotypal personality disorder, brief psychotic disorder, schizophreniform disorder, schizoaffective disorder, schizophrenia, delusional disorder and psychotic affective disorders; Claridge, 1997; Kwapil & Barrantes-Vidal, 2015; Kwapil, Barrantes-Vidal, & Silvia, 2008; Meehl, 1990). For instance, epidemiological studies have demonstrated that weaker expressions of psychotic symptoms ("psychotic experiences") are also present in non-clinical populations (Linscott & van Os, 2013) suggesting an "extended psychosis phenotype" (Kaymaz & van Os, 2010), which shares demographic, etiological, familial and psychopathological factors with clinical forms of psychosis (e.g. Poulton et al., 2000; Tien, 1991; Verdoux & van Os, 2002). Although psychotic experiences in non-ill individuals have been shown to increase the risk for later onset of psychotic disorder (van Os, Kenis, & Rutten, 2010), only a small proportion may become persistent over time and progress into a clinical psychotic state (Kelleher & Cannon, 2011; Linscott & van Os, 2013; van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009). The extended psychosis phenotype, considered as the behavioral expression of vulnerability for psychotic disorders in populations (van Os & Linscott, 2012), allows to examine the processes involved in the extension of this phenotypic continuum. This is fundamental for the identification of individuals possessing vulnerability to psychosis and for the examination of the etiological risk and protective factors that contribute to the development of schizophrenia spectrum disorders.

The hypothesis of a psychosis or dimensional continuum poses that schizotypy and schizophrenia are not qualitatively distinct or separate entities; rather, schizophrenia, related spectrum disorder, and the prodrome represent the most extreme expressions of the schizotypy continuum (Kwapil & Barrantes-Vidal, 2015). This also implies that psychosis may be conceived as an extreme expression of continuously distributed quantitative traits in the general population (see Figure 1) (Claridge, 1997; Eysenck, 1952; Kretschmer, 1925; van Os & Reininghaus, 2016). Thus, schizotypy would be the psychological diathesis underlying the schizophrenia spectrum, whose disorders would differ in their degrees of severity, frequency, chronicity and outcome, but sharing etiological, risk factors and developmental processes (Barrantes-Vidal, Grant, & Kwapil, 2015).

Figure 1: Continuum hypothesis of psychosis (Barrantes-Vidal, personal communication).



Schizotypy and schizophrenia are characterized by a common multidimensional structure. As revealed by factor-analytic studies, the positive, negative and disorganized symptom dimensions are the most consistently identified (Kwapil, Barrantes-Vidal, & Sílvia, 2008; Raine et al., 1994; Stefanis et al., 2004; Vollema & Hoijtink, 2000). The positive or psychotic-like dimension encompasses features that reflect distortion or excess in normal functioning and is characterized by the presence of odd beliefs and unusual perceptual experiences, which in their extreme form manifest as delusions and hallucinations. The negative or deficit-like dimension reflect diminution or impairment in normal functions and

encompasses deficits such as affective flattening, anhedonia, anergia, avolition, social disinterest and alogia. The disorganized dimension encompasses features characterized by disruptions in the capacity of organization and expression of thoughts, behaviors and affect; it ranges from mild disturbances to grossly disorganized behavior and formal thought disorder (Kwapil & Barrantes-Vidal, 2015).

Research on the multidimensional model of schizotypy has supported the validity of positive and negative schizotypy by demonstrating that these dimensions are related to differential patterns of symptoms and impairment in cross-sectional studies (e.g., Barrantes-Vidal et al., 2013; Barrantes-Vidal, Ros-Morente, & Kwapil, 2009). Importantly, studies using momentary assessments have also supported the ecological validity of the schizotypy dimensions by showing that they relate to distinct patterns of daily life experiences (e.g., Barrantes-Vidal, Chun, Myin-Germeys, & Kwapil, 2013; Kwapil, Brown, Silvia, Myin-Germeys, & Barrantes-Vidal, 2012). Furthermore, the schizotypy dimensions have been found to predict the development of schizophrenia-spectrum disorders longitudinally (kwapil, Gross, Silvia, Barrantes-Vidal, 2013).

Prospective and cross-sectional investigations in individuals with clinical psychosis have significantly improved our phenomenological understanding of psychotic disorders. However, they are essentially limited in their potential for studying the progression, expression, and prevention of psychosis. In this sense, schizotypy is a promising construct for understanding the development of schizophrenia spectrum disorders through assessment of etiological mechanism without the bias associated to clinical status; and lastly, for enhancing the identification of resilience factors that may be protective against the development of the psychotic phenomena (Barrantes-Vidal et al., 2015).

2.2. From Chronic Schizophrenia to Early Psychosis: Early detection and Intervention in Psychosis

Over the last century, the traditional diagnostic system for psychotic disorders has been characterized by artificial divisions of cross-sectional symptom sets and has focused exclusively on course and outcome variables. Thus, one of the limitations of this approach is that do not contemplate the onset of the disorder, since as it cannot offer a differentiation between early clinical manifestations and those more characteristic of a persistent disorder (McGorry, Nelson, Goldstone, & Yung, 2010). The traditional diagnostic concept of psychotic disorders comes from the more prevalent subsamples of chronic individuals, thereby giving a misleading impression of stability and validity of diagnosis. However, in clinical practice, these operational criteria may generate a lack of diagnostic precision, and questions of validity and utility remain to be solved (Regier, Narrow, Kuhl, & Kupfer, 2009; Jansson & Parnas, 2007). Pharmacological and psychosocial treatments for psychotic disorders still remain episodic and palliative; and most patients might be better but are not fully recovered and/or do not respond to the available treatments (Insel, 2007). As a result, an adverse combination of pessimism, stigma and neglect have limited therapeutic advances in schizophrenia for more than a century (McGorry, Killackey, & Yung, 2008).

Nevertheless, in the last decades, an international collaborative task between clinicians and researchers have sought to implement the principles and practice of early diagnosis and staged treatment in the field of schizophrenia and related disorders (McGorry, 2002). Consequently, psychiatry has undergone a paradigm shift toward the identification of the early stages of mental disorders and preventive intervention, including increased focus on "prodromal" or "at risk mental states" for psychosis (ARMS) and first episode psychosis (FEP) individuals. In relation to this, the clinical staging model has proven to be especially useful in the distinction between early subclinical phenomena and those characteristics that

accompany illness progression and chronicity (McGorry et al., 2010). Staging model differs from conventional diagnostic practice in that it defines not only the extent of progression of disease at a specific point in time, but also where a person is currently located along the continuum of the course of the illness (McGorry et al., 2007). This approach enables clinicians to refine diagnosis and to select specific treatments for earlier stages and assumes that such interventions will be more effective and less damaging than those indicated later during the illness course (McGorry, Yung, Bechdolf, & Amminger, 2008).

Early identification and prospective assessment of individuals at risk for psychotic disorders have been considered crucial to isolate the mechanism underlying psychosis onset (Cannon et al., 2007). In addition, studying ARMS individuals enable us to identify the biological, social, and psychological vulnerability factors implicated in the development of psychotic spectrum disorders, prior to the onset of prominent clinical symptoms and impairment. Thus, a better understanding of the origins and development of psychosis is essential for identifying novel targets for early treatment interventions (Cornblatt et al., 2003) and, fundamentally, for reducing the morbidity and mortality associated with psychosis (McGorry, 2009). Hence, a focus on prevention in prodromal or ARMS individuals provides a unique opportunity to forestall or minimize the emergence and course of psychosis.

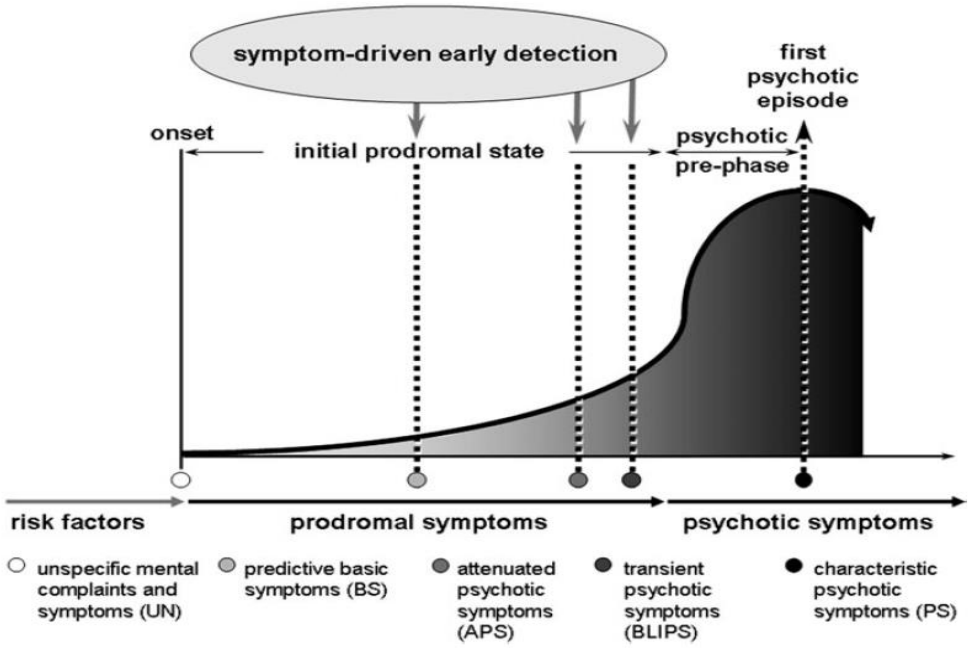
Two different clinical approaches have been widely applied to identify individuals with an at-risk mental state for psychosis. The first approach is based on Huber's Basic Symptoms (BS) concept (Huber & Gross, 1989; Schultze-Lutter, Ruhrmann, Berning, Maier, & Klosterkötter, 2008), which focuses on a detailed way of describing subtle, subjectively experienced disturbances in the cognitive, affective and physical domains. Because the basic symptom approach refer only to subtle subjectively experienced anomalies, it may reflect an earlier phase in the disease process than the Ultra-High Risk (UHR) approach, which identifies ARMS on the basis of three inclusion criteria which have been validated

internationally: (i) Attenuated Psychotic Symptoms (APS): individuals who have experienced attenuated positive psychotic symptoms during the previous year; (ii) Brief Limited Intermittent Psychotic Symptoms (BLIPS): individuals who have experienced episodes of frank psychotic symptoms, no longer than a week, with spontaneous full recovery; and (iii) Trait and State Risk Factor: individuals with a first degree relative with a psychotic disorder or who have a schizotypal personality disorder in addition to a significant decrease in functioning over the past year (Yung et al., 2003; Yung, Phillips, Yuen, & McGorry, 2004).

The UHR criteria have been extensively tested in recent decades and have been found to predict psychosis onset over a 12-months period, with transitions rates varying approximately between 13% and 50% (Ruhrman et al., 2010; Woods et al., 2009; Yung et al., 2006; Yung et al., 2008). However, the rate of transition to psychosis has been markedly declined over the last few years (Fusar-Poli et al., 2012; Nelson et al., 2013; Simon, Umbricht, Lang, & Borgwardt, 2014), which is partly explained because ARMS individuals are being detected and provided with care earlier than in the past (Yung et al., 2007). Furthermore, prospective data of individuals with basic symptoms (Klosterkötter, Hellmich, Steinmeyer, & Schultze-Lutter, 2001) show that the 12-month transition rate to psychosis is lower (19%) and the long-term transition rate higher (70% after 5.4 years) than the 12-month conversion rate of the ARMS individuals (Ruhrmann et al., 2010; Cannon et al., 2008).

Although the UHR approach has prevailed because it is closer in severity to psychotic disorders (Cannon et al., 2008), the basic symptom approach has also shown to be effective for an earlier detection of risk (Schultze-Lutter et al., 2008). For this reason, some researchers have used a combination of the two approaches and have classified those who meets the basic symptoms criteria as being in an early prodromal stage, with the UHR criteria indicating a later prodromal stage (see Figure 1) (Bechdolf et al., 2012).

Figure 1: Model of psychopathological development of psychosis related to the definition of the Early and Late Initial Prodromal State (Schultze-Lutter et al., 2008)



It is important to note that in the literature, as well as in this current thesis, the terms "prodrome" and ARMS are used inter-changeably. Nevertheless, the assessment of a prodromal state is only possible from a retrospective strategy and cannot be deemed to have occurred until the onset of full-blown psychotic symptoms indicative of a psychotic disorder (Woods et al., 2009; Yung et al., 1996). For this reason, is technically most appropriate the use of the term At-risk Mental States (ARMS) to refer to those individuals that are at heightened risk of developing psychosis.

On the other hand, the criteria for diagnosing psychosis require to specify a precise date of the beginning of the illness and to distinguish prodromal symptoms from those signaling an acute psychotic episode (Beiser, Erickson, Fleming, & Iacono, 1993). However, there remains a lack of consensus on operational definition for what is commonly referred to as "First-Episode Psychosis" (FEP) and the existing diagnostic approaches (e.g., DSM-V; American Psychiatric Association, 2013), only offer a little guidance for FEP

characterization. Hence, despite the implementation of successful clinical research programs aimed at promoting early detection and intervention in psychosis, further research is still required in in order to achieve a better characterization of the early stages of psychosis with the main goal of improving early identification and effective treatment options (Domínguez-Martínez, Cristóbal-Narváez, Barrantes-Vidal, & Kwapil, 2017).

2.3. Etiological factors in the Emergence of Psychosis

Despite intensive research over the past century, the causes and pathogenesis of psychosis are not fully understood, and multiple approaches are still attempting to provide responses to one of the major challenges in psychopathology research. Currently, the most widely accepted framework continues to be the neurodevelopmental hypothesis, which postulates that the emergence of psychosis could be explained by the interaction of both pre and postnatal environmental factors with genetic vulnerability, which in turns would result in different pathophysiologic processes that would impair brain development (e.g., Cannon et al., 2003; Murray & Lewis, 1987; Weinberger, 1987). These neurodevelopmental abnormalities have been proposed to lead to the activation of pathological neural circuits during adolescence or early adulthood (sometimes provoked by high levels of stress), which would lead to the emergence of psychotic symptoms (Brown et al., 2004; Fatemi, 2005).

Although genetic and neurodevelopmental theories have guided the conceptualization of psychosis, stress has not lost its value in the etiological models of psychosis (Holtzman et al., 2013). The vulnerability-stress model (or diathesis-stress model) of psychosis (Zubin & Spring, 1977) suggests that psychosis will develop as a result of the interplay between individual's genetic vulnerability and the stress caused by life experiences. This model provides a valuable framework for describing the relationships among provoking agents (stressors), vulnerability (diathesis) and symptom formation in schizophrenia-related disorders (Zubin, Steinhauer, & Condray, 1992). According to this, a genetically vulnerable

individual, whose innate tolerance for stress is incompatible with exposure to either excessive internally or externally generated stressors, may experience the onset of the disorder. This assumption underlies the biopsychosocial model (Engel, 1977), which states that psychotic disorders are the result of the continuous interaction of specific biological disorders with specific psychosocial and other environmental factors. These psychosocial and/or environmental stressors are the proximal causes of an initial psychotic episode or can even contribute to a relapse in established cases of psychosis (McFarlane, 2016b). Specifically, one of the strongest influences on the prevailing level of environmental stress is probably the emotional family atmosphere (Nuechterlein & Dawson, 1984). In this sense, it is well known that families not only provide emotional support but can also become a powerful source of psychological tensions (Leff & Vaughn, 1985). Within this causal biopsychosocial model, subtle symptoms, behavioral alterations, and functional decline would induce anxiety, anger, rejection, and other negative reactions in family members, which in turn would aggravate those same symptoms by inducing psychological and finally physiological and neurochemical reactions in the genetic vulnerable individual. The result would be a positive feedback process that leads to deterioration of both the patient and the family (McFarlane, 2016b). For this reason and in order to prevent bad outcomes, stressful interpersonal family environments have been studied extensively as an influential psychosocial factor that relates to the development and course of psychosis (Butzlaff and Hooley, 1998; Kavanagh, 1992; Tienari et al., 2004).

2.3.1. Environmental Risk Factors: The Role of Family Environment

There is a long and unfortunate history in psychiatry of blaming parents for causing their family members' psychotic illness through poor parenting styles (Bateson, Jackson, Haley, & Weakland, 1956; Cook, 1988; Cohler, Picket, & Cook, 1991). Fortunately, these theories have been abandoned since they have not received clear support from empirical

research, and moreover have been quite alienating to families of schizophrenic patients (Dixon et al., 2001; Hatfield, Spaniol, & Zipple, 1987). Modern approaches do not view the family as the primary causal agent in the patient's illness. Instead, modern approaches have reconceptualized the role of family on psychiatric illness as the product of a dynamic interaction between patients and their families, rather than as static family characteristics that contribute unidirectionally to the emergence of the illness (Jenkins, 1993; Miklowitz, 2004; Wynne, Shields, & Sirkin, 1992). Hence, the role of the family environmental risk factors on the development and course of the illness emerge within an interpersonal context that includes the reciprocal influences between the patients and their families.

Keeping these theoretical assumptions in mind, we now turn to the evidence that family relationships have a significant impact on the development and course of psychosis. One of the most important studies showing the risk and protective influences of the family environment on the development of psychosis is a longitudinal study conducted by Tienari and his colleagues (2004). They have demonstrated that negative family interactional patterns, measured by high levels of criticism or deviant styles of communication, do not predict the development of schizophrenia in adopted individuals who have no genetic risk for psychosis. However, when individuals with genetic vulnerability are adopted into dysfunctional families, they are more likely to develop the disorder later than if they were raised in a healthier family environment. Even further, the most powerful finding of this study is that when individuals with high genetic risk for psychosis were raised in a healthy family context, the probability that they would later develop the disorder was the same as it was for individuals who had no genetic risk. Although these results demonstrate the strong impact of family environmental stress on increased risk for developing psychosis in genetically vulnerable individuals, another relevant finding is the degree to which a healthy environment can protect at-risk individuals from developing psychosis. Thus, the family environment only influences genetically vulnerable individuals, demonstrating that the family

environment alone cannot promote the emergence of schizophrenia. In this sense, while genetic risk factors are more difficult to identify, environmental risk factors are more easily recognizable, which favours early identification and targeted interventions focused on preventing the stress induced by dysfunctional family environments (Schlosser et al., 2012).

Another important perspective on the relationship between family environmental stressors and the course of psychotic disorders arise from the "expressed emotion" research, since it has been consistently established that the course and prognosis of schizophrenia is highly correlated with a negative family atmosphere (Weisman, Nuechterlein, Goldstein, & Snyder, 1998; Peris & Miklowitz, 2015). The expressed emotion construct fits well within the stress-vulnerability model of schizophrenia, and further supports that persistent chronic stressors may play a significant role in the onset and course of psychotic spectrum disorders (Gleeson, Jackson, Stavely, & Burnett, 1999; Wearden et al., 2000).

2.3.1.1 Expressed Emotion and Schizophrenia Relapse

The Expressed Emotion (EE) construct was developed in the late 1950s by a British sociologist named George Brown (Brown, Birley, & Wing, 1972). In a preliminary work, Brown and his colleagues realized that patients with schizophrenia did better clinically if they were discharged from the hospital to live in lodgings or with their siblings. Contrary, many of those patients who returned to live with their parents experienced clinical worsening and greater relapse rates (Brown, Castairs, & Topping, 1958). This prompted Brown to consider the possibility that something about family interactions might be influencing the clinical outcomes of schizophrenic patients. During the next few years, Brown, in collaboration with Michael Rutter, recognized that it was essential to develop a consistent method to measure "the range of feelings and emotions to be found in ordinary families" (Brown, 1985; Brown & Rutter, 1966; Rutter & Brown, 1966). The result of this work was the development of the EE construct (Brown et al., 1972).

The construct of EE is now well-established as an important measure of the family emotional environment used to describe relatives' affective attitudes and behaviors towards an ill family member. The key aspects of family interpersonal relationships comprised within this construct are criticism, hostility, Emotional Over-Involvement (EOI), warmth and positive remarks. Of the five initial proposed components of EE, criticism, hostility, and EOI have shown to be the most predictive of clinical relapse in schizophrenia (Butzlaff & Hooley, 1998; Kuipers, 1992). In this sense, the term "High-EE" is specifically used to define the presence of higher levels of criticism, hostility and/or EOI in the family environment (Brown et al., 1972; Vaughn & Leff, 1976). As described by Leff and Vaughn (1985), criticism reflects obvious dislike or disapproval of some aspects of the patients' behavior or personality. Hostility is conceived as more generalized critical attitude and dislike of the patient as a person, which could lead to a rejection of the patient. Finally, EOI reflects an unusually marked concern toward the patient, indicating evidence of overprotective or self-scarifying attitudes.

The traditional way of measuring EE status in family members is through a semi structured interview named the Camberwell Family Interview (CFI; Leff & Vaughn, 1985; Vaughn & Leff, 1976). The CFI is a well-known gold-standard measure of EE and is conducted with the patient's closest relative in the absence of the patient. It approximately takes 1-2 hours, and it is always recorded for later coding. Although it was designed to measure the emotional attitudes of a particular caregiver, it is thought to reflect the disruptions in the organization, emotional atmosphere, and interactional patterns of the entire family system (Miklowitz, 2004). However, given that the CFI needs for specific training and is also time-consuming to administer and to rate, alternative shorter measures for assessing EE have been designed. Magaña et al. (1986) have introduced the Five-Minute Speech Samples (FMSS) as a relatively brief assessment method based on the original CFI. In addition, numerous questionnaires have been developed to assess EE as the Perceived

Criticism Rating (PC; Hooley & Teasdale, 1989); the Parental Bonding Instrument (PBI; Parker, Tupling, & Brown, 1979); the Level of Expressed Emotion Scale (LEE; Cole & Kazarian, 1988; Kazarian, Malla, Cole, & Baker, 1990); the Patient Rejection Scale (PRS; Kreisman, Simmens, & Joy, 1979); the Family Attitude Scale (FAS; Kavanagh et al., 1997); the Family Questionnaire (FQ; Wiedemann, Rayki, Feinstein, & Hahlweg, 2002) and the Brief Dyadic Scale of Expressed Emotion (BDSEE; Medina-Pradas, Navarro, López, Grau, & Obiols, 2011).

Research over the past five decades has established EE as a reliable psychosocial predictor of relapse in psychiatric disorders. The first study to demonstrate the relationship between EE and relapse in patients with schizophrenia was conducted by Brown et al. (1972). In this study, patients were followed up for 9 months after they have discharged from hospital. It was found that prolonged contact of patients with high-EE relatives (relatives with high levels of criticism, hostility and/or EOI) was strongly related with symptomatic relapse during the 9 months following discharge. The main results of this study were supported successfully in subsequent prospective studies (Vaughn & Leff, 1976; Vaughn, Snyder, Jones, Freeman, & Fallon, 1984). In each study, patients returning to high-EE family environments after hospital discharge were at significantly elevated risk of relapse during the 9 months following hospitalization than were patients returning to low-EE homes. In a review of 26 studies, Kavanagh (1992) reported that the mean relapse rate was 48% for patients living in high-EE environments and 21% for those residing in low-EE households. Bebbington and Kuipers (1994) analyzed 25 worldwide EE outcomes studies and further supported the association of relatives' EE with patients' symptomatic relapse. Moreover, they demonstrated the protective effect of low face-to-face contact for patients living in high-EE families. Once again, a meta-analysis of 27 prospective studies (Butzlaff & Hooley, 1998) showed that patients living in high-EE environments are more than twice likely to relapse compared to patients living in low-EE families. The negative consequences of relatives'

high-EE attitudes on patient outcomes are not restricted to short-term (e.g., 12 months). In this line, some studies have reported higher rates of relapse among those patients living with high-EE caregivers as a part of a 5-year follow up (Huguelet, Favre, Binyet, Gonzalez, & Zabala, 1995) and 7-year follow-up (Marom et al., 2005). Furthermore, the predictive validity of EE has also been found for a broad range of other psychiatric disorders (Butzlaff & Hooley, 1998; Chambless, Steketee, Bryan, Aiken, & Hooley, 1999; O'Farrell, Hooley, Fals-Stewart, & Cutter, 1998). Thus, the reported evidence shows on the one hand, that regular contact with high-EE relatives has an adverse effect on the course of a range of psychiatric disorders and, on the other hand, that EE represent the most consistent psychosocial predictor of relapse across a wide range of psychopathological conditions (Hooley, 2007; Wearden et al., 2000).

The replicability and magnitude of the relationship between relatives' high-EE and patients' relapse has led to the need of numerous interventions particularly designed to reduce high-EE attitudes in relatives of schizophrenia patients (for a review, see McFarlane, 2016a). These family interventions are based on the postulate that in daily interactions, relatives' high-EE attitudes can increase patients' stress levels resulting in symptoms exacerbation and, lastly, relapse (Nuechterlein & Dawson, 1984). However, the presence of a reliable association between relatives' EE and patients' symptom exacerbation does not allow us to state that EE plays a causal role in the relapse process. While it is possible that relatives' high-EE attitudes cause vulnerable patients to relapse, it is also plausible to propose that some of the illness features of relapse-prone patients might elicit high-EE in family caregivers. Considering this, EE could be associated with relapse and yet play no causal role in the patients' relapse process (Hooley, 2015). Nevertheless, studies that have statistically controlled for potentially important patient variables have further supported the independent contribution of relatives' EE on patients' poor clinical outcomes (e.g., Heikkilä et al., 2002; Nuechterlein et al., 1992).

Although the success of family based-interventions in reducing patients' relapse rates further supports the assumption that relatives' EE may play a causal role in the symptomatic relapse, the question of directionality is still not fully resolved and thus, there is still an ongoing discussion as to whether EE is more a cause of poor clinical outcomes among patients or a parental reaction to patients' disorder severity (Heikkilä et al., 2002). However, it is important to avoid an overly simplistic and unidirectional interpretation of EE (see Hooley, Rosen, & Richters, 1995 for a review). Therefore, a bidirectional and interactional model of the relationship between relatives' EE and patients' poor clinical outcomes has been suggested and now EE is widely accepted as a bidirectional construct, which reflects the product of the interaction between the relative and the patient. Thus, EE is perhaps best regarded in interactional terms, considering a bidirectional pattern of effects and reciprocal influences between patients' clinical features and the reactions of family caregivers that are important for the relapse process (Hooley, 2007; Hooley & Gotlib, 2000; Miklowitz, 2004).

Although the predictive validity of EE has been consistently established in schizophrenia and other psychiatric conditions, the factors involved in its ontogenesis have not yet been fully clarified. In this sense, research on the etiological factors of EE is limited by the fact that most of the studies have been conducted on families containing individuals already diagnosed with chronic forms of the psychosis phenotype (Bebbington & Kuipers, 1994; Cutting, Aakre, & Docherty, 2006; Kavanagh, 1992; Wearden et al., 2000). Hence, it is crucial to examine the mechanisms underlying the ontogenesis of EE in the early stages of psychosis without the bias created by the chronic course the illness and relatives' long-term burden.

2.3.1.2 The Early Development of Expressed Emotion

Over the last 20 years, the recent focus of research on early psychosis has led to a growing interest in the study of EE at early stages of the psychosis continuum. This is of

high relevance given that the specific circumstances of early psychosis vary greatly from those of chronic schizophrenia, in which the illness is clearly established and assumed by relatives. Moreover, exploring the role of EE in its early stages provides the opportunity to clarify which are the mechanisms involved in its early manifestation and its influence on patients' clinical and functional status. This is crucially important to future designing of family-focused interventions aimed at preventing the development and entrenchment of EE attitudes over time.

Preliminary studies examining EE in early psychosis have shown that high-EE is already present in over half of the relatives of persons with First-Episode of Psychosis (FEP) (Bachmann et al., 2002; González-Blanch et al., 2010; McNab, Haslam, & Burnett, 2007) and even is present in relatives of At-Risk Mental State (ARMS) (O'Brien et al., 2006; Schlosser et al., 2010). However, the relevance of the EE concept in the early phase of psychosis has been questioned because the impact of relatives' EE on patients' symptomatic relapse is less conclusive (Bird et al., 2010; Haidl et al., 2018; Linszen et al., 1996). Some prospective studies have pointed to the role of relatives' critical attitudes as predictors of worsening attenuated psychotic symptoms (Schlosser et al., 2010) or even as predictors of an early clinical relapse in FEP samples (Koutra et al., 2015). On the other hand, other studies on ARMS have underlined the importance of EE positive components, thus indicating that relatives' warmth and/or positive remarks predicted decreased symptoms and enhanced social functioning over time (O'brien et al., 2006, 2008). Besides, it seems that relatives' EOI seems to act more as a protective factor at this early stage, since it has been found to be related with improvement in patients' clinical and or functional status (O'brien et al., 2006; Schlosser et al., 2010).

2.3.1.2.1 Expressed Emotion as a reaction to patients' clinical and functional outcomes

Ever since the formulation of the EE construct, several alternative models have aimed to explain the origins of high EE (for review, see Hooley, 2007; Kavanagh, 1992; Miklowitz, 2004). One ongoing discussion has focused on whether relatives' EE represents a unidirectional reaction to clinical characteristics of patients, but the data on this issue are inconclusive. Schizophrenia studies generally have not found cross-sectional relationships between the severity of patients' concurrent symptoms during or after acute illness episodes and relatives' EE (Cutting et al., 2006; Miklowitz, Goldstein, Nuechterlein, Snyder, & Mintz, 1988; Nuechterlein, Snyder, & Mintz, 1992). In the same way, schizophrenia patients living in high-EE environments have not appear to be sicker than those living in low-EE families (e.g., Brown, Birley, & Wing, 1972; Miklowitz, Goldstein, & Fallon, 1983; Vaugh & Leff, 1976). Stated simply, EE does not appear to be simple reaction to patients' psychopathological characteristics. The fact that two relatives of the same patient can sometimes have different levels of EE constitutes further proof of this (Weisman, Nuechterlein, Goldstein, & Snyder, 2000). However, some isolated reports of schizophrenia studies do link EE to patients' concurrent symptoms (Barrowclough & Tarrier, 1990; Bentsen et al., 1998; Karno et al., 1987).

Likewise, findings on the association between patients' illness-related characteristics and relatives' EE are still controversial and inconclusive in the early psychosis literature. Recent investigations conducted in ARMS and FEP samples have suggested that patient's symptomatology and psychosocial functioning have limited or no impact upon relatives' EE (Álvarez-Jiménez et al., 2010; Bachmann et al., 2002; Heikkila et al. 2002, 2006; Meneghelli et al., 2011; Raune, Kuipers & Bebbington, 2004), whereas others studies have revealed that patients' symptoms/functioning were positively correlated with family EE (Domínguez-

Martínez, Medina-Pradas, Kwapil, Barrantes-Vidal, 2014; Koutra et al., 2016; McFarlane & Cook, 2007; Mo et al., 2007).

Rather than supporting simplistic and unidirectional models between patients' symptoms and EE, the evidence seems to be pointing to a more holistic model that involves reciprocal influences between patients' clinical attributes and the reactions of relatives, in which certain characteristics of relatives (e.g., a more inflexible personality style) render them more vulnerable to responding to patients' difficulties in a certain way. Thus, a diathesis-stress conceptualization of EE (Hooley, 1987; Hooley & Gotlib, 2000; Hooley, 2007) states that EE is a product of the interaction of both patient and relatives' characteristics in which bidirectional processes are contributing to the development of high-EE attitudes. This approach facilitates the view that both patients and relatives are involved in a system of mutual influence in which each contributes to the stress that acts on the intrinsic vulnerabilities of the other. In doing so, it implicitly recognizes the role of two moderator variables: the interpretations that each actor makes of the other's behavior, and the coping skills of each for dealing with the situation.

2.3.1.2.2 Expressed Emotion as a product of relatives' attributions about patients' symptoms

The attributional model of EE that Barrowclough et al. (1994) and Barrowclough and Hooley (2003) established based on schizophrenia samples provides a useful explanatory framework for understanding the development of relatives' EE attitudes. It postulates that relatives' beliefs about the nature of the illness and the symptomatology are related to their emotional attitudes towards patients. It seems that critical relatives are more likely to blame patients for their behaviors and to perceive symptoms as controllable by patients rather than illness driven (Brewin, 1994; Hooley & Campbell, 2002; Weisman et al., 1998). They, therefore, attempt to reduce the undesired behaviors through persuading or coercing the patient, making more use of criticism. In contrast, relatives high in EOI are especially unlikely to attributing responsibility or blame patients for their problematic behaviors. In fact,

emotionally overinvolved relatives tend to attribute symptoms to external and uncontrollable factors by the patient (Barrowclough et al., 1994; Brewin et al., 1991). They, therefore attempt to ameliorate events by acting as a buffer between the patient and the outside world and, through their use of intrusive and/or self-sacrifying attitudes. Further observations indicate that relatives with marked EOI can also perceive patients' symptoms under their own control or even could report high levels of guilt and/or self-blame attributions (Bentsen et al., 1998; Bolton et al., 2003; Peterson & Docherty, 2004).

Recently, the attributional model of EE has become a theoretical framework increasingly used for understanding the development of EE attitudes in the very beginning stages of psychosis. Consistent with the attributional model, some studies have shown that critical relatives of FEP patients tend to belief that symptoms are within the patients' control (McNab et al., 2007; Vasconcelos e Sa et al., 2013) and also, that attributions of blame toward the patients predict the early emergence of relatives' critical attitudes (Domínguez-Martínez, et al., 2017). In addition, Domínguez-Martínez et al. (2014) indicated that relatives' attributions of blaming patient for their illness-related difficulties mediated most of the relationships between patients' illness severity and relatives' EE at both subclinical and onset stages of psychosis. Thus, relatives' cognitive representations of psychosis are strongly related to their emotional and behavioral attitudes toward patients even at early stages of the disorder (Onwumere et al., 2008).

2.3.1.2.3 The stress and coping model and its relationship to Expressed Emotion

An increasing body of evidence suggests the 'stress and coping model' (Lazarus & Folkman, 1984; Lazarus, 1993) may be helpful in understanding the genesis of EE (Barrowclough & Parle, 1997; Scazufca & Kuipers, 1999; Barrowclough, Lobban, Hatton, & Quinn, 2001). Lazarus and Folkman (1984) proposed that individuals' cognitive appraisals play a critical role in assessing stressors and determining appropriate coping responses. This

theory distinguishes two basic forms of appraisals: primary appraisals involve determining whether a stressor constitutes a threat and secondary appraisals involve the individual's evaluation of the coping strategies at his or her disposal for addressing any perceived threat. Then, coping refers to "cognitive and behavioral efforts to manage (reduce, minimize, master, or tolerate) the specific external and/or internal demands of the person-environment transaction that is appraised as taxing or exceeding the resources of the person" (Lazarus, 1993, p.19). Coping has two major functions. One is the management of the problem that is causing distress by directly changing the elements of the stressful situation (problem-focused coping). The other is the regulation of emotions or distresses that come with the stressful situation (emotion-focused coping). Problem-focused coping strategies involve an active response, which includes solving the problem, managing or changing the situation and seeking information, seeking instrumental help, planning and direct action. Emotion-focused coping strategies involve emotion-oriented reactions such as minimizing, distancing, self-control, seeking social support, avoidance, self-blame, venting, and positive reappraisal (Felsten, 1998; Folkman, Lazarus, Gruen, & DeLongis, 1986).

This approach provides a useful framework to better understand the range of adaptational responses made by family members in response to the stress of caring for a psychiatrically impaired relative (Hatfield, 1987) and might contribute to a better understanding of the mechanisms underlying EE attitudes.

However, only few studies in the schizophrenia field have assessed the relationship between relatives' EE and their coping strategies. Smith, Birchwood, Cochrane and George (1993) found that relatives of schizophrenia high on EE perceive their ability to cope with patients' disturbing behaviours as less effective and more impaired than those with low-EE. Barrowclough and Parle (1997) indicated that relatives who doubted in their ability to cope with patient's schizophrenia symptoms were more likely to be rated as high EE-hostile, while EOI relatives reported greater certainty in their coping skills. Scazufca and Kuipers (1999)

showed that high EE relatives tended to use more maladaptive emotion-focused coping strategies, such as avoidant coping, than low EE relatives.

Based on the stress and coping model, Raune et al. (2004) and Kuipers et al. (2006) proposed the 'carer appraisal model of EE' to account for the nature of EE in relatives of FEP patients. According to this model, caregivers' negative appraisals of their living situation results in negative emotional states such as distress and depression, precipitating high EE among relatives in an attempt to neutralize these emotions. Then, high-EE behaviors (e.g., criticism and EOI) could be deemed as maladaptive coping strategies used to reduce the perceived stress related to the caregiving role (Álvarez-Jiménez et al., 2010; Kuipers et al., 2006). In fact, emotion-focused strategies, such as avoidant coping, has been related to critical attitudes in relatives of FEP patients (Kuipers et al., 2006; Raune et al., 2004). Furthermore, avoidant coping strategies have been found to be strongly related to caregivers' distress in the early stages of psychosis (Omnuwere et al., 2011). It is well known that caring for a family member in the early stages of psychosis, can lead to experience elevated levels of distress, including anxiety and depression (Addington, Coldham, Jones, Ko, & Addington, 2003; Addington, McCleery, & Addington, 2005). Thus, it seems plausible to suggest that caregivers may feel overwhelmed by the negative emotions that arise from this new situation of caregiving, and consequently they adopt coping strategies designed to shield themselves from distress.

2.3.1.2.4 Expressed Emotion and family members' perceived loss: the role of attachment

Given the magnitude of the impairment associated with psychotic disorders, relatives often experience grief reactions This grief results from the loss of the healthy relative, loss of specific hopes and aspirations for the relatives' future and/or loss of the pre-existing relationship to illness (Miller, 1996; Parker, 1993; Young, Bailey, & Rycroft, 2004). Grief reactions has been mostly examined in relatives of schizophrenia patients (Jones, 2004;

Ozgul, 2004; Richardson et al., 2011), but recently, further research has revealed that high levels of perceived loss are already present in the early stages of the illness (Mulligan, Sellwood, Reid, Riddell, & Andy, 2013; Patterson et al., 2000, 2005). Importantly, high appraisals of loss have been found to be related with the early manifestation of high-EE (Mulligan et al., 2013; Patterson et al., 2000, 2005; Raune et al., 2004). Therefore, it has been suggested that EE attitudes may be conceived as a reaction to relatives' grief and perceived loss (Patterson, 2013; Patterson et al., 2000, 2005). In this regard, attachment theory has been highlighted as a helpful framework for understanding how loss appraisals may contribute to the development of EE (Patterson, 2013; Patterson et al., 2000, 2005), since it is extensively assumed by attachment theorists that threats to an attachment bond tend to activate the attachment system (Mikulincer and Shaver, 2016, 2007). In light of this, Patterson (2013) proposed a theoretical model to explain how family illness leads to an activation of relatives and patients' attachment behaviors with increased high EE attitudes from relatives as an initial normative reaction. In doing so, it is theoretically suggested that an initial response of high EE may be adaptive rather than dysfunctional or maladaptive (Hooley, 1986; Patterson, 2013; Patterson et al., 2000, 2005). However, empirical research is required to better account for the relationship among relatives' perceived loss, attachments processes and EE.

To summarize, further studies should be conducted to provide a clear picture of the mechanisms underlying the ontogenesis of EE in the early stages of psychosis. Investigating the potential mechanisms accounting for relatives' EE should improve early family interventions, thereby enhancing the prognostic of both patients and their relatives.

3. AIMS AND OUTLINE OF THIS THESIS

The present thesis consists of two main sections: a theoretical investigation and an empirical investigation. Both sections aim at examining specific family environmental factors that have been demonstrated to be related with the course and outcome of psychotic disorders in the early stages of psychosis. Based on this overarching goal, the theoretical investigation section sought to review empirical studies focused on the examination of family factors in samples of At-Risk Mental State (ARMS) patients. The focus on ARMS patients derives from the lack of selective reviews of the accumulating data in this specific population. The empirical investigation section attempted to 1) address issues related to the measurement and validity of Expressed Emotion (EE) in daily life; 2) to examine the role of relatives' insecure attachment dimensions as potential mediating factors in the association of relatives' perceived loss with EE dimensions; and 3) to investigate whether relatives' psychological distress and subjective appraisals of the illness predicted EE dimensions over-and above-patients' poor clinical and functional status.

The theoretical investigation section, ***Family environment research in at-risk mental state stages of psychosis*** includes one chapter (i.e., ***chapter 1***), which is dedicated to review the literature that has examined family environment variables in the ARMS stage. The more recent reviews about the family environment in early psychosis have exclusively focused on the examination of family factors in samples of first-episode psychosis patients. Thus, this review provides the opportunity to explore distinctive features of family functioning in individuals at risk for psychosis. The review covers the examination of: 1) cross-sectional studies investigating the association of EE and other family environment constructs with ARMS symptoms and/or functioning; 2) prospective studies exploring the predictive value of EE and other family environment constructs on ARMS symptomatic

and/or functional outcomes; and finally, 3) the effect of family-based interventions on ARMS symptomatic and/or functional outcomes.

The empirical investigation section is subdivided into three further sections. The first section, ***The measurement of relatives' EE in daily Life***, is dedicated to research on the assessment and validity of EE dimensions (i.e., criticism and Emotional Over-Involvement (EOI) in daily life. The study presented in ***Chapter 1*** explores for the first time the real-life expression of EE dimensions using the Experience Sampling Method with the general purpose of examining the ecological validity of EE. It was hypothesized that momentary EE dimensions (i.e., momentary criticism and EOI) would be related with the gold-standard psychometric EE dimensions derived from the Family Questionnaire (FQ), thus providing evidence for the criterion validity of momentary EE domains. In addition, it was expected that momentary EE dimensions as well as FQ-EE dimensions would show meaningful associations with real-world experiences in the domains that are theoretically related to EE. This would support the construct validity of momentary EE dimensions as well as the construct and ecological validity of the FQ as a sensitive measure of EE dimensions.

The second section, ***Mediating mechanisms in the link between relatives' perceived loss and EE: the role of relatives' attachment dimensions*** sought to increase our understanding of the pathways linking relatives' perceived loss and EE dimensions. ***Chapter 2*** describes a study that aimed to examine the relationship among relatives' attachment dimensions, perceived loss and EE as well as the mediating effect of relatives' attachment dimensions (i.e., anxiety and avoidance) in the association between perceived loss and EE attitudes. Based on the reviewed theorization, it was hypothesized that relatives' relatives' attachment anxiety would play a mediating role between perceived loss and EOI, as well as between perceived loss and criticism.

The third section, ***Predictors of EE in early psychosis,*** further investigated the potential mechanisms underlying the ontogenesis of EE considering the contribution of

patients' illness-related variables in conjunction with relatives' psychological factors. The study presented in ***Chapter 3*** examines the association of patients' clinical and functional status as well as relatives' psychological distress and illness attributions with relatives' EE dimensions at baseline and at the 6-month follow-up. This study also aims to explore whether relatives' psychological distress and subjective appraisals of the illness predicted EE dimensions over-and-above patients' poor clinical and functional status at baseline and follow-up assessments. Based on previous suggestions from the EE literature, it was expected that relatives' baseline psychological distress and negative illness attributions would predict relatives' EE dimensions at both time points over-and-above patients' baseline clinical and functional variables.

Finally, a global discussion and conclusions are presented at the end in a different section, including a summary of main findings, research and clinical implications, limitations and directions for future research.

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THEORETICAL INVESTIGATION

SECTION 1

FAMILY ENVIRONMENT RESEARCH IN AT-RISK MENTAL STATE STAGES OF PSYCHOSIS

Chapter 1

Family environmental factors in At-Risk Mental States for Psychosis

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Abstract

Objectives: To review the literature regarding family environment variables in the At-Risk Mental State/ (ARMS) stage.

Method: Publications were retrieved by an extensive search on three electronic databases: MEDLINE, PsycINFO and SCOPUS (1990-2018). A supplemental manual search in relevant journals was also carried out. In total, 18 studies investigating expressed emotion (EE) and/or other relevant family environment variables as well as family interventions in individuals at-risk for psychosis were identified and met the inclusion criteria.

Results: Cross-sectional findings regarding the relationships of EE and/or other family environment constructs with ARMS patients' characteristics were inconclusive. Relatives' beliefs about the disorder played a significant role, either as mediators of these relationships, or as predictors of EE attitudes. Although the evidence regarding the predictive value of EE on ARMS clinical outcome was limited, longitudinal studies pointed to the role of family positive factors as predictors of ARMS clinical/functional improvement. Family-based interventions demonstrated great potential to reduce high-EE attitudes and/or to improve ARMS patients' outcomes.

Conclusions: Research on family environment in ARMS is still in an incipient stage, which impacts on the heterogeneity of findings and still lack of conclusive findings. An increased focus on the impact that the at-risk stage of illness has on relatives' mental well-being is necessary to clarify the mechanisms leading to dysfunctional family dynamics in the critical ARMS period.

Keywords: Family environment, At-Risk Mental State, Expressed Emotion, Review.

Introduction

At the early stages of the psychotic illness most of individuals live at home (50-70%) with their families (Addington, Addington, Jones, & Ko, 2001). This entails that family members become the main informal caregivers of individuals with early psychosis (Addington, McCleery, Collins, & Addington, 2007). Unfortunately, they often experience burden and/or significant stress because of this increased responsibility (Addington & Burnett, 2004; Jansen, Haahr, et al., 2015; Jansen, Gleeson, & Cotton, 2015). This is crucially important given that the way that families way react to and organize themselves around the psychotic condition has been found to have considerable influence on illness course and outcome (Hooley, 2007; Miklowitz, 2004). Consequently, family environment has been extensively studied as an influential psychosocial factor that impacts on psychosis prognosis (Butzlaff & Hooley, 1998; Kavanagh, 1992; Schlosser, Pearson, Perez, & Loewy, 2012; Tienari et al., 2004)

In this regard, family members' attitudes toward an ill relative, as measured by the level of Expressed Emotion (EE), have received most of the psychosocial research attention (Leff and Vaughn, 1985). Given that high-EE, characterized by the presence of elevated levels of criticism, hostility, and/or Emotional Over-Involvement (EOI), has consistently shown to be a robust predictor of relapse in schizophrenia (Butzlaff & Hooley, 1998; Cechnicki, Bielańska, Hanuszkiewicz, & Daren, 2013; Marom, Munitz, Jones, Weizman, & Hermesh, 2005; Wearden, Tarrier, Barrowclough, Zastowny, & Rahill, 2000), recent research has focused on the study of EE in the early stages of psychosis (Domínguez-Martínez, Medina-Pradas, Kwapil, & Barrantes-Vidal, 2017; Koutra, Vgontzas, Lionis, & Triliva, 2014; Meneghelli et al., 2011; Schlosser et al., 2010) in order to examine its ontogeny without the plethora of confounds associated to chronic stages of the illness and, ultimately, prevent the entrenchment of high-EE attitudes and related poor prognosis.

To date, most of the research related to the study of family environment has mainly been carried out on patients with the chronic form of the psychosis phenotype or individuals experiencing the recent onset of psychosis [i.e., First-Episode of Psychosis (FEP) patients]. Conversely, family environment has been less studied in the phases preceding the illness onset [i.e., At-Risk Mental State (ARMS) stages]. The ARMS stage comprises a heterogeneous group of symptoms traditionally described in the prodromal phase of psychosis. Current standard definitions and operationalization yield three cluster of individuals: 1) people with attenuated positive psychotic symptoms; 2) people who have experienced episodes of frank psychotic symptoms but no longer than a week with spontaneous full recovery; and 3) individuals with either genetic risk (having a first degree relative diagnosed with psychotic disorder) or meeting criteria for Schizotypal Personality Disorder in addition to, in both cases, a significant decrease in social functioning (Yung et al., 2003; Yung, Phillips, Yuen, & McGorry, 2004). Thus, the ARMS stage constitutes a perfect "laboratory" to study relevant factors related to the family environment prior to the onset of marked clinical symptoms, impairment, the emergence of large comorbidity, and the deleterious effects of medication secondary effects.

Since family factors might play a critical role in the management and outcome of psychosis, developing understanding of the family functioning in the very early stages of psychosis can help to design early interventions aimed at preventing negative dynamics in the family environment. Furthermore, by studying family functioning in ARMS populations, we expect to achieve a clear overview of family interactions without the bias created by the chronic course of psychosis and/or the onset of frank psychotic symptoms, and long-term caregiving burden.

Previous reviews on the study of family environment in early psychosis have exclusively focused on samples of FEP patients (Jansen, Gleeson, et al., 2015; Koutra et al., 2014). However, no systematic investigation has explored the potential distinctive features

of family functioning in individuals 'at-risk' for psychosis, which is the focus of the present review.

The purpose of this paper is to provide a review of the literature on the relationship between family factors and ARMS patients characteristics or outcome. The reviewed research is addressed in three different sections:

1. Cross-sectional studies investigating the association of EE and other family environment constructs with ARMS symptoms and/or functioning.
2. The predictive value of EE and other family environment constructs on ARMS symptoms and/or functional outcomes.
3. The effect of family interventions on ARMS symptoms and/or functional outcomes.

Methods

Publications were retrieved by an extensive search on three electronic databases: MEDLINE, PsycINFO and SCOPUS (1990-2018). The search was conducted using the terms "expressed emotion", "family expressed emotion", "emotional over-involvement", "criticism", "family environment", "family functioning", "family cohesion", "family adaptability", "at-risk mental states", "prodrome" and "ultra-high risk". All published studies that met the following criteria were included in the review: (a) published in peer-reviewed journals in English; (b) date of publication from 1990 to 2018; (c) samples of ARMS patients and/or their relatives; (d) focused on investigating

1) the impact of illness on family members' attitudes or psychological health; 2) the influence of family environment variables on ARMS' clinical and/or functional outcomes; 3) relatives' psychological factors accounting for EE; 4) the effects of family interventions on both ARMS' clinical and/or functional outcomes. In addition, studies had to contain at least one family measure and/or relevant constructs to understand the early emergence of EE. Exclusion criteria were: (a) secondary publications (commentaries, editorials and letters); (b)

Theses, dissertations and conference papers; and (c) case reports. We did not limit the search to studies that included biological mothers and fathers, but also included studies that recruited other relatives, such as step-parents, siblings or partners. Additionally, we also included studies assessing family factors in mixed samples of ARMS and FEP patients given that it is a common practice in this literature. Furthermore, to guarantee that our search was as comprehensive and updated as possible, we also specifically searched for relevant and specialized journals such as Schizophrenia Bulletin, Schizophrenia research, Clinical Psychology Review, Psychiatry Research, Family Process, Social Psychiatry, Psychiatric Epidemiology and Early Intervention in Psychiatry.

In total, 18 studies met the inclusion criteria. Table 1 summarizes the main characteristics of the studies included.

Results

Study aims

The aims and scope of the reviewed studies varied greatly. Regarding the family environment variables, ten studies (55.5%) explored EE (Domínguez-Martínez, Medina-Pradas, Kwapil, & Barrantes-Vidal, 2014; Domínguez-Martínez et al., 2017; Haidl et al., 2018; Hamaie et al., 2016; McFarlane & Cook, 2007; Meneghelli et al., 2011; O'Brien et al., 2006, 2008; Schlosser et al., 2010; Tsai et al., 2015) and five (27.77 %) explored other relevant family environment constructs (e.g., burden, problem-solving skills, communication, cohesion, adaptability, perception of the quality of relationships within the family, etc.) (Bentley et al., 2016; O'Brien et al., 2009; Wang et al., 2015; Welsh & Tiffin, 2015; Wong et al., 2008) as the main outcome. Finally, three studies focused on family-based interventions and its effects on ARMS clinical outcomes, high-EE attitudes and/or family communication (Miklowitz et al., 2014; O'Brien et al., 2014; O'Brien, Miklowitz, & Cannon, 2015). Reviewed studies also varied in their assessment methods; while some of them assessed family's

emotional climate through relatives' self-reports and/or interviews based on relatives' reports (Domínguez-Martínez et al., 2014, 2017; Hamaie et al., 2016; McFarlane & Cook, 2007; Meneghelli et al., 2011; O'Brien et al., 2006, 2008, 2009; Wong et al., 2008), other studies assessed family variables from the patient's viewpoint (Bentley et al., 2016; Haidl et al., 2018; Tsai et al., 2015; Wang et al., 2015; Welsh & Tiffin, 2015), with only two studies considering both patients and relatives perspectives (O'brien et al., 2015; Schlosser et al., 2010). Family interactional tasks were also used for the assessment of family-related variables (O'Brien et al., 2008, 2009, 2014).

Cross-sectional studies investigating the association of EE and other family environment constructs with ARMS symptoms and/or functioning

The extant sparse literature on the relationship between EE and specific symptoms and functioning in ARMS patients presents a substantial level of contradictory findings, much more so than that conducted in patients with chronic forms of psychosis.

Despite the cross-sectional nature of the designs, some studies have aimed to explore the assumption that EE develops as reaction to patients' illness severity by comparing groups at different stages of illness severity and/or using retrospective reports (McFarlane & Cook, 2007; Meneguelli et al., 2011). McFarlane and Cook (2007) did not use patients' measures but compared patients with clinical psychosis with ARMS individuals. They found that parents of offspring with established psychotic disorders reported higher levels of criticism and EOI and lower levels of warmth than parents of offspring who were in the ARMS stage. Further analyses conducted only within the ARMS sample revealed that levels of maternal criticism and EOI increased since the first signs of illness began to appear, whereas maternal and paternal warmth decreased over the course of prepsychotic development. The latter analyses were conducted using retrospective reports from parents regarding the duration of the subpsychotic syndrome. Authors concluded that EE is a reaction to patients' deterioration, that is, increasing symptom severity and disability, across the ARMS stage.

Contrarily, Meneguelli et al. (2011) indicated that duration of untreated illness (DUI) was not related to EE in relatives of ARMS patients; however, in the FEP group, high-EE (i.e., high hostility, criticism and EOI) correlated with a longer DUI period, whereas only higher paternal EOI correlated with a longer duration of untreated psychosis (DUP). EE was not related to severity of symptoms or psychosocial functioning in either group. Authors concluded that results partially support the assumption that high-EE attitudes develop as a reaction to patients' clinical/functional status. In a more recent Japanese study, Hamaie et al. (2016) showed that ARMS caregivers' criticism was not related to patients' clinical status but to caregivers' higher educational levels, which also made a significant independent contribution to critical attitudes in the regression analysis. It was speculated that high levels of education may contribute to develop higher expectations regarding the capacity of control of their offspring over illness-related behaviors, and that this would imply the manifestation of critical attitudes. Conversely, criticism in FEP caregivers was related to FEP patients' negative and general symptoms as well as to FEP caregivers' depression symptoms. Regression analyses revealed that caregivers' depression symptoms and patients' general symptoms significantly predicted criticism in FEP caregivers.

Another study examining the impact of EE on ARMS patients' symptoms (Tsai et al., 2015) found that higher levels of patients perceived maternal criticism were associated with lower levels of negative symptoms. Further analysis indicated that race/ethnicity moderated the relationship between patients' perceived levels of maternal criticism/warmth and patients' symptom expression. Thus, a contrasting role of relationships were reported between perceived criticism and/or warmth and patients' symptomatology depending upon the patient's ethnicity. Domínguez-Martínez et al. (2014) showed that relatives' criticism was related to increased positive, negative, and general symptoms, whereas EOI was related to increased negative and general symptoms at both ARMS and FEP stages of psychosis. Both dimensions were also related to patients' functional impairment. The relationship between

EE and patients' symptoms/functioning did not differ between ARMS and FEP groups, suggesting that both patients' samples were similarly influenced by family environment variables. Going a step further, this study analyzed the potential role of relatives' attributions in the association between EE and patients' symptoms. It was found that relatives' attributions of blaming patients for their illness-related difficulties mediated most of the relationships between EE and illness severity. The role of cognitive representations of illness in explaining EE attitudes was also highlighted by the same researchers in a more recent study (Domínguez-Martínez et al., 2017). Relatives' distress and attributions of blaming patients for their illness predicted criticism in both ARMS and FEP caregivers, whereas beliefs that symptoms are within patients' control and an emotional negative representation about the illness predicted EOI in both groups. Relatives' EE dimensions were highly associated with relatives' distress, and with several types of illness attributions. Anxiety was more strongly related with criticism in ARMS than in FEP-relatives, and it was related with EOI in ARMS' relatives but not in FEP relatives. In a small exploratory study also aimed at exploring relatives' emotional distress in the early stages of psychosis, Wong et al. (2008) indicated that levels of both subjective and objective burden were comparable between ARMS and FEP caregivers.

Other studies have examined how other family variables, as rated by ARMS patients' perceptions, are related to patients' symptom expression in the subclinical stages of psychosis. Welsh &Tiffin (2015) showed that ARMS patients are likely to report poorer perceived problem solving and lower levels of nurturing behavior in their families compared to a control community sample. Self-reported family perceptions were not related to symptom severity in either ARMS or FEP groups; although higher scores on the EE subscale of the self-reported family perceptions measure were significantly related to manic symptomatology in both ARMS and FEP groups. Bentley et al. (2016) found that ARMS individuals reported less positive parent-child relationships and higher levels of social stress

than a help-seeking control group. Parent-child relationships moderated the relationship between a psychosis risk (ARMS) diagnosis and social stress. Severity of social stress was dependent on the quality of family relationships only for the ARMS group. ARMS individuals who informed poorer parent-child relationships tended to report greater perceptions social stress, whereas those who described positive parent-child relationships tended to report decreased perceptions of social stress.

Predictive value of EE and other family environment constructs on ARMS symptoms and/or functional outcomes

Preliminary research examining family environment as a predictor of outcome in ARMS patients points out the important role of positive family environment. In a longitudinal study of 26 ARMS patients and their primary caregivers O'Brien et al. (2006) indicated that caregivers' criticism at baseline was not related to changes in symptoms or social functioning at a 3-month follow-up; however, caregivers' EOI at baseline was associated with improvement in negative symptoms and social functioning at follow-up. Similarly, caregivers' positive remarks were related with improvement in negative and disorganized symptoms at follow-up, and caregivers' warmth was also associated with enhanced social functioning at follow-up. These findings were replicated by O'Brien et al. (2008) using a larger sample (n=40) of ARMS individuals and their respective parents. Caregivers' warmth predicted an improvement in social functioning and caregivers' positive remarks were associated with a decrease in negative symptoms 4 months later. In addition, it was shown that parents who expressed more positive remarks regarding their ill family member during the Camberwell Family Interview (CFI; Vaughn and Leff, 1976) tended to exhibit more constructive behaviors during an interactional task. Also, criticism was positively related to parents' conflict engaging behaviors during the interactional task. Finally, the behaviors exhibited by relatives during the interactional task were not predictive of ARMS patients' symptoms/functioning at the 4-month follow-up. However, in a 6-month

follow-up report O'Brien et al. (2009) showed that ARMS individuals' skillful problem solving and constructive communication as well as caregivers' constructive communication exhibited during face-to-face problem-solving discussions were associated with patients enhanced social functioning at follow-up. Contrarily, ARMS individuals' conflictual communication during the problem-solving discussion with their parents was associated with increased positive symptoms at follow-up. Wang et al. (2015) in their longitudinal study of 32 ARMS from a non-clinical population, found that self-reported family functioning, specifically, better perceived problem solving and affective responsiveness from their parents predicted less severe positive and negative symptoms at 6-month follow-up. Perceived family cohesion and adaptability were negatively associated with general symptoms at baseline, but also were negatively associated with general and disorganized symptoms at follow-up. In another study by Schlosser et al. (2010) it was shown that ARMS patients' perceived parental criticism predicted the worsening of attenuated positive symptoms at follow-up. Also, CFI-rated hostility and criticism significantly predicted change in positive symptoms at follow-up. CFI-rated warmth interacted with an optimal level of EOI to predict improved functioning over time. Recently, as part of the European Prediction of Psychosis Study (EPOS), Haidl et al. (2018) followed up a large cohort of 235 ARMS individuals during an 18-month period. Results revealed that patients' perceived irritability of a key relative, as assessed by the Level of Expressed Emotion Scale (LEE; Cole & Kazarian, 1988, 1993; Gerlsma, Van der Lubbe, & Van Nieuwenhuizen, 1992; Gerlsma & Hale III, 1997) predicted conversion from high-risk status into FEP. The predictive value of this environmental risk factor was further underpinned by an improvement of risk estimation in the EPOS prediction model.

Effect of family interventions on ARMS symptoms and/or functional outcomes

All the reviewed trials were conducted within the eight-site North American Prodrome Longitudinal Study (NAPLS). A family-focused therapy consisting of an 18-

session intervention that included explicit training in communication and problem solving was administered to clinical high-risk (FFT-CHR) relatives and patients. Results from O'Brien et al. (2014) indicated that ARMS individuals and their respective families showed greater improvement from baseline to the 6-month follow-up in constructive communication (e.g., active listening) and greater decreases in conflictual behaviors (e.g., criticism) than those who participated in a brief psychoeducational intervention. Importantly, the FFT-CHR was found to be effective in reducing high-EE attitudes and improving positive communication within the family. Miklowitz et al. (2014) examined the effects of the FFT-CHR in reducing risk for the onset of psychosis among 129 ARMS individuals. Patients undertaking FFT-CHR showed greater improvement in positive symptoms from baseline to 6 months than those assigned to a brief family psychoeducational intervention. Changes on psychosocial functioning over time were dependent of age, such that patients over 20 years demonstrated greater functional improvement in FFT-CHR, whereas those between ages of 16-19 showed greater functional improvement in the brief psychoeducational intervention. O'Brien et al. (2015) explored whether FFT-CHR can reduce levels of perceived criticism (PC), and whether decreases in PC predicted improvement in symptoms. Findings indicated that PC reduced from baseline to 6 months for both treatment groups (FFT-CHR and brief family psychoeducational intervention). A reduction in ARMS individuals' PC from baseline to 6 months predicted improvement in attenuated positive symptoms at 12 months over and above symptom improvement at 6 months.

Discussion

To the best of our knowledge, this is the first review examining family environmental variables in the ARMS stage. Given that high-EE environments have been consistently related to poor outcomes among patients with schizophrenia (Butzlaff & Hooley, 1998;

Cechnicki et al., 2013; Marom et al., 2005; Wearden et al., 2000), some of the reviewed cross-sectional studies aimed to explore the impact of EE on ARMS patients' symptoms and/or functioning (Domínguez-Martínez et al., 2014; Tsai et al., 2015). Findings were mixed and somewhat contradictory across these investigations. Whereas Domínguez et al. (2014) showed that relatives' EE was associated with ARMS/FEP patients' symptom severity and worse functioning, Tsai et al. (2015) informed that increased appraisals of criticism were related with patients' lower levels of negative symptoms. Using similar measures, further cross-sectional studies examined whether other family variables (e.g., nurturing behavior, problem solving, quality of parent-child relationships), as rated by ARMS patients' perceptions, were related to their concurrent clinical status (Welsh & Tiffin, 2015) or perceptions or social stress (Bentley et al., 2016). Once again, the latest studies reported mixed results.

Another line of enquiry has been the examination of whether ARMS concurrent clinical status impacted on relatives' EE (Hamaie et al., 2016; McFarlane & Cook, 2007; Meneguelli et al., 2011), as it has been suggested that patients' clinical features predict relatives' levels of EE (Miklowitz, 2004). Except for the study of McFarlane & Cook (2007), all studies showed that relatives' high-EE status did not seem to be reactive to ARMS patients' poor clinical status (Hamaie et al., 2016; Meneguelli et al., 2011) or to ARMS relatives' depressive symptoms (Hamaie et al., 2016). In summary, findings on the cross-sectional associations of EE and/or family functioning (as rated by patients or relatives) with patients' status seem to be contradictory and thus inconclusive in the ARMS literature. However, it must be noted that not all studies on family environment in schizophrenia and/or FEP samples find correlations between levels of EE and the severity of patients' concurrent clinical status (Álvarez-Jiménez et al., 2010; Bachmann et al., 2002; Cutting, Aakre, & Docherty, 2006; Heikkilä et al., 2002; Nuerchterlein, Snyder, & Mintz, 1992). Probably, accurate predictions of the influence of EE on ARMS patients' status cannot be

identified with the use of cross-sectional designs. Likewise, understanding EE as a unilateral relative's reaction to patient's clinical characteristics is an incomplete approach to study the ontogenesis of EE (Hooley, 2007; Miklowitz, 2004). In fact, a different picture emerges when considering EE as a more relational variable in which relatives' cognitive representations of the illness and/or generalized stress reactions to the patient's status are contributing to the emergence of EE. In this way, one of the reviewed studies highlighted the significant role of relatives' illness attributions (i.e., attributions of blame toward the patient) as mediators of the association between relatives' EE and patients' clinical/functional features. Also, Domínguez- Martínez et al. (2017) pointed to the contribution of relatives' distress and illness attributions in explaining EE attitudes. However, there is still a great need of studies exploring relatives' beliefs about the illness in ARMS stages to provide a comprehensive comparation of relatives' attributions and its relationship to EE attitudes across the different stages of the disorder. Likewise, only one of the reviewed studies (Wong et al., 2008) aimed to assess the experience of ARMS caregivers' burden independently of the course of the illness in their ill relative and/or its relationship to EE. Overall, the study of relatives' distress and/or burden in ARMS stages is still very scarce in comparation to its examination in relatives of schizophrenia (for a review, see Awad & Voruganti, 2008; Baronet, 1999; Saunders, 2003) and/or FEP patients (for a review, see Jansen, Gleeson, et al., 2015; Koutra, Vgontzas, et al., 2014).

Regarding the reviewed studies exploring the longitudinal impact of family environment variables on ARMS symptomatic relapse, it seems that most of the reviewed investigations pointed out the role of family positive aspects. Interestingly, studies revealed that: (1) relatives' EE positive components (i.e., positive remarks and warmth) (O'brien et al., 2006; O'brien et al., 2008); (2) observed positive interactional patterns within the family (O'brien et al., 2009) and positive self-reported family functioning (Wang et al., 2005) were predictors of improvement in ARMS patients' symptoms and/or functioning over time. By

comparison, fewer schizophrenia (Greenberg, Knudsen, & Aschbrenner, 2006; López et al., 2004; Medina-Pradas, Navarro, Pousa, Montero, & Obiols, 2013) and/or FEP studies (González-Pinto et al., 2011; Lee, Barrowclough, & Lobban, 2014) have examined the relationship between positive affect in the family environment and clinical outcome, such as relapse or symptom severity. Another differential aspect of ARMS stage is that relatives' EOI seemed to act more as protective factor, given that it was found to be related with improvement in patients' clinical/functional status (O'brien et al., 2006, Schlosser et al., 2010). In this line, it is important to assess the differential predictive power of the two EE components (i.e., criticism and EOI) given that criticism has been found to make a greater contribution to symptomatic relapse in schizophrenia (Cechnicki et al., 2013; Kavanagh et al., 1992; Marom et al., 2005) and even in the FEP period (Koutra et al., 2015). However, results regarding the predictive value of criticism in ARMS samples are somewhat mixed, while one of the studies found that relatives' criticism predicted worsening of attenuated psychotic symptoms over time (Schlosser et al., 2010), others did not report the same association (Haidl et al., 2018; O'brien et al., 2006). Notwithstanding, Haidl et al. (2018), as being the first study exploring the predictive value of perceived EE in conversion into FEP, highlighted how other valuable constructs, as patients' perceived irritability of a key relative, were predictive of ARMS conversion into FEP. These significant results should lead future studies to adopt a more holistic approach to study family environment variables contributing to relapse, not only restricted to relatives' criticism and EOI attitudes.

In comparison to longer-term illness (Barrowclough & Tarrier, 1992; Berglund, Vahlne, & Edman, 2003; Chien & Norman, 2009) and recent-onset psychosis groups (for a review, see Askey, Gamble, & Gray, 2007; Bird et al., 2010; Claxton, Onwumere, & Fornells-Ambrojo, 2017; Penn, Waldheter, Perkins, Mueser, & Lieberman, 2005), there have been fewer family-based intervention studies in ARMS stage and the evidence based on its efficacy during this pre-illness stage is still limited. However, reviewed studies suggested that, as in

schizophrenia or FEP stages, family-based interventions were effective in reducing both relatives' high-EE attitudes (O'brien et al., 2014) and patients' perceived levels of criticism (O' brien et al., 2015) as well as in improving ARMS patients' clinical and functional outcomes over time (Miklowitz et al., 2014; O'brien et al., 2015). The primary objective of the reviewed family-based interventions in ARMS stages was to prevent the likelihood of patients' symptomatic relapse. Notwithstanding, relatives' own needs and the emotional impact of caregiving are still a neglected intervention area in ARMS stages. Thus, further understanding of relatives' adaptation to the prodromal period is required to empirically validate intervention protocols focused on alleviating relatives' suffering.

Methodological limitations and future research

We identified several important methodological limitations in the reviewed literature. First, there was high heterogeneity amongst included studies. There were differences regarding study designs, methods of assessment (family and patients' measures), follow-up or other features that make studies different. This make comparison between studies difficult. Second, most of the studies were cross-sectional and contained small samples. Future studies may elucidate variations in patient-family dynamics over time using longitudinal designs and large samples of ARMS patients and their respective relatives. Another limitation is that EE and/or other family environment constructs were assessed from relatives' or patients' independent perspectives. Only two study assessed both patients' and relatives' perceptions of EE (O'brien et al., 2015; Schlosser et al., 2010). Given that EE reflects a transactional process between patients and relatives (Strachan, Feingold, Goldstein, Miklowitz, & Nuechterlein, 1989) further studies should consider the importance of obtaining information from both relatives' and patients' perspectives. A final limitation is that only a minor part of studies considered the role of relatives' psychological features (e.g., illness beliefs, stress reactions) in explaining EE attitudes and/or other stressful family environment variables. Besides, only one study (Mo et al., 2008) was focused on relatives'

emotional reactions to illness (i.e., burden), whereas all the rest, although few, measured relatives' distress to test its relationship to EE. Thus, there is still a great need of studies aimed at exploring the needs of relatives independently of the course of illness in their ill relative.

Clinical Implications

While much research of family-based interventions with ARMS populations remains to be done, the evidence summarized in this review in relation to family treatment in ARMS stages suggested that early interventions benefit individuals at risk for psychosis as well as family dynamics. However, it will be important to take better account of relatives' own psychological needs and not only focus on solely reducing EE in ARMS stages. Thus, family work with ARMS families is of high relevance to maximize adaptive functioning of the family and minimize disruption to family life and the risk of ARMS patients' deterioration given its high vulnerability to environmental stressors (Fusar-Poli et al., 2017).

Conclusions

In conclusion, preliminary evidence synthesized in this present review constitutes just and advance of the state of the art of the study of family environmental factors in ARMS stages. Given the high heterogeneity of the reviewed studies is difficult to make comparisons between studies or to draw meaningful conclusions. Overall, cross-sectional findings regarding relationships of EE and/or other family environment constructs with ARMS patients' status are inconclusive. However, it seems that relatives' cognitive representations of illness may have an important role to play, either as a mediator of the relationship between EE and ARMS clinical/functional features, or as predictors of EE attitudes. However, there is still scarce literature aimed at accounting for relatives' psychological features in terms of its relationship to EE. Likewise, relatives' distress and/or burden have been largely unexplored as main variables of interest in ARMS stages, thus neglecting relatives'

psychological needs in the prodromal period. Although evidence is still limited, an important part of longitudinal studies pointed out the significant role of family positive aspects as predictors of ARMS patients' clinical and/or functional improvement over time. Notwithstanding, there is an urgent need of studies aimed at clarifying which is the predictive value of EE dimensions (i.e., criticism and EOI) on the clinical outcome of ARMS patients. Finally, family-based interventions demonstrated great potential to reduce high-EE attitudes and/or to improve ARMS patients' outcomes. To assess relatives' needs and support family caregivers also deserve further attention.

Table 1. Summary of studies investigating family environment variables and family interventions in the At-Risk Mental Stage (ARMS) stage of psychosis

Study	Location	Design and participants	Family variables	Family measures	Key findings
FAMILY ENVIRONMENT STUDIES					
McFarlane & Cook (2007)	Portland, USA New Rochelle and Kingston, USA	Cross-sectional study 69 subjects with established psychotic disorders and their parents 50 subjects with prodromal symptoms and their parents	EE	SAS-III (relatives' self-reports)	- Criticism and EOI were higher in parents of patients with established psychotic disorders than in parents of ARMS individuals. - Warmth was significantly higher in ARMS families than in parents of ARMS individuals. - Analyses conducted only in ARMS families revealed that maternal criticism and EOI increased over time, whereas maternal and parental warmth decreased over time since the first signs of illness began to appear.
Meneguelli et al. (2011)	Milano, Italy	Cross-sectional study 77 FEP and their relatives 66 ARMS and their relatives	EE	CFI (Interview based on relatives' reports)	FEP families: - High-EE (i.e., high hostility, criticism and EOI) related to longer DUI. - High paternal EOI related to DUP. - Patients' severity of symptoms/functioning not related to EE. ARMS families: - High-EE not related to DUI. - Severity of illness/functioning not related to EE.
Hamaie et al. (2016)	Sendai, Japan	Cross-sectional study 43 FEP and their relatives 56 ARMS and their relatives	EE	FAS (relatives' self-reports)	- FEP criticism was associated with relatives' higher depression symptoms and with FEP patients' negative and general symptoms. - Criticism of FEP relatives was explained by relatives' depression symptoms and FEP patients' general symptoms in the regression analyses. - Criticism of ARMS relatives was not related to ARMS patients' clinical status, while it was related to ARMS relatives' higher educational levels - Criticism of ARMS relatives was explained by relatives' higher educational levels in the regression analyses.

Tsai et al. (2015)	Los Angeles, USA	Cross-sectional study 49 ARMS Non-Latino White:38 Latino:11	EE	PC and PW (patients' self-reports)	- Analyses examining sample as a whole revealed that patients' perceived levels of criticism were negatively associated with ARMS negative symptomatology. - Race/Ethnicity moderated the relationship between Perceived Criticism/Warmth and CHR clinical symptomatology.
Domínguez-Martínez, Medina-Pradas, Kwapil, & Barrantes-Vidal (2014)	Barcelona, Spain	Cross-sectional study 24 FEP and their relatives 20 ARMS and their relatives	EE Illness' perceptions	FQ (relatives' self-reports) IPQS-R (relatives' self-reports)	- Relatives' EOI was associated with patients' higher negative and general symptoms and worse social and role functioning. - Relatives' criticism was associated with patients' higher positive, negative and general symptoms, depressive symptoms and worse social and role functioning. - The association between EE and patients' symptoms/functioning did not differ between FEP and ARMS groups. - Attributions of blame toward the patient mediated most of the relationships between EE and illness severity.
Domínguez-Martínez et al. (2017)	Barcelona, Spain	Cross-sectional study 37 FEP-relatives 41 ARMS-relatives	EE Illness' perceptions Distress	FQ (relatives' self-reports) IPQS-R (relatives' self-reports) SCL-90-R (relatives' self-reports)	- Anxiety, depression and attributions of blame toward the patient predicted relatives' criticism in both ARMS and FEP relatives' groups. - Attributions of control by the patient and emotional negative representation of the disorder predicted relatives' EOI. - Anxiety more strongly associated with relatives' criticism in ARMS-relatives than in FEP-relatives. - Anxiety associated with relatives' EOI in ARMS but not in FEP-relatives.
Wong et al. (2008)	New York, USA	Cross-sectional study 12 FEP and their relatives 11 ARMS and their relatives	Burden	FEIS (Interview based on relatives' reports)	- Levels of both subjective and objective burden were comparable between ARMS and FEP relatives.

Welsh & Tiffin (2015)	North East of England, UK	Cross-sectional study 26 FEP 44 ARMS 140 Control Group (CG)	Family perceptions	FPS (patients' self-reports)	- ARMS and FEP showed more maladaptive family perceptions than CG. - ARMS showed poorer perceived problem solving and nurturing Behavior than CG. - Family perceptions not related to symptom severity in either ARMS and FEP groups; however higher scores on the EE subscale of the FPS were related to manic symptomatology in both ARMS and FEP groups.
Bentley et al. (2016)	Baltimore, USA	Cross-sectional study 36 ARMS 60 Help-seeking Control Group (CG)	Quality of parent-child relationship	BASC-2 (patients' self-reports)	- ARMS reported less positive parent-child relationships (P-CH-R) and higher perception of social stress than CG. - P-CH-R moderated the relationship between ARMS diagnosis and perception of social stress. - ARMS informing poorer P-CH-R reported increased perceptions of social stress. - ARMS informing positive P-CH-R reported decreased perceptions of social stress.
O'brien et al. (2006)	Los Angeles, USA	Prospective study, 3-months follow-up 26 ARMS and their primary caregivers at baseline and follow-up	EE	CFI (Interview based on relatives' reports)	- Relatives' criticism at baseline was not associated with changes in symptoms or social functioning at follow-up. - Relatives' EOI at baseline was associated with improvement in negative symptoms and social functioning at follow-up. - Relatives' positive remarks at baseline were associated with improvement in negative and disorganized symptoms at follow-up. - Relatives' warmth at baseline was associated with improvement in social functioning at follow-up.
O'brien et al. (2008)	Los Angeles, USA	Prospective study, 4-months follow-up 40 ARMS and their primary caregivers at baseline and follow-up	EE Supportive and conflict-engaging behavior	CFI (Interview based on relatives' reports) FIT (interactional patterns)	- Relatives' positive remarks at baseline were associated with a decrease in negative symptoms at follow-up. - Relatives' warmth at baseline predicted an improvement in social functioning at follow-up. - Relatives' behaviors exhibited during the interactional task were not predictive of ARMS patients' symptoms/functioning at follow-up.

O'brien et al. (2009)	Los Angeles, USA	Prospective study, 6-months follow-up 33 ARMS and their primary caregivers at baseline 27 ARMS and their primary caregivers at follow-up	Social problem-solving behavior	Problem-solving discussion (interactional patterns) FIT (interactional patterns) CFI (Interview based on relatives' reports)	- Baseline ARMS' skillful problem-solving and constructive communication & relatives' constructive communication were associated with ARMS' enhanced social functioning at follow-up. - Baseline ARMS' conflictual communication was associated with increased positive symptoms at follow-up.
Wang et al. (2015)	Shanghai, China	Prospective study, 6-months follow-up 32 ARMS from general population at baseline 25 ARMS from general population at follow-up 256 Control Group (CG)	Perceptions of family functioning Family cohesion Family adaptability	FAD (ARMS' self-reports) FACES-II (ARMS' self-reports)	- ARMS reported worse family functioning than CG. - Positive perception of problem solving and affective responsiveness from parents at baseline predicted less severe positive and negative symptoms at follow-up. - Better family cohesion and adaptability was associated with decreased general symptoms at baseline. - Better family cohesion and adaptability at baseline was associated with decreased disorganized and general symptoms at follow-up.
Schlosser et al. (2010)	Los Angeles, USA	Prospective study, 6- month follow-up 63 ARMS and their relatives at baseline and follow-up	EE	CFI (Interview based on relatives' reports) PC and PW (patients' self-reports) FMPC and FMPW (relatives' self-reports)	- Patients' perceived criticism at baseline significantly predicted worsening of attenuated positive symptoms at follow-up. - Relatives' criticism and hostility at baseline (as measured by CFI) significantly predicted worsening of attenuated positive symptoms at follow-up. - Relatives' EOI (moderate levels) and relatives' warmth (as measured by CFI) interacted such that the two jointly predicted improved functioning at follow-up.

Haidl et al. (2018)	Multicentric European study	Prospective study, 18-month follow-up 235 ARMS at baseline 205 ARMS at follow-up	EE	LEE (patients' self-reports)	- Patients' Perceived irritability was found to be a predictor of conversion for ARMS into FEP. - The importance of this family environmental risk factor was further demonstrated by an improvement of risk estimation in the original European Prediction of Psychosis Study (EPOS) predictor model.

FAMILY INTERVENTION STUDIES

Miklowitz et al. (2014)	8 research centers of the NAPLS-2 consortium	Randomized control trial Duration of Family Focused-Therapy for individuals at clinical high risk (FFT-CHR): 18 x 1 sessions over 6 months FFT-CHR was administered to patients and their parents. 129 ARMS at baseline 102 ARMS at follow-up	-	-	- ARMS participants assigned to FFT-CHR showed greater improvement in positive symptoms from baseline to follow-up than those participants assigned to a brief family psychoeducational intervention (3 sessions of family psychoeducation). - Negative symptoms improved independently of psychosocial treatments. - Changes on psychosocial functioning over time were dependent on age: patients over 19 years showed greater role improvement in FFT-CHR, whereas participants between 16-19 showed more role improvement in the brief psychoeducational intervention.
O'brien et al. (2014)	8 research centers of the NAPLS-2 consortium	Randomized control trial Duration of Family Focused-Therapy for individuals at clinical high risk (FFT-CHR): 18 x 1 sessions over 6 months FFT-CHR was administered to patients and their parents.	Family communication	Problem-solving discussion (interactional patterns)	- ARMS and their respective families assigned to FFT-CHR showed greater improvement from baseline to follow-up in constructive communication and greater decreases in conflictual behaviors than those who participated in a brief psychoeducational intervention. - FFT-CHR was found to be effective in improving active listening and calm communication and decreasing irritability, anger, complaints and criticism in either patients and family caregivers.

		51 ARMS and their relatives at baseline 38 ARMS and their relatives at follow-up			
O'brien, Miklowitz, & Cannon (2015)	8 research centers of the NAPLS-2 consortium	Randomized control trial Duration of Family Focused-Therapy for individuals at clinical high risk (FFT-CHR): 18 x 1 sessions over 6 months FFT-CHR was administered to patients and their parents. 90 ARMS and their mothers at baseline 41 ARMS and their mothers at follow-up	EE	PC (patients' and mothers self-reports)	- Perceived maternal criticism decreased from pre- (baseline) to posttreatment (6-months) for both treatment groups (FFT-CHR and brief psychoeducational intervention) and this changes in criticism predicted decreases in attenuated positive symptoms at 12-month follow-up. - Decreases in mothers' reports of criticism were marginally significant predictors (p=.06, two tailed).

Abbreviations and notes: The order of appearance of studies follows the comments of the body text to ease the reading.
EE: Expressed Emotion; EOI: Emotional Over-Involvement; SAS-III: Social Adjustment Scale-III; CFI: Camberwell Family Interview; DUI: Duration of Untreated Illness; DUP: Duration of untreated psychosis; FAS: Family Attitude Scale; NLW: Non-Latino White; PC: Perceived Criticism Scale; PW: Perceived Warmth Scale; FQ: Family Questionnaire; SCL-90-R: Symptom Checklist-90-Revised; IPQS-R: Illness Perception Questionnaire for Schizophrenia Relatives' version; FEIS: Family Experiences Interview Schedule; FPS: Family Perception Scale; BASC-2: Behavior Assessment System for Children, Second Edition; FIT: The Family Interaction Task; FAD: Family Assessment Device; FACES-II: Family cohesion and adaptability evaluation Scale II; FMPC: Family member's perceived criticism; FMPW: Family member's perceived warmth; LEE: Level of Expressed Emotion Scale; NAPLS-2 : North American Prodrome Longitudinal Study; NAPLS-2 consortium: Emory University, Harvard University, University of Calgary, University of California Los Angeles, University of California San Diego, University of North Carolina, Yale University, and Zucker Hillside Hospital.

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EMPIRICAL INVESTIGATION

SECTION 1

THE MEASUREMENT OF RELATIVES' EXPRESSED EMOTION IN DAILY LIFE

Chapter 1

Ecological Validity of Expressed Emotion in Early Psychosis

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Abstract

Expressed Emotion (EE) has been conceptualized as a relevant measure of the family environment. However, there is limited research about how EE dimensions (i.e., criticism and Emotional Overinvolvement; EOI) behave in real-world settings. The present study used experience sampling methodology to investigate: (1) the criterion and construct validity of daily-life, momentary measures of criticism and EOI, and (2) the construct and ecological validity of psychometric EE-dimensions as assessed with the Family Questionnaire (FQ). A total sample of 55 relatives (34 from ARMS and 21 from FEP patients) were prompted randomly six times daily for 1-week period to assess their current emotional experiences and cognitive appraisals. Relatives also completed the self-reported FQ. Findings revealed that momentary criticism and EOI were significantly associated with the two FQ-EE dimensions respectively, supporting the criterion validity of momentary EE dimensions. As hypothesized, momentary and FQ-EE dimensions were associated with decreased positive affect as well as to appraisals of less effective coping in daily life. Only momentary EE dimensions were associated to increased momentary negative affect. Partly in contrast with our hypotheses, momentary criticism and FQ-criticism were more consistently related to situational stress and burden than momentary EOI and FQ-EOI. Finally, neither momentary nor FQ-EE dimensions showed a distinct pattern of associations with illness attributions. Findings partly support the construct validity of momentary criticism and EOI as well as the construct and ecological validity of the FQ as a sensitive measure of EE dimensions.

Keywords: Experience Sampling Methodology (ESM), criticism, emotional over-involvement, early psychosis, family environment.

Introduction

The potential prognostic value of factors identified in the early stages of psychosis has (Fusar-Poli et al., 2013; McGorry, 1998; Morrison et al., 2011) renewed the interest in environmental stressors as co-participating factors in the risk, onset, expression and progression of psychosis (Bentall and Fernyhough, 2008; Brown, 2011; Read et al., 2014).

One of the most significant factors in psychosocial research in psychosis has been Expressed Emotion (EE), a measure of the family environment used to describe relatives' attitudes towards an ill family member (Leff and Vaughn, 1985). High-EE attitudes, particularly criticism and Emotional Over-Involvement (EOI), have been considered the strongest psychosocial predictor of relapse in schizophrenia (Butzlaff and Hooley, 1998; Cechnicki et al., 2013; Marom et al., 2005)

Although most studies on EE have been carried out in patients with the chronic form of the psychosis phenotype (Hooley, 2007; Kavanagh, 1992), recent research has focused on the study of EE in the early stages of the illness (Koutra et al., 2014; Meneghelli et al., 2011; Raune et al., 2004) in order to prevent the entrenchment of high-EE and the potentially associated bad outcomes. Increasing evidence suggests that high-EE levels are observed in relatives of persons with First-Episode of Psychosis (FEP) (Bachmann et al., 2002; Gonzalez-Blanch et al., 2010; McNab et al., 2007) and At-Risk Mental State (ARMS) (O'Brien et al., 2006; Schlosser et al., 2010). Moreover, relatives of patients with early psychosis often report high levels of burden, distress, depression and anxiety related to high levels of EE (Domínguez-Martínez et al., 2017; Jansen et al., 2015a, 2015b; Möller-Leimkühler et al., 2005; Raune et al., 2004; Sadath et al., 2017; Tomlinson et al., 2014). Specifically, there is converging evidence suggesting that EOI is more related to distress and burden than criticism (Álvarez-Jiménez et al., 2010; Gonzalez-Blanch et al., 2010; Jansen et al., 2015a, 2015b; Jansen et al., 2014). Given the large variety of negative outcomes associated

with high-EE, both for relatives and patients, it is crucial to examine the psychological underpinnings of EE in early psychosis without the bias created by the chronic course of the illness and relatives' long-term burden.

The attributional model of EE posits that relatives' beliefs about patients' illness-related behaviors are linked to relatives' emotional attitudes towards patients (Barrowclough and Hooley, 2003). It seems that critical relatives are more likely to perceive symptoms as controllable by patients, even at recent-onset psychosis stages (McNab et al., 2007; Vasconcelos e Sa et al., 2013).Consequently, they attempt to reduce the undesired behaviors through critically persuading or coercing the patient. In contrast, overinvolved relatives tend to attribute symptoms to external and uncontrollable factors by the patient (Barrowclough et al., 1994; Brewin et al., 1991). However, they can also perceive patients' symptoms under their own control (Bolton et al., 2003) or even can report high levels of guilt and/or self-blame attributions (Bentsen et al., 1998; Peterson and Docherty, 2004). This is turn makes them more likely to exhibit intrusive and/or self-sacrifying attitudes. A different explanatory model of EE proposes that high-EE attitudes may represent a maladaptive attempt to cope with the stress of caring for an impaired ill relative; thus, EE behaviors could be deemed as maladaptive coping strategies used to reduce the perceived stress related to the caregiving role (Álvarez-Jiménez et al., 2010; Kuipers et al., 2006). In fact, relatives of patients with schizophrenia with high EE perceive their ability to cope as less effective and more impaired than those with low-EE (Smith et al., 1993). Also, emotion-focused strategies, such as avoidant coping, have been related to high-EE attitudes in relatives of FEP patients (Kuipers et al., 2006; Raune et al., 2004).

Significant contributions to the characterization of EE in early psychosis have been achieved by using retrospective reports and a few studies have examined it in early psychosis patients. However, an important limitation of this literature is that the vast majority of studies have not considered how EE is displayed within the natural family environment. This is a

notable limitation given that EE is conceptualized within an interactional framework (Hooley, 2007; Hooley and Gotlib, 2000; Miklowitz, 2004). Therefore, it is crucial to examine how EE behaves when interactions with ill relatives occur and how it is expressed in relation to daily appraisals and caregivers' subjective states in real-world settings.

The construct and ecological validity of EE has been supported by research showing that high-EE relatives tend to be more critical and intrusive in their direct transactions with patients than low-EE relatives (Miklowitz et al., 1989, 1984; Valone et al., 1983). However, most of these studies have assessed family interactions as a function of global EE, without considering that criticism and EOI measure heterogeneous attitudes and could be related with different type of behaviors and prognostic estimates (Chambless et al., 1999; Scazufca and Kuipers, 1998; Van Os et al., 2001). Work examining the two EE dimensions separately suggests that relatives high on criticism manifest critical attitudes at a behavioral level (Cruise et al., 2011; O'Brien et al., 2008; O'Brien et al., 2009) and/or make disgust and harsh statements in parent-patient interactions (McCarty et al., 2004). However, findings supporting the construct validity of EOI have been less consistent (McCarty et al., 2004; Mueser et al., 1993). Some studies have found that high-EOI relatives make intrusive (Strachan et al., 1986) or ambiguous statements (Hubschmid and Zemp, 1989), whereas others have reported that they show high rates of positive and supportive statements in interaction studies (Hahlweg et al., 1989). These studies offer valuable information of the behavioral correlates of EE in laboratory settings. However, as these paradigms focus on objectively defined family interactional tasks (e.g., interactions lasting 10 min or longer), they are unable to capture how EE components are expressed in daily life and relate to the wide variety of caregiver's subjective states and appraisals within the natural family environment.

Unlike previous research, the current study used experience sampling methodology (ESM) to examine the daily life expression of EE. ESM provides several benefits compared to conventional laboratory or clinic-based assessment paradigms (e.g., deVries, 1992; Conner

et al., 2009; Hektner et al., 2007): 1) it enhances ecological validity because it allows to evaluate participants in their daily life environment, 2) it captures participant's experience in the moment, thus minimizing retrospective bias, and 3) allows for the examination of the context where the experience is occurring. To the best of our knowledge, the only study that has used an ecologically valid methodology to examine family interactions in EE environments reported that relatives' high-EE status did not influence relatives' affect when relatives were in contact with patients (Vasconcelos e Sa et al., 2016). Although this work provided an ecologically valid insight on EE dynamics, it did not measure specifically the expression of EE dimensions in daily life.

Therefore, the general purpose of this study was to test the ecological validity of the EE dimensions (i.e., criticism and emotional over-involvement) in a sample of relatives of early psychosis patients. To this end, we first analyzed the criterion validity of momentary criticism and EOI (i.e., as measured with ESM) by examining their association with the EE-dimensions of the Family Questionnaire (FQ; Wiedemann et al., 2002), a widely-used psychometric measure of EE. It was predicted that the analogous momentary and psychometric indicators of criticism and EOI would be significantly and more strongly related to each other than to the other dimension. Secondly, we examined the construct validity of momentary criticism and EOI as well as the construct and ecological validity of psychometric EE dimensions by relating them to emotional, cognitive and interpersonal correlates occurring in the flow of daily life. We expected momentary and psychometric criticism and EOI to show both common and distinctive correlates. Both EE dimensions (momentary and psychometric) were expected to be related to: increased negative affect and decreased positive affect, appraisals of less effective coping in daily life, and momentary reports of increased situational stress and burden. Based on the attributional model of EE and previous findings, different correlates were expected for criticism and EOI in relation to illness attributions. Momentary and psychometric criticism would be associated with

attributions of control toward the patient, whereas momentary EOI and FQ-EOI would be related to attributions of personal control over the disorder in daily life. Additionally, we explored whether criticism and EOI, as measured by momentary and psychometric self-reports, showed differential associations with negative and positive appraisals about the self, positive appraisals about the patient, as well as with negative and positive appraisals about patients' behaviors in situations of direct and/or recent contact with the patient. It was expected that high criticism would be related to negative appraisals about the patient, whereas EOI would show some associations with positive appraisals of the patient.

Methods

Participants and Procedure

The present study is embedded in a larger longitudinal study carried out in three Mental Health Centres in Barcelona (Spain) within the Sant Pere Claver-Early Psychosis Program (SPC-EPP; Domínguez-Martínez et al., 2011). A total of 55 relatives (34 from ARMS and 21 from FEP patients) were included in this study. An additional six participants were enrolled in the study and completed the questionnaires but were omitted from the analyses due to failing to complete the ESM protocols.

The recruited relatives were those who had the most regular contact and/or the most significant relationship with the patient. Patients had to meet ARMS criteria as assessed by the Comprehensive Assessment of At-Risk Mental States (CAARMS; Yung et al., 2005) and/or the Schizophrenia Proneness Instrument Adult- Version (SPI-A; Schultze-Lutter et al., 2007). FEP patients met DSM-IV criteria (APA, 2002) for any psychotic disorder or affective disorder with psychotic symptoms as established by the Structured Clinical Interview for DSM-IV (SCID-I; First et al., 1995). All relatives provided written informed consent to participation. The project was developed in accordance with the Code of Ethics

of the World Medical Association (Declaration of Helsinki). Ethical approval for the study was obtained from the local ethical committee.

Measures

Relatives completed the Family Questionnaire (FQ; Wiedemann et al., 2002), a well-established instrument to measure EE. The FQ consists of 20 items equally distributed into two subscales (criticism and EOI). They are scored on a 4-point scale ranging from 'never/very rarely' to 'very often'. The internal consistency (Cronbach's alpha) of the scores for the two subscales in our sample was good, 0.89 for criticism and 0.86 for EOI.

Experience sampling methodology data were collected with personal digital assistants (PDAs). The PDAs signaled each of patient relatives' randomly six times a day (between 11 a.m. and 22 p.m.) for one week to complete brief questionnaires. When prompted by the signal, the participants had 5 min to initiate responding. After this time interval or the completion of the questionnaire, the PDA became inactive until the next signal. Each questionnaire took approximately 2 minutes per beep to complete. All ESM items reported in the current study were answered on 7-point scales ranging from 'not at all' to 'very much', except for the dyad contact items (i.e., 'Are you with your son/daughter right now?', 'Since the last beep, did you have contact with he/she', 'Right now, I wish he/she was here') which were responded dichotomously (yes/no).

The ESM questionnaire included items that inquired about the following global domains: (1) momentary criticism; (2) momentary EOI; (3) affect in the moment; (4) appraisals of effective coping in the moment (5) appraisals about the current situation; (6) appraisals of burden; (7) illness attributions; (8) appraisals related to the self; (9) positive appraisals about the relative; and (10) a variety of appraisals that are only prompted if there is direct and/or recent contact with the patient. As it can be seen in Table 2, some domains were subdivided into further specific domains.

The ESM items comprised in the domain: 'appraisals in situations of direct and/or recent contact with the patient' were only prompted when relatives reported 'Yes' to the dyadic contact items: 'Are you with your son/daughter right now?' or 'Since the last beep, did you have contact with he/she'. The rest of the ESM items were asked by participants at all beeps.

The momentary criticism index was created using the following 4 items: 'I feel exhausted by he/she', 'I feel disappointed by he/she', 'I feel angry with the he/she' and 'It is difficult to deal with he/she' (Cronbach's α=0.83). Momentary EOI was assessed with the item 'I am worried about he/she'. Momentary EE items were developed on the basis of construct definitions and the items of the FQ (Wiedemann et al., 2002). Summary indices were also computed for negative affect (NA) (Cronbach's α=0.81), positive affect (PA) (Cronbach's α=0.87) and relatives' positive appraisals about patients' behaviors in situations of direct and/or recent contact with the patient (Cronbach's α=0.81). Table 1 displays the ESM items and indices.

Statistical Analysis

Pearson correlations were computed to explore the association of momentary EE constructs (i.e., criticism and EOI) with psychometric EE dimensions (FQ) using the Statistical Package for Social Sciences (SPSS), Version 22.0. The effect size of the correlations was interpreted following Cohen's (1992) guidelines (correlations of 0.10 indicate small effect sizes, 0.30 indicate medium effect sizes, and 0.50 indicate large effect sizes).

The statistical analyses involving the ESM data were conducted with Mplus 6 (Muthén and Muthén, 2010). ESM data have a multilevel structure in which ESM ratings (level 1 data) are nested within participants (level 2 data). Multilevel or hierarchical linear modeling techniques are a standard approach for the analysis of ESM data (Bolger and Laurenceau, 2013; Nezlek, 2001). Level 1 predictors were group-mean centered, level 2 predictors were grand-mean centered, and parameter estimates were calculated using robust

standard errors. Two types of multilevel analyses were conducted in the present study. Firstly, a series of multilevel regressions were conducted to test the impact of momentary criticism and EOI (level 1 predictors) on emotional, cognitive and interpersonal experiences in daily life. Secondly, multilevel regressions were performed to explore the impact of FQ-EE psychometric dimensions (level 2 predictors) on ESM domains in daily life (level 1 dependent measures).

Results

Sample characteristics

Relatives were predominantly female (67.3%), specifically patients' mothers (63.6%), with the remaining caregivers being fathers (25.5 %), partners or siblings (11%). Mean age of the relatives was 50.7 years old (*SD*=8.96). Most relatives lived with the patient (85.5%). Participants completed an average of 28.5 usable ESM questionnaires (*SD* = 11.4).

Associations between momentary EE and FQ-EE dimensions

Pearson's correlations revealed strong associations between momentary criticism and FQ-criticism ($r=0.66$, $p<0.001$), as well as between momentary EOI and FQ-EOI ($r=0.51$, $p<0.001$). Following Cohen (1992), effect sizes were of large magnitude.

Significant associations were also found between momentary criticism and FQ-EOI ($r=0.42$, $p<0.01$) as well as between momentary EOI and FQ-criticism ($r=0.45$, $p<0.01$); however, these associations were of a medium effect size.

Associations between momentary EE and emotional, cognitive and interpersonal experiences in daily life

Momentary criticism and momentary EOI were significantly correlated in the present sample ($r=0.59$, $p<0.001$).

Table 2 presents the direct effects of both momentary EE dimensions on relatives' daily life experiences. As expected, momentary criticism and EOI were associated with increased NA and decreased PA in daily life. Specifically, both momentary EE dimensions were related to increased feelings of sadness (momentary criticism: 0.439, *SE*=0.124, $p<0.001$; momentary EOI: 0.152, *SE*=0.035, $p<0.001$) and anxiety (momentary criticism: 0.373, *SE*=0.091, $p<0.001$; momentary EOI: 0.069, *SE*=0.029, $p=0.019$), as well as to decreased ratings of happiness (momentary criticism: -0.385, *SE*=0.092, $p< 0.001$; momentary EOI: -0.150, *SE*=0.041, $p<0.001$) and relax (momentary criticism: -0.414, *SE*=0.082, $p< 0.001$; momentary EOI: -0.145, *SE*=0.030, $p<0.000$). Momentary criticism, but not EOI, was related to feeling irritable in daily life (momentary criticism: 0.508, SE=0.134, $p< 0.000$; momentary EOI: 0.055, *SE*=0.038, $p= 0.153$). Additionally, both momentary EE dimensions were related with decreased appraisals of effective coping in everyday life.

In terms of appraisals about the situation, momentary criticism and EOI were associated with a decreased enjoyment of current activities and perceiving the current situation as less positive. Momentary criticism was associated with reports that the current situation was stressful, whereas contrary to expectations, momentary EOI was not related to appraisals of situational stress. In relation to burden, both momentary EE domains showed significant associations with increased appraisals of feeling burdened by the patient. Also, contrary to our hypotheses, no differential associations emerged for each momentary EE dimension in relation to illness attributions. Both momentary EE dimensions were significantly associated with attributions of patients' control over the disorder as well as with attributions of relatives' personal control over the disorder in daily life.

Regarding negative and positive appraisals related to the self, momentary criticism was related to appraisals of feeling less emotionally supported, whereas momentary EOI was

associated with feelings of being lonely. No associations were found between momentary EE and appraisals of hope and guilty. In relation to relatives' positive appraisals about the patient, momentary criticism and EOI were associated with expressing decreased feelings of happiness in relation to the patient and less reports of feeling emotionally close to the patient.

As for relatives' appraisals in situations of direct and/or recent contact with the patient, momentary criticism and EOI were associated with current appraisals of feeling exhausted by the patient as well as with perceiving the current patient's behavior as disruptive. There were no associations between momentary EE and appraisals of burden. Moreover, both momentary EE dimensions were inversely related to positive appraisals about patients' behaviors when relatives were interacting and/or had recently interacted with the patient.

Impact of psychometric EE dimensions on emotional, cognitive and interpersonal experiences in daily life

Criticism and EOI dimension scores, as measured by FQ, were significantly correlated in the present sample (r=0.72, $p< 0.001$).

Table 3 presents the direct effects of FQ-EE dimensions on relatives' daily life experiences. FQ-criticism was related with the momentary criticism index (0.091, *SE*=0.014, $p< 0.001$) and its four individual items. Specifically, FQ-criticism was associated with increased reports of feeling exhausted by the patient (0.091, *SE*=0.018, $p< 0.001$), disappointed (0.081, *SE*=0.021, $p< 0.001$) and angry with the patient (0.048, *SE*=0.014, $p= 0.001$), as well as with an increased perception of difficulties for dealing with the patient (0.144, *SE*=0.021, $p< 0.001$) in daily life. FQ-criticism was also related to momentary EOI (0.117, *SE*=0.028, $p< 0.001$). On the other hand, FQ-EOI was related to momentary EOI (0.141, *SE*=0.028, $p< 0.001$) that is, to increased reports of worry about the patient in daily life. In addition, FQ-EOI was associated with the momentary criticism index (0.062,

SE=0.018, *p*=0.001)., specifically with feeling exhausted by the patient (0.093, *SE*=0.018, *p*< 0.001) and perceiving difficulties in dealing with the patient (0.088, *SE*=0.032, *p*= 0.006), but not with feeling disappointed (0.045, *SE*=0.024, *p*=0.065) or angry with the patient (0.022, *SE*=0.018, *p*=0.226).

Although none of two FQ-EE dimensions showed significant relationships with momentary NA, both of them were inversely related to momentary PA. Both dimensions were associated with decreased ratings of happiness (FQ-criticism: -0.069, *SE*=0.029, *p*= 0.017; FQ-EOI: -0.076, *SE*=0.030, *p*=0.010) and relax (FQ-criticism: -0.061, *SE*=0.024, *p*= 0.012; FQ-EOI: -0.071, *SE*=0.025, *p*= 0.004). Also, unlike FQ-criticism, FQ-EOI was related to increased feelings of sadness (FQ-criticism: 0.063, SE=0.034, *p*= 0.062; FQ-EOI: 0.078, *SE*=0.033, *p*= 0.018). Furthermore, both dimensions were related to decreased appraisals of effective coping in daily life.

In terms of situational appraisals, both dimensions were associated to perceiving situations as less positive and more stressful. No associations were found with appraisals of enjoyment with current activities. Unlike FQ-EOI, FQ-criticism was associated with increased momentary reports of feeling burdened by the patient. Regarding illness attributions, both dimensions were associated with attributions of relatives' personal control over the disorder. However, only FQ-criticism was associated with increased attributions of patients' control over the disorder as expected.

As for negative and positive appraisals related to the self, both dimensions were related with increased feelings of guilt and decreased ratings of hopefulness. There were no associations with appraisals of feeling supported or lonely. In relation to positive appraisals of the ill relative, both dimensions were associated with decreased feelings of happiness with the patient. However, only FQ-criticism was associated with feeling less emotionally close to the patient.

No differential associations were found in relation to the appraisals in situations of direct and/or recent contact with the patient. Both FQ-criticism and FQ-EOI displayed significant relationships with increased reports of feeling exhausted by the patient as well as with perceiving the patient's behavior as disruptive in the current situation. No associations were found between EE and burden. Moreover, both psychometric dimensions were inversely related to positive appraisals about patients' behaviors.

Discussion

To the best of our knowledge, this is the first study to explore how EE dimensions (i.e., criticism and EOI), as measured by momentary and psychometric self-reports, are expressed in daily life by using ESM in a sample of early psychosis caregivers. Consistent with our hypotheses, momentary criticism and FQ-criticism as well as momentary EOI and FQ-EOI displayed significant associations of a large magnitude, providing support for the criterion validity of momentary EE dimensions. Furthermore, findings showed that both momentary EE and FQ-EE dimensions were meaningfully and significantly associated with real-world experiences pertaining to psychological domains that have been previously related to EE in retrospective and psychometric studies and that are critical to the definition of EE from a theoretical standpoint. On the other hand, it was expected that criticism and EOI, as measured by momentary and psychometric self-reports, would show a clearer differential pattern of relationships with real-world experiences in accordance to EE research suggestions. Overall, these findings partly support the construct validity of momentary criticism and EOI as well as the construct and ecological validity of the FQ.

The strong association between analogous EE momentary and psychometric dimensions supported the criterion validity of momentary criticism and EOI assessments. However, there were also significant associations between momentary criticism and FQ-EOI, as well as between momentary EOI and FQ-criticism—although of a medium, not

large, magnitude. Hence, momentary criticism and momentary EOI appear to be a relatively non-specific indicators of each respective EE dimension (i.e., criticism and EOI).

On the other hand, multilevel regression analyses indicated FQ-criticism was significantly related with the momentary criticism index as well as its four individual items, and that FQ-EOI was associated with momentary EOI. This further supports the criterion validity of each momentary EE dimension as well as the construct and ecological validity of the psychometric EE dimensions. However, multilevel analyses also indicated a low-specificity pattern, thus showing that FQ-criticism displayed significant associations with momentary EOI and that FQ-EOI was related to momentary criticism index. Further analyses regarding relationships between FQ-EOI and the four individual items of momentary criticism index showed that FQ-EOI was associated to increased reports of feeling exhausted by the patient, and with increased difficulties for dealing with the patient, but not with feeling disappointed or angry with the patient. This provides some discriminant validity to EOI dimension by the fact that it was not related with the most conceptually representative critical appraisals of the momentary criticism index (i.e., 'I feel disappointed by he/she', 'I feel angry with the he/she').

Overall, the results regarding the daily life expression of criticism and EOI dimensions partly confirmed our research and theory-based predictions. Momentary criticism and EOI were related to increased NA and decreased PA, consistent with previous work indicating that early psychosis relatives often report high levels anxiety and depression associated to high levels of EE (Domínguez-Martínez et al., 2017; Jansen et al., 2015a, 2015b; Tomlison et al., 2014). However, FQ-EE dimensions were only associated to decreased PA in daily life, suggesting that the momentary measure of EE is more sensitive to capture daily negative affective experiences. Furthermore, both momentary and psychometric EE indicators were related to appraisals of less effective coping in daily life. This finding is in

accordance with previous results from the schizophrenia literature showing that relatives with high EE perceive their ability to cope as poorer and more impaired than those with low EE (Smith et al., 1993), and further supports the assumption that EE could be deemed as a maladaptive coping strategy used in an attempt to reduce the perceived stress related to the caregiving role (Álvarez-Jiménez et al., 2010; Kuipers et al., 2006).

Regarding appraisals about the situation, results showed that both momentary criticism and EOI as well FQ-criticism and FQ-EOI were associated with reports that the current situation was less positive. Unlike FQ-EE dimensions, momentary EE dimensions also displayed associations with expressing decreased enjoyment regarding current activities. Consistent with our results, Hooley and Hiller (2000) found that relatives of schizophrenia patients with high-EE reported reduced satisfaction about their individual activities compared to low-EE relatives. It is likely that the momentary nature of ESM measures allows to capture with higher sensitivity the rewarding capacity of situations encountered in the flow of daily life as compared with the psychometric inventory.

In line with our hypotheses, momentary criticism and FQ-criticism were related to daily appraisals of situational stress and burden. However, momentary EOI and FQ-EOI showed discrepancies in their association to burden and stress. FQ-EOI, but not momentary EOI, was associated with increased appraisals of situational stress, whereas only momentary EOI was related with increased appraisals of feeling burdened by the patient. Thus, criticism had a clearer association with situational stress and burden than EOI. Overall, these results seem to be partly consistent with previous early psychosis studies indicating relationships of EE with relatives' distress and/or burden (Domínguez-Martínez et al., 2017; Jansen et al., 2015a, 2015b; Möller-Leimkühler et al., 2005; Raune et al., 2004; Sadath et al., 2017; Tomlinson et al., 2014), but do not replicate previous early psychosis research suggesting that EOI is more related to distress and burden than criticism (Álvarez-Jiménez et al., 2010; González-Blanch et al., 2010; Jansen et al., 2015a, 2015b, 2014).

Partly in contrast with our hypotheses, a distinct pattern of associations was not observed for momentary and FQ-EE dimensions in relation to illness attributions. As expected, momentary criticism and FQ-criticism were associated with increased attributions of patients' control over the disorder. This result agrees with previous findings in early psychosis (McNab et al., 2007; Vasconcelos e Sa et al., 2013) and is also consistent with the attributional model of EE (Barrowclough and Hooley, 2003). However, momentary EOI was also associated with attributions of control over the disorder by the patient. This seems to be partly incongruent with the attributional model of EE referred above, which posits a specific relationship between criticism and attributions of the patients' ability to control their behaviors. However, EOI has also been related with attributions of control by the patient in the early stages of psychosis (Domínguez-Martínez et al., 2017). Therefore, it is attractive to speculate that at the early stages, when there is great confusion and still a low level of knowledge about the disorder, a great majority of relatives still trust that patients can have a significant control over their behavior, which may explain the finding of a lack of a differential pattern. In line with previous studies relating EOI with relatives' self-control attributions (Bolton et al., 2003), both momentary EOI and FQ-EOI were related with attributions of relatives' control over the disorder. However, in contrast with our hypotheses, both momentary criticism and FQ-criticism were also related to self-control attributions. Probably, relatives' self-control attributions could be interpreted as a feeling that the patient is powerless (Rexhaj et al., 2013) and, thus, relatives would assume illness control and would react with critical attitudes to persuade or coerce the patient to gain control over symptoms/behaviors.

Regarding positive and negative appraisals related to the self, our results showed that, unlike momentary EE, both FQ-EE dimensions were associated with increased reports of feeling guilt in daily life. Previous studies have reported associations between relatives' guilt and/or self-blame related to the patient's illness and EOI behaviors (Bentsen et al., 1998;

Peterson and Docherty, 2004). However, Wasserman et al. (2012) also found relatives' guilt/self-blame associated high-EE overall status and posited that relatives may defend against the experience of blaming themselves by putting the blame onto the patient in a critical manner, or by behaving in an emotionally over-involved way to repair their wrong-doing. Furthermore, unlike momentary EE, both FQ- EE dimensions were associated to decreased reports of hopefulness in everyday life. Surprisingly, hopefulness has not been studied in relation to EE, although it has been conceived as crucial in the process of coping with a psychiatric disorder in a close family member (Bland and Darlington, 2002; Tseng et al., 1995). Finally, only momentary criticism was related to appraisals of feeling less emotionally supported, whereas momentary EOI was associated with feelings of being lonely. In essence, these appraisals could be conceived as indicators of perceived social support. Of note, recent research has found EE to be related with a decreased perception of social support in schizophrenia relatives (Gupta and Mohanty, 2016).

In regard to the association of criticism and EOI with daily positive appraisals about the ill relative, both momentary and FQ-EE dimensions were related to decreased feelings of happiness with the ill relative. Also, both momentary EE domains and FQ-criticism (but not FQ-EOI) were associated with reports of feeling less emotionally close to the patient. Given that EOI is characterized by expressing extreme emotional closeness with the patient (i.e., overidentification) (Leff and Vaughn, 1985), it is not surprising that FQ-EOI was not related to decreased feelings of closeness. Therefore, the relationship between momentary EOI and appraisals of decreased emotional closeness constitutes an inconsistent result, and possibly indicates that our measure of EOI, based on the core element of 'worrying' but restricted to it, has not been sufficient to capture all the nuances of this construct.

As for relatives' appraisals about the ill relative when relatives were in direct contact and/or had had recent contact with the patient, all momentary and FQ-EE dimensions were related with decreased positive appraisals about patients' behaviors, as well as with increased

reports of feeling exhausted by the patient and/or with perceiving the patient's behavior as disruptive in the current situation. Momentary and FQ-EE dimensions did not show associations with appraisals of feeling burdened by the patient in situations of direct and/or recent contact with the patient. Our findings are consistent with research indicating that relatives of schizophrenia patients holding highly critical or emotional overinvolved attitudes (high-EE) tend to show lower levels of accepting behavior (Hooley, 1986) and make more negative statements (e.g., criticism, statements of disagreement) during face-to-face interactions with patients than do low-EE relatives (Miklowitz et al., 1984; Simoneau et al., 1998; Valone et al., 1983). Also, our results concur with previous studies indicating that criticism is related to "belittling and blaming" statements (Hubschmid and Zemp, 1989) and/or with statements of disgust and harshness in parent-patient interactions (McCarty et al., 2004). However, contrary to our findings, some researchers have found EOI associated with high rates of positive/supportive statements in interaction studies (Hahlweg et al., 1989). An interesting finding emerged thanks to ESM methodology employed. The item about feeling that the ill relative is a burden was prompted at all assessment points and appeared again at the end of the questionnaire if relatives answered that they were in direct or recent contact with the patient since the last beep as it was part of the appraisals regarding the patient and the interaction. Of note, both momentary EE dimensions and FQ-criticism, but not FQ-EOI, showed associations with burden when this item was asked at the beginning of the questionnaire. However, when answering exactly the same item in the assessments where relatives had been asked whether they were with their offspring, they reported negative appraisals as mentioned (being disruptive, makes me feel exhausted), but not feeling burdened.

The following limitations should be acknowledged when interpreting the results. First, our ESM measure of EOI (ESM item: 'I am worried about he/she') was necessarily brief and concentrated on an essential element but is arguably rudimentary. Although EOI

is characterized by relatives' over-concern, it is also defined by excessive self-sacrifice, over-identification and extreme over-protective behavior with the patient (Leff and Vaughn, 1985). Thus, our momentary EOI measure was probably not comprehensive enough to capture the heterogeneous collection of behaviors defining EOI attitudes. Second, although it has been suggested that the two dimensions of EE are uncorrelated, relate to different variables and are best examined separately (Chambless et al., 1999; Scazufca and Kuipers, 1998; Van Os et al., 2001), strong relationships were detected between momentary criticism and momentary EOI ($r=0.59$, $p<0.001$) as well as between FQ-criticism and FQ-EOI ($r=0.72$, $p< 0.001$). It is likely that such large overlap in both momentary and psychometric dimensions involved a poor differential pattern of relationships with real-world experiences. Third, it should be noted that we have examined the impact of momentary EE dimensions on momentary emotional, cognitive and interpersonal correlates to investigate the daily life expression of criticism and EOI; nevertheless, given the correlational nature of these data, the opposite interpretation is also plausible (e.g., increased NA contributing to increased reports of momentary EE). Future research should examine whether specific patterns of momentary emotional, cognitive and/or interpersonal experiences predict the emergence of momentary EE at subsequent assessments using longitudinal designs. Likewise, it would be also important to examine whether ARMS and FEP relatives differed in terms of levels of EE dimensions across the ecological and psychometric measures.

The expression of EE dimensions in real time as relatives navigate their real-life settings has remained an area largely unexplored by research in the EE field. This study provided a novel contribution by using momentary as well as psychometric measures to examine the expression of relatives' EE in relation to a wide variety of real-world experiences in the domains that are theoretically related to EE. Although criticism and EOI, as measured by momentary and psychometric self-reports, were expected to show relatively differential relationships with daily-life appraisals and caregivers' subjective states in real-world settings,

these results partly support the construct validity of momentary EE assessments and the construct and ecological validity of the FQ dimensions. This 'low-specificity' pattern might be related to a developmental issue. The fact that this is a very early risk or onset stage of the illness process may involve that relatives hyperactivate both the caregiving behavioral system to protect their relative as well as coercive and critical attitudes as an attempt to restore the lost normal behavior and healthy person; these would, respectively, raise EOI and criticism attitudes. It is possible that if illness progresses and becomes chronic relatives start to display a stronger tendency towards either criticism or EOI depending on a complex number of factors pertaining to both the relative (e.g., illness attributions, attachment style, type of relationship with the relative in the past, etc.) and the ill person (e.g., severity, disability). This work points to the utility of ESM as a promising method for assessing how the predictions derived from EE theory play out in the natural family environment. Moreover, from a clinical viewpoint, our results underscore the need for early family interventions including assessments of relatives' daily life experiences of EE in order to assist relatives to manage the manifestation of high-EE attitudes as well as its negative emotional and cognitive correlates in the specific moment that is needed.

Table 1. Relatives' ESM questionnaire and summary indices

Questionnaire	Summary indices
1. Right now, I feel happy	
2. Right now, I feel sad	Indices are computed as the means of the items indicated
3. Right now, I feel I can cope with things well	
4. Right now, it is difficult to concentrate or make decisions	Momentary criticism: 20, 21, 22 and 24
5. Right now, I feel relaxed	Negative affect: 2, 7 and 8
6. Right now, I feel lonely	Positive affect: 1, 5
7. Right now, I feel irritable	Positive appraisals about patients' behaviors: 31, 32 and 34
8. Right now, I feel anxious	
9. Right now, I feel hopeful	
10. Right now, I feel guilty	
11. Right now, I have difficulty controlling my thoughts and emotions	
12. Right now, I like what I am doing	
13. Right now, I feel tired	
14. Right now, I don't feel physically well	
15. Right now, I feel supported	
16. My current situation is positive	
17. My current situation is stressful	
18. Right now, I feel happy with my son/daughter	
19. Right now, I am worried about my son/daughter	
20. Right now, I feel exhausted by my son/daughter	
21. Right now, I feel disappointed by my son/daughter	
22. Right now, I am angry with my son/daughter	
23. Right now, I feel close to my son/daughter	
24. Right now, it is difficult to deal with my son/daughter	
25. Right now, I feel that my son/daughter doesn't make an effort to be well	
26. Right now, my son/daughter is a burden to me	
27. Right now, I feel my son/daughter cannot function without me	
28. ¿Are you with your son/daughter right now? *[If YES selected: Q31-Q36/If NO selected: Q29]*	
29. Since the last beep, did you have contact with he/she? *[If YES selected: Q31-36 /If NO selected: Q30 and END of SURVEY]*	
30. Right now, I wish he/she was here	
31. Right now, he/she is functioning well	
32. Right now, he/she is in a good mood	
33. Right now, he/she is being disruptive	
34. Right now, it is good to have he/she around	
35. Right now, he/she makes me feel exhausted	
36. Right now, he/she is a burden to me	

Table 2. Direct effects of momentary ESM-EE on relatives' daily life experiences

Level 1 criterion	Level 1 predictors	
	Momentary Criticism	**Momentary EOI**
Affect in the moment		
Negative Affect Index	0.440(SE=0.103)***	0.092(SE=0.028)**
Positive Affect Index	-0.399(SE=0.081)***	-0.150(SE=0.030)***
Appraisals of effective coping		
Right now, I feel I can cope with things well	-0.173(SE=0.056)**	-0.070(SE=0.034)*
Appraisals about the current situation		
My current situation is positive	-0.214(SE=0.070)**	-0.073(SE=0.030)*
Right now, I like what I am doing	-0.190(SE=0.056)**	-0.057(SE=0.028)*
My current situation is stressful	0.366(SE=0.062)***	0.033(SE=0.030)
Appraisals of burden		
Right now, he/she is a burden to me	0.321(SE=0.097)**	0.112(SE=0.039)**
Illness attributions		
Attributions of patients' control over the disorder		
Right now, I feel that he/she doesn't make an effort to be well	0.473(SE=0.102)***	0.157(SE=0.042)***
Attributions of relatives' control over the disorder		
Right now, I feel that he/she cannot function without me	0.167(SE=0.070)*	0.090(SE=0.030)**
Appraisals related to the self		
Positive Appraisals		
Right now, I feel hopeful	-0.077(SE=0.050)	-0.036(SE=0.019)
Right now, I feel supported	-0.157(SE=0.063)*	-0.055(SE=0.035)

Negative Appraisals		
Right now, I feel lonely	0.211(SE=0.151)	0.063(SE=0.028)*
Right now, I feel guilty	0.089(SE=0.062)	0.037(SE=0.024)
Positive Appraisals about the ill relative		
Right now, I feel happy with my son/daughter	-0.605(SE=0.128)***	-0.183(SE=0.051)***
Right now, I feel close to my son/daughter	-0.324(SE=0.094)**	-0.056(SE=0.026)*
Appraisals in situations of direct and/or recent contact with the patient		
Negative Appraisals about patients' behaviors		
Right now, he/she is being disruptive	0.498(SE=0.072)***	0.198(SE=0.039)***
Right now, he/she makes me feel exhausted	0.462(SE=0.082)***	0.116(SE=0.048)*
Right now, he/she is a burden to me	0.264(SE=0.154)	0.044(SE=0.053)
Positive appraisals about patients' behaviors - Index	-0.359 (SE=0.052)***	-0.181(SE=0.036)***
Other ESM items		
Right now, it is difficult to concentrate or make decisions	0.219(SE=0.078)**	0.114(SE=0.040)**
Right now, I have difficulty controlling my thoughts and emotions	0.252(SE=0.080)**	0.118(SE=0.036)**
Right now, I feel tired	0.320(SE=0.134)*	0.034(SE=0.045)
Right now, I don't' feel physically well	0.301(SE=0.098)**	0.081(SE=0.054)

Momentary Criticism was computed by averaging the scores of the following 4 items: 'I feel exhausted by he/she', 'I feel disappointed by he/she', 'I am angry with he/she' and 'It is difficult to deal with he/she' (α= 0.83)

Momentary EOI was assessed with the item 'I am worried about he/she'.

Negative affect index was computed by averaging the scores of the following 3 items: 'I feel sad', 'I feel irritable' and 'I feel anxious' (α= 0.81).

Positive affect index was computed by averaging the scores of the following 2 items: 'I feel happy' and 'I feel relaxed' (α= 0.87).

Positive appraisals about patients' behaviors index was computed by averaging the scores of the following 3 items: 'He/she is functioning well', 'He/she is in a good mood' and 'It is good to have he/she around'. (α= 0.81).

$*p < 0.05$, $**p < 0.01$, $***p < 0.001$.

Table 3. Direct effects of psychometric FQ-EE dimensions on daily life experiences

Level 1 criterion	Level 2 predictors	
	FQ-Criticism	**FQ-EOI**
Affect in the moment		
Negative Affect- Index	0.043(SE=0.025)	0.045(SE= 0.025)
Positive Affect-Index	-0.065(SE=0.024)**	-0.074(SE=0.025)**
Appraisals of effective coping		
Right now, I feel I can cope with things well	-0.075(SE=0.017)***	-0.070(SE=0.018)***
Appraisals about the current situation		
My current situation is positive	-0.071(SE=0.019)***	-0.083(SE=0.022)***
Right now, I like what I am doing	-0.032(SE=0.020)	-0.038(SE=0.020)
My current situation is stressful	0.082(SE=0.023)***	0.065(SE=0.030)*
Appraisals of Burden		
Right now, he/she is a burden to me	0.117(SE= 0.048)*	0.090(SE=0.048)
Illness Attributions		
Attributions of patients' control over the disorder		
Right now, I feel that he/she doesn't make an effort to be well	0.091(SE= 0.024)***	0.054(SE=0.028)
Attributions of relatives' control over the disorder		
Right now, I feel that he/she cannot function without me	0.134(SE=0.032)***	0.135(SE=0.032)***
Appraisals related to the self		
Positive Appraisals		
Right now, I feel hopeful	-0.041(SE=0.017)*	-0.046(SE=0.019)*
Right now, I feel supported	-0.049(SE=0.030)	-0.048(SE=0.027)

Negative Appraisals		
Right now, I feel lonely	0.053(SE=0.032)	0.047(SE=0.030)
Right now, I feel guilty	0.089(SE=0.042)*	0.106(SE=0.040)**
Positive Appraisals about the ill relative		
Right now, I feel happy with my son/daughter	-0.083(SE=0.026)**	-0.099(SE=0.028)***
Right now, I feel close to my son/daughter	-0.065(SE=0.027)*	-0.044(SE=0.027)
Appraisals in situations of direct and/or recent contact with the patient		
Negative Appraisals about patients' behaviors		
Right now, he/she is being disruptive	0.117(SE=0.022)***	0.072(SE=0.028)*
Right now, he/she makes me feel exhausted	0.088(SE=0.025)***	0.083(SE=0.025)**
Right now, he/she is a burden to me	0.012(SE=0.041)	-0.032(SE=0.048)
Positive appraisals about patients' behaviors Index	-0.066(SE=0.017)***	-0.054(SE= 0.018)**
Other ESM items		
Right now, it is difficult to concentrate or make decisions	0.083(SE=0.031)**	0.055(SE=0.033)
Right now, I have difficulty controlling my thoughts and emotions	0.092(SE=0.029)**	0.066(SE=0.031)*
Right now, I feel tired	0.073(SE=0.049)	0.091(SE=0.040)*
Right now, I don't' feel physically well	0.050(SE=0.032)	0.045(SE=0.033)

Momentary Criticism was computed by averaging the scores of the following 4 items: 'I feel exhausted by he/she', 'I feel disappointed by he/she', 'I am angry with he/she' and 'It is difficult to deal with he/she' (α= 0.83)

Momentary EOI was assessed with the item 'I am worried about he/she'.

Negative affect index was computed by averaging the scores of the following 3 items: 'I feel sad', 'I feel irritable' and 'I feel anxious' (α= 0.81).

Positive affect index was computed by averaging the scores of the following 2 items: 'I feel happy' and 'I feel relaxed' (α= 0.87).

Positive appraisals about patients' behaviors index was computed by averaging the scores of the following 3 items: 'He/she is functioning well', 'He/she is in a good mood' and 'It is good to have he/she around'. (α= 0.81).

$*p < 0.05$, $**p < 0.01$, $***p < 0.001$

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SECTION 2

MEDIATING MECHANISMS IN THE LINK BETWEEN RELATIVES' PERCEIVED LOSS AND EXPRESSED EMOTION: THE ROLE OF RELATIVES' ATTACHMENT DIMENSIONS

Chapter 2

Relatives' Attachment anxiety mediates the association between Perceived Loss and Expressed Emotion in Early Psychosis

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Abstract

The mechanisms underlying the relationship between relatives' perceived loss and Expressed Emotion (EE) attitudes in the early stages of psychosis are still not fully understood. The current study aimed to examine: (1) whether relatives' perceived loss was associated with relatives' EE dimensions [i.e., criticism and emotional overinvolvement (EOI)], and (2) whether such associations were mediated by relatives' attachment dimensions (i.e., anxiety and avoidance). Seventy-eight early psychosis relatives completed the Mental Illness Version of the Texas Inventory of Grief for the assessment of loss reactions. Attachment dimensions and EE attitudes were assessed by the Psychosis Attachment Measure and the Family Questionnaire, respectively. Findings indicated that relatives' perceived loss was associated with EE dimensions. Relatives' attachment anxiety, but not avoidance, mediated the relationship of perceived loss with both criticism and EOI. Findings highlight the importance of examining the role of relatives' attachment characteristics for understanding how perceptions of loss might impact the manifestation of EE attitudes in the early stages of psychosis. Family interventions aimed at assisting relatives to improve their management of negative emotional reactions to loss are fundamental to prevent impairing loss reactions and the entrenchment of high-EE attitudes.

Key words: Grief, Attachment Style, Criticism, Emotional Over-Involvement, Family, Early Psychosis.

Introduction

A prominent reaction described by family members of individuals with psychosis is grief (Davis and Schultz, 1998; Miller et al., 1990; Osborne and Coyle, 2002). This grief results from a deep sense of loss: loss of the healthy relative, loss of specific hopes and aspirations for the relatives' future and/or loss of the pre-existing relationship to illness (Miller, 1996; Parker, 1993; Young et al., 2004). Perceived loss has been found to have negative implications for relatives' physical and psychological health, and also affects interactions with their ill family member (Geraghty et al., 2011; Richardson et al., 2013). However, to grieve is not necessarily a pathological phenomenon, but rather a natural process of adapting to or accommodating a changed reality (MacGregor, 1994).

Relatives' perceived loss has been mostly examined in schizophrenia caregivers (Jones, 2004; Ozgul, 2004, Richardson et al., 2011). However, the few studies examining relatives' loss reactions in the early stages of psychosis indicated that high levels of perceived loss are already present in this very early phase (Mulligan et al., 2013; Patterson et al., 2005, 2000). Moreover, high levels of loss appraisals are related to the manifestation of high expressed emotion (EE) attitudes [i.e., criticism and emotional over-involvement (EOI)]; (Mulligan et al., 2013; Patterson et al., 2005, 2000; Raune et al., 2004). Patterson et al. (2005, 2000) found that high levels of perceived loss were related to high EOI attitudes, whereas low levels of perceived loss were linked to high criticism. It seems that relatives' perception of loss could motivate high EOI attitudes with the aim of reestablishing what has been lost (Patterson et al., 2005, 2000). However, coercive criticism has also been theoretically interpreted as a coping mechanism to deal with the pain of loss (Stirling et al., 1995). As argued by Patterson et al. (2005, 2000), this interpretation is consistent with attachment theory, which states that coercive angry or critical attitudes are a natural response to any perceived loss, with the goal to bring the person "back into line" through an activation of attachment responses (Bowlby, 1982, 1980, 1973). Since the perception of loss may be a

major driver of high EE attitudes (Birchwood, 1992; Birchwood and Spencer, 1999), it would be relevant to identify the mediating mechanisms by which perceived loss influences the manifestation of EE in early psychosis relatives. In this regard, attachment theory has been highlighted as a helpful framework for understanding how loss appraisals may contribute to the development of EE (Patterson, 2013; Patterson et al., 2005, 2000). Specifically, relatives' attachment styles have received theoretical attention as potential underlying mechanisms in the association between perceived loss and EE attitudes (Patterson, 2013).

Attachment theory has become one of the foremost paradigms for understanding the grieving process after the loss of a significant person (Shaver and Fraley, 2008; Shear and Shair, 2005; Stroebe et al., 2005). Insecure attachment has been proposed as a major risk factor for complications in adaptation to loss (Fraley and Bonanno, 2004; Neimeyer et al., 2002). Regarding the dimensions underlying attachment style, attachment anxiety and avoidance (Bartholomew and Horowitz, 1991; Mikulincer and Shaver, 2007), it seems that anxious attachment is more consistently associated with elevated grief symptoms than avoidant attachment after the loss of a loved one (Burke and Neimeyer, 2012; Meier et al., 2013). Moreover, anxious/ambivalent attachment has been related to increased parental grief in response to a family member's mental illness (Godress et al., 2005).

It is extensively assumed by attachment theorists that threats and stressors to an attachment bond such as illness or loss tend to activate the attachment system (Mikulincer and Shaver, 2016, 2007). Indeed, persons with high levels of attachment anxiety or avoidance tend to rely on secondary attachment strategies (Cassidy and Kobak, 1988; Main, 1990), either hyperactivating or deactivating their attachment system for regulating threat-related distress. Hyperactivating strategies observed in anxious individuals cause them to amplify negative emotional responses to threats. In contrast, avoidant individuals attempt to inhibit emotional reactions with the goal of maintaining the attachment system deactivated (Mikulincer and Shaver, 2016, 2008a, 2007). Taking this into account, anxiously attached

individuals' tendency to intensify negative emotions would involve a heightened risk of distress after an actual or perceived loss, whereas avoidant individuals' tendency to suppress negative emotions would promote an absence of conscious grieving (Mikulincer and Shaver, 2012, 2008b; Shaver and Fraley, 2008).

According to Bowlby (1982), parents develop their caregiving behaviors in consonance with their attachment systems and the associated working models (Collins and Ford, 2010; George and Solomon, 2008; Jones et al., 2015; Kunce and Shaver, 1994). For instance, avoidant individuals' lack of interpersonal engagement and negative working models of others may also translate into a lack of caregiving behaviors, probably driven by deactivating strategies across both attachment and caregiving systems (Canterberry and Gillath, 2012; Feeney and Collins, 2001). Conversely, anxious individuals, who adopt a hyperactivating attachment strategy (Canterberry and Gillath, 2012; Feeney and Collins, 2001; Karantzas and Simpson, 2015), show a pattern of hyperactivated caregiving, which is intrusive or overinvolved, poorly timed, and burdensome (Mikulincer and Shaver, 2016, 2007). The parallelism between these caregiving behaviors and those exhibited by high EE individuals could suggest that relatives' insecure attachment styles may influence their caregiving behaviors, contributing to high EE levels under acute levels of stress (Chen, 2006). In this line, insecure attachment has been hypothesized to contribute to the development of critical or EOI parenting styles (Diamond and Doane, 1994; Paley et al., 2000). Specifically, attachment anxiety has been related to intrusive, overinvolved, and controlling forms of caregiving (Adam et al., 2004; Bosquet and Egeland, 2001; Feeney and Collins, 2001; Kunce and Shaver, 1994), as well as with the use of authoritarian and dominant behaviors in high anxiety situations (García-Ruíz et al., 2013; Millings et al., 2013). Altogether, this emphasizes attachment theory as a potential framework for understanding how relatives' attachment history influences the development of EE (Berry et al., 2007).

The relationship between relatives' attachment styles and perceived loss in the early stages of psychosis has not yet been explored. Similarly, no studies have directly considered the possible mediating role of insecure attachment styles in the association between relatives' perceived loss and high EE attitudes. This study addressed these issues in a sample of relatives of early psychosis participants by: 1) examining whether relatives' perceived loss is associated with EE dimensions (i.e., criticism and EOI); and 2) testing whether such associations are mediated by relatives' dimensions of attachment (i.e., anxiety and avoidance). Despite the lack of previous studies, it was hypothesized based on the reviewed theorization that relatives' attachment anxiety would play a mediating role between perceived loss and EOI, as well as between perceived loss and criticism.

Methods

Participants

The study comprises 78 relatives of early psychosis participants, 48 of At-Risk Mental State (ARMS) and 30 of First-Episode (FEP) participants. They were recruited in the Sant Pere Claver-Early Psychosis Program conducted in Barcelona, Spain (Domínguez-Martínez et al., 2011). Participating relatives were those who had most regular contact and/or the most significant relationship with the patient. Early psychosis participants met ARMS criteria as assessed by the Comprehensive Assessment of At-Risk Mental States (CAARMS; Yung et al., 2005) or FEP criteria according to DSM-IV (APA, 2002).

All relatives provided written informed consent to participation. The project was developed in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and was approved by the local ethical committee.

Measures

Relatives completed the Mental Illness Version of the Texas Inventory of Grief (MIV-TIG; Miller et al., 1990) for the assessment of loss reactions. The MIV-TIG is a self-reported questionnaire that consists of 24 items and measures the relatives' initial response

to the loss of a family member's mental health and the current feelings about their perceived loss. Responses were rated on a five-point Likert scale from 'completely true' to 'completely false'. The Cronbach's alpha of the instrument was excellent in this sample (0.95).

Attachment was assessed with the Psychosis Attachment Measure (PAM; Berry et al., 2006), a self-reported adult attachment questionnaire referring to self-identified thoughts, feelings and behaviors in interpersonal relationships. The PAM is comprised of 16 items that assess the two dimensions of adult attachment, anxiety and avoidance. Respondents rated on a four-point Likert scale ranging from 'not at all' to 'very much'. Alpha for these subscales was good in this sample (Anxiety=0.71; Avoidance= 0.68).

Finally, relatives completed the Family Questionnaire (FQ; Wiedemann et al., 2002), a well-established instrument to measure EE. The FQ consists of 20 items equally distributed into two subscales (EOI and criticism) and scored on a four-point Likert scale ranging from 'never/very rarely' to 'very often'. The Cronbach's alpha for the two subscales in this sample was 0.84 for EOI and 0.87 for criticism.

Statistical Analysis

All analyses were performed using the Statistical Package for Social Sciences (SPSS), Version 22.0. Pearson correlations were calculated to explore the association of relatives' perceived loss with EOI and criticism, as well as association of these variables with the two attachment dimensions. The effect size of the correlations was interpreted following Cohen's (1992) guidelines (correlations of 0.10 indicate small effect sizes, 0.30 indicate medium effect sizes, and 0.50 indicate large effect sizes). Parallel multiple mediation analyses were performed using PROCESS (Hayes, 2013). These analyses examined the unique mediating effect of attachment anxiety and avoidance on the significant associations found between perceived loss and the EE dimensions. For each model, attachment anxiety and avoidance were entered simultaneously as mediators. The 95% bias-corrected confidence intervals were

generated using bootstrapping with 10,000 resamples. Indirect effects were considered significant when the 95% bias-corrected confidence intervals did not include zero.

Results

Most relatives were parents who lived with the patient. Over half of them were females, specifically patients' mothers (see Table 1 for details about relatives' socio-demographic characteristics). For the sake of completeness, descriptive data for all relatives' measures are presented in Table 2.

Firstly, we examined whether relatives of ARMS and FEP participants differed on levels of perceived loss. No significant differences emerged between them ($t(76)=-1.17$; $p=0.25$; $d=0.27$). Consequently, ARMS and FEP relatives were grouped together in the remaining analyses.

Relatives' perceived loss was significantly related to both EOI ($r=0.49$, $p<0.001$) and criticism ($r=0.27$, $p<0.05$). Following Cohen (1992), effect sizes were of a medium and small magnitude, respectively.

As seen in Table 3, relatives' attachment anxiety showed significant associations with relatives' perceived loss and both EE dimensions. All effect sizes were of medium magnitude. In contrast, relatives' attachment avoidance was significantly associated with relatives' perceived loss but was not associated with the EE dimensions.

Table 4 displays the results of the parallel multiple mediation analyses using relatives' perceived loss as the independent variable. Two models were tested (one for EOI and one for criticism), with the two attachment dimensions entered simultaneously as mediators. The total, direct, and indirect effects are shown in Table 4. The specific indirect effect of attachment anxiety was significant in the models for both EOI and criticism. Avoidant attachment was not a significant mediator of the association between relatives' perceived loss and EE dimensions.

Discussion

To the best of our knowledge, this is the first study examining the relationship among relatives' perceived loss, attachment styles, and EE as well as the mediating role of relatives' attachment dimensions in the association between perceived loss and EE in the early stages of psychosis. Results showed that relatives' perceived loss was associated with EE attitudes as well as with relatives' attachment anxiety and avoidance. This finding points out the significance of considering the role of relatives' perceived loss along with other psychological mechanisms for understanding the ontogenesis of EE in the family environment. In addition, the current study indicated that relatives' attachment anxiety, but not attachment avoidance, mediated the relationship between perceived loss and EE, both for criticism and EOI attitudes. Altogether, these results emphasize the importance of considering the role of loss in the development of EE attitudes and that relatives' attachment style is relevant to understand how appraisals of loss might impact the formation and/or expression of EOI and criticism in the critical period of the emergence of the disorder.

Consistent with our predictions, relatives' perceived loss was positively associated with both EOI and criticism. These results are in consonance with theoretical suggestions from the EE literature that relatives' perception of loss may be a main driver of high EE attitudes (Birchwood, 1992; Birchwood and Spencer, 1999). The positive association between perceived loss and relatives' EOI attitudes supports previous findings reported by Patterson et al. (2005, 2000) in relatives of early psychosis patients. However, in contrast to Patterson et al. (2005, 2000), the present study also found a positive association between perceived loss and relatives' criticism. This finding seems to be consistent with attachment theorization, which indicates that coercive criticism is not an uncommon response to perceived loss as an attempt to restore what has been "lost" through the activation of attachment responses (Bowlby, 1982, 1980, 1973).

Concerning the mediating role of relatives' attachment dimensions in the association between the perception of loss and EE, attachment anxiety, but not avoidance, mediated the relationship of appraisals of loss with both EOI and criticism. As hypothesized, this differential role of attachment styles might be explained by the specific distress regulation strategies characterizing anxious and avoidant attachment. Anxious individuals respond to appraisals of loss with hyperactivating strategies of the attachment system, which impairs their capacity to regulate negative emotions and thus contributes to an intensification of distress (Mikulincer and Shaver, 2016, 2008a, 2007). Moreover, ineffective emotional regulation strategies make them feel overwhelmed by personal distress, which may interfere with the normative functioning of the caregiving behavioral system (Mikulincer and Shaver, 2016, 2007). Theoretically, the caregiving system is activated by cues generated from care recipients in times of need (Bowlby, 1982), but it can also be activated by caregivers' appraisals of danger or threat, which are directly influenced by caregivers' own attachment system (George and Solomon, 2008; Jones et al., 2015). Specifically, attachment anxiety has been associated with high levels of proximity and compulsive caregiving that are inconsistent and lack sensitivity (Collins and Feeney, 2000; Kunce and Shaver, 1994). Following Canterberry and Gillath (2012), this type of caregiving behaviors could reflect the hyperactivation of the caregiving system. Therefore, anxious individuals, who rely on hyperactivating strategies in their attachment system, seem to adopt this strategy with their caregiving system (Canterberry and Gillath, 2012; Feeney and Collins, 2001; Karantzas and Simpson, 2015). Drawing on previous theoretical suggestions based on the interplay between the attachment and caregiving systems (Karantzas and Simpson, 2015; Millings et al., 2013), our findings could be interpreted to suggest that relatives' perceived loss might trigger the concurrent hyperactivation of the attachment and caregiving systems in anxiously attached relatives. The inability to regulate the negative emotions provoked by perceived loss may lead to excessive ruminations about the perceived loss, amplifying the negative

affective/cognitive reactions to loss. This would contribute to the hyperactivation of the caregiving system and lead to EE-like intrusive, overinvolved or even critical patterns of caregiving, probably driven by an attempt to restore the pre-illness situation and to mitigate the loss perceived (see Fig.1). This explanation is partly consistent with previous suggestions (e.g., Patterson et al. 2005, 2000), even though the contribution of the caregiving behavioural system as the mechanism through which EE attitudes manifest had not been considered. Specifically, Patterson (2013) proposed a theoretical model suggesting that family illness leads to an activation of carers' and patients' attachment behaviors and that relatives increased high EE attitudes should be conceived as an initial normative reaction.

Previous work has linked attachment anxiety to caregiving behaviors that clearly resemble aspects of EOI behaviors (i.e., overinvolved, intrusive, controlling and/or compulsive forms of caregiving; Adam et al., 2004; Bosquet and Egeland, 2001; Feeney and Collins, 2001; Kunce and Shaver, 1994). This has even led to the interpretation of EOI as a type of anxious attachment/caregiving behavior (Álvarez-Jiménez et al., 2010; Wynne, 1981). In addition, attachment anxiety has also been related to the expression of critical attitudes through the use of authoritarian (Millings et al., 2013), aggressive (O'Connell-Corcoran and Mallinckrodt, 2000; Simpson et al., 1996), dominant (García-Ruíz et al., 2013) and demanding behaviors in high anxiety situations (Feeney, 2006). Therefore, relatives' insecure attachment could contribute to the development of either critical or EOI parenting styles (Diamond and Doane, 1994; Paley et al., 2000) and these two dimensions of EE could be considered as "special forms of attachment/caregiving" that are likely to lead to dysfunctional patterns of communication and problem solving (Wynne, 1981).

Interestingly, an unexpected positive correlation between perceived loss and attachment avoidance was observed. It is well recognized that the tendency to suppress negative emotions encourages an absence of conscious grieving (Mikulincer and Shaver, 2008b, 2012; Shaver and Fraley, 2008). Nevertheless, some studies have found an association

between attachment avoidance and severe grief symptoms after the loss of a loved one (Currier et al., 2015; Jerga et al., 2011; Wijngaards-de Meij et al., 2007). These findings have been interpreted as indicating that strategies of emotional deactivation might collapse under conditions of high cognitive load produced by highly stressful situations, thereby causing avoidant individuals to be less able to suppress separation thoughts. Therefore, it is attractive to speculate that the powerful threat of loss experienced by relatives of early psychosis individuals might weaken the suppression of the negative emotional experience of loss in relatives with avoidant attachment.

Some limitations of the present study must be considered. First, the cross-sectional design limits drawing causal conclusions, which can only be determined by further longitudinal studies. Second, it is important to note that attachment and EE-related constructs are dynamic processes influenced by bidirectional and interactional patterns within familiar relationships (Bowlby, 1988; Miklowitz, 2004). Future studies should consider how the clinical features and attachment styles of care recipients contribute to the manifestation of high-EE attitudes within the family environment.

In conclusion, this study shows that relatives' perception of loss is significantly associated with EE-criticism and EE-EOI attitudes in the early stages of coping with psychosis, and that relatives' attachment anxiety is a mediator of the association between perceived loss and the manifestation of EE attitudes in early psychosis relatives. These results have important clinical applications. Considering the negative implications of perceived loss for relatives' psychological health and the potential etiological role of perceived loss on the manifestation of high EE attitudes, family interventions should specifically take into consideration the psychological aspects related to loss and the grief process experienced by relatives during the at-risk and onset stages of psychosis. This emphasizes the importance to go beyond educating relatives about psychosis (e.g., Crisp and Gleeson, 2009) by implementing treatments in which the provision of information is adapted to caregivers'

needs and allows emotional processing (Lobban et al., 2013). Consequently, this would help relatives to gain a better understanding of their own psychological situation. In addition, these findings highlight the need of tailoring interventions to relatives' attachment needs. This would include assessing relatives' attachment patterns, since the specific subtypes of insecure attachment style will provide guidance to moving forward in the therapeutic process, for example in building the working alliance or setting relevant treatment goals (Harris, 2004). Early psychosis is a critical period where relatives' appraisals and attitudes are forming and might be more malleable; therefore, it is fundamental to support relatives in adjusting to the grief process with the aim of preventing unresolved loss reactions and the entrenchment of high-EE attitudes over time.

Table 1. Descriptive data on socio-demographic characteristics of early psychosis relatives (n=78)

	n (%)
Age*(mean, SD)*	51.05(9.7)
Gender	
Males	25 (32.1)
Females	53 (67.9)
Ethnicity	
Caucasian-white	66 (84.6)
Other	12 (15.4)[a]
Occupation	
Unemployed/unoccupied	34 (43.6)
Employed	44 (56.4)
Marital Status	
Single	4 (5.1)
Married or analogous	50 (64.1)
Separated/divorced/widowed	24 (30.8)
Relationship to patient	
Father	19 (24.4)
Mother	47 (60.2)
Other	12 (15.4)
Living with patient	
Yes	65 (83.3)
No	13 (16.7)
Frequency of contact[b]	
Between 1 and 14h a week	28 (35.9)
Between 15 and 27h a week	14 (17.9)
≤ 28h a week	28 (35.9)

Abbreviations: SD: Standard Deviation.

[a]Other ethnicity was comprised by Latin Americans=5 (6.4), Asians=2 (2.6), Eastern Europeans=3 (3.8) and Arabs=2 (2.6).

[b]Information about frequency of contact was available only for n=72.

Table 2. Descriptive data on perceived loss, attachment and expressed emotion (N=78)

	Mean	SD	Possible score range	Observed score range
Perceived loss (MIV-TIG)	63.44	20.95	24-120	24-116
Attachment (PAM)				
Anxious Attachment	0.90	0.43	0-3	0-2.38
Avoidant Attachment	1.22	0.45	0-3	0.38-2.25
Expressed Emotion (FQ)				
EOI	24.33	5.85	10-40	11-37
Criticism	20.63	6.02	10-40	11-37

Abbreviations: SD: Standard Deviation; MIV-TIG: Mental Illness Version of the Texas Inventory of Grief; PAM: Psychosis Attachment Measure; FQ: Family Questionnaire; EOI: Emotional Over-Involvement.

Table 3. Pearson correlations of attachment dimensions with perceived loss and expressed emotion (N=78)

	Attachment-Anxiety	Attachment-Avoidance
Perceived loss (MIV-TIG)	**0.38*** **	**0.30** **
Expressed Emotion (FQ)		
EOI	**0.46*** **	0.22
Criticism	**0.38*** **	0.21

Abbreviations: MIV-TIG: Mental Illness Version of the Texas Inventory of Grief; FQ: Family Questionnaire; EOI: Emotional Over-Involvement.
***p≤ 0.001, **p≤0.01. Medium effect sizes in bold.

Table 4. Mediation analyses examining the indirect effects of perceived loss on EOI and criticism via anxious and avoidant attachment

			95 % Bias-corrected Confidence Interval	
	Raw Parameter Estimate	SE	Lower	Upper
EOI (FQ)				
Total Effect	0.136*	0.028	0.080	0.191
Direct Effect	0.098*	0.030	0.039	0.157
Total Indirect Effect	0.038*	0.016	0.012	0.078
Indirect Effect via Anxiety	0.034*	0.014	0.013	0.071
Indirect Effect via Avoidance	0.003	0.009	-0.012	0.026
Criticism (FQ)				
Total Effect	0.077*	0.032	0.014	0.140
Direct Effect	0.035	0.034	-0.033	0.103
Total Indirect Effect	0.042*	0.019	0.012	0.091
Indirect Effect via Anxiety	0.033*	0.016	0.009	0.076
Indirect Effect via Avoidance	0.009	0.011	-0.007	0.037

Abbreviations: FQ: Family Questionnaire; EOI: Emotional Over-Involvement.
Note: Results are based on 10,000 bias-corrected bootstrap samples.
**95% Confidence Interval does not include zero.*

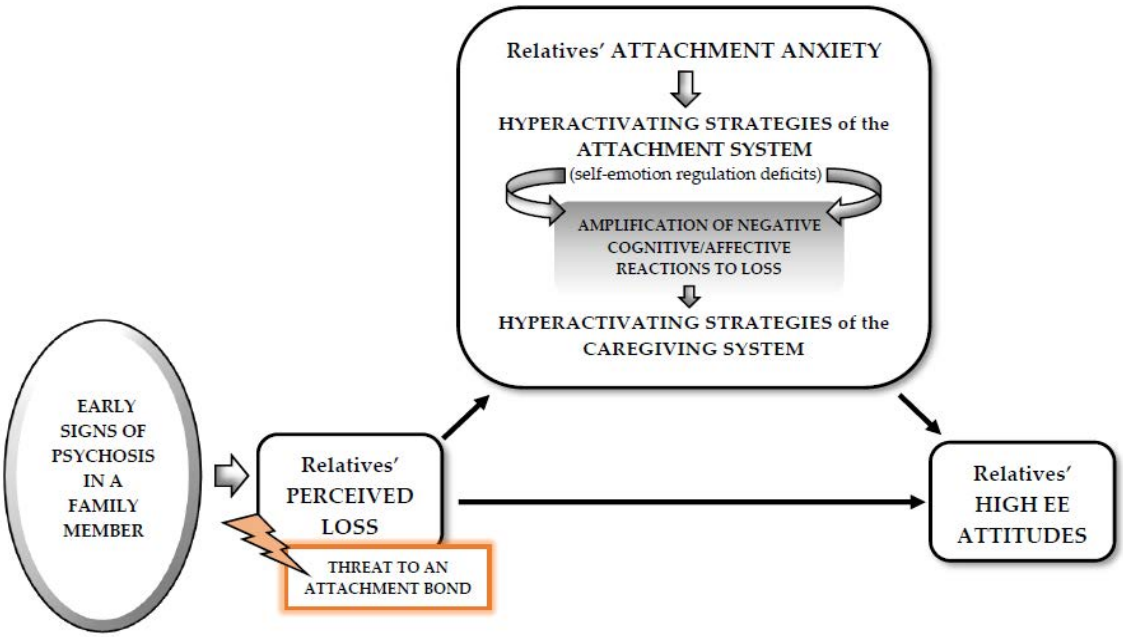

Figure 1. Proposed mediational model of the relationship between perceived loss and high EE attitudes in anxiously attached relatives. Adapted from Patterson (2013).

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SECTION 3

PREDICTORS OF EXPRESSED EMOTION IN EARLY PSYCHOSIS

Chapter 3

Predictors of Criticism and Emotional Over-Involvement in relatives of early psychosis patients

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Abstract

Mechanisms underlying the ontogenesis of EE attitudes in the early stages of psychosis are still not properly understood. The present study aimed to examine whether relatives' psychological distress and subjective appraisals of the illness predicted EE dimensions over-and-above patients' poor clinical and functional status. Baseline patient-related variables and relatives attributes comprising criticism, EOI, psychological distress and illness attributions were assessed in a sample of 91 early psychosis patients and their respective relatives. Relatives were reassessed regarding EE dimensions at a 6-month follow-up. Relatives' psychological distress and illness attributions predicted criticism and EOI over-and-above patients' illness characteristics at both time points. Relatives' increased levels of anxiety, attributions of blame toward the patients, an emotional negative representation of the disorder and decreased levels of self-blame attributions predicted EE-criticism at baseline. Relatives' anxiety was the only significant predictor of EE-criticism at follow-up, whereas anxiety, attributions of control by the relative and an emotional negative representation of the disorder predicted EE-EOI both at baseline and follow-up assessments. Dissecting the components that construe and maintain EE attitudes should help to consider the specific needs of early psychosis caregivers in family interventions, enhancing a proper management of psychological distress and the reduction of negative appraisals about the illness. The prevention of high-EE attitudes over time in a sensitive period such as early psychosis might be critical in shaping the health of caregivers and the outcome of the affected relatives.

Key words: Expressed Emotion, Distress, Illness attributions, Family, At-Risk Mental States, First-Episode Psychosis.

Introduction

A substantial body of research has consistently shown that Expressed Emotion (EE; Brown et al., 1972), particularly criticism and Emotional Over-Involvement (EOI), is a reliable psychosocial predictor of relapse in schizophrenia (Butzlaff and Hooley, 1998; Cechnicki et al., 2013; Hooley, 2007; Marom et al., 2005). However, while the predictive validity of EE has been repeatedly demonstrated, the developmental precursors of EE are still not well understood.

Over the last 50 years, most studies in EE and related factors have been carried out with patients with the chronic form of the psychosis phenotype (Bebbington and Kuipers, 1994; Kavanagh, 1992; Wearden et al., 2000). Nevertheless, recent research has focused on the study of EE in the early course of the illness (Koutra et al., 2016, 2014; Meneghelli et al., 2011; Raune et al., 2004) in order to prevent the entrenchment of high-EE and associated poor prognosis. Preliminary studies have shown that high-EE is already present in over half of the relatives of persons with First-Episode of Psychosis (FEP) (Bachmann et al., 2002; Gonzalez-Blanch et al., 2010; McNab et al., 2007), and is even present in relatives of At-Risk Mental State (ARMS) (O'Brien et al., 2006; Schlosser et al., 2010). Since the association of relatives' EE with patients' symptomatic relapse is less conclusive in early psychosis samples (Bird et al., 2010; Gleeson et al., 2010; Haidl et al., 2018; Schlosser et al., 2010), there has been an increased interest in examining the impact that EE has on relatives' mental well-being. In this sense, multiple studies suggest that early psychosis relatives often report high levels of burden, depression and anxiety related with high levels of EE (Domínguez-Martínez et al., 2017; Jansen et al., 2015a, 2015b; Möller-Leimkühler et al., 2005; Raune et al., 2004; Sadath et al., 2017; Tomlinson et al., 2014). Given that the presence of EE is associated with a large variety of negative outcomes, both for relatives and patients, it is crucial to examine the mechanisms underlying the ontogenesis of EE in the early stages of psychosis, when

most of the changes are emerging and it is still possible to examine these factors without the bias created by the chronic course of psychosis and relatives' long-term burden.

Although patients' poor clinical and functional status have been related with increased relatives' EE in several early psychosis studies (Domínguez-Martínez et al., 2014; Koutra et al., 2016; McFarlane and Cook, 2007; Mo et al., 2007). Other studies have suggested that patients' symptoms/functioning have limited or no impact upon relatives' EE (Álvarez-Jiménez et al., 2010; Bachmann et al., 2002; Heikkilä et al., 2002; Meneghelli et al., 2011; Raune et al., 2004).

Some studies have shown that the effects of patients' clinical features on EE may be mediated by relatives' attributions (Domínguez-Martínez et al., 2014).Relatives' beliefs about the nature of the illness would explain relatives' emotional attitudes better than the unidirectional reactivity of relatives to patients' illness characteristics (Barrowclough et al., 1994; Barrowclough and Hooley, 2003). Möller-Leimkühler (2005) also suggested that EE is not accounted for by a unilateral response to patients' illness characteristics, but rather by beliefs of control and/or a generalized negative stress reaction.

The attributional model of EE (Barrowclough et al., 1994; Barrowclough and Hooley, 2003) suggests that relatives' beliefs about the patients' illness and symptoms are related to relatives' emotional attitudes towards patients. Particularly, critical relatives are more prone to blame patients for their behaviors and perceive symptoms as controllable by patients rather than illness driven; as a result, they react with criticism to reduce undesired behaviors. Some studies conducted with families of FEP patients have shown that critical relatives tend to belief that symptoms are within the patients' control (McNab et al., 2007; Vasconcelos e Sa et al., 2013) and also that attributions of blame toward the patient predict relatives' criticism in the early stages of psychosis (Domínguez-Martínez et al., 2017). In contrast, overinvolved relatives tend to attribute symptoms to external and uncontrollable factors by the patient (Barrowclough et al., 1994; Brewin et al., 1991). Additionally, they belief

that they have contributed in some way to the patients' problems, so they could report higher levels of self-blaming attributions (Bentsen et al., 1998; Bolton et al., 2003; Peterson and Docherty, 2004).

It is well known that caring for a family member in the early stages of psychosis can lead to experience elevated levels of distress, including anxiety and depression (Addington et al., 2005, 2003). In this sense, a different explanatory model of EE proposes that high-EE attitudes could be conceived as a coping strategy that reduces the perceived stress related to the caregiving role (Álvarez-Jiménez et al., 2010; Kuipers et al., 2006). Accordingly, greater levels of psychological distress in caregivers seem to be related with increased levels of EE (Domínguez-Martínez et al., 2017; Jansen et al., 2015a, 2015b). Converging evidence suggests that EOI is more related to distress than criticism (Álvarez-Jiménez et al., 2010; Jansen et al., 2015a, 2015b, 2014), although criticism has also been linked to psychological distress in early psychosis caregivers (Domínguez-Martínez et al., 2017; Tomlinson et al., 2014). Of note, relatives' perceived distress has been shown to be an important predictor of EE in FEP relatives (Sadath et al., 2017) and also has been found to predict the early emergence of relatives' criticism in cross-sectional studies (Domínguez-Martínez et al., 2017).

Notwithstanding, little is known about psychological factors related to relatives' levels of EE in the early course of the illness and further research is required at this point. The possible contribution of patients' clinical and functional characteristics on EE in conjunction with relatives' psychological factors has been scarcely investigated (Álvarez-Jiménez et al., 2010; Raune et al., 2004). Understanding the specific and common underlying factors of relatives' criticism and EOI in the early stages of psychosis should improve the design and personalization of early family interventions, thereby enhancing the prognostic of both patients and their relatives.

Despite intensive research aimed at disentangling the multiple correlates of EE, little is known about the developmental precursors of EE in the early stages of psychosis. Most

of the studies have used cross-sectional data to examine EE correlates (Domínguez-Martínez et al., 2017; Gómez-de-Regil et al., 2014; Sadath et al., 2017). To date, only a few longitudinal studies have explored potential predictors of criticism and EOI in relatives of FEP patients (Álvarez-Jiménez et al., 2010; Patterson et al., 2005, 2000).

The goals of the present study were: (1) to examine the association of patients' clinical and functional status as well as relatives' psychological distress and illness attributions with relatives' EE dimensions (criticism and EOI) at baseline and at the 6-month follow-up; and (2) to explore whether relatives' psychological distress and illness attributions at the initial assessment predicted relatives' EE dimensions both at baseline and follow-up assessments over-and-above patients' baseline clinical and functional status. Based on previous suggestions of the EE literature, we hypothesized that relatives' baseline psychological distress and negative illness attributions would predict relatives' EE dimensions over-and-above patients' baseline clinical and functional variables at both time points. Based on the attributional model of EE, we also expected common as well as distinctive predictors of criticism and EOI at both baseline and follow up assessments: (a) Both criticism and EOI would be predicted by relatives' psychological distress (anxiety and depression); (b) Beliefs of self-blame, self-control and negative emotional representation of the illness would predict relatives' EOI, whereas beliefs of control and blame toward the patient would predict relatives' criticism.

Methods

Participants

Ninety-one early psychosis patients (55 ARMS and 36 FEP) and their respective relatives were initially recruited in the present study. Of these, 46 completed the 6-month follow-up assessment due to a variety of reasons (n=25 were non-contactable or refused to participate, n=10 did not have a complete set of follow-up data, and n=10 abandoned the study because of patient withdrawal from the clinic or the study). Therefore, the follow-up

sample included 46 families (33 of ARMS and 13 of FEP). Please note that patients' data only belongs to the baseline phase.

The relatives recruited were those who have most regular contact and/or the most significant relationship with the patient. Patients had to meet ARMS criteria as assessed by the Comprehensive Assessment of At-Risk Mental States (CAARMS; Yung et al., 2005) and/or the Schizophrenia Proneness Instrument Adult-Version (SPI-A; Schultze-Lutter et al., 2007). FEP patients met DSM-IV criteria (APA, 2002) for any psychotic disorder or affective disorder with psychotic symptoms as established by the Structured Clinical Interview for DSM-IV (SCID-I; First et al., 1995). Exclusion criteria for patients were: (a) Evidence of organically based psychosis; (b) any previous psychotic episode that involved pharmacotherapy; and (c) mental retardation.

Measures

Relatives' outcome measure at baseline and 6-month follow-up

EE was measured with the Family Questionnaire (FQ; Wiedemann et al., 2002), which consists of 20-items equally distributed in two subscales (criticism and EOI) scored on a 4-point Likert scale ranging from 'never/very rarely' to 'very often'.

Patient predictor factors at baseline

Patients' current clinical status was rated with the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987), a widely used scale for the assessment of positive and negative symptoms, and general psychopathology. Patients' current functional status was measured with the short version of the Social Functioning Scale SFS; Birchwood et al., 1990), a self-reported measure that assesses social functioning by addressing multiple facets of social adjustment.

Relatives predictor factors at baseline

Relatives' distress was measured with the Depression and Anxiety subscales of the Symptom Checklist (SCL-90-R; Derogatis and Cleary, 1977). The SCL-90-R is a psychiatric

self-report inventory intended to measure symptom intensity on a five-point scale from 0 'not at all' to 4 'extremely'. The Illness Perceptions Questionnaire for Schizophrenia-Relatives version (IPQS-R; Lobban et al., 2005) was used to measure relatives' beliefs about the disorder. Each item is rated from 1 'strongly disagree' to 5 'strongly agree'. For the purposes of this study, we used the following subscales: personal control-patient and personal control-relative (control over the disorder), personal blame-patient and personal blame relative (blame toward the patient or self-blame about the disorder), and emotional representation of the illness (negative emotions about the disorder including sense of fear, frustration, anger, worry).

Procedure

The present study is part of a larger, longitudinal study carried out in three Mental Health Centers of Barcelona (Spain) taking part of the Sant Pere Claver-Early Psychosis Program (Domínguez-Martínez et al., 2011).

The project was developed in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). Ethical approval for the study was obtained from the local ethical committee. All patients and relatives provided written informed consent to participation. All the interviews were conducted by experienced clinical psychologists. The time gap between patients and relatives' assessments ranged from 3 to 15 days.

Statistical analyses

First, Pearson correlations were used to analyze the associations between each of the baseline predictors and relatives' outcome variables (EE-criticism and EE-EOI) at baseline and at the 6-month follow-up. Secondly, hierarchical regression analyses were computed to predict relatives' EE-criticism and EE-EOI at baseline and 6-month assessments using patients' and relatives' baseline predictors. The main goal of the regression analyses was to test whether relatives' baseline predictors accounted for variance in relatives' EE-criticism

and EE-EOI (at baseline and at the 6-month follow-up) over-and-above patients' baseline symptom severity and social functioning. The following steps were entered in all regression analyses. The PANNS total score was entered at step 1 to examine the variance accounted for by patients' symptom severity. Patients' SFS score was entered at step 2 to examine the variance accounted for by patients' social functioning. Relatives' Depression and Anxiety SCL-90-R subscales were entered at step 3 to examine the variance accounted for by relatives' psychological distress. The five IPQ-S subscales were entered as a block at step 4 to examine the variance accounted for by relatives' beliefs about the disorder.

Results

Sample characteristics

At baseline, relatives were mainly female (74.7%), particularly patients' mothers (71.4%), with the remaining caregivers being fathers (17.6%), siblings (5.5%), partners (4.4 %) or adoptive parents (1.1%). Mean age of the relatives was 51.7 years old (S.D = 10.0). Patients were predominantly male (69.2%) and lived with their families (91.2%). The mean age of the patients was 22.4 years old (S.D.=4.9). Over half of them (58.3%) were studying, working or carrying out any daily activity, 36.3% were unemployed/unoccupied, and 5.5% had a sick leave.

At six-month follow-up, most relatives were also females (80.4%), mothers who lived with the patient (89.1%). The relationship with the patient was motherhood (76.1%), fatherhood (15.2%), siblingship (2.2%), partnership (4.3%) or adoptive parent (2.2%). The mean age of the relatives at follow-up was 51.9 years old (S.D = 8.7).

Descriptive baseline data for all relatives' and patients' measures are presented in Table 1. Dependent T-tests revealed that, on average, the levels of EE-criticism (t (45) = -0.670, p =0.51) and EE-EOI (t (45) = 0.834, p =0.41) did not differ significantly between baseline and follow-up assessments.

Association of relatives' EE with patients' clinical and functional variables and relatives' variables

Results of the association of patients' and relatives' baseline measures with relatives' levels of criticism and EOI at both baseline and follow-up are provided in Table 2. Regarding the cross-sectional associations, only patients' social functioning was significantly associated with relatives' EE-criticism, such that worse social functioning in patients at baseline was related to relatives' increased levels of criticism. No associations were found between patients' baseline clinical status and relatives' baseline EE indices. Furthermore, no longitudinal associations were found between patients' variables at baseline and relatives' EE at follow-up.

As for the associations between relatives' baseline psychological distress and relatives' EE dimensions, both relatives' baseline levels of anxiety and depression were strongly associated with relatives' EE dimensions at both time points. Moreover, relatives' baseline attributions of blame toward the patient were significantly related with relatives' EE-criticism at baseline, whereas relatives' baseline attributions of control by the relative were significantly associated with relatives' EE-EOI at baseline.

Finally, relatives' emotional negative representation about the disorder at baseline showed significant associations with both EE dimensions at both time points. Neither attributions of control toward the patient nor self-blame attributions were associated with EE indices.

Predictors of EE at baseline

Hierarchical regressions showed that neither patients' baseline clinical status nor baseline psychosocial functioning accounted for significant variance in the prediction of baseline EE indices (see Table 3). Relatives' baseline data revealed that high levels of anxiety (but not depression), attributions of blame toward the patient, emotional negative representation of the disorder as well as low scores on self-blame attributions significantly accounted for variance in relatives' EE-criticism at baseline. In addition, high levels of

anxiety, attributions of control and emotional negative representation about the disorder significantly accounted for variance in relatives' EE-EOI.

Baseline predictors of EE at follow-up

Hierarchical regressions showed that neither patients' baseline clinical status nor baseline psychosocial functioning accounted for significant variance in the prediction of follow-up EE indices (see Table 4). Only relatives' high levels of anxiety at baseline significantly accounted for variance in relatives' EE-criticism at follow-up. For EE-EOI, relatives' high levels of anxiety (but not depression), attributions of control by the relative and emotional negative representation about the disorder at baseline significantly accounted for variance at follow-up.

Discussion

The most relevant finding is that, as expected, both at baseline and 6 months, relatives' levels of anxiety and negative illness attributions accounted for significant variance over-and-above patient-related variables in the prediction of criticism and EOI in the early stages of psychosis. These results confirm the main predictions of this study and are consistent with findings in the schizophrenia literature, as they demonstrate that relatives' distress and cognitive representations of psychosis are strongly related to their emotional and behavioral attitudes towards patients.

Consistent with previous early psychosis studies (Álvarez-Jiménez et al., 2010; Bachmann et al., 2002; Heikkila et al., 2002; Meneghelli et al., 2011; Raune et al., 2004), no associations were found between patients' clinical status and relatives' EE attitudes neither at baseline nor follow-up. Of the patient-related variables, only patients' poor social functioning appeared to be significantly related to relatives' criticism at baseline, consistent with previous cross-sectional findings (Domínguez-Martínez et al., 2014; Raune et al., 2004). In contrast, other studies have not detected relationships between patients' functional status

and EE (Heikkila et al., 2002; Koutra et al., 2016; Meneguelli et al., 2011). It is likely that the large heterogeneity characterizing psychosis even in the early stages of the disorder and cultural differences in the attitudes towards mentally ill relatives make it difficult to find a homogeneous and conclusive pattern on the association between patients' illness-related characteristics and relatives' EE.

As for the association of relatives' psychological distress with EE dimensions, relatives' levels of anxiety and depression were strongly related with both baseline and follow-up EE indices. This is consistent with preliminary cross-sectional findings (Álvarez-Jiménez et al., 2010; Domínguez-Martínez et al., 2017; Jansen et al., 2014; Jansen et al., 2015a, 2015b; Tomlinson et al., 2014) and with the longitudinal relationships between relatives' distress and EE-EOI reported by Álvarez-Jiménez et al. (2010) in relatives of FEP patients. Although relatives' distress and EE may have a complex pattern of interactions, our findings suggest that early psychosis has a profound impact on relatives' emotional state that leads to significant levels of distress (Addington and Burnett, 2004; Martens and Addington, 2001), which in turn may exacerbate EE attitudes.

Regarding the association between illness attributions and EE, findings indicated that attributions of blame toward the patient were significantly related with EE-criticism at baseline. This result agrees with previous findings (Weisman et al., 1998; Domínguez-Martínez et al., 2014; Domínguez-Martínez et al., 2017) and is also consistent with the attributional model (Barrowclough and Hooley, 2003), which states that relatives who believe that patients are guilty of their behaviors rather than these being a product of the disorder are more prone to be critical with them to reduce the undesired behaviors. Moreover, in agreement with Bolton et al. (2003), it was found that relatives' self-control attributions were significantly associated with EE-EOI at baseline. Thus, relatives' who perceive themselves excessively responsible for their child's behaviors are more likely to exhibit intrusive and/or self-sacrifying attitudes. Finally, strong relationships were observed between relatives'

negative emotional representation of the disorder and EE dimensions (criticism and EOI), both at baseline and follow-up. This further supports the assumption that EE attitudes may be driven by relatives' negative emotional responses to illness such as sense of fear, frustration, anger or worry (Álvarez-Jiménez et al.,2010; Domínguez-Martínez et al., 2017; McNab et al., 2007).

In line with our hypothesis, relatives' distress and negative illness attributions at baseline predicted relatives' EE dimensions at both time points over-and-above patients' poor clinical and functional status. Hence, as suggested (Möller-Leimkühler, 2005), EE attitudes might be better explained by specific characteristics of relatives, particularly for their beliefs of control and/or generalized negative stress response, rather than as a unilateral reaction to patients' clinical features. In accordance with Domínguez-Martínez et al. (2017), our results indicated that EE-criticism at baseline was predicted by relatives' anxiety levels. Moreover, relatives' anxiety at baseline was the only significant baseline predictor of relatives' criticism at follow-up. This seems to support that the emergence of relatives' criticism arises from distressing affective states. In this line, Álvarez-Jiménez et al. (2010) suggested that EE-criticism may be conceived as a reaction to the stress related to the caregiving role; however, this study failed to find evidence to support that relatives' distress predicted EE-criticism at the follow-up assessment. Furthermore, attributions of blame toward the patient and negative emotional representations of the disorder, as well as decreased levels of self-blame attributions, significantly accounted for variance in EE-criticism at baseline. Previous studies have also reported that attributions of blame toward the patient predict the early emergence of relatives' criticism (Domínguez-Martínez et al., 2017). Again, this result is consistent with the attributional model (Barrowclough and Hooley, 2003), which posits that relatives who attribute responsibility or blame to the patients for their behaviors are more likely to exhibit critical attitudes towards them. Our results also showed that decreased levels of self-blame attributions were predictive of relatives' criticism at baseline. This finding is not surprising

given that critical relatives place the blame or attribute the responsibility of the illness behaviors mainly to internal or personal causes of the patients (Barrowclough et al., 1994; Hooley and Licht, 1997), which could lead to reduce the possibility of feeling themselves guilty or responsible of the patients' problems. Finally, EE-criticism at baseline was predicted by relatives' negative emotional representation of patients' illness, which is likely given that emotional representation assesses the presence of feelings typically found in EE-criticism, such as frustration or anger.

About EE-EOI predictors, our results showed that relatives' anxiety levels at baseline predicted EE-EOI at both baseline and follow-up assessments. This finding provides further evidence to support that relatives' EOI may be driven by negative affective experiences (McNab et al., 2007), as suggested by the strong relationships reported between EOI and distress within the early psychosis literature (Álvarez-Jiménez et al., 2010; Jansen et al., 2015a, 2015b, 2014). Besides, EE-EOI at baseline and at follow-up was predicted by relatives' self-control attributions. One study has reported relationships between EOI and self-control attributions (Bolton et al., 2003) but there exists little consistency in this aspect, mainly because it has been repeatedly shown that EOI relatives are more likely to attribute the patient's behavior to the illness and/or external factors that are outside the patient's control (Barrowclough et al., 1994; Brewin et al., 1991; Yang et al., 2003), and rarely attribute the patient's problems to factors that are internal, personal and controllable by them (Brewin et al., 1991). However, our results confirmed that those relatives' who hold the belief that they can control patients' problems are more likely to exhibit overinvolved behaviors, taking control and doing this for the patient (Bolton et al., 2003). Finally, consistent with other cross-sectional studies (Domínguez-Martinez et al., 2017) a negative emotional representation of the disorder was predictive of EE-EOI at baseline and at follow-up. This adds even more weight to the argument that negative emotional representations of the illness

such as initial responses of fear and worry may lead to the early emergence of overinvolved attitudes (McNab et al., 2007).

Contrary to what it was expected, attributions of control toward the patient did not predict relatives' criticism either at baseline or follow-up. This would appear to be inconsistent with the attributional model of schizophrenia but in accordance with previous cross-sectional studies conducted in early psychosis caregivers (Domínguez-Martínez et al., 2014; Domínguez- Martínez et al., 2017). It seems that attributions of blame toward the patient, rather than attributions of control, have a significant impact on relatives' criticism. We speculate that attributions of blame toward the patient may be emotionally-driven in response to the early course of the disorder, but in later stages they may turn into stronger beliefs of patient's personal control over the illness. Moreover, although attributions of blame toward the patient predicted relatives' criticism at baseline this was not significantly maintained at follow-up, as we initially expected. It might be that attributions of blame toward the patient have a significant impact on the early emergence of EE-criticism but not over a longer period of 6-months, thus indicating that they are not stable over time. This may be because relatives receive adequate information during the treatment that helps them to better understand the cause of the problem. As a result, they stop blaming patients for their behaviors. Furthermore, contrary to our hypotheses and in contrast with some schizophrenia studies (Bentsen et al., 1998; Peterson and Docherty, 2004), self-blame attributions did not predict relatives' EOI at neither baseline nor follow-up. According to Vasconcelos e Sa et al. (2017), the use of self-reported items that directly ask about relative's own causality on the patient's disorder is not the most convenient way to assess this construct. It might be that self-blame attributions tend to become more evident over time when diagnoses are clearly established, and then relatives wonder about how they might have contributed on the development of illness.

Several limitations of the present study need to be acknowledged. First, it is likely that the most accurate way of examining relationships among patient-relatives variables could be through an ecological assessment, which would allow to capture the manifestation of EE attitudes when interactions with patients occur within the natural family environment. A second limitation is that the FQ assessment does not contemplate the positive components of the EE construct (e.g., warmth). Considering that preliminary research emphasizes the protective effect of warmth in both chronic (López et al., 2004; Medina-Pradas et al., 2013) and early psychosis samples (Lee et al., 2014; Schlosser et al., 2010), further research should examine the psychological mechanisms underlying the expression of the positive components of EE.

In conclusion, this study shows that relatives' psychological distress and negative illness attributions accounted for significant variance over-and-above patients' clinical and functional status in the prediction of the early emergence of EE attitudes at both baseline and 6-month follow-up assessments. This highlights the importance of considering how relatives' affective states and the early formation of cognitive representations of psychosis can adversely affect the emotional attitudes they take towards the patient's disorder at the at-risk and recent onset stages of psychosis. Moreover, our results underscore the need for early family interventions aimed at: (i) providing relatives with proper information and specific guidance about the illness functioning at every stage and (ii) design psychological interventions to address relatives' emotional distress and negative appraisals of illness, which may offer a protective benefit for both the patient and the family. Furthermore, family treatment strategies should consider the specific needs of early psychosis caregivers, assisting them to properly manage beliefs about the illness in its different stages, with the aim to reduce their psychological distress, negative illness attributions and the presence of high-EE attitudes in the family environment.

Table 1. Descriptive baseline data of early psychosis patients and their respective relatives (*n*= 91).

	α	Possible score range	Observed Score Range	*Mean (SD)*
Patients				
Clinical status (PANSS)				
Positive symptoms	-	7-49	7-24	12.74 (3.40)
Negative symptoms	-	7-49	7-34	17.40 (5.80)
General symptoms	-	16-112	18-66	32.93 (7.51)
Functional status (SFS)				
Social Functioning	0.76	0-43	2-36	21.19 (6.12)
Relatives				
Expressed Emotion (FQ)				
Criticism	0.86	10-40	10-36	20.86 (6.15)
EOI	0.82	10-40	11-36	23.98 (5.82)
Distress (SCL-90-R)				
Anxiety	0.90	0-40	0-34	7.13 (7.41)
Depression	0.91	0-52	0-39	14.73 (10.62)
Illness Attributions (IPQS-R)				
Personal control-Patient	0.63	4-20	8-20	14.69 (2.58)
Personal control-Relative	0.61	4-20	6-20	13.45 (2.68)
Personal blame-Patient	0.81	3-15	3-15	9.93 (2.94)
Personal blame-Relative	0.83	3-15	3-15	7.45 (2.76)
Emotional representation	0.81	9-45	10-41	27.76 (7.10)

Abbreviations: SD: Standard Deviation; PANSS: Positive and Negative Syndrome Scale; SFS: Social Functioning Scale; FQ: Family Questionnaire; EOI: Emotional Over-Involvement; SCL-90-R: Symptom Checklist-90-Revised; IPQS-R: Illness Perception Questionnaire for Schizophrenia Relatives' version.

Table 2. Pearson Correlations between baseline predictors (patient and relative factors) and relatives' EE dimensions at baseline and follow-up.

	Baseline (n= 91)		**Follow-up (n= 46)**	
	EE- Criticism	**EE- EOI**	**EE- Criticism**	**EE- EOI**
Patient factors				
Clinical status (PANSS)				
Positive symptoms	0.14	0.09	0.28^{+}	0.12
Negative symptoms	0.05	0.08	-0.08	0.06
General symptoms	0.15	0.11	0.25	0.02
PANSS total score	0.13	0.12	0.18	0.07
Functional status (SFS)				
Social Functioning	-0.21*	-0.03	-0.12	-0.10
Relative factors				
Distress (SCL-90-R)				
Anxiety	***0.60******	***0.51******	***0.61******	***0.62******
Depression	***0.59******	***0.50******	***0.63******	***0.62******
Illness Attributions (IPQS-R)				
Personal control-Patient	0.13	0.02	0.28^{+}	0.06
Personal control-Relative	0.02	0.21*	0.09	0.29^{+}
Personal blame-Patient	0.27**	0.07	0.27^{+}	0.23
Personal blame-Relative	0.04	0.09	0.10	0.27^{+}
Emotional representation	**0.44***	***0.61******	***0.52******	***0.56******

$^{+}$ p<.10; *p <0.05; **p ≤ 0.01; *** p <0.001. Medium effect sizes (r ≥ 0.30) in bold, large effect sizes (r ≥ 0.50) in bold and italics.
Abbreviations: EOI: Emotional Over-Involvement; PANSS: Positive and Negative Syndrome Scale; SFS: Social Functioning Scale; SCL-90-R: Symptom Checklist-90-Revised; IPQS-R: Illness Perception Questionnaire for Schizophrenia Relatives' version.

Table 3. Predictors of Expressed Emotion at baseline (N=91 patients and their respective relatives).

		EE- Criticism *(at baseline)*			**EE- EOI** *(at baseline)*		
Step	**Baseline Predictors**	β	p	Δr^2	β	p	Δr^2
1	**Patients' clinical status (PANSS)**			0.017; p=0.22			0.014; p=0.27
	PANSS total score	0.131	0.22		0.117	0.27	
2	**Patients' functional status (SFS)**			0.030; p=0.10			0.000; p=0.92
	Social Functioning	-0.188	0.10		0.012	0.92	
3	**Relatives' distress (SCL-90-R)**			**0.403; p=0.000**			**0.279; p=0.000**
	Anxiety	**0.466**	**0.001**		**0.331**	**0.04**	
	Depression	0.196	0.17		0.223	0.17	
4	**Relatives' illness attributions (IPQS-R)**			**0.125; p=0.001**			**0.220; p=0.000**
	Personal control-Patient	0.116	0.15		0.048	0.58	
	Personal control-Relative	0.001	0.99		**0.207**	**0.02**	
	Personal blame-Patient	**0.240**	**0.008**		0.024	0.80	
	Personal blame-Relative	**-0.238**	**0.01**		-0.160	0.10	
	Emotional representation	**0.250**	**0.004**		**0.465**	**0.000**	

Abbreviations: EOI: Emotional Over-Involvement; PANSS: Positive and Negative Syndrome Scale; SFS: Social Functioning Scale; SCL-90-R: Symptom Checklist-90-Revised; IPQS-R: Illness Perception Questionnaire for Schizophrenia Relatives' version.
Significant at $p < 0.05$ (two-tailed) are bolded.

Table 4. Baseline predictors of Expressed Emotion at follow-up (N=46 patients and their respective relatives).

		EE- Criticism *(at follow-up)*			**EE- EOI** *(at follow-up)*		
Step	**Baseline Predictors**	β	p	Δr^2	β	p	Δr^2
1	**Patients' clinical status (PANSS)**			0.032; p=0.24			0.005; p=0.65
	PANSS total score	0.178	0.24		0.070	0.65	
2	**Patients' functional status (SFS)**			0.006; p=0.61			0.006; p=0.60
	Social Functioning	-0.080	0.61		-0.082	0.60	
3	**Relatives' distress (SCL-90-R)**			**0.458; p=0.000**			**0.465; p=0.000**
	Anxiety	**0.449**	**0.02**		**0.410**	**0.04**	
	Depression	0.279	0.144		0.326	0.10	
4	**Relatives' illness attributions (IPQS-R)**			0.098; p=0.151			**0.139 p=0.041**
	Personal control-Patient	0.185	0.13		-0.018	0.88	
	Personal control-Relative	0.024	0.84		**0.233**	**0.04**	
	Personal blame-Patient	0.141	0.28		0.101	0.42	
	Personal blame-Relative	-0.089	0.50		-0.005	0.97	
	Emotional representation	**0.278**	**0.04**		**0.346**	**0.01**	

Abbreviations: EOI: Emotional Over-Involvement; PANSS: Positive and Negative Syndrome Scale; SFS: Social Functioning Scale; SCL-90-R: Symptom Checklist-90-Revised; IPQS-R: Illness Perception Questionnaire for Schizophrenia Relatives' version.
Significant at $p < 0.05$ (two-tailed) are bolded.

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6. GENERAL DISCUSSION

The main goal of this thesis was to examine specific family environmental risk factors in early psychosis that have been demonstrated to be related with the course and outcome of psychotic disorders. In the process of working toward this aim, the theoretical investigation of this thesis first sought to review, for the first time, the empirical studies analyzing family factors in samples of ARMS patients. Thereafter, the empirical investigation section provides a novel contribution to the field of EE research by investigating the measurement and validity of EE dimensions in daily life. Then, the role of relatives' insecure attachment dimensions as potential mediators of the relationship between relatives' perceived loss and EE dimensions was investigated. Finally, the thesis sheds new light on the potential mechanisms underlying the ontogenesis of EE by considering patients' illness-related variables in conjunction with relatives' psychological factors in a longitudinal design. The key results of the work presented in each section of the thesis are summarized below, followed by a consideration of their implications for theory and clinical practice. Finally, strengths and limitations of the studies included in this thesis are discussed, before outlining suggestions for future research.

6.1 Summary of Main Findings

The work presented in this thesis is divided in two parts, a theoretical and an empirical investigation sections.

Theoretical Investigation

The theoretical investigation consisted in a review of the available literature examining family environment variables at the ARMS stage. The overview of the existing literature suggested that the relationship of EE and/or other family environment constructs with ARMS patients' clinical/functional status is still controversial and thus inconclusive at

the ARMS stage. However, relatives' cognitive representations of the illness could have an important role, either as a mediator of the relationship between EE and ARMS clinical/functional features or as a predictor of EE attitudes. Although the evidence regarding the predictive value of EE on ARMS clinical outcome was still limited, an important proportion of longitudinal studies pointed to the role of family positive aspects as predictors of ARMS clinical/functional improvement over time. Finally, the evidence in relation to family treatment in ARMS stages suggested that family-based interventions had a great potential to reduce EE attitudes and/or to improve ARMS patients' outcomes. The present review concluded by highlighting the current challenges and future perspectives for research in the field.

Empirical Investigation

Section one of the empirical investigation section was dedicated to the assessment and validity of EE dimensions (i.e., criticism and EOI) in daily life. The work presented in *Chapter 1* explored for the first time the way in which EE dimensions, as measured by momentary and psychometric self-reports, were expressed in real-world settings in relation to a wide variety of caregivers' emotional states and subjective appraisals. Firstly, it was tested whether the newly designed items tapping both EE dimensions in the ESM questionnaire (momentary EE) were meaningfully associated with their analogous psychometric EE dimensions using a gold-standard measure (FQ). The findings showed that momentary criticism and FQ-criticism displayed significant associations, as also did momentary EOI and FQ-EOI, thus providing support for the criterion validity of momentary EE dimensions. As hypothesized, momentary and FQ-EE dimensions were associated with decreased positive affect as well as to appraisals of less effective coping in daily life. Only momentary EE domains were associated to increased momentary negative affect. Partly in contrast with our hypotheses, momentary criticism and FQ-criticism were more consistently related to

situational stress and burden than momentary EOI and FQ-EOI. Finally, a clear distinct pattern of associations was not observed for momentary and FQ-EE dimensions in relation illness attributions in daily life. The preliminary findings of this study partially supported the construct validity of momentary criticism and EOI and the construct and ecological validity of the FQ as a sensitive measure of EE dimensions. Given the relational nature of the EE construct, these results underscore the importance of investigating how EE behaves within the natural family environment when interactions with ill relatives occur and how it is expressed in relation to daily appraisals and caregivers' subjective states.

Section 2 was aimed at increasing our understanding of the mechanisms underlying the relationship between relatives' perceived loss and EE dimensions. In *chapter 2,* a study was described that examined the relationships among relatives' attachment dimensions (i.e., anxiety and avoidance), perceived loss, and EE dimensions as well as the mediating effect of relatives' attachment dimensions in the association between perceived loss and EE attitudes. The results showed that relatives' perceived loss was associated with EE dimensions as well as with relatives' attachment anxiety and avoidance. In addition, the current study provided a novel contribution by indicating that relatives' attachment anxiety, but not attachment avoidance, mediated the relationship between perceived loss and EE, both for criticism and EOI attitudes. This work underscores the importance of investigating the role of loss in the development of EE attitudes and that relatives' attachment styles are relevant to understand how appraisals of loss might impact the formation and/or expression of EOI and criticism in the critical early stages of the disorder.

Section 3 presented one study examining the contribution of patients' illness-related variables together with relatives' psychological factors as potential mechanisms underlying the ontogenesis of EE. The work presented in *Chapter 3* described the associations of patients' clinical and functional status as well as relatives' psychological distress and illness

attributions with relatives' EE dimensions at baseline and at the 6-month follow-up. In addition, this study aimed to explore whether relatives' psychological distress and subjective appraisals of the illness predicted EE dimensions over-and-above patients' poor clinical and functional status at either baseline or follow-up assessments. Overall, findings demonstrated that relatives' EE is highly associated with relatives' psychological distress and with several kinds of illness attributions. Of the patients-related variables, only patients' poor social functioning appeared to be significantly related to relatives' criticism at baseline. Relatives' psychological distress and illness attributions predicted criticism and EOI at both time points over-and-above patients' illness characteristics. Specifically, relatives' increased levels of anxiety, attributions of blame toward the patient, emotional negative representation of the disorder and decreased levels of self-blame attributions predicted EE-criticism at baseline. Relatives' anxiety was the only significant predictor of EE-criticism at follow-up, whereas relatives' anxiety levels, self-control attributions and emotional negative representation of the disorder predicted EE-EOI at both baseline and follow-up assessments. Taken together, these findings highlight the relevance of considering how relatives' affective states and the early formation of cognitive representations of psychosis can adversely affect the emotional attitudes they take towards the patient's disorder at the at-risk and recent onset stages of psychosis.

6.2 Integration and Theoretical Implications

Overall, the findings of this thesis contribute to a growing body of evidence underscoring the importance of investigating the early expression of specific family risk factors at the most vulnerable stages of the psychosis development. Specifically, they emphasize the relevance of examining the role of relatives' perceived loss, subjective appraisals of the illness as well as relatives' emotional distress to unravel the psychological mechanisms underlying the early manifestation of EE (*Chapters 2-3*). In the study presented

in *Chapter 2,* the relationship between relatives' perceived loss and EE dimensions was hypothesized to be mediated by relatives' attachment anxiety given the characteristics of hyperactivating attachment strategies. The predictions in this study were confirmed. Although the contribution of relatives' attachment anxiety was not considered in *Chapter 1 (empirical investigation section)* and *Chapter 3*, it is proposed here that the emotion regulation aspects of hyperactivating attachment strategies can provide clues about the ways in which relatives appraise and emotionally react to stressful events (i.e., illness of a close family member). Thus, the hyperactivating models of distress regulation (e.g., increased stress, amplification of negative emotional responses) and the effect of hyperactivating strategies on relatives' cognitive appraisals (e.g., exaggerated or biased appraisals of threats) might confer vulnerability to distressing affective states and/or might contribute to the formation of negative cognitive representations of illness. This, in turn, might also promote the manifestation of EE attitudes.

Altogether, the above-mentioned results emphasize the need to take a comprehensive approach in order to improve our understanding of EE development. This probably involves the reformulation of strictly cognitive-oriented paradigms that set this research in motion but that probably can nowadays be enriched by more integrative approaches. In *Chapter 3* we also aimed to explore the longitudinal impact of patients' illness characteristics on EE attitudes, as it has been suggested that patients' poor clinical and functional status might engender EE in family members (Hooley, 2007; Hooley & Richters, 1995; McFarlane & Cook, 2007; Miklowitz, 2004). Consistent with previous studies (Álvarez-Jiménez et al., 2010; Bachmann et al., 2002; Heikkilä et al., 2002; Meneghelli et al., 2011; Raune et al., 2004), findings revealed that patients' psychopathological features were not related with relatives' EE either at baseline or the follow-up assessment. Of the patient-related variables, only patients' poor social functioning appeared to be significantly related to relatives' criticism at baseline, consistent with previous cross-sectional findings (Domínguez-

Martínez et al., 2014; Raune et al., 2004). All this shows that findings on the association between patients' illness-related characteristics and relatives' EE are still controversial and inconclusive in the early psychosis literature. Probably, the psychopathological condition of ARMS and FEP patients is not severe enough to elicit high-EE in relatives. Likewise, it also seems plausible that relatives' EE increases over time as function of the longevity of the psychotic disorder, given that relatives become overexposed to repeated episodes of illness, medical nonadherence and low functioning (Miklowitz, 2004). In fact, it has been suggested that in the early stages of psychosis high-EE attitudes might be better explained by specific characteristics of relatives, particularly by their beliefs of control and/or generalized negative stress response, rather than by a unilateral reaction to patients' clinical features (Möller-Leimkühler, 2005). Consistent with this view, findings from *chapter 3* indicated that relatives' anxiety levels and negative illness attributions at baseline predicted relatives' EE dimensions at both time points over-and-above patients' poor clinical and functional status. These results are also in agreement with the attributional model of EE (Barrowclough & Hooley, 2003), which states that relatives' beliefs about the illness are related to their emotional attitudes toward patients. Likewise, the current findings also provide support to the carer appraisal model of EE (Raune et al., 2004; Kuipers et al., 2006), which posits that caregivers' negative appraisals of their living situation results in negative emotional states such as distress and depression, precipitating high EE among relatives in an attempt to neutralize these emotions.

The association of EE with relatives' negative affective states is also extended to the realm of daily life. The findings of the study investigating the daily-life expression of criticism and EOI (chapter 1, empirical investigation section) indicated that momentary criticism and EOI were strongly related to momentary experiences of increased negative affect as well as decreased positive affect. Moreover, both momentary EE indicators were associated with expressing decreased enjoyment regarding current activities, as well as with reports that the current situation was less positive. Overall, these findings provide an ecological valid insight

of EE correlates, thus pointing to the role of negative affective states as potential mechanisms underlying the expression of EE.

Another important consideration is that results in *Chapter 3* revealed that in the early stages of psychosis, unlike in the chronic phases of the illness (Brewin, 1994; Hooley & Campbell, 2002; Weisman et al., 1998), attributions of control toward the patient are not determining relatives' critical attitudes. In fact, our results indicated that blame-patient attributions seem to have more influence than control-patient attributions on relatives' critical attitudes. It might be that attributions of blame may be emotionally-driven in response to the early course of the disorder, but that in later stages they become stronger beliefs of control. Furthermore, in contrast with some schizophrenia studies (Bentsen et al., 1998; Peterson & Docherty, 2004), self-blame attributions did not predict relatives' EOI. Our findings showed that self-control attributions, rather than self-blame attributions, were related to relatives' EOI. It seems likely that self-blame attributions tend to become more evident over time when diagnoses are clearly established, and that then relatives wonder about how they might have contributed to the development of illness. Nevertheless, perception of more negative consequences of the disorder in relatives has emerged as an important attribution that impacts on relatives' EE in early psychosis, as it was the attribution most strongly associated with both critical and emotional over-involved attitudes (*Chapter 3*).

The current thesis also pointed to the role of relatives' perceived loss as a major driver of EE attitudes in the early stages of psychosis. Besides, the present results expanded previous findings by investigating the hypothesis that relatives' attachment styles may be a potential mediating mechanism by which perceived loss influences the manifestation of EE (*Chapter 2*). The current study indicated that relatives' attachment anxiety, but not attachment avoidance, mediated the relationship between perceived loss and EE, both for criticism and EOI attitudes. In light of these findings, a theoretical model was proposed based on the reviewed theorization. It is extensively assumed by attachment theorists that threats to an

attachment bond, such as illness or stressors such as loss, tend to activate the attachment system (Mikulincer and Shaver, 2016, 2007). Indeed, persons with high levels of attachment anxiety tend to rely on secondary attachment strategies hyperactivating their attachment system for regulating threat-related distress (Cassidy & Kobak, 1988; Main, 1990). We propose that the inability of anxious individuals to regulate negative emotions provoked by perceived loss due to ineffective strategies for regulating distress may lead to excessive ruminations about the loss perceived, amplifying their negative affective/cognitive reactions to loss. In response to anxious caregivers' stressful appraisals of loss, we also suggest a concurrent hyperactivation of the caregiving system. This would lead to hyperactivating strategies of caregiving such as intrusive, overinvolved or even critical patterns of caregiving, that would become expressed as high EE attitudes probably due to an attempt to restore the pre-illness situation and to mitigate the loss perceived. Although some authors have theoretically approached the role of caregivers' attachment in the expression of high EE attitudes (Chen, 2006; Paley, Shapiro, & Worrall-Davies, 2000; Patterson, 2013; Patterson et al., 2000, 2005), none of them have considered the possible contribution of the caregiving behavioral system as a potential mechanism through which EE attitudes could manifest. Overall, the results from this study suggested that the concurrent hyperactivation of attachment and caregiving systems in anxiously attached relatives may be important in explaining the effects of relatives' perceived loss on EE attitudes.

6.3 Implications for Intervention Initiatives and Clinical Work

The clinical implications of the findings derived from this thesis have been discussed throughout the thesis in the different chapters, but this subsection provides an overview of the main ways in which the present results can inform clinical practice.

Family interventions are an essential component of early psychosis prevention as the onset of illness often occurs when many patients are still living with their families (Garety &

Rigg, 2001; Fisher et al., 2008; Jansen, Gleeson & Cotton, 2015). Growing evidence shows that early family support can be related to significantly fewer rates of relapse (Norman et al., 2005) and treatment engagement (Stowkowy, Addington, Hollowell, & Addington, 2012). Morever, findings suggest that family interventions improve relatives' levels of EE, psychological health, and reduce negative experiences of caregiving (for a review, see Claxton, Onwumere, & Fornells-Ambrojo, 2017). As a result, family interventions, if successful in reducing family stress and promoting intra-familial support, can potentially prevent or delay the onset of psychosis (Leff & Vaughn, 1985).

The evidence summarized in the review (*Chapter 1, theoretical investigation section*) regarding family treatment in ARMS stages suggested that early interventions benefit individuals at risk for psychosis. This highlights the importance of implementing family interventions to prevent poor symptom trajectories in high risk individuals. As previously mentioned, the main aim of the reviewed family-based interventions was to prevent the likelihood of patients' symptomatic relapse either by reducing relatives' EE or encouraging positive family dynamics (consistent with the desirable new attention provided to the effects of increasing *positive* factors and not only reducing negative risk factors). However, relatives' own needs and the emotional impact of caregiving are still a neglected area of intervention in the ARMS stage. Likewise, recent systematic reviews evaluating family interventions in FEP pointed out the importance of meeting the specific needs of caregivers independently of the course of illness (Claxton et al., 2017). Thus, further understanding of relatives' adaptation to early psychosis is required to empirically validate intervention protocols focused on improving relatives' well-being. This, in turn, may offer a protective benefit for both the relative and the patient.

Furthermore, the findings from *Chapter 3* highlight the importance of addressing relatives' affective states and negative appraisals about the illness in designing treatment

interventions. This has been acknowledged in some family interventions for psychosis, suggesting that treatment interventions need to go beyond educating relatives about psychosis (e.g., Crisp & Gleeson, 2009) or reducing relatives' distress, with relatives being involved and supported throughout the recovery process (Lobban et al., 2013). Furthermore, the use of reattribution techniques may prove beneficial in helping relatives to acquire a more balanced attributional stance (Barrowclough & Hooley, 2003). Overall, family treatment strategies should assist relatives to properly manage beliefs about the illness in its different stages, with the aim to reduce their psychological distress, negative illness attributions and the presence of high-EE attitudes in the family environment.

Considering the negative implications of perceived loss for relatives' psychological health and the potential etiological role of perceived loss on the manifestation of high-EE attitudes (*Chapter 2*), family interventions should also assist relatives to prevent impairing loss reactions to avoid the entrenchment of high-EE. The work presented in *Chapter 2* also supports that it is essential to consider the role of relatives' attachment styles to inform the delivery of mental health services. There is extensive work on attachment-based interventions for the treatment of psychosis (e.g., Benamer, 2010; Brent, Holt, Keshavan, Seidman, & Fonagy, 2014) which could also be helpful to inform caregiver interventions. Highlighting the role of insecure attachment responses in maintaining unhelpful patterns of caregiving along with offering alternative and more adaptive strategies would be important for early psychosis caregivers.

Moreover, from a clinical viewpoint, our results (*Chapter 1, empirical investigation section*) underscore the importance of the use of experience sampling methodology (ESM) to assess the daily life expression of EE. Our results highlight that relatives' criticism and EOI, as measured by momentary and psychometric self-reports, may impact on a wide variety of subjective appraisals and affective states occurring in the flow of daily life. Thus, the use of ESM is another potential route for intervention, as it could greatly help to personalize

treatment needs and the design of recently-devised personalized Ecological Momentary Interventions (EMIs). An immediate intervention could prevent relatives to engage in maladaptive attitudes, which are associated to negative emotional states and/or biased appraisals. The use of EMIs to deliver treatment in real life has been emphasized as a complementary approach to face-to-face treatments in order to extend the therapy beyond the clinical setting into daily life (Myin-Germeys, Klippel, Steinhart, & Reininghaus, 2016). EMIs might also provide an excellent starting point for choosing the most applicable therapeutic intervention in the specific moment that is needed.

6.4 Limitations

The empirical studies presented in this thesis have several limitations. First, the relatively small sample size limits the generalizability of the findings and may have weakened the statistical power to detect significant effects. Second, the cross-sectional nature of the data *(Chapter 1 and Chapter 2, empirical investigation)* is a major limitation that warrants caution in drawing any causal conclusion. In *chapter 3* our data are also correlational, which impedes the establishment of directions of causality. However, the use of a prospective design with the measurement of relatives' attributions and distress preceding the measurement of EE dimensions 6-months later give greater weight to the assumption that relatives' beliefs and distress are predictive of EE indices in early psychosis. Although the interpretations of the results that have been provided throughout this thesis are consistent with EE theory and research, only prospective data will allow covering the timing and sequence of developmental processes leading to the development of EE attitudes. We hope that the longitudinal follow-up studies that are currently being conducted by our group will allow us to clarify the temporal dynamics of EE, illness attributions and perceived loss, as well as to disentangle the causal influences among the different studied variables over time in the near future.

Another limitation is that our measure of EE does not contemplate the positive components of the EE construct (i.e., warmth and positive remarks). Preliminary research has emphasized the protective effect of warmth in both chronic (López et al., 2004; Medina-Pradas et al., 2013) and early psychosis samples (Lee, Barrowclough, & Lobban, 2014; Schlosser et al., 2010). Thus, it would have been interesting to inform of family protective effects and to examine the psychological processes underlying the expression of the positive components of EE. Additionally, the very use of the FQ to examine relatives' self-reported EE attitudes, although being a gold standard in the field, may also be conceived as a limitation given that EE reflects a transactional process between patients and their relatives (Strachan, Feingold, Goldstein, Miklowitz, & Nuechterlein, 1989). Thus, further research should consider the importance of obtaining information of family environmental constructs from both relatives' and patients' perspectives. In fact, we have recently incorporated in the assessment protocol the Brief Dyadic Scale of Expressed Emotion (BDSEE; Medina-Pradas et al., 2011) in order to compare the patients' perception of EE with that expressed by their relatives. This would offer a more comprehensive approach to explore the dyadic view of EE.

A final consideration is that the relatives' sample was comprised of a combination of ARMS and FEP relatives given that this ensured enough statistical power to perform the analyses. However, this precluded a more detailed examination of the differential aspects of ARMS and FEP relatives in relation to family environment variables.

6.5 Future Directions

The findings from the empirical studies presented in this thesis point to several future lines of investigation.

Given the controversial relationship between patients' clinical attributes and relatives' EE in early psychosis, more prospective designs are necessary to clarify whether EE levels

increase over time in the face of repeatedly exposure to psychotic experiences and the wide variety of challenging associated factors (e.g., poor treatment compliance, etc.). However, caution must be taken to avoid an oversimplistic and unidirectional view of EE (i.e., EE as unidirectional reaction to patients' clinical status). As suggested by the findings reported in this thesis, numerous relatives' psychological variables, as well as attachment mediating mechanisms, account for the manifestation of EE attitudes. Thus, it would be crucial to examine prospectively how EE fluctuates as a function of relatives' appraisals of loss, illness attributions as well as psychological distress in the early stages of psychosis. A suitable methodological approach to delineate mechanistic pathways of EE formation would be ESM. Momentary assessment techniques will permit to grasp the essence of EE, since this construct is conceptualized within an interactional framework (Hooley, 2007; Hooley & Gotlib, 2000; Miklowitz, 2004). Therefore, it is crucial to examine how EE emerges when interactions with ill relatives occur and how it is expressed in relation to daily appraisals and caregivers' subjective states in the natural family environment. In fact, longitudinal multilevel models will permit us to assess whether momentary emotional, cognitive and/or interpersonal experiences at a given assessment point predict the increase of momentary EE at a subsequent assessment point. Furthermore, momentary assessment will offer an ecological valid insight into daily interactions between patients and their respective relatives, and how these interactions impact on relatives' EE levels.

Additionally, although this thesis has given much importance to the negative components of EE and to the negative factors that are most critical and predictive of EE maladaptive attitudes, future research should focus on adaptive families' behaviours and on factors that enable families fostering positive interactions (Lobban et al., 2013). In this regard, it has been found that low-EE relatives make significantly more attributions of positive illness-related events and less about negative events than high-EE relatives. Also, low-EE relatives are more likely to attribute responsibility to patients for positive events, but less

likely to attribute responsibility to patients for negative events (Grice et al., 2009). This may act as a protective factor for relatives' distress. Therefore, further investigation is required to examine what are the mechanisms leading to positive attributional styles and to elucidate whether this protects relatives against distressing affective states and/or EE maladaptive attitudes.

In the same vein, this thesis has put more attention to the vulnerability associated with insecure attachment dimensions. However, the protective role of secure attachment is of equal relevance (Read & Gumley, 2008). It has been noted that secure attachment facilitates emotional adjustment after experiencing a significant loss (Fraley & Bonano, 2004). Therefore, further research is needed to examine the influence of secure attachment as a protective factor in the process of grieving the loss of family member's mental health.

Finally, attachment theory suggests that illness in a close family member normally elicits that attachment-based scripts for caregiving become activated. This might be accompanied by heightened emotional reactions which are interpreted as appropriate responses to situations of risk or illness between attached members (Bowlby, 1982, 1980, 1973). On this basis, Patterson (2013) proposed that "some of the normal processes experienced early in a psychosis by family members may involve high EE levels as reflecting the triggering of normative attachment responses". This would imply that an initial response of high EE to a recently unwell family member may be normative. In light of these theoretical suggestions, further studies should empirically examine the developmental attachment processes that naturally occur in response to the onset of psychosis in order to clarify its relationship to EE attitudes.

6.6 Conclusions

The empirical work presented in this thesis provides new insights into the psychological mechanisms underlying the early manifestation of EE attitudes. Collectively, the findings indicated that relatives' perceived loss, negative cognitive representations of the illness and distressing affective states are important factors for refining our understanding of the early development of EE. Moreover, relatives' attachment styles are relevant to understand how appraisals of loss might impact the formation of EE attitudes in the critical stages of the disorder. Finally, the findings emphasize the relevance of using novel techniques for investigating the daily life expression of criticism and EOI in the early stages of psychosis. The specific conclusions of this work, are:

1. Relatives' perceived loss was associated with both criticism and EOI as well as with relatives' attachment anxiety and avoidance. Relatives' attachment anxiety, but not attachment avoidance, mediated the relationship between perceived loss and EE, both for criticism and EOI attitudes.
2. Relatives' psychological distress and negative illness attributions predicted criticism and EOI over-and-above patients' illness characteristics at both baseline and follow-up assessments. Relatives' increased levels of anxiety, attributions of blame toward the patients, an emotional negative representation of the disorder and decreased levels of self-blame attributions predicted criticism at baseline. Relatives' anxiety was the only significant predictor of EE-criticism at follow-up, whereas anxiety, attributions of control by the relative and an emotional negative representation of the disorder predicted EE-EOI both at baseline and follow-up assessments.
3. Momentary criticism and EOI were significantly associated with the FQ-EE dimensions respectively, supporting the criterion validity of momentary EE dimensions. Both momentary EE and FQ-EE dimensions were meaningfully and significantly associated

with real-world experiences pertaining to the psychological domains that have been previously related to EE in retrospective and psychometric studies. Although criticism and EOI, as measured by momentary and psychometric self-reports, were expected to show a clearer differential pattern of relationship with real-world experiences in accordance to EE research suggestions, these results partly support the construct validity of momentary EE assessments and the construct and ecological validity of the FQ dimensions.

Altogether, these results contribute to a better knowledge concerning the expression of family risk factors at the most vulnerable stages of psychosis. Continued investigation of the factors involved in the manifestation of EE attitudes will provide a clear picture of the psychological/emotional/interpersonal pathways leading to dysfunctional family environments, and therefore this would benefit family intervention programs in early psychosis.

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Principal Investigator: Neus Barrantes-Vidal

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Project title: **Consolidated Research Group: Person-Environment Interaction in Psychopathology, Research Group Support-Consolidated Modality (SGR 2014)**

Funding Agency: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR)- Generalitat de Catalunya

Research team: Ballespí, S. (UAB), Cristòbal, P. (UAB), Mitjavila, M. (UAB), Sheinbaum, T. (UAB), Vilagrà, R. (UAB), Racioppi, A. (UAB), Monsonet, M. (UAB), **Hinojosa, L.** (UAB)

Principal Investigator: Neus Barrantes-Vidal.

2015-2017

Project title: **Ecological, Clinical, Psychometric and Longitudinal Trajectories Assessment of Psychosis- Proneness across the Extended Psychosis Phenotype (Evaluación Ecológica, Clínica, Psicométrica y de Trayectorias Longitudinales del Riesgo a la Psicosis en el Fenotipo Extenso de la Psicosis).**

Principal Investigator: Neus Barrantes-Vidal

Project reference: PSI2014-54009-R.

Funding Agency: Ministerio de Ciencia e Innovación, Plan Nacional de I+D+i

Duration: January 2015 to December 2017 (3 years)
Investigators: Ballespí, S. (UAB), Kwapil, T. R. (University of Norh Carolina at Greensboro, USA), Myin-Germeys, I. (Maastricht University, NL), Mitjavila, M. (UAB), Sheinbaum, T. (UAB). Teamwork (non-doctor researchers): Cristóbal, P. (UAB), Guasch, V., Montoro, M., Herrero, S., Racioppi, A. (UAB), **Hinojosa, L.** (UAB), Monsonet, M. (UAB).

2013

Title: **Clitoris Reconstructive Surgery after Female Genital Mutilation (FGM): Sexual Function Assessment and Psychopathology. Pilot study.**
Main Researchers: **Lídia Hinojosa-Marques** (Hospital Quirón-Dexeus) y Dra. Gracia Lasheras-Pérez (Hospital Quirón-Dexeus).
Funding entity: **Asociación Española de Sexualidad y Salud Mental (ASEXSAME)**

- ***SCIENTIFIC POSTERS***

2015

Authors: **Hinojosa-Marqués, L.,** Sheinbaum, T., Cristóbal-Narváez, P., Monsonet, M., Kwapil, T. R., Domínguez-Martínez, T., & Barrantes -Vidal, N.
Title: **Association of early psychosis patients' and relatives' attachment style with clinical and functional presentation.**
Congress: 5th European Conference on Schizophrenia Research 2015 (ECSR 2015). Berlin, Germany. September 24-26th.

2016

Authors: **Hinojosa-Marqués, L.,** Sheinbaum, T., Cristóbal-Narváez, P., Monsonet, M., Kwapil, T. R., Domínguez-Martínez, T., & Barrantes-Vidal, N.
Título: **Early psychosis patients' and relatives' attachment style: Association with clinical and functional presentation.**
Congress: 5th Biennial Schizophrenia International Research Society Conference (SIRS 2016). Florence, Italy. April 2-6th.

Authors: Barrantes-Vidal, N., Cristóbal-Narváez, P., Sheinbaum, T., Monsonet, M., **Hinojosa-Marqués, L.,** Kwapil, T. R., & Domínguez-Martínez, T.
Title: **Childhood trauma is associated to psychotic-like symptoms and stress reactivity in daily life in individuals with an at-risk mental state for psychosis.**
Congress: 5th Biennial Schizophrenia International Research Society Conference (SIRS 2016). Florence, Italy. April 2-6th.

2017

Authors: **Hinojosa-Marqués, L.,** Domínguez-Martínez, T., Cristóbal-Narváez, P., Kwapil, T. R., & Barrantes-Vidal, N.
Título: **Ecological validity of Expressed Emotion in Early Psychosis.**
Congress: 5th Biennial Conference of the Society for Ambulatory Assessment 2017 (SAA 2017). Luxembourg, Luxembourg. June 15-17th.

Authors: **Hinojosa-Marqués, L.,** Domínguez-Martínez, T., Cristóbal-Narváez, P., Kwapil, T. R., & Barrantes-Vidal, N.
Title*:* **Ecological validity of Expressed Emotion in Early Psychosis.**
Congress: 4rt Seminari de la Comunitat de Recerca Estratègica (CORE) en Salut Mental.
(Strategic Research Community in Mental Health 4th Seminar)
Barcelona, Spain. November 9 th.

Authors: Rodríguez-Romero, A. M., **Hinojosa-Marqués, L.,** Sheinbaum, T., Monsonet, M. & Barrantes-Vidal., N.
Title: **Attachment Style, Self-esteem and Psychotic phenomena in an early psychosis sample**.
Congress: X Congreso Internacional y XV Nacional de Psicología Clínica.
(10 th International Congress and 15 th Congress on Clinical Psychology, Santiago de Compostela, Spain. November 16 th-19 th.

- ***ARTICLES IN SCIENTIFIC JOURNALS***

European Network of National Networks Studying Gene Environment Interactions in Schizophrenia (EUGEI). (2017). **Child maltreatment and clinical outcome in individuals at ultra-high risk for psychosis in the EU-GEI high risk study.** *Schizophrenia Bulletin.* doi: 10.1093/schbul/sbw162.

Cristóbal-Narváez, P., Sheinbaum, T., Myin-Germeys, I., Kwapil, T.R., de Castro-Català, M., Domínguez-Martínez, T., Racioppi, A., Monsonet, M., **Hinojosa, L.,** van Winkel, R., Rosa, A., & Barrantes-Vidal, N. **The role of stress-regulation genes in moderating the association of stress and daily-life psychotic experiences**. *Acta Psychiatrica Scandinavica, 136 (*4), 389-399. doi: 10.1111/acps.12789.

Unpublished articles:

Hinojosa-Marqués, L., Domínguez-Martínez, T., Cristóbal-Narváez, P., Sheinbaum,T., Kwapil, T.R., & Barrantes-Vidal, N. (2018). **Relatives' attachment anxiety mediates the association between perceived loss and expressed emotion in early psychosis.** Unpublished manuscript.

Hinojosa-Marqués, L., Domínguez-Martínez, T., Cristóbal-Narváez, P., Kwapil, T.R., & Barrantes-Vidal, N. (2018). **Predictors of Criticism and Emotional Over-Involvement in Relatives of Early Psychosis Patients**. Unpublished manuscript.

Hinojosa-Marqués, L., Domínguez-Martínez, T., Cristóbal-Narváez, P., Kwapil, T.R., & Barrantes-Vidal, N. (2018). **Ecological Validity of Expressed Emotion in Early Psychosis.** Unpublished manuscript.

Hinojosa-Marques, L., Domínguez-Martínez, T., & Barrantes-Vidal, N. (2018). **Family environmental factors in At-Risk Mental States for Psychosis.** Unpublished manuscript.

- ***BOOK CHAPTERS***

2018

Vilagrà, R., Monsonet, M., **Hinojosa-Marqués, L.,** Barrantes-Vidal, N. (2018). Evaluación de la dimensión afectiva de la psicosis (depresión y manía). En: E. Fonseca (Ed.), *Manual para la Evaluación del Síndrome Psicótico,* pp. 225-246. Madrid: Ediciones Pirámide (ISBN: 978-84-368-3890-9)

- ***DISSEMINATION AND PUBLICATION***

2012

Review chapter of the scientific literature from 2011 on sexual dysfunction.
Web publication within the CD SCRITC 2.0, *Actualitzacions de la Societat Catalana de Recerca i Teràpia del Comportament.*
Authors: Farré-Sender, B., & **Hinojosa-Marqués, L.**
Title: Disfuncions sexuals

2013

Review chapter of the scientific literature from 2012 on sexual dysfunction.
Web publication within the CD SCRITC 2.0, *Actualitzacions de la Societat Catalana de Recerca i Teràpia del Comportament.*
Authors: Farré-Sender, B., & **Hinojosa-Marqués, L.**
Title: Disfuncions sexuals

2014

Review chapter of the scientific literature from 2013 on female sexual dysfunction.
Web publication within the CD SCRITC 2.0, *Actualitzacions de la Societat Catalana de Recerca i Teràpia del Comportament.*
Authors: **Hinojosa-Marqués, L.** & Farré-Sender, B.
Title: Disfuncions sexuals femenines

- ***ORAL PRESENTATIONS***

2011

Psiquiatría de Enlace en la cirugía reconstructiva de clítoris. Presentation at XLIV Congreso de la Sociedad Española de Medicina Psicosomática (Teruel, Spain).

2012

Trastorns Sexuals en la Dona. Presentation at the 3rd Congrés Català de Dona i Salut Mental (Hospital de la Santa Creu i Sant Pau, Barcelona, Spain).

2013

Sexualidad Femenina: Nuevos elementos de valoración. Presentation at the VII Curso Internacional de Sexualidad y Salud Mental (Salamanca, Spain).

Cirugía reconstructiva de clítoris en mujeres víctimas de mutilación genital femenina. Valoración de la función sexual y psicopatología. Presentation at the VII Curso Internacional de Sexualidad y Salud Mental (Salamanca, Spain).

Reparació de danys en la reconstrucció de clítoris. **Perspectiva Psicològica.** Ponencia en el 1er congrés de Dret, tradició i creença en la Salut Africana (Parets del Vallès, Spain).

2017

Coauthor of the oral presentation: Cristóbal-Narváez, P., Sheinbaum, T., Rosa, A., Domínguez-Martínez, T., Castro-Catala, M., Monsonet, M., **Hinojosa- Marqués, L.,** Racioppi, A., Peña, E., Kwapil, T.R, Barrantes-Vidal, N. Impact of Gene-Environment **Interaction on the Real-World Expression of Psychosis Risk: Linking Genetic Variation, Early-life and Momentary Experiences**. 5th Biennial Conference of the SAA 2017. (Luxembourg, Luxembourg).

- ***LANGUAGES***
  - **Catalan:** Mother tongue.
  - **Spanish:** Mother tongue.
  - **English:** B2.2 (Upper-Intermediate, MECR).

- ***SOFTWARE***
  - Statistics Software: SPSS, Mplus.
  - Microsoft Office.
  - Mendeley (bibliographic manager).