Universitat Autònoma de Barcelona

Facultat de Psicologia

Departament de Psicologia Clínica i de la Salut

Tesis Doctoral

THE EARLY STAGES OF PSYCHOSIS:

Characterization of At-Risk Mental State and First-Episode Psychosis patients and The Effect of Family Environment on Outcome.

TECELLI DOMÍNGUEZ MARTÍNEZ

JULIO 2012

Universitat Autònoma de Barcelona

Facultat de Psicologia

Departament de Psicologia Clínica i de la Salut

Tesis Doctoral

THE EARLY STAGES OF PSYCHOSIS:

Characterization of At-Risk Mental State and First-Episode Psychosis patients and The Effect of Family Environment on Outcome.

TECELLI DOMÍNGUEZ MARTÍNEZ

Directora:

PROF. NEUS BARRANTES-VIDAL

Doctorado en Psicología Clínica y de la Salud.

JULIO 2012

THE EARLY STAGES OF PSYCHOSIS:

Characterization of At-Risk Mental State and First-Episode Psychosis patients and The Effect of Family Environment on Outcome.

A Ber

A mis papás y a Sebastián

“Et l'être de l'homme, non seulement ne peut être compris sans la folie, mais il ne serait pas l'être de l'homme s'il ne portait en lui la folie comme la limite de sa liberté”.

"Ne devient pas fou qui veut."

J. LACAN

INDEX

I. INTRODUCTION

Nowadays, the treatment of several mental disorders is one of the major social and health problems in society (Alvarez, 2002). According to the World Health Organization (WHO, 2004), 10% (500 million) of the world population suffers from a mental disorder at some point in life and it is estimated that 1% (50 million) currently suffers a severe mental illness. After decades of research and despite advances in pharmacological and psychotherapeutic interventions, schizophrenia-spectrum disorders are still among the most debilitating disorders in medicine (Hegart et al., 1994).

Schizophrenia and related psychotic disorders are conditions that affect approximately 5-6% of the population. The symptoms run a chronic and episodic course that results in impairments in all areas of life, generating huge personal, social and economic costs (Davis and Drummond, 1994). In point of fact, schizophrenia is still one of the most mysterious and costliest mental disorders in terms of human suffering and societal expenditure (van Os and Kapur, 2009). Schizophrenia patients frequently require hospitalization and many are unable to return to independent functioning during residual periods. Symptoms and impairment usually first appear in late adolescence, disrupting patients' transition into adulthood, causing significant levels of disability, loss of psychosocial functioning and negatively impacting the quality of life of both the person and their family (Miller et al., 1990; Caqueo and Lemos, 2008; Lua et al., 2011).

Although schizophrenia may appear to develop suddenly, the onset of psychotic symptoms is often preceded by a period of decreased function that is known as the prodrome or prodromal phase, usually defined as the period from first noticeable symptoms to first prominent psychotic symptoms (Beiser et al., 1993). The psychosis prodrome may be lengthy, lasting on average between 1 and 5 years (Loebel et al., 1992).

In recent years there has been increasing international interest in the prognostic potential of early identification and intervention in the prodromal and first-episode phases of

psychosis, assuming that it could at least help to improve the course of illness, reducing its long-term impact (Corell et al., 2010). The possibility of studying psychosis in its early stages and exploring factors that might signal of vulnerability for psychosis onset and/or predict illness course at short term, allows us to identificate individuals at-risk for develop psychosis prior to the onset of frank psychotic symptoms, enhancing our understanding of the etiology, development, and prevention of psychotic disorders. This new paradigm of early detection and intervention in psychosis is consistent with a recently adopted staging model in psychiatry, which emphasizes that less differentiated early phases of mental illnesses may benefit from simpler and broader spectrum of treatments, allowing young people to receive the help they need in a timely manner, with the potential for improved outcomes across several fronts (McGorry et al., 2010). Thus, the main aims of intervention before the onset of psychosis are to alleviate current distress and impairment and to either prevent, delay or ameliorate the onset of more severe psychotic disorder (Yung et al., 2007a).

Therefore, the 'prodromal intervention' opens up the exciting possibility of the prevention of full-blown psychosis, with all its associated morbidity, risks and stigma, possible prevention of brain damage, minimal duration of untreated psychosis (DUP) even if psychosis does develop, and the opportunity to study risk factors and processes around the onset phase of schizophrenia and related disorders (Yung et al., 2004a). Moreover, evaluating patients at their first episode of any psychosis, limits the potential confounding effects of illness severity, progression, or long-term exposure to antipsychotic drugs. Furthermore, the burgeoning interest in investigating the first-episodes of schizophrenia and related psychosis provides an opportunity to examine how this approach has assisted our understanding of the heterogeneity of psychopathology of this disorder and the trajectories of its outcome (Malla et al., 2005).

The present thesis has been developed within the framework of the new paradigm of early detection and intervention in psychosis. Moreover, the thesis is embedded in a larger longitudinal research study linked to the Sant Pere Claver Early Psychosis Program (SPC-

EPP) currently being carried out in two Communitary Mental Health Centers for Adults (CSMA-Sants y CSMA-Montjuïc), one for adolescents and children (CSMIJ), and one Day Hospital (HD) for adolescents belonging to the Sant Pere Claver Hospital in Barcelona, Spain.

The current thesis consists of two main parts. The first part is comprised by the theoretical framework, in which the main theoretical and methodological constructs, as well as the rational and state of the art of the early detection and intervention in psychosis paradigm are developed. Moreover, in this first part, three theoretical articles that have been recently published on scientific journals are included. The first article presents an overview and update of current research about Schizotypal Personality Disorder in adolescence, emphasizing on its relevance for early detection and intervention of schizophrenia spectrum disorders. The second article presents on the one hand, the basic concepts, rationale and state of the art of the early detection and intervention paradigm. Besides, it presents a review of main detection and intervention programs in early psychosis developed worldwide, which brings us an overview of the current psychotherapeutic approaches in early psychosis. The third article, aims to present and describe the integrated need-adapted treatment approach of the SPC-EPP currently being developed in Barcelona, in which sampling and empirical work of this thesis was conducted.

The second part of the thesis contains four empirical studies conducted with relatives and At-Risk Mental State (ARMS) and First-Episode Psychosis patients who receive treatment and belong to the SPC-EPP. Both groups of patients represent two different stages of the psychosis continuum, on the one hand, the 'prodromal' phase or high risk phase (ARMS), and on the other hand, the onset of first frank psychotic symptoms characterizing the first psychosis episode (FEP).

Study 1 presents an overall description of clinical and psychosocial features (including socio-demographic, background, history of treatment, psychopathology, social functioning, quality of life, etc.) of ARMS and FEP groups. Furthermore, both groups were compared in

order to characterize commonalities and differences between the at-risk and onset of disorder stages. Additionally, Study 2 focused on analyzing how subjective quality of life was associated with symptom severity and functional impairment in ARMS patients.

Study 3 and Study 4 are focused on the study of family factors that have been demonstrated to be related with the course and outcome of psychotic disorders. Thus, Study 3 characterizes the profile of relatives' Expressed Emotion (EE), illness attributions and emotional states in early stages of psychosis on the one hand, and examines how these family factors are associated and how they differ between ARMS and FEP groups, on the other hand.

Study 4 aims to examine if family environment, through the relatives' EE has an effect on clinical and functional status of early psychosis patients, as well as to examine the possible mediating role of relatives' attributions in the association between EE and illness severity.

It is noteworthy that each of the four studies were presented in an article format including their own introduction, methods, results and discussion, since they will be submitted for publication in scientific journals in the near future. Therefore, a general discussion and conclusions of the entire thesis are presented at the end in a separate section, including a summary of main findings, research and clinical implications, limitations and future research directions.

II. THEORETICAL FRAMEWORK

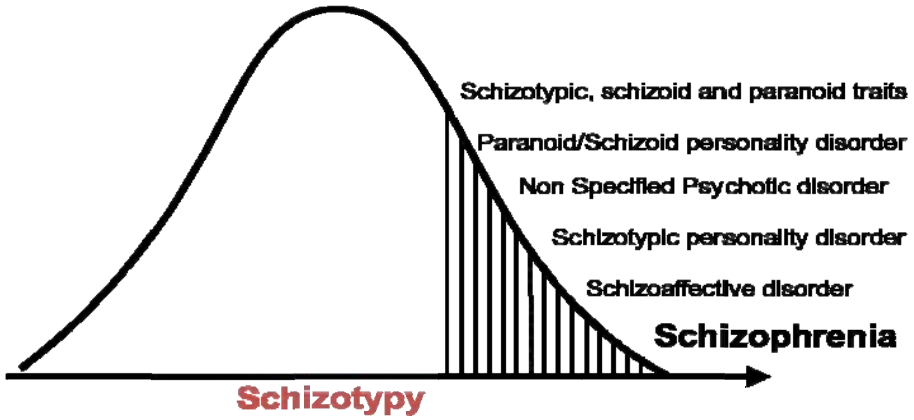
1. THE EXTENDED PSYCHOSIS PHENOTYPE

1.1. Schizophrenia-Spectrum Disorders and The Continuum Hypothesis of Psychosis

Traditional medical models assume a categorical view of psychosis represented by classification systems of mental disorders such as the Diagnostic and Statistical Manual of Mental Disorders (DSM) (APA, 2002) and the International Classification of Disease (ICD) (WHO, 1992). Based on this, the psychosis phenotype has traditionally been thought of as a dichotomous entity that can be identified by applying certain operationalized criteria, also, totally distinguishable from health. Within the cluster of diagnostic categories, the term schizophrenia is applied to a syndrome characterized by long duration, delusions, hallucinations, negative symptoms, and few affective symptoms (non-affective psychosis). However, the diagnosis of schizophrenia encapsulates patients with markedly different clinical features and courses. Patients who present with a psychotic disorder with fewer negative symptoms, but whose psychosis is preceded by a high level of affective symptoms, (depression and mania) are usually diagnosed with psychotic depression or bipolar disorder (affective psychosis) (van Os and Kapur, 2009a). Therefore, psychosis is not exclusive to schizophrenia, but it is spread over a myriad of diagnostic categories in the different classification systems and represents highly variable syndromal clusters of continuous psychotic and affective symptom dimensions, in combination with variable degrees of motivational and neurocognitive impairments (van Os and Kapur, 2009a). In consequence, classification systems have attempted to deal with this categorical approach by proposing subtypes and intermediate syndromes (Peralta and Cuesta, 2001). On the other hand, it has been suggested that the unitary schizophrenia construct, which results hardly amenable to be operationalized in terms of categorical definitions, should be better understood as dimensional construct comprised by underlying psychopathological dimensions (positive, negative, disorganized, etc.) (Cuesta and Peralta, 1995; Peralta and Cuesta, 2005).

In contrast to categorical approach, dimensional models (or continuum models) consider the existence of continuity between health and pathology (Kerr and McClellnd, 1991). So, the question becomes not whether an individual has a particular psychotic disorder, but instead to what degree the person has the experience, measured dimensions, and the extent of its repercussions or need for care (Johns and van Os, 2001). Rado (1952) has postulated that a common schizophrenic diathesis might lead to several phenotypic manifestations, from descompensated schizotype (an abbreviation of 'schizophrenic phenotype') to a deteriorated schizophrenia, which pointed to the existence of an aetiological unit underlying several clinical manifestations along the schizophrenic spectrum (Lenzenweger and Korfine, 1995). The term 'schizophrenic spectrum' is defined as the range that goes from inadequate personality to chronic schizophrenia, based on the qualitative similarities of the traits that characterize the entities that compose this construct (Kety et al., 1968). Thus, schizotypy would be the psychological diathesis underlying the schizophrenia spectrum whose disorders would differ in their severity, frequency, chronicity and outcome, but sharing aetiological and risk factors (Maier et al., 1999). Following this reasoning, two types of syndromes were proposed as components of the schizophrenia spectrum. First, personality features and disorders (sometimes the spectrum concept is restricted to personality traits). Secondly, psychotic symptoms and disorders, often with an episodic course, which are shared clinical features with schizophrenia without meeting its full diagnostic criteria (see Figure 1). The spectrum concept reflects the notion that the diagnostic criteria of schizophrenia are too restrictive to tap the whole variation of symptoms and features induced by its underlying causes. So, schizophrenia-spectrum disorders can be defined as those disorders that resemble and/or are associated to schizophrenia, and that share the same familial-genetic risk factors, similar symptomathology, course, treatment and vulnerability to the development of comparable psychopathology (Widiger et al., 1988).

Figure 1: Schizophrenia-spectrum disorders (Maier et al., 1999).



Furthermore, epidemiological studies have consistently shown the existence of psychotic experiences in non-clinical populations (people who are not readily diagnosable according to ICD/DSM criteria) suggesting an ‘‘extended psychosis phenotype,’’ (Kaymaz and van Os, 2010), which shares demographic, etiological, familial, and psychopathological factors with clinical psychotic disorder (e.g. Tien, 1991; Poulton et al. 2000; Verdoux and Van Os, 2002). Thus, affective dysregulation, psychotic experiences, motivational impairments, and cognitive alterations appear to be distributed and co-expressed to a degree in non-ill individuals and have been shown to index risk for later onset of disorder, particularly if they tend to persist over time (van Os et al., 2010). The extended psychosis phenotype, considered as the behavioral expression of vulnerability for psychotic disorder in populations (van Os et al., 2012), allows to identify subclinical manifestations of the psychosis phenotype, which is essential for understanding the etiology of such conditions and for identifying relevant risk and protective factors.

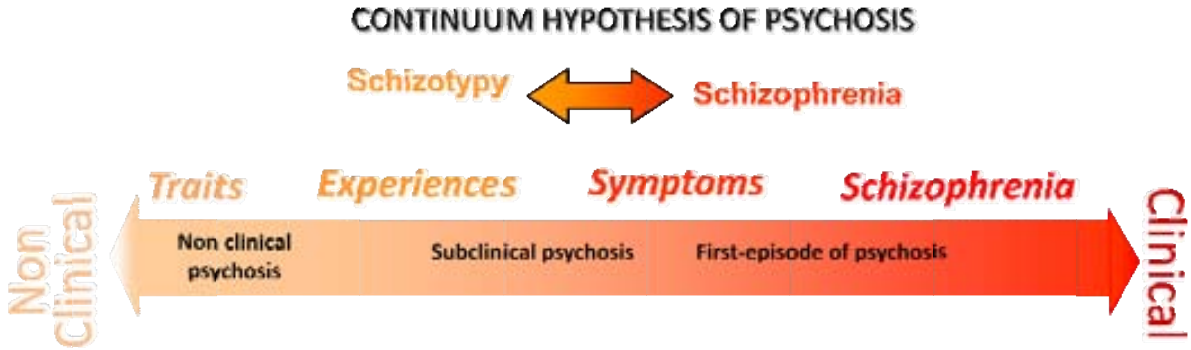
According to dimensional models, schizophrenia-spectrum disorders represent the extreme expressions of a personality disposition, referred to as schizotypy that results from the interaction of multiple genetic, neurodevelopmental, and psychosocial factors (e.g. Claridge, 1997; Meehl, 1999; Van Os et al., 2009b). It is assumed that there are schizotypic individuals who have an underlying vulnerability for schizophrenia, but who may never

transition into clinical psychosis. In fact, it is presumed that the majority of individuals with schizotypy will never descompensate, although they may demostrate mild and/or transient signs of schizophrenic-like or schizotypic adjustment, including neurocognitive and biobehavioral deficits, clinical and subclinical symptoms, and social impairment (Kwapil et al., 2008). This formulation suggests that schizotypy is expressed across a dynamic continuum of clinical and subclinical characteristics ranging from relative psychological health to full blown schizophrenia (see Figure 2) (e.g. Claridge, 1997; Van Os and Kapur, 2009. b.; Kaymaz and van Os, 2010). Therefore, the psychosis phenotype is expressed at levels well below its clinical manifestation, commonly referred to as psychosis proneness, psychotic experiences, schizotypy or at-risk mental states (Meehl, 1962; Chapman et al., 1994; Claridge, 1997; Kwapil, 1998; Stefanis et al., 2002; Yung et al., 2003a). A psychosis continuum phenotype implies that the same psychotic symptoms that are seen in patients with a psychotic disorder can also be observed in non-clinical populations (Van Os et al. 2009b). The assumption of this approach is that experiencing symptoms of psychosis such as delusions and hallucinations is not inevitably associated with the presence of disorder. Thus, even though the prevalence of the clinical disorder is low, the prevalence of the symptoms can conceivably be much higher (van Os et al., 2009b). However, the superposition of a psychosis continuum does not necessarily imply that there is also a continuum of disorder, i.e., that individuals who exhibit subclinical manifestations of psychosis are at heightened risk for developing psychotic disorders (Chapman et al., 1994; Kwapil, 1998; Poulton et al., 2000; Hanssen et al., 2005); although, the majority will never decompensate, and only a minor part of the entire phenotypic continuum will represent clinical psychosis (Johns and Van Os, 2001).

As schizophrenia, schizotypy has also been characterized as a multidimensional construct (e.g. Raine et al., 1994; Claridge, 1996; Stefanis et al., 2004; Kwapil et al., 2008). Thus, positive schizotypy and positive symptom of schizophrenia are characterized by odd beliefs and unusual perceptual experiences, which in their extreme form manifest as

delusions and hallucinations. Negative schizotypy and schizophrenia are characterized by deficits such as affective flattening, anhedonia, social disinterest, and diminution of cognitive functioning (Kwapil et al., 2012). While there is not a universally agreed upon latent structure of schizotypy, the proposed factors are consistent with those hypothesized to comprise schizophrenia (Bilder et al. 1985; Liddle 1987; Peralta et al. 1992), supporting the continuum of psychosis.

Figure 2: Continuum hypothesis of psychosis.



The elucidation of the processes involved in the development of this broad phenotype is essential for the identification of individuals at risk for psychotic disorders and may ultimately hasten the development of prophylactic treatment interventions (Barrantes-Vidal et al., 2009). Moreover, the study of sublicinical manifestations of psychosis also allows us to examine these processes relatively free of the confounding consequences of clinical disorders (e.g., hospitalization, medication, marginalized social status, etc.) that plague the study of patients (Lenzenweger, 2006).

Additionally, systematic review of the literature shows that there is evidence, not only for a psychometric ‘‘continuum’’ (in the sense of an extended psychosis phenotype blending gradually into clinical syndromes) (van Os et al., 2009a), but also for an underlying latent categorical structure of the population, in the sense that, regardless of the presence of a

psychometric continuum, the population may still be composed of two different types of people: those who are liable, some of whom may also have the disorder, and those who are not (Linscott and van Os, 2010). In addition, recent research suggests that onset of psychotic disorder can be understood, in part, as different types of subclinical experiences causally impacting on each other over time, for example, negative symptoms predicting psychotic experiences (Domínguez et al., 2010), affective dysregulation impacting on onset of psychotic symptoms (Krabbendam et al., 2005; van Rossum et al., 2011), or hallucinations giving rise to delusions (Krabbendam et al., 2004; Smeets et al., 2010), suggesting a network model of symptoms onset of psychotic disorder. These reciprocally influencing symptoms, in turn, can be traced to ‘‘microphenotypes’’ of subtle responses of aberrant salience or negative affect to small variations in the environment that possibly constitute the core vulnerability in the way cerebral processing gives rise to subtle alterations in the representation of the social environment in the form, for example, of paranoia (Simons et al., 2009; Myin-Germeys et al., 2005) or hallucinatory experiences (Galdos et al., 2011). An approach that possibly can accommodate this type of variation over time is the clinical staging model which is detail below (McGorry et al., 2007), in combination with a network model of psychopathology (van Os et al., 2012). Thus, reciprocally impacting symptoms sharing degrees of liability may develop across stages of severity and comorbidity (Wigman et al., 2012).

To sumarize, increasing evidence indicates that: a) the psychosis phenotype is expressed across a dynamic continuum of clinical and subclinical expression (Stefanis et al., 2004); b) there is a common multidimensional structure across the continuum (Claridge et al., 1997; Vollema and Hoitjink, 2000; Kwapil et al., 2008); c) psychopathology may be considered as a network of symptom dimensions that reciprocally impact each other over time and are linked as part of a homeostatic mechanism, time, and/or share liability (van Os et al., 2012); and d) identification of individuals at-risk for psychosis should enhance our understanding of the etiology, development, and prevention of psychotic disorders.

1.2. SCHIZOTYPAL PERSONALITY DISORDER

Although schizotypy and schizotypal have frequently been used synonymously (owing no doubt in part to their similar names), it is important to differentiate them. On the one hand, the term schizotypy describe the expression of neurodevelopmental vulnerability for schizophrenia across a broad continuum ranging from minimal impairment to full-blown schizophrenia (as has been explained above), and, on the other hand, term schizotypal refers to the specific personality disorder that is part of the family of schizophrenia-spectrum disorders, i.e. the Schizotypal Personality disorder (SPD). SPD, like schizophrenia and other spectrum disorders, is subsumed within the broader continuum of schizotypy and it is currently characterized as involving marked interpersonal deficits, cognitive and perceptual distortions, as well as odd and eccentric behaviors. SPD stands at a unique crossroads in the characterization and treatment of psychopathology in that it is conceptualized both as stable personality pathology and also as a milder manifestation of schizophrenia. SPD's etiological relation with schizophrenia is supported by extensive genetic, neurobiological, neurocognitive, psychosocial, and clinical research. However, research has also identified biopsychosocial factors that differentiate SPD from schizophrenia and may protect SPD patients from deteriorating into psychosis.

Studying SPD can help to delineate protective factors against the development of schizophrenia (Kirrane and Siever, 2000); an effort that is central to the current focus on prophylactic interventions aimed at preventing, delaying, or minimizing the onset of psychosis (e.g., Ruhrmann et al., 2009).

At follows, it will present a recent publish article in which is explained the SPD and is provided an overview of current research about SPD in adolescence, emphasizing on its relevance for early detection and intervention of schizophrenia spectrum disorders.

Revista de
PSICOPATOLOGÍA Y SALUD MENTAL
del niño y del adolescente

Noviembre / November 2011 18

INVESTIGACIÓN SOBRE EL TRASTORNO ESQUIZOTÍPICO DE LA PERSONALIDAD EN LA ADOLESCENCIA: ACTUALIZACIÓN

Tecelli Domínguez Martínez*, Thomas R. Kwapil** y Neus Barrantes-Vidal***

RESUMEN

[illegible]

[illegible]

ABSTRACT

[illegible]

1.3.1. INTRODUCCIÓN

Cien años de estudios descriptivos, empíricos y clínicos han proporcionado una sólida evidencia de que pueden encontrarse formas atenuadas de psicopatología psicótica, tanto en familiares de pacientes con esquizofrenia como en la población en general. Dichas formas atenuadas pueden preceder el inicio de la esquizofrenia, o, por el contrario, pueden representar formas más estables de psicopatología que no necesariamente avanzan hacia la completa manifestación de la psicosis. Por tanto, se ha establecido el uso del término *esquizotipia* para describir la expresión fenotípica de la vulnerabilidad psicobiológica hacia la esquizofrenia, a través de un amplio proceso continuo que va desde un deterioro mínimo hasta la esquizofrenia plenamente desarrollada, mientras que el término *esquizotípico* se utiliza específicamente para referirse al trastorno de la personalidad que forma parte de la familia de los trastornos del espectro de la esquizofrenia.

Así pues, el Trastorno Esquizotípico de la Personalidad (TEP) se encuentra en una encrucijada en cuanto a la caracterización y tratamiento de la psicopatología ya que, al ser conceptualizado como una patología estable de la personalidad, por una parte, y como una manifestación latente de la esquizofrenia, por la otra, padece de numerosos problemas de delimitación; en particular con trastornos del Eje I, con los trastornos de la personalidad paranoide y esquizoide, así como con presentaciones subclínicas y no clínicas. Además, está rodeado de diversas controversias, algunas de las cuales se acentúan en la publicación de la última revisión del DSM (APA, 2010) sobre todo, en lo que concierne a la clarificación de las conceptualizaciones alternativas de los estados borderline, así como de los pródromos y los modelos multidimensionales de esquizotipia.

La comprensión y el estudio de la psicopatología de la personalidad en jóvenes resultan aún más complejos y multifacéticos que en la adultez, debido, en parte, a la amplia variabilidad individual de la estabilidad de los rasgos (Esterberg et al., 2010) y a que los trastornos de la personalidad generalmente se inician en la adolescencia y la adultez temprana, con lo cual, en muchas ocasiones, resulta muy difícil distinguir sus rasgos

característicos del comportamiento común de los adolescentes (en el TEP, por ejemplo, dificultades de adaptación, aislamiento, desinterés, poca energía e inexpresividad emocional, conductas y vestimenta excéntricas, etc.). Por lo tanto, el estudio del TEP en la juventud es fundamental para ampliar el limitado conocimiento que existe sobre el funcionamiento y la psicopatología de la personalidad en esta etapa, y, sobre todo, porque la evidencia demuestra que representa la expresión fenotípica más común de la diátesis genética subyacente de los trastornos del espectro esquizofrénico (Tienari et al., 2003).

El presente artículo tiene como finalidad presentar una breve revisión y actualización de la investigación del TEP en la adolescencia, así como destacar su relevancia en la detección e intervención temprana de los trastornos del espectro de la esquizofrenia.

1.3.2. EL TRASTORNO ESQUIZOTÍPICO DE LA PERSONALIDAD (TEP) EN LA ADOLESCENCIA: CARACTERÍSTICAS CLÍNICAS, CURSO, ETIOLOGÍA Y FACTORES DE RIESGO.

El TEP es un trastorno de la personalidad (TP) que forma parte del espectro de la esquizofrenia y se caracteriza por "un patrón general de déficits sociales e interpersonales asociados a malestar agudo y una capacidad reducida para las relaciones personales, así como distorsiones cognoscitivas o perceptivas y excentricidades del comportamiento que comienzan al principio de la edad adulta y se dan en diversos contextos" (APA, 2002). Su prevalencia es de 3% en la población en general, aunque las estimaciones han oscilado entre el 1% y el 5% (Torgersen et al., 2001). Al igual que la esquizofrenia, el TEP es un constructo multidimensional (reflejado en la presentación de los síntomas, el deterioro, la patofisiología y la etiología). Aunque no hay un acuerdo general, las principales dimensiones que se han identificado en el TEP y que se asemejan a las de la esquizofrenia son, la positiva (pensamiento mágico, ideas de referencia y anormalidades perceptivas), la negativa (anhedonia, afectividad inapropiada o restringida, desinterés social y abulia) y la desorganizada (comportamiento excéntrico, pensamiento y lenguaje raros). Sin embargo,

los estudios que utilizan análisis de *clusters,* establecen subgrupos de sujetos en función de las características esquizotípicas que presentan. Por ejemplo, Barrantes-Vidal et al. (2010) en una amplia muestra no clínica (n=6,137) exploraron las agrupaciones de las dimensiones de la esquizotipia positiva y negativa y establecieron cuatro *clusters* caracterizados como: baja esquizotipia, alta esquizotipia positiva, alta esquizotipia negativa y esquizotipia mixta (alta tanto en la dimensión positiva como en la negativa).

El TEP es considerado trans-situacional, disfuncional, deteriorante y se encuentra subsumido en el *continuum* más amplio de la esquizotipia (Kwapil et al., 2008; Kwapil & Barrantes-Vidal (2012). Su aparición, curso y estabilidad han sido temas de amplio estudio y controversia (Trull & Durrett, 2005). El DSM-IV-TR advierte que el diagnóstico de TP en niños y adolescentes debe hacerse únicamente en aquellos casos excepcionales en los que los rasgos de personalidad del individuo sean "particularmente maladaptativos" y hayan estado presentes durante, al menos, 1 año (APA, 2002). Por esto, la investigación centrada en la aparición de los TP en niños y adolescentes suele ser polémica, principalmente porque la mayoría asume que la personalidad no se forma completamente hasta la edad adulta. Como consecuencia, la investigación en esta área se ha visto limitada, en parte por el supuesto de que las características de la personalidad en la infancia y la adolescencia son inestables, volubles y no persisten en la edad adulta. En este sentido, la evidencia ha mostrado que la estabilidad de los rasgos de personalidad normal en la infancia es, en el mejor de los casos, moderada, y que los TP son menos estables en los niños que en los adultos. Ésta y otras conclusiones han impulsado el aumento de estudios en el desarrollo de la trayectoria y la evaluación de los TP en la juventud (Skodol, 2005, 2008). Por otra parte, el auge del enfoque actual de prevención e intervención temprana ha estimulado el interés en explorar las vías de desarrollo de los TP en la juventud (Esterberg et al., 2010; Skodol, 2008).

La relación etiológica entre el TEP y la esquizofrenia se fundamenta en la comunalidad hallada entre ambos trastornos desde la investigación genética,

neurobiológica, neurocognitiva y clínica. Dicha comunalidad sería explicada por el hecho de que los trastornos del espectro esquizofrénico tienen una etiología multifactorial. Así, la interacción entre múltiples genes y una serie de factores biopsicosociales ambientales produciría una amplia gama de expresiones fenotípicas que van desde la esquizotipia no clínica, hasta el TEP y los trastornos clínicos del eje I del espectro esquizofrénico.

La mayoría de estudios del TEP, siguiendo los pasos de la investigación en esquizofrenia, se han centrado en los factores genéticos, ambientales de base biológica y en los endofenotipos neurobiológicos. Más recientemente, elementos tales como la importancia de los factores afectivos en la psicosis no afectiva (Garland et al., 2010), o los resultados epidemiológicos que muestran la importancia de los factores de riesgo psicosociales para la esquizofrenia están ampliando el alcance de la investigación etiológica del TEP (Cantor-Graae, 2007). Por otro lado, resultados como los de Barrantes-Vidal et al. (2009) indican que el neuroticismo es etiológicamente relevante para la psicopatología del espectro de la esquizofrenia y puede influir en la transición a través del *continum* de la psicosis.

En general, los estudios sobre los factores de riesgo de alteraciones en el neurodesarrollo son consistentes con la idea de que el TEP comparte con la esquizofrenia factores de riesgo ambientales de base biológica, a la vez que sostienen la hipótesis de un origen neurológico común (Chok et al., 2005; Lathi et al., 2009; Machón et al., 2002; Rosa et al., 2000). En este sentido, Rosa et al. (2000) hallaron que la asimetría en el recuento palmar a-b se asoció específicamente con la esquizotipia negativa en adolescentes de población general, mientras que Chok et al. (2005) en una muestra de estudiantes encontraron que la esquizotipia positiva se asoció con menores recuentos palmares y parámetros más simples. Por otro lado, Barrantes-Vidal et al. (2003) y Kaczorowski et al. (2009) hallaron asociaciones entre los signos neurológicos suaves y la dimensión negativa de la esquizotipia en adolescentes y jóvenes adultos. Asimismo, Walder et al. (2006) demostraron la ausencia del dimorfismo sexual normal prenatalmente determinado en el patrón de la segunda y cuarta huellas digitales en adolescentes con TEP, lo cual, a su vez,

indica ciertas alteraciones de los niveles prenatales de andrógeno/estrógeno en las hormonas gonadales prenatales.

En cuanto a los factores de riesgo psicosociales, la investigación epidemiológica ha mostrado cada vez más asociaciones entre los factores psicosociales (por ejemplo, el estado de migración, exposiciones a traumas, intimidación, acontecimientos estresantes de la vida, relaciones familiares disfuncionales, etc.) y las experiencias psicóticas subclínicas, los síntomas psicóticos y la esquizofrenia (Allardyce & Boydell, 2006; Bendall et al., 2008; Morgan y Fisher, 2007). Por ejemplo, en un estudio longitudinal con una muestra de 2,542 adolescentes de la población general, encontraron una asociación prospectiva más consistente en adolescentes con elevadas puntuaciones de esquizotipia entre el trauma autoinformado en la línea base y la aparición de síntomas psicóticos en el seguimiento (media= 42 meses), lo cual sugiere un sinergismo entre el trauma y la propensión a la psicosis (Spauwen et al., 2006). Asimismo, estudios recientes como el de Powers et al. (2011) indican la importante influencia del abuso emocional en el posterior desarrollo del TEP y sugieren que los síntomas del trastorno de estrés postraumático pueden proporcionar un vínculo entre las experiencias traumáticas de la infancia y los síntomas del TEP en los adultos que las experimentaron. Otros estudios han encontrado que el estrés psicosocial pre y postnatal (por ejemplo, el embarazo no deseado o la separación temprana de la madre) pueden predecir síntomas elevados de TEP y pueden provocar un impacto negativo tanto en el vínculo parental temprano como en los estilos de apego (Anglin et al., 2008; Lahti et al., 2009).

Por otra parte, Read et al. (2008) afirman que el maltrato infantil es un factor causal de la psicosis y plantean que la adversidad social y vital no son meramente exacerbadores de la vulnerabilidad genética, sino también “creadores” de la diátesis a la psicosis, posiblemente a través de la generación de una vulnerabilidad anómala al estrés. En esta línea, algunos estudios han demostrado que adolescentes con TEP suelen tener más experiencias vitales indeseables y no atribuibles a los síntomas que personas sin TP

(Tessner et al., 2011), así como menores acontecimientos vitales positivos y mayor deterioro general en comparación con pacientes con depresión o con otros TP (Skodol et al., 2005). Desafortunadamente, resulta difícil extraer conclusiones firmes sobre las relaciones entre el trauma y las dimensiones específicas del TEP, puesto que no todos los estudios exploran las dimensiones del TEP y la esquizotipia de forma separada.

1.3.3. EL TEP Y LA PROPENSIÓN A LA PSICOSIS

De acuerdo con la presunta etiología compartida entre el TEP y la esquizofrenia, pruebas fehacientes indican que los pacientes con rasgos de TEP tienen un riesgo elevado a desarrollar esquizofrenia y trastornos psicóticos relacionados con respecto a la población en general (Kwapil, 1998; Miller et al., 2002). Aproximadamente el 70% de individuos con TEP presentan síntomas y cumplen criterios para el síndrome prodrómico de psicosis (Shapiro et al., 2011). De manera similar, estudios con pacientes en fase prodrómica que presentan características de TEP han informado de tasas de transición a la psicosis del 20% o superiores (Klosterkotter et al., 2001; Miller et al., 2002; Woods et al., 2009; Yung et al., 2005). No obstante, es importante tener en cuenta la advertencia de O'Flynn et al. (2003) de que los TP del espectro esquizofrénico no son necesariamente las etapas de transición al desarrollo de la esquizofrenia, y que el trastorno premórbido de la personalidad no es específico de las psicosis esquizofrénicas. El hecho de que se presenten formas más estables de psicopatología que no necesariamente avanzan hacia la completa manifestación de la psicosis se ha visto reforzado por la identificación de factores biológicos y psicosociales que establecen una diferencia entre el TEP y la esquizofrenia y que, posiblemente, protegen a los pacientes del deterioro hacia la psicosis.

De esta manera, el TEP representa un importante factor de riesgo para la psicosis y, dadas las estrechas similitudes fenomenológicas entre ambos síndromes, resulta difícil distinguirlo de la fase prodrómica de la esquizofrenia (Trotman et al., 2006). No obstante, a pesar de que se considera que el pródromo y el TEP se solapan (de hecho uno de los

criterios para diagnosticar el pródromo es la presencia de un diagnóstico de TEP y una disminución marcada del funcionamiento (Miller et al., 2003a), éstos no son conceptos sinónimos. En esta línea, Woods et al. (2009) advierten que la presencia del pródromo en algunos pacientes no necesariamente evoluciona hacia la psicosis, sino que podría estabilizarse en un TEP.

A pesar de que el síndrome de riesgo propuesto recientemente por el DSM-V ha provocado una considerable controversia (Carpenter, 2009; Corcoran, et al., 2010; Yung et al., 2010), se debe tomar en cuenta que dichos síndromes de riesgo están centrados en la identificación (y ultimadamente en la prevención) de casos de psicosis incipiente, lo cual, no es el enfoque principal del diagnóstico de TEP. Sin embargo, es importante tener en cuenta la importancia de la identificación de jóvenes con TEP, puesto que nos permite avanzar en la comprensión de los procesos psicosociales y del neurodesarrollo anómalo que pueden producir la esquizotipia, y, además, posibilita el desarrollo de tratamientos y programas preventivos. Hasta ahora, este tipo de intervenciones siguen siendo polémicas, debido en parte, a la limitada capacidad de identificar de forma eficaz a personas en riesgo de desarrollar psicosis y a la falta de comprensión sobre algunas intervenciones verdaderamente profilácticas (Kwapil et al., 2008; Barrantes et al., 2009).

1.3.4. CONCLUSIONES

El diagnóstico de TEP ofrece la mejor estimación actual de un patrón complejo de disfunciones cognitivas, afectivas y del comportamiento que puede proporcionar un punto de partida prometedor para las actuales líneas de investigación centradas en la detección y prevención de la psicosis incipiente.

La investigación etiológica indica, por lo general, que el TEP y la esquizofrenia comparten muchos factores de riesgo genéticos, del neurodesarrollo y psicosociales, así como las versiones atenuadas de endofenotipos que se derivan de las interacciones complejas y dinámicas de estos componentes etiológicos. Sin embargo, es necesario

desarrollar investigaciones que continúen dilucidando los factores que diferencian el TEP y la esquizofrenia, para ampliar el conocimiento sobre riesgo y protección respecto a la psicosis, algo esencial para el desarrollo de intervenciones tempranas y de estrategias de prevención. De este modo, con el reciente enfoque de investigación en las fases prodrómicas, el TEP tendrá un papel cada vez más importante en la identificación de los grupos clínicos de alto riesgo, lo que a su vez, permitirá prevenir, retrasar y/o minimizar el inicio de la psicosis (Ruhrmann et al., 2009).

2. THE CLINICAL STAGING MODEL OF PSYCHOSIS AND THE EARLY DETECTION AND INTERVENTION PARADIGM

2.1. THE CLINICAL STAGING MODEL

The traditional diagnostic system for psychotic and mood disorders is characterized by artificial divisions based on cross-sectional symptom sets, supported on course and outcome variables. Early clinical features are not differentiated from those that become apparent as a persistent disorder, and no consideration is given to the definition of the onset of a disorder (McGorry et al., 2010). The traditional diagnostic concepts the mood and psychotic disorders have been derived from the more prevalent subsamples of chronic patients, thereby enhancing the impression of stability and validity. However, in everyday clinical practice, unfortunately, diagnostic criteria operationally defined create a spurious precision that does not extend far beyond the research setting, and questions of validity and utility remain unresolved (Rieger et al., 2009; Jansson and Pamas, 2007). On the other hand, medications and psychosocial treatments for schizophrenia, mood and anxiety disorders still remain episodic and palliative. Most patients are better but not recovered, many do not responding to available treatments, and many treatments are not accessible to those who need them (Insel, 2007). In consequence, pessimism, stigma, and neglect have confined therapeutic efforts in schizophrenia for more than a century (McGorry et al., 2008).

A clinical staging model mapping the development, progression, and extension of mental illness over time may prove to be heuristically and practically useful in clinical practice and research (McGorry et al., 2010). It differs from conventional diagnostic practice in that it defines not only the extent of progression of a disorder at a particular point in time but also where a person lies currently along the continuum of the course of an illness, which is particularly useful as it differentiates early, milder clinical phenomena from those that accompany illness progression and chronicity (McGorry et al., 2010). Therefore, clinical staging may provide a way forward to refine diagnosis and to select treatments in a safer and more effective manner (i.e., relevant to earlier stages of an illness, where such interventions

are likely to be more effective and less harmful than treatments delivered later in the course of illness). In doing so, a preemptive psychiatry based on the clinical staging paradigm is a welcome departure from the deterministic thinking that has plagued psychiatry for so long, and opens the door for a better understanding of gene-environment interactions in the onset and course of psychiatric illness (Insel, 2007).

During the past decades, a systematic international collaboration of clinicians and researchers has sought to apply the principles and practice of early diagnosis and staged treatment to the field of schizophrenia and related psychoses (McGorry et al., 2002a). Consequently, psychiatry is currently undergoing a paradigm shift towards the identification of the early stages of mental disorders and preventive intervention, including increased focus on “prodromal” or “at risk mental states” (ARMS) for psychosis.

Early detection and prospective evaluation of individuals at risk for psychotic disorders are critical to efforts to isolate the mechanisms underlying psychosis (Cannon et al., 2007) and the perfect “laboratory” to study symptom formation. Besides, studying ARMS patients allows us to identify psychological and biological processes relevant to etiology, prior to the onset of marked clinical symptoms and impairment. This is essential for understanding the origins and development of psychosis and for identifying targets for future interventions (Cornblatt, 2003). Finally, a focus on prevention in prodromal/subpsychotic individuals promises the possibility of forestalling or minimizing the emergence and course of psychosis.

In what follows, it will be described the rationale and state of the art of this new paradigm of early detection and intervention in psychosis. First a review of the main international early psychosis programs will offered and then an overview of the current psychotherapeutic approaches in this field will be presented.

2.2. EARLY DETECTION AND INTERVENTION IN PSYCHOSIS PARADIGM

Salud Mental 2011;34:341-350

Rationale and state of the art in early detection and intervention in psychosis

Tecelli Domínguez Martínez,[1,2] Joan Manel Blanqué,[3] Jordi Codina,[3] Mónica Montoro,[3] Lluis Mauri,[3] Neus Barrantes-Vidal[1,3,4,5]

Artículo original

SUMMARY

Schizophrenia-spectrum disorders have a chronic and episodic course that results in impairment of all life domains. Pharmacological and psychosocial treatments provide symptom relief, but there is not a cure for schizophrenia and many patients suffer chronic impairment. In addition, it is expensive both in economical terms and also in terms of personal costs for both patients and their families.

International interest has grown over the past 15 years in the prognostic potential of early identification and intervention in the prodromal and first-episode phases of psychotic illness. This focus is associated with increasing optimism about the benefits of implementing treatment as early as possible in the course of psychosis at least to help improve the course of illness, reducing its long-term impact.

The most recent epidemiological studies have shown that patients with longer duration of untreated psychosis (DUP) have worse short-term outcomes in terms of treatment response, positive symptoms, negative symptoms, and global functioning. Neuroimaging studies have also indicated that prolonged untreated illness is associated with more pronounced structural brain abnormalities, while this is less prominent earlier in the course of the disorder. Therefore, early detection aims to reduce treatment delay in the hope of improving prognosis and reducing illness severity. Early intervention in psychotic disorders has gained momentum in the last decades, and there is now an estimated 200 centers worldwide offering specialized services for young people experiencing their first episode of psychosis. Each of these programs has unique characteristics and distinctive features in terms of treatment modalities and assessment tools, but most have a number of common elements and goals: a) early detection of new cases, b) reducing DUP, and c) providing better and continued treatment during the «critical period» of the early years of the disease.

Moreover, the role of family work in early psychosis can be crucial given that relatives are the main informal caretakers of persons with mental health problems. Family interventions in early psychosis usually offer psychoeducation and/or individual and group family therapy, communication and problem solving training, which can help to develop coping strategies and reduce distress and burden.

Intervention programs in early psychosis are usually composed by interdisciplinary teams, providing a wide range of integrated services that typically include psychoeducation, clinical case management, and group interventions. Specific interventions generally include pharmacotherapy, stress management, relapse prevention, social and employment rehabilitation support, and cognitive and family therapy.

Given the complex etiology and clinical manifestation of psychosis, treatment packages for people experiencing early psychosis need to be individually tailored to specific needs rather than applied homogenously across early psychosis patients.

The current challenge in the implementation of psychological interventions in the early stages of psychosis are: 1. to adapt treatment modalities that have been proven effective in stable and residual stages of the disease to its early stages; 2. to develop new forms of therapy tailored to the specific characteristics of these early stages of psychosis (prodromal and ultra high-risk phase, onset and first episode psychosis, and «critical period» or post-crisis psychosis); and 3. treatment packages need to be individually tailored to their specific needs rather than applied homogenously across a group of patients.

The aims of this paper are: 1. to present the basic concepts, rationale and state of the art of the early detection and intervention paradigm; 2. to review and present the main detection and intervention programs in early psychosis and 3. to provide an overview of the current psychotherapeutic approaches in early psychosis.

Key words: Early detection and intervention, early psychosis, psychotherapeutic approach, need-adapted treatment.

RESUMEN

Los trastornos del espectro psicótico presentan un curso crónico y episódico que provoca alteraciones en todas las áreas de la vida, generando importantes grados de discapacidad, pérdida de funciones psicosociales, grandes costos económicos, una comorbilidad considerable y sufrimiento tanto para los pacientes como para sus familias. A pesar de que los tratamientos farmacológicos y psicosociales han ayudado a aliviar los síntomas y mejorar la calidad de vida, en muy pocas ocasiones se logra una recuperación satisfactoria a nivel psicológico y funcional.

Durante los últimos 15 años, el optimismo creciente sobre la posibilidad de mejorar el pronóstico de la psicosis y alterar con ello el tradicional curso negativo de la enfermedad ha producido una

[1] Universitat Autònoma de Barcelona, Departament de Psicologia Clínica i de la Salut, Facultat de Psicologia, Barcelona.
[2] Ministerio de Asuntos Exteriores y de Cooperación y la Agencia Española de Cooperación Internacional para el Desarrollo (MAEC-AECID).
[3] Sant Pere Claver Fundació Sanitària, Departament de Salut Mental, Barcelona.
[4] University of North Carolina at Greensboro, Department of Psychology.
[5] Instituto de Salud Carlos III, Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Spain.

Correspondencia: Neus Barrantes-Vidal. Departament de Psicologia Clínica i de la Salut, Facultat de Psicologia, Universitat Autònoma de Barcelona (UAB) 08193 Bellaterra (Barcelona), España. Tel. +34 93 581 38 64. Fax. +34 93 581 21 25. E.mail: Neus.Barrantes@uab.cat

Recibido: 22 de diciembre de 2010. Aceptado: 22 de marzo de 2011.

reforma sustancial en la práctica clínica y en el desarrollo de estrategias de intervención temprana en muchos países. De esta manera, el desplazamiento del foco de atención desde las fases estables o residuales de la psicosis hacia los inicios de la misma está suponiendo una serie de innovaciones y avances, tanto en la evaluación y diagnóstico como en las modalidades terapéuticas y en la consiguiente reordenación de los servicios asistenciales.

Los estudios epidemiológicos más recientes han mostrado que los pacientes con mayor duración de la psicosis no tratada tienen peor respuesta al tratamiento farmacológico, mayor gravedad de síntomas positivos, síntomas negativos y peor funcionamiento global. Por otra parte, los estudios de neuroimagen también indican que un periodo prolongado de enfermedad no tratada produce anormalidades estructurales cerebrales más pronunciadas. Es por esto que la detección temprana en psicosis tiene como objetivo reducir la demora de tratamiento para mejorar el pronóstico y reducir la gravedad del trastorno.

La detección temprana y la aplicación del tratamiento específico más eficaz para cada fase inicial del trastorno son dos elementos que diferencian la intervención temprana de las formas habituales de asistencia actuales.

Cada vez existen más grupos en todo el mundo dedicados a establecer programas clínicos e iniciativas de investigación centradas en la psicosis temprana. Cada uno de estos programas tiene características particulares y rasgos propios en cuanto a las modalidades de tratamiento o los instrumentos de evaluación, pero la mayoría tiene una serie de elementos y objetivos en común: a) detectar de forma precoz nuevos casos; b) reducir el periodo de tiempo desde que el paciente presenta una sintomatología claramente psicótica hasta que recibe un tratamiento adecuado y c) proporcionar un mejor y continuo tratamiento en el «periodo crítico» de los primeros años de la enfermedad.

En el contexto de la prevención e intervención temprana, el trabajo con la familia puede ser crucial, ya que los familiares son los principales cuidadores informales y son una parte fundamental para la recuperación del paciente. La mayoría de las intervenciones familiares ofrecen psicoeducación y/o terapia familiar que ayudan a desarrollar estrategias de adaptación y afrontamiento, disminuir el estrés y la carga a largo plazo, así como mejorar la comunicación y la resolución de problemas.

Los programas de intervención en la psicosis temprana están habitualmente formados por equipos interdisciplinarios que proporcionan una amplia serie de servicios integrados que suelen incluir psicoeducación, manejo clínico de casos e intervenciones grupales. Las intervenciones específicas incluyen generalmente farmacoterapia, manejo de estrés, prevención de recaídas, apoyo y rehabilitación social y laboral, así como terapia cognitiva y familiar.

Dada la compleja etiología y manifestación clínica de la psicosis, los tratamientos para personas con psicosis incipiente deben ser adaptados individualmente a las necesidades específicas en lugar de aplicarlos homogéneamente a todos los pacientes por igual.

El desafío actual en la aplicación de intervenciones en la psicosis temprana consiste en: 1. conseguir adaptar aquellas modalidades de tratamiento que ya han demostrado su eficacia en las fases estables y residuales de la enfermedad o los inicios de la misma; 2. integrar y desarrollar nuevas formas de terapia que se adapten a las características específicas de cada una de las fases iniciales de la psicosis (fase prodrómica o de alto riesgo, inicio de la psicosis o primer episodio de psicosis y «fase crítica» o poscrisis) y 3. acecuar los tratamientos de manera individual en vez de aplicarlos de forma homogénea.

Los objetivos del presente artículo son: 1. presentar los conceptos básicos, la justificación y el estado de la cuestión del paradigma de detección e intervención temprana en psicosis; 2. hacer una revisión y presentar los principales programas de detección e intervención temprana en psicosis y 3. proporcionar una visión general de los enfoques psicoterapéuticos actuales en psicosis incipiente.

Palabras clave: Detección e intervención temprana, psicosis incipiente, tratamiento integrado y adaptado a las necesidades.

2.2.1.1. INTRODUCTION. A Conceptual Change: From Chronic Schizophrenia to Early Psychosis

Schizophrenia-spectrum disorders usually have a chronic and episodic course that results in impairment of all life domains. Patients frequently require hospitalization and many are unable to return to independent functioning in residual periods. Disorders typically start in late adolescence, disrupting patients' transition into adulthood (Yung et al., 1996; McGorry et al., 2003). Pharmacological and psychosocial treatments provide symptom relief, but there is not a cure for schizophrenia and many patients suffer chronic impairment, which has huge social and economic costs.

In recent years there has been increasing confidence that preventive intervention in psychotic disorders might be a realistic proposition in clinical settings (Birchwood et al., 1998;

McGorry et al., 1998). International interest has grown over the past 15 years in the prognostic potential of early identification and intervention in the prodromal and first-episode phases of psychosis, assuming that it could at least help to improve the course of illness, reducing its long-term impact (Corell et al., 2010). This is consistent with a recently adopted staging model in psychiatry, which emphasizes that less differentiated early phases of mental illnesses may benefit from a broader spectrum of and simpler treatments, allowing young people to receive the help they need in a timely manner, with the potential for improved outcomes across several fronts (McGorry et al., 2010). Thus, early intervention programs have been initiated worldwide, beginning with McGorry and colleagues (1996) in Australia and then moving to the United States and Europe shortly thereafter.

The early psychosis movement focused at first on the timely recognition and phase-specific treatment of first-episode psychosis (FEP). However, it was also recognized that for most patients a prolonged period of attenuated symptoms and impaired functioning precedes FEP (Yung et al., 1996). Much of the disability associated with the psychotic disorders, particularly schizophrenia, develops long before the onset of frank psychosis and is difficult to reverse even if FEP is successfully treated (Hafner et al., 2003). This pre-onset period of illness has been termed the “prodromal phase”, characterized by various mental state features, including non-specific symptoms such as depressed mood and anxiety, negative signs and symptoms as well as sub-threshold or attenuated psychotic symptoms. Accordingly, the putative prodromal symptoms and signs can be divided into those that are more distal to the onset of psychosis (*early prodrome*) and those more proximal to the onset of psychosis (*late prodrome*) (Schultze-Lutter et al., 2010b). Nevertheless, the prodrome is a retrospective concept which cannot be deemed to have occurred until the onset of full-blown psychotic symptoms indicative of definitive psychotic disorder, when the opportunity for preventing onset has passed (Woods et al., 2009; Yung et al., 1996).

The possibility to monitor prospectively those people at heightened risk for developing FEP lies in the new identification and follow-up of such population who demonstrate clinical

high risk factors for subsequent psychosis, established as “at-risk mental state” (ARMS) and “ultra-high risk” (UHR) (Yung et al., 2004).

The first study using UHR criteria found a transition rate of 40% to full-threshold psychotic disorder within 1 year, despite the provision of needs-based psychosocial intervention and antidepressant treatment where indicated (Yung et al., 2003a). This finding has subsequently been replicated by several groups internationally (Mason et al., 2004; Miller et al., 2002), including the recent multicentre North American Prodromal Longitudinal Study (NALPS),[15] which reported an average 1-year transition rate of 36.7% in UHR subjects who did not receive antipsychotic treatment. These results indicated that the UHR criteria are valid and reliable for predicting psychosis onset in this population (McGorry et el., 2010).

Unlike the predominant UHR approach, that only takes into account the severity of positive symptoms for meeting UHR criteria, the Hillside Recognition and Prevention (H-RAP) Program in New York[16] takes into account specific combinations of cognitive, academic and social impairments and disorganization/odd behavior.

2.2.1.2. EARLY DETECTION METHODS

Yung et al (2005) were the first to develop operational criteria to detect UHR patients, resulting in the Comprehensive Assessment of at Risk Mental State (CAARMS). They distinguished three distinct high-risk groups to identify and follow prospectively the rate of conversion to psychosis: 1) *attenuated positive symptoms (APS)*; 2) frankly psychotic positive symptoms that appear too brief and too intermittently to constitute a fully psychotic syndrome (*brief limited intermittent psychotic symptoms,* BLIPS); and 3) *vulnerability group*, characterized by functional decline in persons at risk for psychosis (because of meeting criteria for schizotypal personality disorder or having a first-degree relative with a psychotic disorder). Moreover, Miller, McGlashan and colleagues developed the Structured Interview for Prodromal Syndromes (SIPS) and the companion Scale of Prodromal Symptoms (SOPS) (Miller et al., 2003a), which have become the prevailing prodromal instrument in North

American studies, while the CAARMS has a predominating influence in Australia and many studies in Europe.

A different approach to early recognition was taken by German research groups, resulting in a set of criteria that are known as self-perceived cognitive and perceptual deficits, or “basic symptoms”, characterized by subjective disturbances of self-perception, stress tolerance, thought organization, and social and nonverbal interactions that are generally not observed by others (Shultze-Lutter, 2009). The German concept of basic symptoms has been operationalized in the Schizophrenia Pronennes Instrument Adult Version (SPI-A) (Schultze-Lutter et al., 2007) and recently adapted for child and adolescent population, (the Schizophrenia Proneness Instrument, Child and Youth version- SPI-CY) (Schultze-Lutter et al., 2010b).

2.2.1.3. Rationale of early psychosis intervention

A key rationale for the early intervention paradigm has been the association between prolonged illness duration and poor outcome in the psychotic disorders. On the one hand, the duration of untreated psychosis (DUP) is negatively associated with the long-term symptomatic and functional outcomes in schizophrenia (Perkins et al., 2005). Neuroimaging studies have also indicated that prolonged untreated illness is associated with more pronounced structural brain abnormalities, while this is less prominent earlier in the course of the disorder (Keshavan et al., 2007). On the other hand, research indicates that cognitive functioning deteriorates steeply before psychotic symptoms fully manifest (Caspi et al., 2003). Thus, interventions delivered during the early phases of illness manifestation are believed to help preserve the individual’s overall functional ability by reducing DUP and/or addressing the deterioration of functioning before FEP (Liu et al., 2010).

Naturally, early detection raises important ethical issues (Heinimaa et al., 2002) as 60% or more ARMS will not, even without treatment, develop psychosis (Lewis et al., 2006). However, it must be reminded that psychotherapy has been suggested as one approach for

mitigating this problem by offering safe treatments (Ruhrmann et al., 2009) allowing delaying the onset of psychosis or ameliorating its severity once it begins, and thus, it could also be unethical not to provide treatment to help-seeking or already disturbed individuals.

Moreover, the role of family work in early psychosis can be crucial given that relatives are the main informal caretakers of persons with mental health problems. In particular, relatives of schizophrenia patients report burden and distress, anxiety, depression and economic strain (Barrowclough et al., 1996). High Expressed emotion (EE) (Leff and Vaughn, 1985), which comprises over-involvement, criticism and hostility, has been shown to be a robust predictor of relapse in both chronic and FEP patients (Álvarez-Jiménez et al., 2010; Butzlaff et al., 1998). Even though it has been less studied in the early phase of psychosis, some studies have shown that high EE is already present in early psychosis (McFarlane et al., 2007). Given that the majority of ARMS and FEP individuals are adolescents or youngsters, investigation of family risk and protective factors would be essential for the design of developmentally appropriate early interventions (Schlooser et al., 2010).

2.2.1.4. Main Early Detection and Intervention Programs

A clearer framework for guiding, designing, and evaluating preventive interventions in mental disorders has been developed. As a consequence, a series of research projects and real-world services systems are being created. Additionally, several influential international figures and research groups have developed and cooperated in disseminating a more optimistic set of ideas concerning early intervention in psychosis (Birchwood et al., 2002; Gleeson and McGorry, 2005; Martindale et al., 2009)

The focus on specific treatments aimed at preventing progression to psychosis or promoting recovery in those who have experienced a psychotic episode has tended to be classified into 3 main categories: 1) prodromal or “high-risk” phase; 2) onset or FEP; 3) post-

psychosis phase, also known as “critical period”, covering the period following recovery from FEP up to five years subsequently (McGorry, 2002b).

Most groups working with the UHR population have attempted to engage patients in various psychological interventions using a recovery model of treatment. These interventions include case management, individual therapy, psychoeducation and Cognitive-Behavioral Therapy (CBT), multifamily support groups and supported education and employment Bhangoo and Carter, 2009). However, specific family interventions, such as problem solving and communication skills training, have also been suggested as possible interventions that may improve the functional prognosis of young people at UHR for psychosis (O’Brien et al., 2009). The main early detection and intervention services and research programs are presented in Table 1. Given that each program has numerous publications, table 1 only shows the references of those articles that describe the programs and those with the most recent findings. For more information, we also include some of the available websites of the programs.

Table 1 Main international early detection and intervention clinical settings and research programs.

CLINICAL SETTINGS				
PROGRAM	AIMS	METHOD	INTERVENTION	MAIN FINDINGS
Buckingham Integrated Mental Health Care Project (1984-1988) (Fallon et al., 1998) Buckinghamshire, England	Pioneering study in primary prevention; first to organize a very early detection of psychosis.	*Design:* Prospective clinical trial *Sample:* Patients with possible prodromal symptoms identified by the 10-question screening (10-QS) (Fallon et al., 1996).	Low-dose medication, crisis-orientated family intervention, with an emphasis on problem solving, social skills training and education about the nature of schizophrenia.	A 10-fold reduction in the annual incidence of schizophrenia, from 7.4/100 000 to 0.75/100 000 total population, was achieved.
The Early Detection and Intervention Evaluation (EDIE) trial (Morrison et al., 2002; 2007) United Kingdom (UK) www.psych-sci.manchester.ac.uk/edie2	To identify an indicated high-risk group and randomly allocate participants to a psychological intervention or a monthly monitoring condition.	*Design:* A randomized controlled trial *Sample:* People at high risk of psychosis using CAARMS criteria (Yung et al., 2005).	Psychological intervention (cognitive therapy), or a monthly monitoring condition.	Cognitive therapy appears to be is an efficacious intervention for people at high risk of developing psychosis.
The Lambeth Early Onset (LEO) and Outreach & Support in South London service (OASIS) (Power et al., 2007) London, UK	1. To reduce the delays that young people with psychosis experience; 2) to provide intensive follow up for 2 years to maximize their chances of a full recovery to normal functioning; 3) to minimize the potential for relapse during the critical first years; and 4) to reduce the distress and burden on carers.	*Design:* Prospective clinical trial *Sample:* Young people experiencing FEP and their carers.	Intensive case management with a range of psychosocial interventions focusing on recovery and relapse prevention. Specific intervention includes CBT therapy, group interventions, carer support and psychoeducation groups, and pharmacotherapy. OASIS services are also part of a network of 15 early intervention services which uses standard clinical audit system evaluation.	Compared to standard service, patients' delays in accessing treatment are less, and outcomes at 18 months are better.
The Birmingham Early Intervention Service (EIS) (Lester et al., 2007) United Kingdom www.bsmhft.nhs.uk	To support younger people through the critical early phase of FEP.	*Design:* Prospective clinical *Sample:* FEP patients.	Pharmacological treatment at low doses, information, education and work support and support to families.	This service has played a crucial role in the development of the UK National Health Service's plan for radical reform of the mental health system, which involves, among other measures, the creation of 50 specialist early intervention services for the treatment and active support in the community of these patients and their families.
RESEARCH PROGRAMS				
PROGRAM	AIMS	METHOD	INTERVENTION	MAIN FINDINGS
The Detection of Early Psychosis (DEEP) (Salokangas et al., 2004) Turku, Finland www.med.utu.fi/tutkimus/tutkimusprojektit/psykiatria3.html	To describe psychopathology and deficiences in neuropsychological, neuroimaging and neurophysiological examination of subjects vulnerable to psychosis.	*Design :*Prospective and longitudinal study *Sample:* Several groups are selected for a screening of prodromal symptoms (SIPS-SOPS criteria[18]).	-	All the patients are currently being followed-up and no preliminary data are available.

Table 1 Main international early detection and intervention clinical settings and research programs (continued).

The European Prediction of Psychosis Study (EPOS) (Klosterkötter et al., 2005; Ruhrmann et al., 2010) Germany, Finland, The Netherlands, UK and Spain, the study is carried out in Cologne, Berlin, Turku, Amsterdam, Birmingham and Manchester. www.epos5.org	Is the first European multicentre investigation focusing on early detection of persons at risk for psychosis.	*Design:* Prospective multicenter, naturalistic field study. *Sample:* Persons between 16 and 35 years with the UHR criteria use by Yung (2005) and Miller[18] groups. Includes a comprehensive baseline assessment and two follow-ups, at 9 and 18 months.	Psychological and psycho-pharmacological treatment.	The instantaneous incidence rates (iIRs) of transitions to psychosis were 14% after 12 months and 19% after 18 months. The extent and course of EPOS transition rates are consistent with recent reports of lower 12-month transition rates and of a further progression of rates beyond 12 months.
The North American Prodrome Longitudinal Study (NALPS) (Addington et al., 2007) United States www.napls.psych.ucla.edu	To establish consortium of prodromal psychosis research centers and Integrate database.	*Design:* Collaborative multisite investigation, longitudinal database. *Sample*: Non-psychotic subjects enrolled between 1998 and 2005.	Each study of NALPS has its specific type of intervention.	The NALPS represents the largest sample of prospectively followed at risk subjects worldwide and will be used to explore a series of questions related to prodromal psychosis.
CLINICAL SETTINGS WITH RESEARCH PROGRAMS				
PROGRAM	**AIMS**	**METHOD**	**INTERVENTION**	**MAIN FINDINGS**
Early Psychosis Prevention and Intervention Centre (EPPIC) (McGorry et al., 1996) Melbourne, Australia www.eppic.org.au	1. To provide both early detection and specialized treatment for early psychosis and treatment-resistant psychosis; and 2) to evaluate the effectiveness of the EPPIC program on 12 month outcome in FEP, in contrast to the previous model of care.	*Design:* Prospective clinical trial with historical control group. *Sample:* Patients with onset of psychosis between the ages of 16 and 30 using CAARMS criteria (Yung et al., 2005).	Providing necessary education, offering support and attaining a shared explanatory model and intervention plan with the patient and their family. Combined pharmacological, psychological, family and social interventions, which focus on managing triggers and promoting resilience.	During the 1-year follow-up period the EPPIC sample experienced significantly fewer admissions, had shorter periods as in-patients and had a reduction in both acute and post-acute levels of neuroleptic dosage. The patients also had significantly better Quality of Life Scores (QOS) and significantly less negative symptoms at follow-up. This effect was strongest for patients with a DUP of 1–6 months.
The Personal Assessment and Crisis Evaluation Service (PACE) (Yung et al., 2007a) Melbourne, Australia www.cp.oyh.org.au	1) To improve understanding of the neurobiological and psychosocial processes during the pre-psychotic phase and contribute to the onset of acute psychosis; 2) to develop psychological and medical interventions and evaluate their safety and efficacy; 3) to establish an accessible and appropriate clinical service specifically for young people at risk of psychosis.	*Design:* Prospective longitudinal study. *Sample:* Patients between the ages of 16-30 identified as UHR for developing a psychotic disorder using CAARMS criteria (Yung et al., 2005).	Combined psychological therapy/medication intervention in reducing pre-psychotic symptomathology and delaying or preventing the onset of psychosis.	The results seem to indicate that psychological and psychosocial interventions, either alone or in combination with pharmacotherapy, may be effective in at least delaying, if not preventing, the onset of a psychotic disorder.

Table 1 Main international early detection and intervention clinical settings and research programs (continued).

The Early Detection and Intervention Programme of the German Research Network on Schizophrenia (GRNS)[53] (Bechdolf et al., 2005) Cologne, Bonn and Düsseldorf	To promote help-seeking and engagement with early intervention services for individuals at-risk of psychosis.	*Design:* Longitudinal Study. *Sample:* Young people suffering from possible pre-psychotic symptoms using the Early Recognition Inventory (ERIraos) (Maurer et al., 2004).	Comprehensive cognitive behavioural therapy has been developed for patients in the early initial prodromal state. For patients in the late initial prodromal state the atypical neuroleptic amisulpride is explored. Both interventions are evaluated in randomised controlled trials using clinical management as the control condition.	The GRNS Early Detection and Intervention programme including awareness campaigns and a two-stage screening approach, appears to be feasible and effective in recruiting at-risk individuals with putatively prodromal symptoms for interventions in the initial prodromal phase.
The Early Treatment and Intervention of Psychosis (TIPS) project (Larsen et al., 2006) Rogaland County, Norway; Oslo, Norway; and Roskilde County, Denmark www.tips-info.com	To test whether an earlier treatment in FEP can change the natural course of the disorder.	*Design:* Multicenter prospective and longitudinal study *Sample:* FEP-affective psychosis, assessed with the same rating instruments at baseline, 3 months, 1, 2 and 5 years.	Antipsychotic treatment, weekly supportive psychotherapy and psychoeducational multifamily group treatment every second week.	To our knowledge, this study is the first to demonstrate a reduction of DUP in a representative sample of FEP patients. Early detection of psychosis is both possible and important even though it was not found obvious effect on positive symptoms during the first year of treatment.
Early Treatment of Pre-psychosis (TOPP) project (it is part of an ongoing international multisite TIPS study) (Larsen et al., 1999) Stavanger, Norway.	To study whether patient to define prodromal states develop psychosis within a 5-year follow-up period.	*Design:* Longitudinal and prospective study *Sample:* Patients at risk to develop psychosis according to SIPS/SOPS scales (Miller et al., 2003a).	Suportive psychotherapy without use of antipsychotics	At 2006, 30 patients were included; during the first year of follow-up 5 cases have developed psychosis which equals 17%.
Calgary Early Psychosis Program (EPP) (Addington et al., 2001, 2011) Calgary-Canada) www.albertahealthservices.ca/services.asp?pid=service&rid=1003859	1. To identify early psychotic illness, reduction in the delays in initial treatment, reduction of secondary morbidity, reduction of frequency and severity of relapse, promotion of normal psychosocial development; and 2) reduction of burden's family.	*Design:* Prospective clinical trial and longitudinal study. *Sample:* FEP and their families.	Case management, psychiatric medication, CBT, group therapy and family interventions.	Over the 2 years it demonstrates that family intervention can be effective in a real clinical situation and represents an important component of any program for early psychosis. There were no differences between the two treatment groups. However, the improvement in attenuated positive symptoms was more rapid for the CBT group.
The early detection and assertive community treatment of young persons with untreated psychosis (OPUS) (Jorgensen et al., 2000; Bertelsen et al., 2008)) Denmark	This study in Denmark has established early detection teams in one study sector and aims at comparing with 'detection as usual' in the other study sector.	*Design:* Prospective follow-up study *Sample:* Young persons with untreated psychosis	Integrate treatment includes individual case manager and antipsychotic medication, psychoeducational family treatment, social skills training and assertive community treatment.	The initial findings of the OPUS study suggest that better adherence to treatment is possible. The benefits of the intensive early-intervention program after 2 years were not sustainable, and no basic changes in illness were seen after 5 years from the start of the program.
The Prevention Through Risk Identification, Management, and Education (PRIME) (McGashan et al., 2003) New Haven, Connecticut, USA www.camh.net	To test in a double-blind study whether early treatment with an atypical antipsychotic compared to placebo can prevent or delay the onset of psychosis.	*Design:* Double-blind controlled trial *Sample:* Patients who are judged to be at risk for psychosis according to SIPS/SOPS scales (Miller et al., 2003a).	Randomization to olanzapine or placebo (double-blind), individual and family intervention, and psychosocial intervention (stress management and problem-solving skills training)	Preliminary data on the first 35 patients who are judged to be at risk for psychosis report that 24 patients have been randomized into the clinical trial. The conversion to psychosis rate as at January 1, 2000 is 33%.

Table 1 Main international early detection and intervention clinical settings and research programs (continued).

The Recognition and Prevention of Psychological Problems (RAP) (Cornblatt et al., 2002) New York, USA www.northshorelij.com/NSLIJ/RAP	To prevent severe mental illness focusing on patients with possible prodromal symptoms or early symptoms of psychosis.	*Design:* Prospective longitudinal study. *Sample:* Patients between the ages 12 and 25 with prodromal symptoms or early symptoms of psychosis according to RAP prodromal criteria (Cornblatt et al., 2002)	Pharmacotherapy with combination of psychotherapy (individual, family and group).	RAP treatment findings suggest that medications other than anti-psychotics may be effective for treating early prodromal symptoms, challenging the widely held hypothesis that antipsychotics should always be the first line preventive treatment.
The Prevention Program for Psychosis (P3) (Vallina et al., 2003) Torrelavega and Oviedo (Spain) www.p3-info.es	To assess the effectiveness of an intervention program for the prevention of psychosis, in the medium and long term. Research and intervention program have three stages: 1) the assessment of high risk personality traits; 2) the implementation of combined psychological and, where necessary, pharmacological therapies, and 3) a three-year post-treatment follow-up of cases with repeated measures.	*Design:* Prospective intervention and longitudinal study. *Sample:* Patients between 16-30 ages according to the CAARMS criteria. Participants are sequentially assigned to two groups: experimental group and control group.	Clinical protocol includes low-dose atypical antipsychotic drugs, CBT and psychoeducation with patients and relatives after the FEP. Controlled group received no intervention.	The detection of people at high risk of transition to psychosis is possible, and an early intervention in prodromal stages of the disorder produce great impact on the clinical symtomatology, the rate of transition to psychosis, and the recovery course.
Early Assessment Service for Young People with Psychosis (EASY)[63] (Tang et al., 2010) Hong Kong, Japan www3.ha.org.hk/easy/eng/service.html	To raise public awareness, to create an easily accessible chanel for service and to provide phase-specific intervention.	*Design:* Randomized controlled trial and longitudinal study. *Sample:* Young people aged 15-25 years with psychotic symptoms.	Psychosocial intervention provided by case management, intensive medical follow-up, enhanced rehabilitation services, intervention for secondary morbidity and CBT for drug resistant psychotic symptoms.	An average of over 600 patients enter the program for intensive treatment each year. Preliminary data suggest that early intervention in Hong Kong has been effective in improving the outcome of early psychosis.

2.2.1.5. FURTHER CONCEPTUAL DEVELOPMENTS AND THEIR POTENTIAL THERAPEUTIC APPLICATIONS

Psychotherapy takes place in diverse settings, with diverse groups, utilizing a bewildering array of techniques and styles informed by a vast array of theories and ideologies.

Usually, the most widely used interventions in psychosis are psychoeducation and CBT. A multitude of studies have demonstrated clear superiority of psychoeducational family interventions as compared with standard treatments (Bauml et al., 2006), and may be considered both clinically beneficial and costeffective (Breitborde et al., 2009). However, it is well known that psychoeducation by itself may not be sufficient to reduce the consequences of the experience of caregiving for a family member of a psychotic patient and, therefore, it has to be seen as a precursor and catalyst for subsequent complementary psychotherapeutic and psychosocial treatment strategies (Bauml et al., 2006).

Moreover, in regard to CBT, there are controversial results and its effectiveness is still not entirely clear for the early phases of psychosis (Kuipers, 2005), because only a small number of controlled trials of CBT in early stages of psychosis have been published (Erikson, 2010). In contrast to the substantial body of positive findings for individual CBT treatment of chronic psychosis, the majority of data on individual CBT for early psychosis is not favorable (Saksa et al., 2009).

On the other hand, the relative shortage of systematic research in modern dynamic models can give the impression of a lack of positive results, unlike CBT techniques (Cullberg and Johannessen, 2005). In fact, therapies based on psychodynamic traditions do not feature greatly in recent discussions, and more research is needed to provide relevant answers to the unsolved questions regarding their usefulness and efficacy in early psychosis intervention (Verdoux and Cougnard, 2003). However, this tradition probably has most extensive experience and elaborates conceptions for dealing therapeutically with cases in the borderline area of normality and psychosis (Heinimaa and Larsen, 2002).

No single type of therapeutic activity is ideal for all patients. Different subgroups of patients require different approaches within a broad spectrum of psychotherapeutic models. There is a clear need for a broader theoretical foundation of a set of therapeutic techniques, and also for the ability of greater depth and duration of therapy (McGorry, 2009). The stress-vulnerability model, along with advances in research of CBT, has been an opportunity for the fusion of dynamic and cognitive approaches, such as in the cognitive analytic Therapy (Kerr et al., 2008) or the psychodynamic-interpersonal psychotherapy (Guthrie et al., 1998; Gumley and Schwannauer, 2008), which rely less on direct interpretations than in conventional psychodynamic therapy and make more emphasis upon the patient-therapist relationship than in interpersonal therapy or CBT. Although the experience of these integrative models is still limited and requires more extensive and systematic formalization and evaluation, it seems that their recent development could play a useful role in the expansion of psychotherapeutic theory and practice (Kerr et al., 2008).

The current challenges for psychological interventions in early psychosis are: 1) to adapt treatment modalities that have been proven effective in stable and residual stages of the disease to early psychosis and, 2) to develop new forms of therapy tailored to the very specific characteristics of the early stages of psychosis (Vallina et al., 2007).

Given the complex etiology and clinical manifestation of psychosis, treatment packages for people experiencing early psychosis need to be individually tailored to specific needs rather than applied homogenously across early psychosis patients (Haddock and Lewis, 2005). One example is the work of the group leaded by Alanen et al. (1991) in Finland, which has created a need-adapted treatment approach, considering in each case both individual and interactional factors. They combine different forms of treatment in a flexible, individually designed intervention in order to take into account the needs of both patients and families, using psychoeducational principles in combination with medication, family intervention techniques, and individual psychotherapy.

Following this example, the Sant Pere Claver-Early Intervention Program (SPC-EPP) currently being developed in Barcelona, is an integrative model and need-adapted treatment always planned individually and taking into account the therapeutic needs of both patients and the people closest to them, based directly on the work of Alanen and collegues (1991). This clinical program is attached to an early psychosis research project conducted by the Universitat Autònoma de Barcelona (UAB), which is presented in Domínguez-Martínez et al. (2011a).

2.2.1.6 FINAL REMARKS

The shift in focus from the stable or residual phase of the illness towards its initial stages has led to a series of innovations and advances not only in assessment and diagnosis, but also in therapeutic approaches, with the consequent reorganization of care services and health policies (Vallina et al., 2007).

Increasing evidence suggests that it is possible both to identify individuals who may be at risk of developing psychosis, and subsequently reduce or delay the transition to psychosis, as well as to ameliorate the severity of non-psychotic symptoms and distress. Nevertheless, and despite this encouraging work and findings, more research is needed to provide relevant answers to the unsolved questions regarding the usefulness and efficacy of early intervention in psychosis (Verdoux and Cougnard, 2003).

Although recently published reviews on interventions in ARMS concluded that the effects of interventions are currently indecisive (McGorry, 2009), and even though the cost-effectiveness of early intervention is still scarce, recent evidence suggests that early intervention in psychosis may not only improve the clinical course of psychotic disorders, but also make such disorders less costly to treat compared with more traditional forms of care (Mihalopoulos et al., 2009). However, more research on the efficacy of early intervention is needed to demonstrate the extent to which the benefits persist in the longer term (Gaffor et al., 2009).

Bringing treatment more rapidly to a person who has become psychotic is in itself enough to justify early detection efforts (McGlashan and Johannessen, 1996). However, the highlighted ethical issues need to be considered seriously when working with young people thought to be at risk of developing psychosis, and further work is therefore needed to investigate and improve intervention options. Finally, despite the emphasis on prevention, it is also important not to forget those patients with a poorer prognosis in need of a long and continuous attention.

Salud Mental 2011;34:517-524

The need-adapted integrated treatment in Sant Pere Claver-Early Psychosis Program (SPC-EPP) in Barcelona, Spain

Tecelli Domínguez Martínez,[1,2] Elías Vainer,[3] Ma. Antonia Massanet,[3] Iván Torices,[3] Mercè Jané,[3] Neus Barrantes-Vidal[1,3,4,5]

Artículo original

SUMMARY

International interest has grown over the past 15 years in the prognostic potential of early identification and intervention in the prodromal and first-episode phases of psychosis. This focus is associated with increasing optimism about the benefits of implementing treatment as early as possible in the course of psychosis, at least to help improve the course of illness, reducing its long-term impact.

A clearer framework for guiding, designing, and evaluating preventive interventions in mental disorders has been developed. As a consequence, a series of research projects and real-world services systems are currently emerging. Additionally, several influential international figures and research groups have developed and cooperated in disseminating a more optimistic set of ideas concerning early intervention in psychosis.

The early psychosis programs developed worldwide have a number of common elements and goals: a) early detection of new cases, b) reducing the duration of untreated psychosis (DUP), and c) providing better and continued treatment during the «critical period» of the early years of the disorder.

Moreover, family interventions usually offer psychoeducation and/or individual and group family therapy, in conjunction with communication and problem solving training, which can help to develop coping strategies and reduce distress and burden.

Intervention programs in early psychosis are usually composed by interdisciplinary teams, providing a wide range of integrated services that typically include psychoeducation, clinical case management, and group interventions. Specific interventions generally include pharmacotherapy, stress management, relapse prevention, social and employment rehabilitation support, and cognitive and family therapy.

The current challenges in the implementation of psychological interventions in the early stages of psychosis are: 1. to adapt treatment modalities that have been proven effective in stable and residual stages of the disease to its early stages; 2. to develop new forms of therapy tailored to the specific characteristics of these early stages of psychosis; and 3. treatment packages need to be individually tailored to specific needs rather than applied homogenously across early psychosis patients.

One example of the integration of all these aspects is the «need-adapted integrated treatment» developed by Alanen et al. in Finland, which combines different forms of treatment in a flexible, individually designed intervention in order to take into account the needs of both patients and families.

Following the experience and work of Alanen et al., an Early Psychosis Program (EPP) currently is being developed in the Mental Health Services of Sant Pere Claver in Barcelona, addressed to young people between 14 and 35 years with at risk mental states (ARMS), first episode psychosis (FEP), and post-crisis stages of psychosis.

All cases included in the program are derived from various community resources (primary health care, schools, emergency services, and inpatient units for acute patients) and assessed exhaustively by the team to define the treatment plan for each case. The treatment modalities offered by the EPP are: individual and group therapy, unifamiliar and multifamiliar psychotherapy, psychoeducation and pharmacotherapy in those cases where necessary. Furthermore, there is an intensive community support for those patients who have difficulties engaging with mental health services. During the EPP all patients are monitored through weekly visits with their psychiatrist, psychologist, social worker and/or nursing staff.

The aim of this paper is to present and describe the integrated need-adapted treatment approach of the early psychosis program currently being developed in a specialized center in Barcelona (Spain).

Key words: Early detection and intervention, early psychosis, psychotherapeutic approach, need-adapted treatment.

RESUMEN

Los trastornos del espectro psicótico presentan un curso crónico y episódico que provoca alteraciones en todas las áreas de la vida, generando importantes grados de discapacidad, pérdida de funciones psicosociales, grandes costes económicos, una comorbilidad considerable y sufrimiento tanto para los pacientes como para sus familias. A pesar de que el tratamiento farmacológico y psicosocial ha cyudado a aliviar los síntomas y mejorar la calidad de vida, en

[1] Universitat Autònoma de Barcelona, Departamento de Psicología Clínica y de la Salud. Barcelona.
[2] Ministerio de Asuntos Exteriores y de Cooperación y la Agencia Española de Cooperación Internacional para el Desarrollo (MAEC-AECID).
[3] Fundació Sanitària Sant Pere Claver, Serveis de Salut Mental. Barcelona.
[4] CIBERSAM- Instituto de Salud Carlos III, Barcelona.
[5] University of North Carolina at Greensboro, USA.

Correspondencia: Neus Barrantes Vidal. Departament de Psicologia Clínica i de la Salut. Universitat Autònoma de Barcelona, 08193 Bellaterra (Barcelona). Tel.: +3493 581 3864. Fax: +3493 581 2125. E-mail: Neus.Barrantes@uab.cat

Recibido: 11 de enero de 2011. Aceptado: 9 de mayo de 2011.

muy pocas ocasiones se logra una recuperación satisfactoria en los niveles psicológico y funcional.

Durante los últimos 15 años, el optimismo creciente sobre la posibilidad de mejorar el pronóstico de la psicosis y alterar con ello el tradicional curso negativo de la enfermedad, ha producido una reforma sustancial en la práctica clínica y en el desarrollo de estrategias de intervención temprana en muchos países. De esta manera, el desplazamiento del foco de atención desde las fases estables o residuales de la psicosis hacia los inicios de la misma está suponiendo una serie de innovaciones y avances, tanto en la evaluación y diagnóstico, como en las modalidades terapéuticas y en la consiguiente reordenación de los servicios asistenciales.

Cada vez existen más grupos en todo el mundo que establecen programas clínicos e iniciativas de investigación centradas en la psicosis temprana. Cada uno de estos programas tiene características particulares y rasgos propios en cuanto a las modalidades de tratamiento o los instrumentos de evaluación, pero la mayoría comparte una serie de elementos y objetivos en común: a) detectar de forma precoz nuevos casos; b) reducir el periodo de tiempo desde que el paciente presenta una sintomatología claramente psicótica hasta que recibe un tratamiento adecuado (duración de la psicosis no tratada); y c) proporcionar un mejor y continuo tratamiento en el «periodo crítico» de los primeros años de la enfermedad.

En el contexto de la prevención e intervención temprana, el trabajo con la familia puede ser crucial, ya que los familiares son los principales cuidadores informales y son una parte fundamental para la recuperación del paciente. La mayoría de intervenciones familiares ofrece psicoeducación y/o terapia familiar que ayudan a desarrollar estrategias de adaptación y afrontamiento, disminuir el estrés y la carga a largo plazo, así como a mejorar la comunicación y resolución de problemas.

Los programas de intervención en la psicosis temprana están formados habitualmente por equipos interdisciplinarios que proporcionan una amplia serie de servicios integrados que suelen incluir psicoeducación, manejo clínico de casos e intervenciones grupales. Las intervenciones específicas incluyen generalmente farmacoterapia, manejo de estrés, prevención de recaídas, apoyo y rehabilitación social y laboral, así como terapia familiar y cognitiva.

El desafío actual en la aplicación de intervenciones en la psicosis temprana consiste en: 1. conseguir adaptar aquellas modalidades de tratamiento que ya han demostrado su eficacia en las fases estables y residuales de la enfermedad a los inicios de la misma; 2. integrar y desarrollar nuevas formas de terapia que se adapten a las características específicas de cada una de las fases iniciales de la psicosis (fase prodrómica o de alto riesgo, inicio de la psicosis o primer episodio de psicosis y «fase crítica» o poscrisis); y 3. adecuar los tratamientos de manera individual en vez de aplicarlos de forma homogénea.

Un ejemplo de la integración de todos estos aspectos es el «tratamiento integrado y adaptado a las necesidades» desarrollado por el grupo de Alanen et al. en Finlandia, que combina diferentes formas de tratamiento de una manera flexible y diseñadas en función de las necesidades de cada caso. Tomando como base el trabajo del grupo finlandés, actualmente se está llevando a cabo un Programa de Psicosis Incipiente (PPI) en la Fundació Sanitària Sant Pere Claver de Barcelona, destinado a jóvenes entre 14 y 35 años con estados mentales de alto riesgo (EMAR), primeros episodios de psicosis (PEP) y en la fase poscrisis psicótica. Los casos incluidos en el programa derivan de diversos recursos comunitarios (atención primaria, psicólogos de las escuelas, servicio de urgencias hospitalarios, unidad de agudos, etc.) y valorados exhaustivamente por el equipo asistencial para definir el tipo de tratamiento en función de las necesidades particulares del paciente y de su entorno. Las modalidades de tratamiento que ofrece el PPI son: terapia individual y grupal, psicoterapia unifamiliar, psicoterapia multifamiliar, psicoeducación y tratamiento farmacológico en aquellos casos que sea necesario. Además, se cuenta con un profesional que hace visitas a domicilio, da seguimiento y tratamiento asertivo comunitario a aquellos pacientes que tienen dificultades para acceder y mantener una vinculación con los servicios de salud mental. Durante el PPI todos los pacientes tienen visitas de seguimiento semanal con el psiquiatra referente, el psicólogo(a), trabajador(a) social y/o el personal de enfermería.

El objetivo del presente artículo es presentar y describir el tratamiento integrado y adaptado a las necesidades del Programa de Psicosis Incipiente-Sant Pere Claver (PPI-SPC) que se está llevando a cabo actualmente en un centro especializado de Barcelona (España).

Palabras clave: Detección e intervención temprana, psicosis incipiente, tratamiento integrado y adaptado a las necesidades.

2.2.2.1. INTRODUCTION

After decades of research, and despite advances in pharmacological and psychotherapeutic interventions, schizophrenia-spectrum disorders are still among the most debilitating disorders in medicine (Hegarty et al., 1994). Most patients suffer chronic impairment in all life domains, which has huge personal, social and economic costs (Corell et al., 2010).

In recent years there has been increasing confidence that preventive intervention in psychotic disorders might be a realistic proposition in clinical settings (Birchwood et al., 1997; McGorry, 1998). Early detection and intervention programs have been initiated worldwide,

beginning with Yung, McGorry and colleagues (1996) in Australia and then moving to the United States and Europe shortly thereafter.

A clearer framework for guiding, designing, and evaluating preventive interventions in mental disorders has been developed. As a consequence, a series of research projects and real-world services systems, which will steadily add to the evidence regarding the value of early intervention, are currently emerging. Finally, several influential international figures and research groups have developed and cooperated in disseminating a more optimistic set of ideas concerning early intervention in psychosis (Birchwood et al., 2002; Gleeson and McGorry, 2005; Martindale, 2009)

The focus on specific treatments aimed at preventing progression to psychosis or promoting recovery in those who have experienced a psychotic episode has tended to be classified into 3 main categories: 1) prodromal or “at risk mental state (ARMS)” phase; 2) onset or first episode psychosis (FEP); 3) post-psychosis phase, also known as “critical period”, covering the period following recovery from FEP to up to five years subsequently (McGorry, 2002b).

Most groups working with the ultra high risk (UHR) population have attempted to engage patients in various psychological interventions using a recovery model of treatment. These interventions usually include case management, individual therapy, psychoeducation, cognitive-behavioral therapy (CBT), multifamily groups, and also give support for education and employment (Bhangoo and Carter, 2009). Family interventions usually focus on individual and group work, psychoeducation and the development of coping strategies to help reduce distress and burden (Addington et al., 2005). However, specific interventions such as problem-solving and communication skills training have also been suggested as possible interventions that may improve the functional prognosis of young people at UHR for psychosis (O’Brien et al., 2009).

Given the complex etiology and clinical manifestation of psychosis, treatment packages for people experiencing early psychosis need to be individually tailored to specific

needs rather than applied homogenously across early psychosis patients (Haddock and Lewis, 2005). One example is the work of the group leaded by Alanen et al. (1991, 1997) in Finland, which has created a need-adapted treatment approach, considering in each case both individual and interactional factors. They combine different forms of treatment in a flexible, individually designed intervention, in order to take into account the needs of both patients and families, using psychoeducational principles in combination with medication, family intervention techniques, and individual psychotherapy. Based directly on the work of Alanen and collegues, there is an early intervention program currently being developed in a specialized center in Barcelona, which is presented below.

2.2.2.2. The Sant Pere Claver – Early Psychosis Program (SPC-EPP)

The Mental Health and Addictions Plan of the Department of Mental Health from the Catalonian Government promotes specific programs in order to serve young people with early psychotic disorders (PAE-TPI-*Programas de Atención Específica a los jóvenes con Trastornos Psicóticos Incipientes)*. The Early psychosis programs have been implemented in a few settings in Catalonia. One of these programs is set at the Mental Health Centers of the Sant Pere Claver sanitary foundation (SPC), whit a catchment area comprising two large districts of Barcelona, where 44.500 inhabitants are within the at-risk age group (14-35 years).

The SPC is composed of two Communitary Mental Health Centers for Adults (CSMA-Sants y CSMA-Montjuïc), one for adolescents and children (CSMIJ), and one Day Hospital (HD) for adolescents.

2.2.2.3. General aims of SPC-EPP

At the start of the SPC-EPP, Alanen and collaborators provided training to the clinicians directly involved in the program. Consistent with this formative experience and following the pioneering work of Yung, McGorry and colleagues (1996) and based on the

recommendations of a Clinical guide for early psychosis of the Spanish and Catalonia governments (Guía de Práctica Clínica sobre la Esquizofrenia y el Trastorno Psicótico Incipiente, 2009; Fòrum Salut Mental, Proposta de desenvolupament d'un model d'atenció als trastorns psicòtics incipient, 2006) the main aims of SPC-EPP are:

1. To identify within a short period of time people at high risk for developing psychosis and people with FEP.
2. To encourage ARMS and FEP individuals to seek and adhere to earlier effective help.
3. If possible, to provide psychological, pharmacological and psychosocial treatment *prior* to the onset of the frank psychotic symptoms, in order to prevent the onset of the full psychotic disorder and to minimize DUP, associated morbidity, stigma, and possible brain damage.
4. To intensify treatment of the FEP to a) optimize recovery; b) prevent relapse, social exclusion, and vocational disruption; c) reduce co-morbidity such as depression, substance abuse, and suicide.
5. To improve symptomatic and functional outcomes and reduce secondary morbidity to improve the quality of life of both families and patients.
6. To promote sensitization of General Practitioners (GPs) and coordination with different health services, as well as with scholar and social resources.

2.2.2.4. METHOD

2.2.2.4.1. *Inclusion and exclusion criteria.*

SPC-EPP inclusion and exclusion criteria are based on the standard criteria used in programs worldwide (See Table 1)

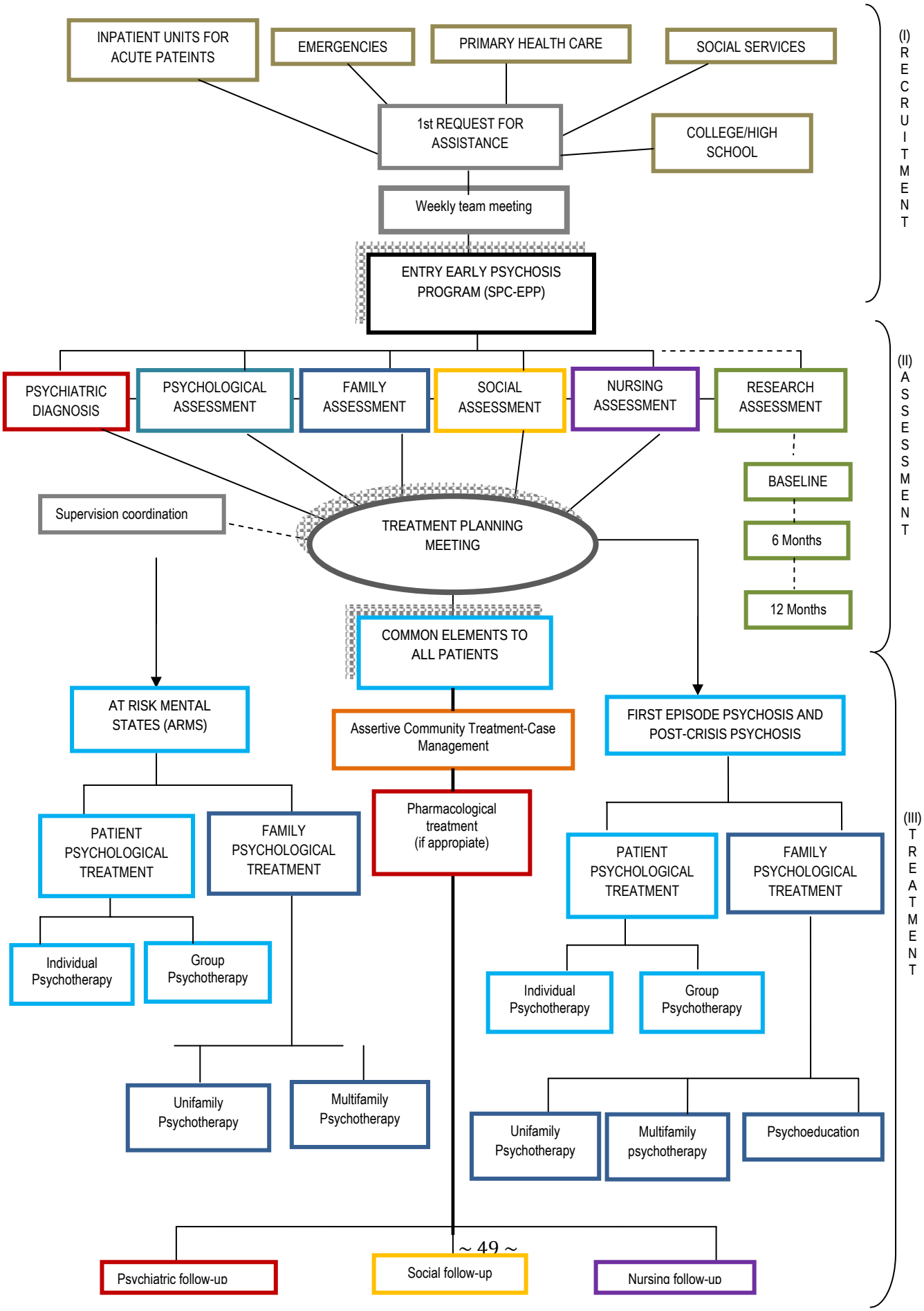
Table 1: Inclusion and exclusion criteria of At Risk Mental State (ARMS) and First-Episode Psychosis patients (FEP):

	At Risk Mental State (ARMS)	First- episode psychosis (FEP)
Inclusion criteria	1. Age between 14 and 35 years. 2. Meets criteria for one or more of the following groups based on Comprehensive Assessment of At Risk Mental State (CAARMS)(Yung et al., 2005) and Schizophrenia Proneness Instrument-Adult version (SPI-A) (Schultze-Lutter et al., 2007: 1. *Attenuated Psychotic Symptoms Group (APS):* substreshold, attenuated positive psychotic symptoms present during the past year; 2. B*rief Limited Intermittent Psychotic Symptoms Group (BLIPS):* episodes of frank psychotic symptoms that have not lasted longer than a week and have spontaneously abated; 3. *Trait and State Risk Factor Group*: family history of psychosis or schizotypal personality disorder with a significant decrease in functioning during the previous year. 3. IQ above 75	4. Age between 14 and 40 years. 5. Diagnosis of a first episode psychosis (FEP) according to DSM-IV. *6.* People who are in a psychotic post-crisis period, or the time span of five years after first episode (with a maximum of three crises, since above this number is no longer considered incipient psychosis). *7.* No current substance dependence *8.* IQ above 75.
Exclusion criteria	9. No evidence of organically based psychosis, 10. Does not meet criteria for psychosis currently, 11. Previous history of antipsychotic treatment (more than a week).	Previous history of antipsychotic treatment (without including the current one)

Abbreviations: DSM-IV: Diagnostic and Statistical Manual of Mental Disorders fourth edition; IQ: Intelligence Quotient.

2.2.2.4.2. *Paths to care and populations*

FIGURE 1. SPC-EPP protocol, paths to care, type of intervention and treated population



As shown in Figure 1, patients are referred to the program from a variety of communitary resources: primary health care (GPs), school psychologists, emergency services, and inpatient units for acute patients.

In order to increase the detection of potential ARMS cases, the SPC-EPP psychologists and psychiatrists visit weekly primary health care units. Also, nurses make regular visits to inpatient units of acute patients to detect FEP and promote their adherence to the program. As shown in Figure 1, after the first request for assistance, there is a *weekly team meeting* where it is evaluated whether the new cases fulfill the criteria for entering the program and assessment is carried out to determine the appropriate treatment.

2.2.2.4.3. Assessment procedures

As it can be seen in Figure 1 there are different types of assessment that have the goal of exploring the case in depth and defining the type of work to be done in each particular case (as outlined in Tables 2 and 3).

1. Psychiatric diagnosis: Initial clinical interview, detailed history, diagnosis and, if necessary, drug prescription (minimum dose) as established by the Clinical Guide of the Spanish Government[16]. Subsequently, the case is reported to the clinicians specifically involved in SPC-EPP for the general team meeting discussion.
2. Family assessment: There are at least 4 family interviews in which all family members are invited to attend with the patient. These interviews aim at analyzing the family status and yield an indication of treatment for both the patient and the family. Before the last interview, the case is discussed in the team meeting to tailor the treatment plan. There is always a feedback meeting with the family and the patient to inform them about the treatment plan, usually done after the case has been monitored and discussed in the *team weekly meeting*.

3. Social assessment: Since the first contact the social worker follows the case, initially weekly and then fortnightly, in order to help the patient to not disengage from studies or work.
4. Nursing assessment: For FEP, the nurse makes an initial contact with the patient before s/he is discharged from acute units (if applicable), and is also involved in following him/her up in the hospital if there is a relapse. Since the first contact with the service, the nurse performs an initial assessment of the patient's health and establishes an action plan including goals to achieve (general health advice to improve quality of life as personal hygiene, nutrition, personal care, etc.) always in accordance with the patient.
5. Nurses are also in charge of making blood extraction for health and genetics analyses.
6. Research assessment: It is undertaken by the research team independently of the treatment team. All patients are assessed prospectively: at baseline (at the moment of inclusion in the program), and at 6 and 12 months with standardized measures to assess changes across time on clinical, functional, psychological and neurocognitive factors. These results are always communicated to the professional responsible for each case in order to contribute in the design of the intervention.

2.2.2.5. Treatment Modalities

Following the work of Alanen and collegues (1991, 1997), known as "need-adapted treatment of psychodynamic orientation", the psychotherapeutic approach is based on the idea of "flexibility in accordance with the needs". Because of the heterogeneous nature of schizophrenic psychoses, the treatment of these patients must always be planned individually and on case-specific premises, taking into account the therapeutic needs of both the patients and the people closest to them (Alanen et al., 1991, 1997; 2009; Räkköläinen, 1991).

The psychodynamic approach used in SPC-EPP places emphasis on increasing self-knowledge and establishing a sense of psychotic experiences in the world within the person.

In addition, the main focus of the treatment process is the relationship between people and their environment.

2.2.2.5.1. The main principles of the need-adapted approach

Following Alanen et al (1991, 1997, 2009) the main principles of the need-adapted approach are:

1. *The therapeutic activities are planned and carried out flexibly and individually in each case.* This principle also implies that unnecessary treatment should be avoided.

2. *Examination and treatment are dominated by a psychotherapeutic attitude,* to understand what has happened and is happening to the patients and their relatives.

3. *The different therapeutic activities should support and not impair each other.* For that, the promotion of cooperation and division of tasks between members of the different staff categories and workers of the different units of a given catchment area is especially important.

4. *Quality of the process of therapy is clearly perceived* through the continuous assessment during the course and outcome of the treatment, which involves the possibility of modifying the therapeutic plans.

5. The *Outreach Assertive Community Treatment* is a key part of the SPC-EPP. It is focused on improving the therapeutic alliance and offering treatment in the community, giving intensive support and follow-up through home visits to all patients who have special difficulties in engaging with mental health service.

6. *Supervisory activities* should become an inseparable part of the therapeutic work.

As shown in Figure 1, patients of SPC-EPP can be treated with individual or group psychotherapy and treatment is also always offered to relatives. The specific modality varies according to the conclusions reached after the assessment and team consensus. We describe in Tables 2 and 3 the specific features and aims of each type of treatment possibilities for both patients (ARMS and FEP) and families. Family psychotherapy, specially

multifamily groups, are based on principles and work of Fulkes & Anthony (1964), Bion (1976), García Badaracco (2000) and Räkköläinen (1991).

In addition to the therapeutic modalities defined, all patients are visited and followed-up individually by the referent psychiatrist, psychologist, social worker, and nurse at least during the entire program (5 years). Also, the Outreach Assertive Community Treatment gives an intensive support and follow-up through home visits to all patients who have special difficulties in engaging with mental health service, in order to improve their therapeutic alliance and offer them treatment in the community.

2.2.2.5.2. Pharmacotherapy

In ARMS patients, pharmacological treatment is prescribed only if necessary, for example, when there is a rapid deterioration, when there is a risk of suicide or a risk of aggression to others or to patients themselves.

In the case of FEP, it is recommended to prescribe the minimum antipsychotic dose that is needed to bring the patient's contact and communication abilities to a level that is optimal for the situation. In practice, this means notably lower doses and shorter periods of medication than is currently customary in treating schizophrenic patients, given that it has been shown that long-term antipsychotic medication with heavy dosage has adverse effects on the psychosocial prognosis of these patients (Alanen et al., 1991, 1997; Guía de Práctica Clínica sobre la Esquizofrenia y el Trastorno Psicótico Incipiente. Madrid: Plan de Calidad para el Sistema Nacional de Salud del Ministerio de Sanidad y Consumo, 2009; Lieberman, 1996; McGlashan et al., 2006; Woods et al., 2003).

Table 2. Description of individual and group psychotherapeutic treatments for patients.

TARGETS OF THERAPY:	ARMS AND FEP PATIENT	
	INDIVIDUAL PSYCHOTHERAPY	**GROUP PSYCHOTHERAPY**
AIMS	1) To promote therapeutic alliance 2) To improve the capacity of insight 3) To recognize the prodrome and identify high stress situations to prevent future decompensation 4) To understand psychotic symptoms and integrate them with the subject's experience 5) To encourage her/his emotional expression and to improve emotional management	1. To improve communication through contact with group members 2. To improve insight and adherence to treatment, both pharmacological and psychological 3. To promote awareness by sharing similar experiences with other patients, which helps them feel more accompanied in the recovery process 4. To find a sense of psychotic experiences in the world within the person 5. To promote the communication of his/her emotions and feelings about all his social and family relationships 6. To work with all the process that happened in the group because they serve to tolerate his/her own daily relationships
INDICATIONS	Patients who show some initial insight into the connection between their symptoms and their life situation, as well as patients with some ability to recognize their difficulties, and have motivation to address them and the capacity for commitment and maintenance of the therapeutic alliance.	1. All patients included in the program that have a minimal capacity to keep a relationship. 2. There are two different groups for ARMS and FEP, the aims are the same but tailored to each population (e.g. in the ARMS group there is not a focus on psychosis and the nature of problems is different).
CONTRA-INDICATIONS	1. Intense paranoid and narcissistic features that prevent the ability to relate. 2. In cases where there is an active consumption of substances, it is considered the need for referral to specialized resources.	Acute states that require great restraint.
FREQUENCY	45 minutes weekly or fortnightly depending on the characteristics of each patient.	1 hour weekly and duration of over 2-3 years

Abbreviations: ARMS: At Risk Mental States;FEP:First Episode.

Table 3. Description of psychotherapeutic treatments for family and patients.

TARGET OF THERAPY:	ARMS AND FEP PATIENT AND THEIR RELATIVES		FAMILY
	UNIFAMILY GROUP	**MULTIFAMILY GROUP**	**PSYHOEDUCATION**
AIMS	1. To clear up the conflicts that interfere in the communication between all family members 2. To identify possible triggers or risk factors of a possible relapse; 3. To improve treatment compliance.	1. To help families to improve communication between their members 2. To enable patients and their families to identify early relapse signs and symptoms 3. To share experiences between the different families and understand the mental functioning of their children	1. To establish a bond of trust between the family and different professionals; 2. To provide basic information about psychosis and its management; 3. To help the family recognize the impact that the illness process will have in family dynamics; 4. To enable families to identify early relapse signs and symptoms to prevent future crises; 5. To collect and treat the emotions that could difficult the relation between family and patient (guilt, fear, reproach, distress, etc.).
INDICATIONS	Cases in which the pathology of the family system is very serious and will be interfering with the course the disease.	All relatives of patients included in SCP-EPP. The group is always active (permanent) and open to everyone, but each participant can attend a maximum of five years, which is the duration of the early intervention program.	It is only applied to FEP and post-crisis psychosis relatives.
CONTRA-INDICATIONS	None	Families considered unstructured or that have severe difficulties to maintain a dialogue between its members.	None.

Abbreviations: ARMS: At Risk Mental States;FEP:First Episode Psychosis;SPC-EPP:Sant Pere Claver-Early Psychosis Program.

2.2.2.6. Sant Pere Claver Research Project (SPC-RP)

There is a joint research project between SPC and the Autonomous University of Barcelona (UAB) on the SPC-EPP: "*The Interaction between Daily-Life Stressors and Subjective Appraisals of Psychotic-Like Symptoms in the Psychosis Prodrome during One Year Follow-up: Ecological and Dynamic Evaluation with the Experience Sampling Methodology and Analysis of Gene-Environment (Stress) Interactions*" (P.I: N. Barrantes-Vidal), funded by "*La Fundació la Marató TV3*", a charity foundation focused on scientific research of diseases that currently have no definitive cure.

This project prospectively examines dynamic relations between daily-life stressors and psychotic-like symptoms in ARMS and FEP individuals, and will delineate disorder and resilience trajectories over one year using Experience Sampling Methodology (ESM). ESM is an intensive research method that can be used to study emotional reactivity to stress through a structured diary technique, assessing cognition, affect, symptoms and contextual factors in daily life (.Myin-Germeys and Van os, 2007). The participants are assessed on clinical, functional, neurocognitive, and genetic assessments at baseline, 6 months and 1-year follow-up. Preliminary results from this study have recently presented (Domínguez-Martínez et al., 2010.a; Domínguez-Martínez et al., 2010.b; Vilagrà et al., 2010).

2.2.2.7. FINAL REMARKS

Our program is designed to meet the special needs of young people in the early stages of psychosis, people recovering from early psychosis and their families. We offer early treatment including both individual and group therapies designed to meet specific needs. Through our family intervention component, families are actively included and involved in the program. Finally, we have an ongoing evaluation of patients' outcomes; these results will be detailed elsewhere.

The training in early psychosis that has been given to the clinicians facilitated the detection and led to greater inclusion of cases in the program. Thus, the number of cases treated in SPC-EPP has tripled since 2007.

In our experience, the integration of psychodynamic concepts can have a significant contribution to contemporary approaches, especially if different techniques are used as an integrated model that emphasizes the tailoring of treatments according to the patients and family needs.

Regarding the early psychosis intervention, the ethical issues need to be seriously considered. The establishment of first contact with young psychotic patients requires a high level of experience and professionalism, and the task of detection and assessment should preferably be performed by a specialized team (Jorgensen et al., 2000).

3. CHARACTERIZATION OF AT-RISK MENTAL STATES AND FIRST-EPISODE OF PSYCHOSIS

3.1. Definitions of the high risk status

3.1.1. The psychosis prodrome

In clinical medicine, a *prodrome* refers to the early symptoms and signs of an illness that precede the characteristic manifestations of the acute, fully developed illness. In schizophrenia and other psychotic disorders there are usually a “prodomal” or “pre-psychotic” phase of illness in which a change from premorbid functioning occurs (Yung et al., 1996). Essentially, the term refers to a period of pre-psychotic disturbance, representing a deviation from a person's previous experience and behavior, usually defined as the period from first noticeable symptoms to first prominent psychotic symptoms (Beiser et al., 1993). It may be lengthy, lasting on average between 1 and 5 years (Loebel et al., 1992; Häfner et al., 1993), and is often associated with substantial levels of psychosocial impairment and disability (Jones et al., 1993; Yung and McGorry, 1996).

Detailed studies of psychotic prodromes revealed that this period is characterized by various mental state features, including nonspecific symptoms such as depressed mood and anxiety, sleep disturbance, irritability, social withdrawal and attenuated (or sub-threshold) psychotic symptoms typically occurring late, just prior to the development of full blown psychotic symptoms (Yung and McGorry, 1996). Besides, negative and ‘basic’ symptoms have also been described in prodromes. Basic symptoms refer to subjectively experienced abnormalities in the realms of cognition, attention, perception and movement and are thought by many to be important precursors of schizophrenia (Klosterkötter et al, 1997).

The psychotic prodrome is potentially important for early diagnosis and management of psychotic disorders, early detection of relapse, prospective studies of high-risk individuals, and prognosis (Yung and McGorry, 1996). However, the concept of prodrome and its

implications for early diagnosis and treatment runs into problems due to the wide variability between individuals and the lack of specificity of many of its features. That is, many prodromal symptoms and signs are non-specific and could be the result of a number of conditions, such as major depression, substance misuse and physical illness, as well as a psychotic prodrome. Because of this lack of specificity, there are problems with using prodromal symptoms and signs alone to identify people thought to be at incipient risk of onset of psychotic disorder as this would result in a high false positive rate, i.e., many people not actually at risk of psychosis would be falsely labeled as such (Yung et al., 2007b). Even attenuated or isolated psychotic symptoms may not necessarily progress to a frank psychotic disorder, as these are now known to be quite common in the general population (Tien, 1991; Van Os et al, 2001). So far, however, the diverse range of symptoms and signs manifest in a psychotic prodrome, has only limited predictive power in relation to subsequent psychosis, (McGorry, 1998).

On the other hand, as in clinical medicine, prodrome is a retrospective concept, diagnosed only after the development of definitive symptoms and signs and cannot be appropriately applied to prospective investigations (Yung and McGorry, 1996). Thus, some added criteria are needed to identify those most likely to be at highest risk (Yung et al., 2007b). The term ‘‘at risk mental states’’ (ARMS) has been suggested instead, implying that a subthreshold syndrome can be regarded as a risk factor for subsequent psychosis, but that psychosis is not inevitable (McGorry and Singh, 1995). Therefore, indicated prevention will need to be based upon the delineation of ARMS features with increased sensitivity and specificity for subsequent psychosis (Yung et al., 2003a).

3.1.2. At Risk Mental States (ARMS) and Ultra High Risk (UHR) criteria

Yung et al (2005) were the first to develop operational criteria to define three groups thought to be at Ultra High Risk (UHR) of developing a psychotic disorder in the near future

(‘‘prodromal’’) or also called At-Risk Mental States (ARMS). Having defined these UHR criteria, the next step was to develop an instrument which could include all dimensions of psychopathology needed for the definition. That is, one that could measure intensity, frequency, duration and recency of subthreshold psychotic symptoms. The Comprehensive Assessment of At-Risk Mental States (CAARMS) was designed for this purpose and additionally, also measured other symptoms thought to be indicative of imminent psychotic disorder such as negative, dissociative and basic symptoms (Klosterkötter et al., 1992, 1997). The CAARMS has two functions: (i) to provide a comprehensive assessment of psychopathology thought to indicate imminent development of a first-episode psychotic disorder; and (ii) to determine if an individual meets UHR status based on criteria derived from the CAARMS assessment.

The current and widely accepted standards for the UHR criteria are identified as fitting into one of three categories: 1) patients with Attenuated Positive Symptoms (APS): have experienced sub-threshold, attenuated positive psychotic symptoms during the past year; 2) patients with Brief Intermittent Psychotic Symptoms (BLIPS): have experienced episodes of frank psychotic symptoms that have not lasted longer than a week and have been spontaneously abated; 3) trait and state risk factor group: have schizotypal personality disorder or a first-degree relative with a psychotic disorder and have experienced a significant decrease in functioning during the previous year. Besides, other criteria have also been developed to define the onset of frank psychotic disorder (Yung et al., 2005), which are not identical to DSM–IV criteria, but are designed to define the minimal point at which antipsychotic treatment is indicated. This definition is arbitrary, and is defined by the persistence of frank psychotic symptoms for over 1 week (Yung and McGorry, 2007).

Alternatively, Miller et al., (2002) modified the UHR criteria to produce the Criteria of Prodromal Syndromes (Woods et al., 2001), based on the three groups criteria defined by CAARMS (APS, BLIPS or genetic risk plus functional deterioration), but with some modifications incorporated (e.g., referencing a new rating scale, requiring recent onset or

change) with intended to increase the reliability of identification of positive symptoms and to improve identification of patients at imminent risk for schizophrenic psychosis (Miller et al., 2002).

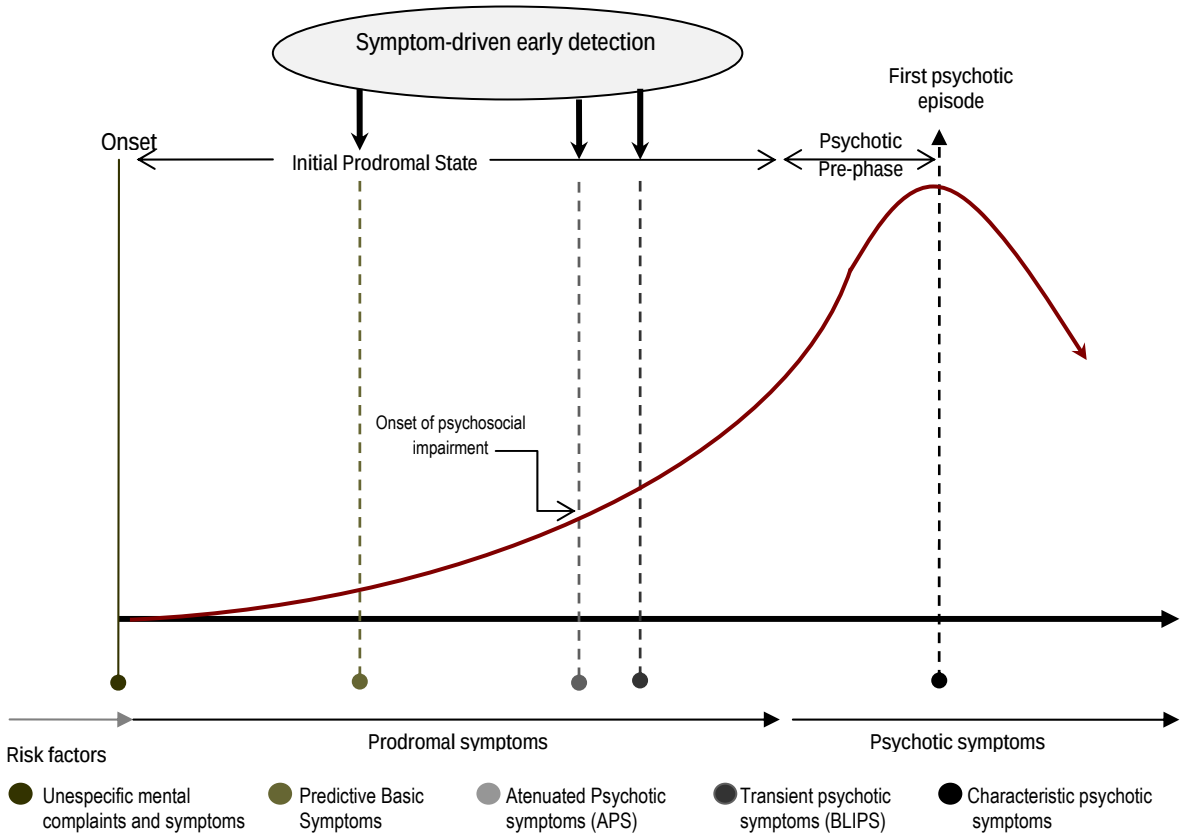
The UHR criteria have been adopted and adapted by a number of settings around the world, with 12-month transition rates varying between 10 and 50% (for a summary see Haroun et al., 2006; Olsen and Rosenbaum, 2006). However, a reduction in the rate of transition to psychosis has been suspected over the last few years. Findings from the Personal Assessment and Crisis Evaluation (PACE) Clinic in Australia, found a 6-month transition rate of only 9.2% (Yung et al., 2006), which has implications for the use of interventions in this population and for the validity of research findings. The decreased transition rate was partly explained by a reduction in the duration of symptoms of patients prior to receiving help. That is, UHR individuals are being detected and provided with care earlier than in the past. Thus, the decline in transition rate may be due to treatment being more effective at this very early stage of illness or it may be due to finding more false positives (those who were never at risk of psychosis). However, it is still not possible to distinguish between these alternatives, at least phenotypically (Yung et al., 2007b). Although there has been a declining in transition rate in clinical settings, meeting the criteria is still considered to significantly predict transition compared to not meeting criteria (Yung et al, 2006).

In Germany, a different and complementary approach is used to define those they considered at high risk of schizophrenia (Klosterkotter et al., 1997, 2001). They studied the predictive capacity of the basic symptoms in a cohort of non-psychotic patients attending a tertiary referral psychiatric setting and who were suspected as being ‘susceptible to schizophrenia’ on the basis of their psychopathology. Participants were followed upon average eight years after initial assessment, and during this period over 50% of them had developed schizophrenia (Klosterkotter et al., 1997).

By definition, basic symptoms differ from what is considered to be one's 'normal' mental self and are not evoked by substance misuse or somatic illness. Being subjective, they remain predominately private and apparent only to the affected person (Shultze-Lutter et al., 2009). Basic symptoms were suggested as a complement to the UHR approach to an early detection of psychosis, and two partially overlapping criteria were derived from it thought to differ in imminence of psychotic breakdown, the risk criterion Cognitive-Perceptive basic symptom (COPER) and the high-risk criterion Cognitive Disturbances (COGDIS), based on the data of the Cologne Early Recognition study (Klosterkötter et al., 2001; Schultze-Lutter et al., 2006). COGDIS criteria is defined by the presence of at least two of the following 9 symptoms suggestive of a schizophrenia prodrome: inability to divide attention, thought interference, thought pressure, thought blockages, disturbance of receptive speech, disturbance of expressive speech, disturbances of abstract thinking, unstable ideas of reference, and captivation of attention by details of the visual field (Klosterkotter et al, 1997). The predictive validity of these criteria is currently being examined in a multi-site European study (Klosterkotter et al., 2005). On the other hand, COPER was included in the Early Initial Prodromal State (EIPS) criterion of the German Research Network Schizophrenia (Häfner et al., 2004; Ruhrmann et al., 2003). It is defined by the presence of any one of the 10 predictive basic symptoms (Klosterkötter et al., 2001; Schultze-Lutter et al., 2006) in the absence of APS and BLIPS (i.e., thought interference, perseveration, pressure or blockages, disturbance of receptive language, decreased ability to discriminate between ideas and perception, unstable ideas of reference, derealization, and visual or acoustic perception disturbances) and, alternatively, by the combination of a genetic or obstetric risk factor for psychosis and recent functional decline. Unlike early initial prodromal state, the "Late Initial Prodromal State" (LIPS) is used to characterize those which meet the APS and, alternatively, the BLIPS criteria (Ruhrmann et al., 2003; Häfner et al., 2004). Based on empirical data, the Schizophrenia Proneness Instrument, Adult (SPI-A; Schultze-Lutter et al.,

2007) as well as the Child and Youth version (SPI-CY; Schultze-Lutter et al., 2010a) had been developed for the quantitative clinical assessment of basic symptoms.

Figure 1: Model of psychopathological development of psychosis related to the definition of the Early and Late Initial Prodromal State (Schultze-Lutter et al., 2010b).



3.1.3. The problems of the False positives in Early Detection

Identifying a population that has a 40–50% conversion to psychosis within 1 to 2 years is impressive, though it still means that 50–60% of individuals identified as at risk for a stigmatizing condition may never develop psychosis (Corcoran et al., 2003). However, there is no method of screening a population for susceptibility to schizophrenia existing or

envisaged that can eliminate the issue of false positives. In prodromal populations the apparent false positive group also includes those for whom treatment was effective at halting the progression to illness—the “false false positives”; therefore on an individual basis no one can ever be certain that their at-risk designation was actually false *per se* (Corcoran et al., 2005).

One problem of false positives is the risk of over-treatment, and therefore, important ethical implications arise for the use of interventions in this population. If a high proportion of those treated to prevent or delay psychosis are in fact ‘‘false positives’’ and were not actually at risk of developing psychotic disorder, at least in the short term, then intervention may not be justified. This would particularly be the case with biological treatments such as antipsychotics, which have potentially harmful side effects. Psychosocial treatment may too be harmful, if it involves educating individuals about psychosis and informing them that they are at risk, if they are not actually at risk. Treatment may needlessly alarm them, result in possible curtailment of activities, and cause stigma including self- stigmatization (for example, they may decide to cease attending university or work to avoid stress) (Yung et al., 2004; Corcoran et al., 2005; Heinssen et al., 2001).

Nevertheless, it has already been pointed out that false positives may benefit from treatment, particularly false positives that are symptomatic. It should also be pointed out that the reverse is true as well; early intervention may pose some hazards even for the true positives, to be set against benefits which, though potentially very great, are as yet not well characterized (Corcoran et al., 2005). There is therefore a mandate to improve the predictive value of the prodromal designation (Corocoran et al., 2003).

3.2. Onset of psychosis

With the recent growing interest in early psychosis it has been raised that the provision of treatment early in the course of illness allows the possibility to prevent or reduce

the morbidity that rapidly occurs during the first few years of a psychotic disorder (Birchwood et al., 1998). Clinical research findings in recent decades suggest that applying existing schizophrenia treatments as soon as possible in the course of the disorder may slow or stop deterioration (McGlashan and Johannessen, 1996).

The criteria for diagnosing psychosis require accurate the dating of the beginning of the disorder and distinguishing prodromal symptoms from those heralding an acute psychotic episode (Beiser et al., 1993). However, despite the establishment of multiple successful clinical and research programs, there is an important conceptual difficulty and there is no consensus operational definition for what is commonly referred to as 'First-Episode Psychosis' (FEP). On the other hand, the existing diagnostic systems as DSM-IV (APA, 2002) and ICD-10 (WHO, 1994) provide little guidance with regard to defining this construct. The significant variability in definition and application across different clinical and research programs threatens meaningful integration of findings from these populations (Keshavan and Schooler, 1992) and may ultimately hinder our progress in identifying key elements of the early course and treatment of psychotic disorders (Breitborde et al., 2009).

Determining when the deficit process begins in psychosis results difficult. It is undoubtedly present when positive psychotic symptoms emerge at onset and most likely actively contributes to the nonspecific symptoms characteristic of the prodromal phase. If and when the process begins in the premorbid phase is more a matter of conjecture. In cases where the presentation of illness is slow, insidious, and characterized primarily by loss of function and increasing negative symptoms (Kelley et al. 1992), the process most likely starts quite early and can even evolve into disorder without prodromal or onset stages (simple schizophrenia). In most cases, however, the process probably begins shortly before the first manifest signs and symptoms of distress in the prodromal phase (McGlashan and Johannessen, 1996).

The term FEP, as used within clinical and research settings, is misleading regardless of which operational definition is used. This term is typically used to refer to individuals early

in the course of a psychotic illness or treatment rather than individuals who are truly in the midst of a first 'episode' of illness (Breitborde et al., 2009). Operational definitions for FEP fall largely into three categories: (i) first treatment contact; (ii) duration of antipsychotic medication use; and (iii) duration of psychosis (Breitborde et al., 2009). According to this operational definition, an individual who presents at a clinical setting with psychosis, and who has never previously presented at a clinical setting with psychosis, is identified as experiencing their 'first-episode' (Breitborde et al., 2009).

Nevertheless, emerging data regarding the pathways to care taken by individuals with psychotic disorders, reveal key limitations of this approach. The first and second operational definitions, it seems that are used to refer to individuals who have experienced a short duration of illness (e.g. 2–5 years) (Miller at al., 1999) or treatment for a psychotic illness, rather than individuals in the midst of a first 'episode' of mental illness (Breitborde et al., 2009). For example, concerning to the 'first treatment contact' for individuals with psychotic disorders, it has to be consider that it often occurs well after the initial onset of symptoms (Häfner et al. 1992; McGlashan et al., 1999). In fact, a recent multi-study review of the Duration of Untreated Psychosis (DUP), or the time between the onset of psychosis and receipt of adequate treatment, found a mean DUP of almost 2 years (Marshall et al., 2005). Also, an individual's 'first contact' (i.e. when psychotic symptoms are first identified) is often not the first attempt to seek treatment. Individuals can make up to five unsuccessful attempts at obtaining treatment prior to successfully engaging with a FEP program (Lincoln et al., 1998). Finally, available evidence suggests that the 'first treatment contact' operationalization may be an overly conservative proxy for identifying people early in the course of a psychotic illness. Thus, on examination, the 'first treatment contact' definition appears neither simple nor necessarily able to collect individuals who meaningfully share service needs or research characteristics (Breitborde et al., 2009). Similarly, the 'duration of antipsychotic medication use' definition can be an unsatisfactory proxy for the first episode of a psychotic illness. For example, this definition would identify an individual who has not received adequate treatment

with antipsychotic medication as experiencing a FEP, even if he or she had experienced psychotic symptoms for many years (Breitborde et al. 2009). On the other hand, the variability in the definition of acceptable duration of medication use and the variable populations recruited even within a single duration criterion, hinder the ability to accurately integrate findings across studies for clinical or research purposes. Additionally, many FEP programs limit enrolment to individuals who have yet to receive adequate treatment for psychosis, with adequate treatment defined as the receipt of antipsychotic medication for a specific duration of time (Addington et al., 2001; Jørgensen et al., 2000; Johannessen et al., 2001; Lieberman et al., 1992; Malla et al., 2003). Therefore, both definitions, whether based on 'first treatment contact' or 'duration of antipsychotic medication', in practice, may overly excludes individuals who are still early in the course of a psychotic disorder but who have experienced psychotic symptoms for 1 year or more (Breitborde et al., 2009).

Alternatively, the third approach, 'recent-onset psychosis', based on duration of psychosis, attempts to most directly address the goal of identifying individuals early in the course of illness and, conceptually, may be more accurate than the term 'first-episode psychosis' given that psychotic disorders do not always follow an episodic course (Flaum et al., 1992). Yet, the most significant problem with regard to the 'duration of psychosis' operational definition is the lack of a validated durational criterion for demarcating the end of the first-episode of a psychotic disorder. Given that most of the deterioration in functioning that accompanies psychotic disorders occurs within the first 2–5 years following the onset of psychotic symptoms (McGlashan, 1998), one may wish to demarcate the first-episode as ending at some point 2–5 years later. However, the speed at which this functional deterioration occurs varies across individuals (Lieberman et al., 2001), and there is a strong lack of scientific evidence to inform an appropriate cut-off point for the end of the first episode within this 2- to 5-year period (Breitborde et al., 2009).

Although dating the onset of illness phases is probably feasible, efforts to improve reliability must continue (Beiser et al., 1993).

4. FAMILY ENVIRONMENT IMPACTING ON EARLY PSYCHOSIS OUTCOMES

The stress-vulnerability model, developed by Zubin and Spring (1977) suggests that psychotic disorders and their associated disabilities are the result of the interaction between specific brain disorders and psychosocial environmental factors. According to this, the experience of stress is essential to the onset of acute psychosis, i.e., a vulnerable person, whose inborn tolerance for stress is incompatible with exposure to either internally or externally generated stimulation may experience a first or a recurring episode of the illness (McFarlane, 2002). This model provides a widely accepted, empirically supported, and useful framework for describing the relationships among provoking agents (stressors), vulnerability (diathesis), and symptom formation and functional outcomes in schizophrenia (Zubin et al., 1992). On the other hand, it also provides a possible explanation for some of the otherwise unexplained features of psychotic disorders, such as their episodic nature (Phillips et al., 2007).

Following this line, one of the prominent influences on the prevailing level of environmental stress is likely to be the emotional family atmosphere (Nuecherlein and Dawson, 1984). It has been universally recognized that the family not only provides a supportive environment, but is also a potent source of psychological tensions (Leff and Voaughn, 1985). Therefore, another perspective on the relationship between stress and the course of psychosis comes from the literature of “expressed emotion”, since it has consistently demonstrated that the course of schizophrenia is highly correlated with the family atmosphere (Weisman et al., 1998). The expressed emotion concept fits well within the stress-vulnerability model of schizophrenia and psychosis, and further supports that ongoing chronic stressors may play a role in the onset and course of psychotic disorders (Gleeson et al., 1999; Wearden et al., 2000).

4.1. Expressed emotion and schizophrenia relapse

Expressed emotion (EE) refers to the emotional environment and attitude of relative towards the ill family member and particularly focuses on negative interactions. Key aspects of interpersonal relationships that are incorporated within this construct are criticism, hostility, Emotional Over-Involvement (EOI), warmth and positive remarks. High EE is defined by the presence of higher levels of criticism, hostility and/or EOI (Brown et al., 1972; Vaughn and Leff, 1976). EE represents a measure of attitudes and behavioral patterns of relatives traditionally assessed through a semi structured interview called the Camberwell Family Interview (CFI) (Vaughn and Leff, 1976, 1985). The CFI is conducted to patient's family member in the absence of the patient. It typically takes 1–2 hours, and it is always audio-taped for later coding. Although it is designed to assess emotional attitudes of the particular family member interviewed, it is thought to reflect disturbances in the organization, emotional climate, and transactional patterns of the entire family system (Hooley, 2007). Nevertheless, given that the CFI needs for specific training and is a very time-consuming procedure (4 hours per relative for recording and evaluation), a number of shorter procedures for assessing EE have been developed, for example, the Five-Minute Speech Sample (FMSS; Magaña et al., 1986), an abbreviate evaluation based on the original CFI, as well as a numerous of questionnaires like the Perceived Criticism Rating (PC, Hooley and Teasdale,1989); the Parental Bonding Instrument (PBI, Parker et al., 1979, 1982); the Level of Expressed Emotion Scale (LEE, Cole and Kazarian, 1988; Kazarian, 1990); the Patient Rejection Scale (PRS, Kreisman et al., 1979); the Family Attitude Scale (FAS, Kavanagh et al., 1997); the Family Questionnaire (FQ; Wiedemann et al., 2002) and the Brief Dyadic Scale of Expressed Emotion (BDSEE; Medina-Pradas et al., 2011).

The original impetus for research on the impact of families on schizophrenia arose from the Brown and colleagues research in the 50's who developed the concept of EE through the study of the relation between family variables and the likelihood of relapse on the

part of patients with schizophrenia who had recently been discharged from the hospital. They found that patients who went to live with family members who were highly emotionally involved were much more likely to relapse than those patients who went to families who exhibited less EE (Brown et al., 1958). Further studies supported these findings, demonstrating that the rate of relapse among patients with schizophrenia during the year following hospitalization was significantly related to the living situation into which they were discharged (Leff and Vaughn, 1985; Vaughn and Leff, 1976), being higher the risk of relapse of those living within a high EE environment than those who live on a low EE environment (Bachman et al., 2002; Kavanagh, 1992). From this evidence, several studies have been developed to explore and clarify the role of EE on the course and outcome of mental illness, whose findings show on the one hand, that regular contact with high EE family members has a deleterious effect on the course of a range of mental and physical disorders and, on the other hand, that EE represents the most consistent predictor of psychiatric relapse across a broad range of disorders (Butzlaff and Hooley, 1998; Hooley et al., 2007; Wearden et al., 2000).

In schizophrenia, EE show more predictive power of relapse as duration of the illness is more longstanding (Butzlaff and Hooley, 1998, Marom et al., 2005; Warden et al., 2000) and, it seems that influences outcome independently of other predictors such as age, gender, marital status, premorbid functioning, illness duration, social adjustment, and medication compliance (Heikkilä et al., 2002). The replicability and magnitude of the high EE-relapse association have spawned a number of interventions specifically designed to reduce EOI and criticism in families of schizophrenia patients (Hahlweg et al., 1989). These family interventions are based on the assumption that attitudes of high-EE relative in daily interactions can increase the patient's stress level resulting in symptoms exacerbation and, ultimately, relapse (Nuechterlein and Dawson, 1984). However, the hypothesis that high EE cause symptoms exacerbation has still not been fully tested. Inversely, it has been argued that some symptoms of the disorder can engender criticism, hostility or EOI in relatives and

that EE may develop in response to cumulative difficulties of living with a family member who has a psychotic disorder, explaining the links with relapse in an indirect or actually reverse way (Meneguelli et al., 2011). Thus, there is an ongoing discussion as to whether EE is more a cause of clinical outcome or a parental reaction to disorder severity (Heikkilä et al., 2002). Therefore, a bidirectional and interactional model of the relationship between relatives' EE and patients' symptoms has been proposed, allowing understanding EE in interactional terms, considering a bidirectional pattern of effects and reciprocal influences between symptoms and the reactions of family members (Kavanagh, 1992; Miklowitz, 2004). Consequently, if the behavior of both patients and relatives are a reaction to stress and their resultant attempts to cope, there implicitly recognizes the role of two moderating variables: the interpretations that each person makes of the other's behavior and the coping skills that each brings to bear (Kavanagh, 1992).

4.2. The attributional and coping models as a Framework to Understand the Development of Expressed Emotion

The 'attributional model' (Barrowclough et al., 1994; Barrowclough and Hooley, 2003) could be potentially useful for elucidating the developmental pathway through which family stress and psychotic processes are related. It postulates that relatives' beliefs about problematic behaviors of the ill family member are related to their emotional attitudes towards them. It seems that critical relatives are more likely to blame patients for their behaviours and attribute symptoms as controllable by them rather than as a result of illness, and, consequently, they critically attempt to coerce the patient to change those behaviours. In contrast, overinvolved relatives are more likely to attribute symptoms to external and uncontrollable factors by the patient. Besides, they believe that they have somehow contributed to the patients' problems, so they usually present self-blaming attributions. Following this line, it has been suggested that patients' behaviours which more clearly reflect

signs of mental disorder, such as positive symptoms, are more likely to provoke uncontrollable attributions in their relatives, and therefore, engender EOI attitudes (exaggerated emotional responses or overprotectiveness) (Brewin et al., 1991). Conversely other kinds of symptoms, such as negative negative symptoms and poor functioning, are more probable to be thought under the patient's control, raising a more critical attitude from relatives (Weisman et al., 1998, Wearden et al., 2000). Based on this, some interventions for relatives of chronic schizophrenia patients have included efforts to modify attributions in an attempt to reduce EE (Barrowclough ant Tarrier, 1992).

On the other hand, there is growing evidence that a 'carer appraisal model' also known as 'stress and coping model' (Lazarus and Folkman, 1984; Lazarus, 1993) could be helpful for understanding the development of EE (Scazufca and Kuipers, 1996; Barrowclough and Parle, 1997; Patterson et al., 2000; Hooley and Campbell, 2002). Coping refers to the person's cognitive and behavioral efforts to manage (reduce, minimize, master, or tolerate) the internal and external demands of the person-environment transaction that is appraised as taxing or exceeding the person's resources (Lazarus and Folkman, 1984). External demands refer to the features of the event itself and internal demands refer to emotional reaction that a person has toward the event. Coping has two major functions: dealing with the problem that is causing the distress (problem-focused coping) and regulating emotion (emotion-focused coping) (Folkman and Lazarus, 1980). Several forms of problem and emotion-focused coping have been identified in previous research (Folkman and Lazarus, 1985; Magliano et al., 1996; Stanton et al., 2000). For example, problem-focused forms of coping include aggressive interpersonal efforts to alter the situation (coercion), as well as cool, rational, deliberate efforts to problem solving (positive communication), and emotion-focused forms of coping include avoidance, self-controlling, seeking information, seeking social support, accepting responsibility, and positive reappraisal.

Stress and coping framework is a paradigm that provides an opportunity to understand in more detail the range of adaptational responses made by family members to

the stress of caring for a psychiatrically impaired relative (Harfield, 1987). The coping strategies of the relatives of patients with schizophrenia are frequently mentioned in literature, on account of their involvement in the genesis of expressed emotions (Fallon, 1988; Kuipers and Bebbington, 1985) and their influence on both objective and subjective family burden (Kuipers and Bebbington, 1988; Grandón et al., 2008).

Several studies demonstrated that stress and coping model is helpful in understanding how EE develops (Scazufca and Kuipers, 1996; Barrowclough and Parle, 1997; Patterson et al, 2000; Barrowclough et al, 2001; Hooley and Campbell, 2002). It has been shown that emotion-focused strategies, such as avoidant coping, seem to be directly related to criticism (Kuipers et al., 2006; Raune et al., 2004). Moreover, it has been suggested that instead of the severity of particular symptoms, it is also important how families try to cope with patients' more difficult and challenging behaviors. Thus, relatives' willingness and ability to make such accommodations is what may underlie the development of higher EE attitudes such as criticism (Hooley, 2007). Smith et al., (1993) show that high-EE relatives perceived themselves as coping less effectively than low-EE relatives (Smith et al., 1993). Thus, high-EE behavior (e.g. criticism and EOI) then may be an attempt to reduce the perceived stressfulness of the caring role (Raune et al., 2004).

4.3. The early development of expressed emotion

Most EE studies in the field of psychosis have been carried out with chronic schizophrenia patients (e.g. Hooley, 2007; Cutting et al., 2006; Kopelowicz et al., 2002; Werker et al., 2002). Nevertheless, the recent focus of research on early psychosis has led to an increasing interest on the study of EE at early stages of the psychosis continuum, which becomes crucial, given that circumstances are different than in schizophrenia where illness is more established and assumed. In addition, exploring the role of EE in early stages of psychosis allows clarifying its early ontogenesis and its impact on the clinical and

functional outcome in (pre)psychotic patients, which is important to future designing of suitable early interventions focused on preventing the development and entrenchment of EE over time.

So far, there are few studies exploring EE in early psychosis, showing that high-EE is present on average, in over half of the patient–carer relationships and appears to be independent of illness chronicity (Bachmann et al., 2002; Heikkila et al., 2002). Some studies have suggested that EE is a weaker predictor of early relapse on FEP patients, compared to those with multiple episodes (Birchwood et al., 2002). Moreover, findings on FEP have shown that EE is not a stable factor (or family trait) but a much more fluid characteristic that changes over time, usually from high to low as patient exhibit improvement in severity of symptoms (Brown et al., 1972; Leff et al., 1985; Lenior et al., 2002; Scazufka and Kuipers, 1998; Stirling et al., 1993). However, the differential relationships between EE indices and specific symptoms and functioning in early psychosis remain unclear, since certain results at this regard are scarce and contradictory. On the one hand, some studies found no association between EE with symptoms and/or functioning (e.g. Álvarez-Jiménez et al., 2010; McFarlane and Cook, 2007; Meneguelli et al., 2011). On the other hand, some studies on FEP showed associations between general and negative symptoms with both criticism and EOI (King et al., 2000; Mo et al., 2007). In addition, preliminary research on at-risk of psychosis patients points the important role that EE seems to play in the evolution of early psychosis outcome. Particularly, in prodromal adolescents, attitudes related to positive affect such as warmth, positive remarks and EOI, predicted improvement in negative symptoms and functioning (O'Brien et al., 2006, 2008), while negative affect in form of criticism and hostility predicted worsening of positive attenuated psychotic symptoms (Schlooser et al., 2010). Other studies have yielded evidence to suggest that the effects of symptoms and functioning on EE may be mediated by parental attributions, coping and burden of care, which have explained the relatives' emotional responses better than the patients' clinical features directly (e.g. Scazufca and Kuipers, 1996, 1998; Magliano et al., 1998; Hinrichsen

and Lieberman, 1999; Raune et al., 2004). On the other hand, although Ownmere et al., (2008) demonstrated that caregivers' cognitive representations of psychosis may play an important role in their emotional appraisals, even at an early stage of the illness, as we know, there is only one study examining the association of attributions with EE in FEP relatives (McNab et al., 2007), whose findings support the attributional model also at this stage of the illness.

Two main explanatory models have been proposed to account for the nature of EE in relatives of FEP patients. It has been argued that EE is a coping strategy that reduces the perceived stress and burden of the caring role (Raune et al. 2004; Kuipers et al. 2006). According to this model, carers' negative appraisals of their living situation results in negative emotional states such as anxiety, precipitating high-EE among relatives in an attempt to neutralize these emotions. An alternative model suggests that EE may be understood as an adaptive reaction to grief and perceived loss (Patterson et al. 2005). This model proposes that, during the early stage of adaptation to the illness, families may fear the loss of the young person developing psychosis, which, according to attachment theory, is fundamental in the development of an anxious attachment style (Bowlby, 1980, 1988). Relatives' EE could then be deemed as a particular form of anxious attachment that is likely to lead to stress, maladaptive relationships and, consequently, burden of care (Wynne, 1981). In so doing, high-EE relationships involving high EOI and criticism could be playing an adaptive function for relatives as an expression of concern in response to the crisis of a close family member developing psychosis. Furthermore, it is possible that low EE response may in fact be unusual when faced with a psychosis (Patterson et al., 2005). It could be that low EE is reached if there is already experience of mental illness in the family, where coercive measures have been previously tested and rejected, or perhaps in response to a psychosis that has had a long and insidious development, where adaptation within the family has already taken place over many months or years during the prodrome phase (Patterson et al., 2005). Nevertheless, further research should be addressed to clear these questions.

Coping strategies in relatives of early psychosis patients has rarely been studied and there is still scarce knowledge about the differences of relatives coping with the onset of psychosis compared to those coping with the chronicity and the multiple episodic stage of the disorder. Tenakoon et al., (2000) show that families of FEP similarly to those of schizophrenia patients, used approach coping strategies, including emotion-focused and problem-solving coping strategies to manage problematic behaviors, and spiritual coping to deal with stigma (Tennakoon et al., 2000). On the other hand, findings of recent exploratory studies of coping styles used by families of individuals with emerging psychotic illness, show that families reported moderate use of 'approach' coping (e.g. planning, seeking social support, positive reinterpretation, acceptance and turning to religion) and rare use of 'avoidant' coping strategies, which is consistent with findings for relatives of FEP patients, but contrary to those of more chronic psychotic illness (Gerson et al., 2011).

To summarize, further research is needed on EE during the early stages of psychosis to better understand its effect on outcome, and to explore psychological factors like relatives' illness attributions and coping strategies at outset of psychosis to better understand their link to the EE' ontogenesis, in order to design effective early interventions aimed to improve their resilience to problematic family environment, and to log-term benefit both individuals with psychosis and their relatives (Patterson et al., 2000).

III. AIMS AND HYPOTHESIS

GENERAL AND PARTICULAR AIMS OF THE THESIS

1. The first aim of the thesis was to create and implement an adequate assessment protocol and adapt it to the context and specific characteristics of the sample of this study, based on the new paradigm and international research and clinical experience of early detection and intervention in psychosis.

2. The second general aim was to characterize At-Risk Mental State (ARMS) and First-Episode of Psychosis (FEP) patients, which represent two different stages of the psychosis continuum, and to test the comparability of our sample with international reports (considering that ARMS is not a formal diagnosis and thus this aspect becomes relevant). Therefore, we established the following particular aims:

   a. To examine socio-demographic, clinical background, treatment history, current service use, psychopathological and psychosocial characteristics of ARMS and FEP patients who are being treated in the Sant Pere Claver Early Psychosis Program (SPC-EPP) in Barcelona.

   b. To compare ARMS and FEP groups in order to characterize commonalities and differences between the at-risk and onset of disorder stages, with the purpose of increasing our knowledge of the ARMS definition.

3. An additional objective was to test if subjective quality of life was associated with symptom severity and functional impairment in ARMS patients.

4. The thesis also focused on some of the family factors that have been demonstrated to be related with the course and outcome of psychotic disorders. Thus, we aimed to characterize the profile of Expressed Emotion (EE), illness attributions and emotional states

in relatives of ARMS and FEP patients, as well as to examine how these family factors are associated and how they differ between ARMS and FEP groups.

5. Finally, we aimed to examine if relatives' negative affect expressed in the form of criticism and Emotional Over-Involvement (EOI) was associated with patients' symptom severity and functional impairment in the early stages of psychosis. Moreover, given that the literature in chronic schizophrenia suggests that relatives' cognitive representations of psychosis may play an important role in their emotional appraisals, we aimed to test the possible mediating role of relatives' attributions in the association between EE and illness severity. Thus, we established the following particular aims:

a. To examine the effect of relatives' EE (criticism and EOI) on patients' symptoms and functioning and whether this potential association is different in ARMS and FEP patients.
b. To test whether the association between EE and symptoms/functioning is mediated by relatives' attributions of control and blame.

HYPOTHESIS

1. Regarding the comparisons between ARMS and FEP in terms of socio-demographic, clinical, and functional characteristics, we hypothesized on the one hand, that both groups would be comparable regarding demographic and clinical background, as well as in their profile of premorbid functioning. On the other hand, we expected that FEP patients would present greater severity of symptoms and functional impairment than ARMS patients.

2. With respect to the associations of subjective quality of life with symptom severity and functional impairment in ARMS patients, we hypothesized that negative symptoms, general psychopathology, and functional impairment would be determine overall subjective quality of life.

3. Regarding the characterization of family factors, and differences between ARMS and FEP relatives, we hypothesized that:

   a. Criticism would be associated with relatives' belief that the patient can control his/her symptoms and with the attribution of blame toward the patient in both ARMS and FEP relatives.
   b. EOI would be associated with relatives' self-blame attributions and relatives' levels of anxiety in both ARMS and FEP relatives.
   c. Relatives of FEP patients would have higher levels of EOI than those of ARMS patients, while levels of criticism would be higher in ARMS than in FEP relatives.

4. Finally, regarding the effect of family environment on patients' clinical and functional features, and the mediating role of relatives' attributions on the association between expressed emotion and patients symptoms/functioning, we expected that:

   a. EOI would have an effect on positive symptoms, whereas criticism would have an effect on negative symptoms and functioning.
   b. Considering that, theoretically, signs of illness are more evident in FEP than in ARMS, the association between EOI and positive symptoms would be stronger in the FEP group, while the association between criticism and negative symptoms/functioning would be stronger in the ARMS group.
   c. Relatives' attributions of self-control and self-blame would mediate the association between EOI and positive symptoms, whereas relatives' attributions of control and blame toward the patient would mediate the association between criticism and negative symptoms and functioning.

IV. EMPIRICAL WORK

STUDY 1:

Clinical and Psychosocial Characterization of At-Risk Mental State and First-Episode of Psychosis patients from the Sant Pere Claver Early Psychosis Program in Barcelona (Spain): Preliminary Baseline Results.

Abstract

Aims: This study aims to describe and compare socio-demographic, background, treatment history, service use, psychopathological and psychosocial characteristics of At-Risk Mental States and First-Episode Psychosis (FEP) patients who receive treatment in the Sant Pere Claver Early Psychosis Program in Barcelona, Spain.

Methods: The sample was comprised by 34 ARMS meeting criteria for the Comprehensive Assessment of At-Risk Mental States and 31 FEP patients meeting DSM-IV-TR criteria for any psychotic disorder or affective disorder with psychotic symptoms. Patients were assessed with several clinical and psychosocial measures at study baseline.

Results: Clinical and psychosocial characteristics of the SPC-EPP sample are comparable with those of previous early psychosis studies. Significant differences were found between ARMS and FEP groups on age and living situation. The higher prevalence of previous psychiatric hospitalizations in FEP group and differences between current psychiatric and psychological treatment among groups was to be expected. The age at onset of both unspecific and prodromal symptoms, and age of first specialized psychiatric/psychological treatment were earlier in ARMS than in FEP patients. Overall, no significant differences on most clinical and functional ratings between ARMS and FEP patients were found. However, FEP patients showed more positive symptoms, overall severity of symptoms and lower quality of life respect to its environment than ARMS patients. Nevertheless, ARMS patients show more global symptom severity than FEP patients.

Conclusions: Findings support the notion that ARMS have to be considered as 'ill' with a need and right for treatment, given that they already suffer from multiple mental and functional disturbances.

Key Words: At-Risk Mental States, First-Episode Psychosis, Early Psychosis Program, Psychopathology, Functioning.

1. INTRODUCTION

Clinical research findings in recent decades suggest that the benefits of implementing treatment, as early as possible in the course of psychotic disorders, may at least help to improve the course of illness and reduce its long-term impact (McGlashan and Johannessen, 1996). Moreover, investigating and evaluating patients at the early stages of psychosis, either prior to the onset of frank psychotic symptoms or at their First Episode of Psychosis (FEP), limits the potential confounding effects of illness severity, progression, or long-term exposure to antipsychotic drugs.

The possibility to monitor prospectively those people at heightened risk for developing psychosis lies in the new identification and follow-up of a population that demonstrates clinical high risk factors for subsequent psychosis, established as “At-Risk Mental State” (ARMS) or “Ultra-High Risk” (UHR) for psychosis (Yung et al., 2004). However, although several studies have indicated that the UHR criteria are valid and reliable for predicting psychosis onset (McGorry et al., 2010), its implications for early diagnosis and treatment runs into problems due to the wide variability between individuals and the lack of specificity of many of its features (Yung et al., 2007b). On the other hand, despite the establishment of multiple successful clinical and research programs, there is a lack of consensus and operational definition for what is commonly referred to as FEP, since it is typically used to refer to individuals early in the course of a psychotic disorder or treatment rather than individuals who are truly in the midst of a first ‘episode’ of illness (Breitborde et al., 2009).

Given the complex etiology and clinical manifestation of psychosis, an important goal of research is to better characterize the early phases of psychosis with the purpose of improving the early detection of high-risk populations and deliver treatment as early as possible at the onset of the disorder. In this sense, this study aims to examine socio-demographic, clinical background, treatment history, current service use, psychopathological and psychosocial characteristics of ARMS and FEP patients who are being treated in the Sant Pere Claver Early Psychosis Program (SPC-EPP) in Barcelona, Spain (Domínguez-

Martínez et al., 2011b). Additionally, these two groups are compared in order to characterized commonalities and differences between the at-risk and onset of disorder stages, with the aim of increasing our knowledge of ARMS definition.

2. METHOD

2.1. Inclusion and Exclusion criteria

Patients' inclusion criteria were: age between 14 and 35 years old, IQ ≥ 75, and a proper command of Spanish language. ARMS patients met criteria for at least one of the operationally UHR groups defined by the Comprehensive Assessment of At-Risk Mental States (CAARMS; Yung et al., 2005): 'Attenuated Psychotic Symptoms (APS)' group; 'Brief Limited Intermittent Psychotic Symptoms (BLIPS)' group; and 'Trait and State Risk Factor' group. If ARMS patients were excluded as ARMS but included as FEP, if they met criteria for the 'psychosis threshold/anti-psychotic treatment threshold' as determined by the CAARMS.

FEP patients met DSM-IV-TR (APA, 2002) criteria for any psychotic disorder or affective disorder with psychotic symptoms. For both ARMS and FEP patients, exclusion criteria were: a) evidence of organically based psychosis, and b) any previous antipsychotic treatment (without considering that for the current episode).

2.2. Measures

Patients were interviewed to complete ad-hoc demographic, clinical background and psychiatric/psychological treatment history schedules.

2.2.1. *Clinical and Subclinical Psychopathology Measures*

Prodromal symptoms of ARMS patients were assessed with the CAARMS (Yung et al., 2005), a semi-structured interview designed to identify subjects at imminent risk of psychosis. FEP patients were assessed with Affective and Psychotic modules of the

Structured Clinical Interview for DSM-IV (SCID-I; First et al., 1996) to determine categorical diagnosis. Psychopathology of all patients was assessed with the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987; Peralta and Cuesta, 1994), the Calgary Depression Scale (CDS; Addington et al., 1990; Sarró et al., 2006); and the Young Mania Rating Scale (YMRS; Young et al., 1978; Colom et al., 2002). Personality dysfunction was assessed with the Cluster A Module Personality Disorders (SCID-II; First et al., 1999). Substance Abuse and Dependence DSM-IV criteria were established by the Structured Clinical Interview for DSM-IV (SCID-I; First et al., 1996). The Schizophrenia Proneness Instrument-Adult version (SPI-A; Schultze-Lutter et al., 2007; Medina-Pradas et al., 2012), a semi-structured interview for assessing basic symptoms was also administrated to both ARMS and FEP patients. However, as the Spanish adaptation was not available at the beginning of the study, not all patients have completed this assessment.

2.2.2. Functional and Psychosocial Measures

The Social and Occupational Functioning Assessment Schedule (SOFAS; Goldman et al., 1992; García-Portilla et al., 2011), the Social Functioning Scale–Brief (SFS-Brief; Birchwood et al. 1990; Alonso et al., 2008) and Global Functioning: Social and Role Scales (GF:Social and GF:Role; Cornblatt et al., 2007) were used to assessed functional impairment, and social and role performance. The Premorbid Adjustment Scale (PAS; Cannon-Spoor, 1982; López et al., 1996) was used to assess premorbid functioning. Finally, the World Health Organization Questionnaire of Quality of Life-Bref Version (WHOQOL-BREF; WHO, 1993; Espinoza et al., 2011) was administered to assess subjective quality of life.

2.3. Procedure

The present study is part of a larger longitudinal study currently being carried out in the SPC-EPP in Barcelona, Spain (Domínguez-Martínez et al., 2011b). The data presented here

were obtained from 2009 to 2012. The project is being developed in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. It has been approved by the local ethic committee. Written informed consent was obtained from all participants. If the patient was less than 18 years old, consent was given by parents or a legal guardian. All the assessments were conducted by experienced clinical psychologists.

3. RESULTS

3.1. Participants

Of the 93 patients invited to participate in the study, 12 (5 ARMS and 7 FEP) refused to participate and 16 (6 ARMS and 10 FEP) were excluded for not meeting fully inclusion criteria. Thus, the sample was comprised by 65 patients, 34 ARMS and 31 FEP.

3.2. Intake Diagnosis and Socio-demographic Characteristics

Table 1 summarizes the diagnostic intake criteria for all patients. Almost all ARMS patients met criteria for the APS group and 26.4% belonged to more than one high-risk group criteria according to CAARMS (Yung et al., 2005). In the FEP group, almost half met criteria for Psychotic Disorder *Not Otherwise Specified. Additionally, 24 ARMS and 16 FEP were assessed with the SPI-A to establish the COPER and COGDIS risk criteria.*

The socio-demographic details of the sample are shown in Table 2. Chi-square or Fisher's exact test (when appropriate) were used to compare categorical variables. The comparison of ARMS and FEP patients indicated significant differences on age and living situation. ARMS group were younger and therefore, lived with their family of origin more often than FEP the group.

Table 1. ARMS and FEP patients' diagnostic intake criteria.

	ARMS N=34 n (%)	FEP N=31 n (%)
Intake CAARMS criteria		
Group 1. Attenuated Psychotic Symptoms (APS)	32 (94.1)	NA
Group 2. Brief Limited Intermittent Psychotic Symptoms	3 (8.8)	NA
(BLIPS)	6 (17.5)	NA
Group 3. Trait and state risk factors	1 (2.9)	NA
Groups 1 +2	5 (14.7)	NA
Groups 1 + 3	2 (5.9)	NA
Groups 2 + 3	1 (2.9)	NA
Groups 1 + 2 + 3		
Intake FEP criteria (DSM-IV SCID-I diagnostic)		
Schizophrenia	NA	4 (13)
Psychotic Disorder NOS	NA	14 (45.1)
Schizophreniform disorder	NA	3 (9.7)
Brief psychotic disorder	NA	1 (3.2)
Bipolar disorder NOS	NA	1 (3.2)
Bipolar disorder I	NA	8 (25.9)
Intake SPI-A criteria	N=24	N=16
COPER	19 (55.9)	8 (25.8)
COGDIS	18 (52.9)	6 (37.5)

Abbreviations: ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; CAARMS: Comprehensive Assessment of At-Risk Mental States; DSM-IV: Diagnostic Statistic Manual; SCID-I: Structured Clinical Interview Axis I Disorders; SPI-A: Schizophrenia Proneness Instrument for Adults; COPER: Cognitive-Perceptive basic symptom; COGDIS: Cognitive Disturbance high-risk criterion; SD: Standard Deviation; NA: Not applicable; NOS, Not Otherwise Specified.

Table 2. Socio-demographic characteristics of the sample.

	ARMS N=34 n (%)	FEP N=31 n (%)	Statistics
Age (mean, SD)	21.21 (4.3)	25.42 (6.1)	t=3.21*
Gender			X^2=.639
Males	23 (67.6)	18 (58.1)	
Females	11 (32.4)	13 (41.9)	
Education			Fisher=8.526
Primary education	2 (5.9)	-	
Secondary education	29 (85.3)	22 (71.1)	
University studies	3 (8.8)	8 (25.8)	
Postgraduates	-	1 (3.2)	
Occupation			Fisher=9.671
Unemployed/unoccupied	11 (32.4)	11 (35.5)	
Student	13 (38.2)	6 (19.4)	
Pensioner due to psychiatric illness	1 (2.9)	4 (12.9)	
Worker/Employee	9 (26.4)	10 (32.2)	
Marital Status			Fisher=5.166
Single	30 (88.2)	23 (74.2)	
Goin out with someone.	3 (8.8)	2 (6.5)	
Married or analogous	-	4 (12.9)	
Separate/Divorced	1 (2.9)	2 (6.5)	
Living situation			Fisher=9.984**
Alone	1 (2.9)	-	
With the family of origin	33 (97.1)	23 (74.2)	
With Partner	-	4 (12.9)	
With friends	-	4 (12.9)	
Nationality			$X^{2=}$.263
Spanish	25 (73.5)	21 (67.7)	
Foreign	9 (26.2)	10 (32)	
Ethnicity			Fisher=2.966
Caucasian-white	24 (70.6)	23 (74.2)	
Eastern European	1 (2.9)	1 (3.2)	
Arab	-	1 (3.2)	
Sub-Saharan	1 (2.9)	-	
Latino American	7 (20.6)	6 (19.4)	
Non-Arab middle east countries	1 (2.9)	-	

Abbrev.: ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; SD: Standard Deviation; * p<0.05; ** p<0.01.

3.3. Clinical Background and History of Treatment

The clinical background and history of previous treatments is presented in Table 3. Most ARMS and FEP patients have not received psychiatric or psychological treatments prior to the current SPC-EPP treatment. Regarding previous hospitalization because of psychiatric reasons, significant differences were found between groups, given that most of FEP patients were previously hospitalized, unlike ARMS patients, as to be expected. Note that 20.6% of ARMS patients have a history of suicide attempts in contrast with the 9.7% of those FEP patients, however, differences at this regard were not significant. Moreover, about less than a half of both ARMS and FEP patients met criteria for lifetime cannabis abuse. Regarding family psychiatric history, the most frequent disorders present in relatives of both ARMS and FEP patients were psychotic and affective disorders, followed by substance abuse/dependence.

On the other hand, ARMS patients show earlier age at onset of both unspecific and prodromal symptoms, as well as earlier age of first specialized psychiatric/psychological treatment than the FEP group. Note that three of the ARMS patients who met BLIPS criteria have presented psychotic symptoms although brief or intermittent and leasting less than one week, thus the mean age of the onset of psychotic symptoms of these particular three ARMS are also presented in Table 3. No differences were found between groups on Duration of Untreated Illness (DUI) and Duration of Untreated Psychosis (DUP).

Information about the current treatment and current use service at SPC-EPP is detailed in Table 4. The origin of psychiatric/psychological demand of almost half of FEP patients was from themselves. Moreover, significant differences were found on current use of psychopharmacological and psychological treatment. FEP patients were taking more antipsychotic and anticholinergic medication than ARMS patients, whereas ARMS group were taking more antidepressant medication and most of them were in psychological treatment, unlike FEP patients. Furthermore, mean of time from the first specialized visit to

the inclusion in the early psychosis program was significantly longer in ARMS than in FEP patients, probably because of the severity of psychotic symptoms of the latter ones.

3.4. Clinical and Psychosocial Characteristics

Descriptions and comparisons of clinical measures are presented in Table 5. Student's t-test was used to compare clinical and psychosocial measures. There were no significant differences on most of clinical ratings between ARMS and FEP patients, except for the positive symptoms and overall severity of symptoms both assessed by CGI, in which the FEP patients were significantly more severe than ARMS patients. Moreover, ARMS patients showed higher score than FEP patients in the GAF-S and in the Schizoid Personality Disorder assessed with SCID-II.

In ARMS group, the most severe prodromal symptoms assessed with CAARMS were negative and anxiety symptoms, with an average level of severity varying between moderate and moderately severe, followed by positive symptoms, cognitive change attention/concentration and depression, ranging between mild and moderate severe. The most frequent symptoms were subjective cognitive change and abolition/apathy, followed by disorganized speech, subjective emotional disturbance, anhedonia, social isolation, impaired role function, depression and anxiety. The average of frequency of these symptoms ranging from twice a week/once a month (the less frequent) and, from 3 to 6 times a week or daily (the most frequent). The less severe and frequent symptoms were dissociative and mania, both absent in most of the ARMS patients.

In both ARMS and FEP patients, the average levels of severity for all of the PANSS symptoms dimensions vary between absent and moderate severe. The most severe symptom in ARMS group was anxiety, and in FEP group, it was passive/apathetic social withdrawal. For depression (CDS) and mania (YMRS) the average symptom severity lies between absent and mild. Furthermore, the average level of clinical severity, as measured by the CGI, lies between borderline mentally ill to moderately ill.

Table 3. Clinical background and history of previous treatment

	ARMS N=34	FEP N=31	Statistics
	n (%)	n (%)	
Previous Psychiatric demand (lifetime)			X^2=.668
No	29 (85.3)	24 (77.4)	
Yes	5 (14.7)	7 (22.6)	
Previous Psychopharmacological Treatment (lifetime)			Fisher=2.321
No	31 (91.2)	24 (77.4)	
Yes, Anxiolytic	1 (2.9)	-	
Yes, Antidepressant	1 (2.9)	4 (12.9)	
Yes, Unknown (not information available)	1 (2.9)	3 (9.7)	
Previous Psychological Treatment (lifetime)			X^2=.253
No	21 (61.8)	21 (67.7)	
Yes	13 (38.2)	10 (32.3)	
Previous Psychiatric Hospitalization/s			X^2=36.887***
None	30 (88.2)	4 (12.9)	
Yes	4 (11.8)	27 (87.1)	
History of Suicide Attempts			Fisher=1.460
None	27 (79.4)	28 (90.3)	
Yes	7 (20.6)	3 (9.7)	
History of Substance Abuse/Dependence			
Lifetime Alcohol Abuse	7 (20.6)	3 (9.7)	Fisher=1.460
Lifetime Alcohol Dependence	3 (8.8)	2 (6.5)	Fisher=.127
Lifetime Cannabis Abuse	7 (20.6)	5 (16.1)	X^2=.072
Lifetime Cannabis Dependence	3 (8.8)	5 (16.1)	Fisher=1.097
Lifetime Other Substance Abuse	1 (2.9)	2 (6.5)	Fisher=.447
Lifetime Other Substance Dependence	1 (2.9)	2 (6.5)	Fisher=.447
Family Psychiatric History			Fisher=17.019
None	5 (14.7)	2 (6.5)	
Psychotic Disorder	11 (32.3)	13 (41.9)	
Affective Disorder	13 (38.2)	10 (32.3)	
Substance Abuse/Dependence	7 (20.6)	5 (16.1)	
Anxiety Disorder	5 (14.7)	2 (6.5)	
Personality Disorder	-	1 (3.2)	
Suicide (death)	1 (2.9)	1 (3.2)	
Neurodegenerative diseases	3 (8.8)	2 (6.5)	
Others	-	4 (12.9)	
Unknown	4 (11.8)	1 (3.2)	
History of current disorder			
Age at onset of unspecific symptoms (mean, SD)	13.6 (4.2)	20.7(6.6)	t=-5.02*
Age of onset of prodromal symptoms (mean, SD)	17.3 (3.9)	22 (6.2)	t=-3.64**
Age of onset of psychotic symptoms (mean, SD) (ARMS, n=3)[1]	17.2 (8.0)	23.4 (6.4)	t=-1.94
Age of first specialized psychiatric/psychological visit (mean, SD)	18.9 (4.9)	23.5 (6.5)	t=-3.2*
Duration of Untreated Illness (DUI)[2] (weeks) (mean, SD)	86.4 (224.4)	79 (117.5)	t=.08
Duration of Untreated Psychosis (DUP)[3] (weeks) (mean, SD) (ARMS, n=3)[1]	22.75 (60.3)	61.3 (115.5)	t=-.65

Abbreviations: ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; SD: Standard Deviation

[1] Three ARMS patients have presence of Psychotic Symptoms but brief, latent or intermitent and during less than a week; [2] Time since onset of unspecific symptoms to receiving the first specialized psychiatric and/or psychotherapeutic treatment; [3]Time since onset of prodromal symptoms to receiving the first antipsychotic treatment; * p<0.05; ** p<0.01; ***p<0.001

Table 4. Treatment History and Current Service Use.

	ARMS N=34 n (%)	FEP N=31 n (%)	Statistics
Origin of current psychiatric/psychological demand			Fisher=8.673
Patient	12 (35.3)	14 (45.2)	
Family	11 (32.4)	12 (38.7)	
Medical service	9 (26.5)	2 (6.5)	
Judicial service/police	-	2 (6.5)	
Other communitary service	2 (5.9)	1 (3.2)	
Current psychiatric treatment			
Antipsychotic medication	11 (32.4)	31 (100)	X^2=32.454***
Anxiolytic medication	19 (55.9)	21 (67.7)	X^2=.964
Antidepressant medication	20 (58.8)	8 (25.8)	X^2=7.209**
Mood stabilizer medication	-	2 (6.5)	Fisher=2.228
Anticholinergic medication	-	8 (25.8)	Fisher=11.281***
Anticonvulsant medication	1 (2.9)	1 (3.2)	Fisher=.111
Current Psychotherapeutic treatment			
None	2 (5.9)	10 (32.3)	X^2=7.494**
Individual Psychotherapy	1 (52.9)	13 (41.9)	X^2=.787
Group Psychotherapy	20 (58.8)	16 (54.8)	X^2=.105
Family psychotherapy	8 (23.5)	6 (19.4)	Fisher=1.108
Assertive Community Treatment-Case Management	2 (5.9)	1 (3.2)	Fisher=.256
Private psychotherapy	2 (5.9)	2 (6.5)	Fisher=.009
Mean of time (weeks) from first specialized visit to inclusion in Early Psychosis Program (mean, SD)	47.6 (99.8)	11.5 (45.4)	t=1.91*
Mean of time (weeks) from first specialized visit to interview assessment (mean, SD) (n=36)	93.4 (97.3)	67 (65.3)	t=1.23

Abbreviations: ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; SD: Standard Deviation.

* p<0.05; ** p<0.01; ***p<0.001

Table 5. Descriptive and mean differences of clinical patients' measures

		ARMS N=34		FEP N=31		
	Possible range	Range	Mean (SD)	Range	Mean (SD)	Mean Comparison t-test
Prodromal symptoms (CAARMS)						
Possitive symptoms-S	0-24	0-18	9.8 (3.6)	NA	NA	NA
Possitive symptoms-F	0-24	0-21	10.9 (3.9)	NA	NA	NA
Cognitive change/attent./concent-S	0-12	1-10	4.6 (1.9)	NA	NA	NA
Cognitive change/attent./concent-F	0-12	1-6	3.6 (1.5)	NA	NA	NA
Emotional disturbance-S	0-18	0-13	5.7 (2.9)	NA	NA	NA
Emotional disturbance-F	0-18	0-18	7.4 (4.4)	NA	NA	NA
Negative symptoms- S	0-18	3-16	8.6 (3.2)	NA	NA	NA
Negative symptoms-F	0.18	3-18	9.7 (3.0)	NA	NA	NA
Behavioural change-S	0-24	3-16	9.4 (3.3)	NA	NA	NA
Behavioural change-F	0-24	3-17	9.4 (3.9)	NA	NA	NA
Motor/physical changes-S	0-24	0-12	5.2 (3.4)	NA	NA	NA
Motor/physical changes-F	0-24	0-17	4.8 (4.3)	NA	NA	NA
General psychopathology-S	0-48	2-26	14.2 (6.1)	NA	NA	NA
General psychopathology-F	0-48	1-34	13.1 (6.9)	NA	NA	NA
Affective Symptoms						
YMRS	0-60	0-34	5.8 (6.4)	0-20	3.1 (3.9)	2
CDS	0-27	0-17	7.3 (4.9)	0-18	5.4 (5.2)	1.5
Symptom severity						
PANSS-Positive	7-49	7-24	13.9 (3.4)	7-24	13.7 (4.3)	0.2
PANSS-Negative	7-49	8-34	20.5 (6.1)	7-31	18.1 (6.6)	1.5
PANSS-General	16-112	25-66	39.4 (8.6)	18-52	32.4 (8.5)	3.3
CGI-Positive	1-7	1-4	2.1 (0.9)	1-6	2.4 (1.4)	-1*
CGI-Negative	1-7	1-5	3.3 (1.1)	1-5	3.5 (1.2)	-0.5
CGI-Depressive	1-7	1-5	3.1 (1.4)	1-5	3 (1.5)	0.3
CGI-Cognitive	1-7	1-5	2.4 (1.2)	1-5	2.8 (1.3)	-1.2
CGI-Overall	1-7	1-5	3.1 (0.8)	1-5	3.4 (1.1)	-1.1*
GAF-S	0-100	35-75	55.7 (8.1)	40-90	56.8 (11.8)	-0.4*
Personality Disorders (SCID-II)						
Schizotypic Personality Disorder	9-27	10-23	14.6 (3.0)	9-21	13.4 (3.7)	1.1
Schizoid Personality Disorder	7-21	7-18	10.5 (3.2)	7-12	8.8 (1.6)	1.9*
Paranoid Personality Disorder	7-21	7-18	10.7 (3.3)	7-18	10.8 (4.3)	-0.04

Abbreviations: ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; SD: Standard Deviation; CAARMS: Comprehensive Assessment of At-Risk Mental States; S: Severity; F: Frequency; YMRS: Young Mania Rating Scale; CDS: Calgary Depression Scale; PANSS: Positive and Negative Syndrome Scale; CGI: Clinical Global Impression; GAF-S: Assessment of Functioning-Symptom Severity; SCID-II: Structured Clinical Interview-Axis II; NA: Not applicable; $p<0.05$; ** $p<0.001$

Table 6. Descriptive and mean differences of psychosocial patients' measures

		ARMS N=34		FEP N=31		
	Possible range	Range	Mean (SD)	Range	Mean (SD)	Mean comparison t-test
Premorbid adjustment (PAS)						
Childhood	0-24	0.4-0.5	0.3 (0.1)	0.0-0.6	0.3 (0.2)	1.3
Early adolescence	0-30	0.1-0.9	0.4 (0.2)	0.0-0.9	0.3 (0.2)	1.9
Late adolescence (ARMS, n=28)	0-30	0.2-0.9	0.5 (0.2)	0.0-0.6	0.3 (0.2)	1.8
Adulthood (ARMS, n=22)	0-18	0.3-0.8	0.5 (0.2)	0.17-0.8	0.4 (0.2)	2.2
Social functioning						
SFS-Overall	0-41	5-35	21.3 (5.9)	12-36	24 (4.9)	-2
SOFAS	0-100	25-75	55.8 (10.1)	40-80	59 (10.2)	-1.3
GF:Social	0-10	2-8	5.6 (1.3)	3-8	6.1 (1.3)	-1.7
GF:Role	0-10	3-7	5.6 (1.2)	4-8	5.7 (1.3)	-0.4
Quality of Life (WHOQoL-BREF)[1]						
Physical Health	4-20	4.5-18.7	13.2 (2.8)	8.6-17.7	14.3 (2.5)	-1.3
Psychological state	4-20	6-18.7	11.9 (3.5)	9.3-18	13 (2.6)	-1.2
Social relationship	4-20	4-17.3	11.6 (3.8)	6.7-18.7	11.7 (3.5)	0.1
Environment	4-20	7.5-18	12.9 (2.9)	11.5-17.5	14 (1.7)	-1.7*
Overall QoL	2-10	2-10	5.7 (2.0)	4-10	6.6 (1.5)	-1.6
Level of Insight	1-7	1-6	2.9 (1.5)	1-6	2.9 (1.7)	1.5

Abbreviations: ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; SD: Standard Deviation; PAS: Premorbid Adjustment Scale; SFS: Social Functioning Scale; SOFAS: Social and Occupational Functional Assessment Scale; GF: Global Functioning; WHOQOL: World Health Organization for Quality of Life-Bref.

[1] FEP n=16 in WHOQoL-BREF

* p<0.05; ** p<0.001

Descriptoion and comparisons of premorbid adjustment, social and role functioning, quality of life and level of insight are presented in Table 6. PAS scores in ARMS patients tend to increase with age, indicating a gradual decline of premorbid functioning from early adolescence, whereas in FEP patients the decline of premorbid functioning occurs in adulthood. Current level of functioning, as reflected in all functional measures, was considerably low and similar in both groups. Moreover, subjective quality of life seems to be already compromised in both groups, although FEP patients showed lower quality of life in the environment domain than ARMS patients. Finally, levels of insight in both groups are comparable, ranging between mild and moderate.

4. DISCUSSION

The current study describes and compares the socio-demographic, clinical background, treatment history, psychopathological and psychosocial characteristics of ARMS and FEP patients treated in the SPC-EPP.

Socio-demographic and clinical background characteristics appeared to be mostly similar between ARMS and FEP patients. However, the older age of FEP patients accounts for differences in the living situation between both groups. Furthermore, the higher prevalence of previous psychiatric hospitalizations in FEP than in ARMS patients, as well as differences between current pharmacological and psychological treatments among groups was to be expected.

On the other hand, the earlier onset of both unspecific and prodromal symptoms in ARMS patients reflect a long course of symptoms since early adolescence, which could be related with gradual decline on its premorbid functioning, as shown in PAS scores. In contrast, the onset of both unespecific and prodromal symptoms in FEP patients occurs until the adulthood, by marking a decline on its premorbid functioning at the adult phase. Moreover, the fact that onset of prodromal symptoms in ARMS patients has been earlier than FEP group, also explain why the age at onset of receiving first specialized

psychiatric/psychological treatment was earlier than in FEP patients. Interestingly, ARMS group have sought professional help on his prodromal phase, whereas FEP patients received their first specialized treatment after the onset of psychotic symptoms.

The mean of DUI in our sample was within the average of 22 and 166.4 weeks reported by several studies (Norman and Malla, 2001). Furthermore, according with most previous studies, the mean DUP in our sample shows to be long but with a mean of around 1-2 years (Loebel et al., 1992; McGlashan, 1999), although it was much longer than that reported by the EPPIC large long-term follow-up study of FEP in Australia (Henry et al., 2007).

Comparison between clinical and psychosocial characteristics of SPC-EPP with other previous studies is not entirely easy, given the differences on measurements between research programs worldwide. However, it can be said that overall socio-demographic, clinical and functional features of SPC-EPP sample are comparable with previous studies. According with literature, ARMS patients showed prominent negative and anxiety symptoms, as well as marked functional impairment (Addington et al., 2004; Velthorst et al., 2009; Yung et al., 2004). Furthermore, socio-demographic features and clinical scores of our ARMS sample were similar to those of the prodromal sample of the European Prediction of Psychosis Study (EPOS) (Ruhrmann et al., 2010a). Consistent with previous findings, attenuated psychotic symptoms were by far the commonest feature of the ARMS (Broome et al., 2005; Miller et al., 2003b; Young et al 2003b). Moreover, severity and frequency of prodromal positive symptoms scores assessed by the CAARMS were comparable to those of the EDIE-2 multi-site randomized trial for ARMS in UK (Morrison et al., 2011), except the disorganized speech subscale, which was more severe and frequent in our sample. The global functioning impairment in our ARMS patients assessed by SOFAS was within the range of 41 and 61 showed by most of ARMS studies, including the North American Prodrome Longitudinal Study (NALPS) and the PRIME clinic in Canada (e.g., Addington et al., 2010; Marshall et al., 2012; Morrison et al., 2011; Thompson et al., 2011). Besides, social

and role functioning scores in ARMS group, assessed by the GF scales, designed specifically to prodromal samples, were very similar to those obtained in a New York young prodromal sample in which these scales were validated (Cornblatt et al., 2007).

On the other hand, our FEP sample showed some differences from previous studies, maybe because of heterogeneity of FEP samples across studies. Socio-demographic data of FEP was comparable with baseline sample of the Lambeth Early Onset (LEO) trial in South London (Gafoor et al., 2010) and with the large epidemiological cohort of EPPIC study in Australia (Henry et al., 2010). However, psychotic symptoms assessed with PANSS were more severe in our FEP sample, than those of the quasi-experimental program in Norway and Denmark (Larsen et al., 2006), although comparing with this same sample, severity of global symptoms by assessing with the GAF, were similar. Nonetheless, both GAF and SOFAS scores were higher in our FEP sample, compared with those of the EPPIC study (Henry et al., 2007) and the OPUS Danish trial sample (Bertelsen et al., 2008). Finally, GF scores showed to be comparable with the only study, as we know, using these functional scales on FEP sample (Piskulic et al., 2011).

Overall, findings show scarce psychopathological and functional differences between ARMS and FEP groups, suggesting that ARMS are almost as ill as FEP patients, which supports the notion that, besides being a population at-risk, they have to be considered as 'ill', i.e., as 'patients' with a need and right for treatment, given that they already suffer from multiple mental and functional disturbances, because they were seeking help (Ruhrmann et al., 2010a). This, in turns, leads us to the ongoing debate about the inclusion of a risk syndrome for psychosis into the fifth revision of the Diagnostic Statistical Manual (DSM-V). However, despite risk syndromes facilitate the early detection and prevention of psychosis, further research and reliable assessment in specialized centers and in clinical practice should improve their diagnostic validity to transfer the syndrome from research to diagnostic criteria (Ruhrmann et al., 2010b). On the other hand, given that ARMS and FEP patients present similar illness severity and functional impairment, it becomes evident that the APS

criteria may detect patients at the late prodromal phase, who were probably at the edge of their FEP. Therefore, unlike the predominant UHR approach that only takes into account the severity of positive symptoms for meeting UHR criteria, it is important to consider and implement the COPER and COGDIS risk criteria (Schultze-Lutter et al., 2007) on the early detection and interventions programs, in order to detect the 'early psychosis prodrome' instead of the 'late prodrome'. Noteworthy that EPOS study has already suggested that the combination of UHR and COGDIS criteria could yield best sensitivity (Ruhrmann et al., 2010a). On the other hand, since the decline in psychosocial functioning has repeatedly been demonstrated in at-risk samples (e.g. Addington et al., 2004; Cannon et al., 2008, Cornblatt et al., 2007; Riecher-Rössler et al., 2007; Ruhrmann et al., 2010a; Yung et al., 2006), and shown to be predictor of conversion to psychosis, it becomes crucial to take into account the specific combinations of cognitive, academic and social impairments and disorganization/odd behavior, as has been proposed by the the Hillside Recognition and Prevention (H-RAP) Program in New York (Cornblatt, 2002).

Consistent with several studies, our findings demonstrated significant decline in psychosocial functioning and in quality of life in early stages of the psychosis continuum (e.g. Addington et al., 2004; Ruhrmann et al., 2008). Therefore, it is important to improve early detection, reduce DUP/DUI and offer adequate treatment as soon as symptoms cause significant distress, but, specially, before functional impairments develop.

STUDY 2:

Is Subjective Quality of Life related with Symptom Severity and Functional Impairment in At-Risk Mental State patients?

Abstract

Aims: Quality of life emerges as a unifying concept in assessing the impact of sickness on person's day-to-day lives. The present study aims to examine associations of symptom severity, functional impairment and Duration of Untreated Illness (DUI) with subjective Quality of Life (sQoL) in At-Risk Mental State patients (ARMS).

Methods: 34 ARMS patients were included and assessed on symptom severity, social and role functioning, and quality of life.

Results: A large number of significant and negative correlations between several symptom dimensions (especially negative, behavioural and depression) and sQoL domains were found. Notably, all of these correlations had medium-large effect sizes. Furthermore, social functioning was significant positive related with almost all sQoL domains and role functioning show strongly significant positive associations with all sQoL domains with medium-large effect sizes. Nevertheless, DUI was not related with sQoL.

Conclusions: Findings show that different domains of sQoL are differentially and meaningfully associated with symptom severity, suggesting that greater symptom severity is associated with decreased sQoL in ARMS patients. Consistent with previous studies depression appears to be the most important predictor of sQoL in the initial prodromal states. Furthermore, the clear association of sQoL with social and role functioning indicates that functioning in ARMS patients could already be an important determinant of sQoL, so it should be considered in future research about sQoL in the ARMS stage of psychosis. These findings underscore the importance of specifically addressing the social and occupational dysfunctions present in early psychosis with psychosocial interventions.

Key Words: At-Risk Mental States, Psychopathology, Functioning, Subjective quality of Life, Early Psychosis.

1. INTRODUCTION

Quality of life (QoL) is a multidimensional construct defined as individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. According to this definition, QoL consists of four domains: physical health, psychological state, social relationships, and relationship to salient features of the environment (WHO, 1996). QoL has emerged as a unifying concept in the assessment of the impact of sickness on people's day-to-day lives (Pinikahana et al., 2002) and it has gained increasing importance as a global measure of the social and clinical outcome in schizophrenia spectrum disorders (Browne et al., 2000). Moreover, the possibility to understand QoL from the subjective perspective of patients, i.e., the subjective quality of life (sQoL) has been increasingly used as an outcome measure to evaluate the impact of illness on the everyday life of patients or as a therapy outcome measure in health programs and services in clinical practice (Sartorius et al., 1997).

sQoL is a complex construct likely influenced by multiple factors (Roseman et al., 2008). However, most studies addressing sQoL in schizophrenia patients and other severe mental illness have focused on its association with psychiatric symptoms. Some studies have demonstrated associations between sQoL with positive and negative symptoms (e.g. Packer et al., 1997; Ritsner et al., 2000; Huppert and Smith, 2001), such that greater symptom severity is associated with decreased sQoL. Nevertheless, numerous studies have demonstrated that general psychopathology consistently emerge as the strongest contributor to poor sQoL in schizophrenia (Eack and Newhill, 2007). Also, it has been suggested that anxiety and depression have a substantial and independent influence on sQoL (e.g. Dickerson et al., 1998; Huppert and Smith, 2001).

There is evidence that sQoL changes across stages of the illness being lower in First-Episode Psychosis (FEP) than in chronic schizophrenia (Priebe et al., 2000). Moreover, in FEP patients, poor sQoL has been generally related to negative and depressive symptoms, longer duration of untreated psychosis and poor premorbid adjustment (e.g., Brown et al.,

2000; Priebe et al., 2000; Malla et al., 2004). In order to better understand the factors related to the worsening of sQoL in early psychosis, it is important to examine which features are already associated with poor sQoL in individuals presenting clinical high risk. Two studies have shown that sQoL is markedly lower in ARMS compared to both healthy controls and FEP patients (Bechdolf et al., 2005; Ruhrmann et al., 2008). These findings lend support to the notion that this population is already in need for mental health care, especially considering their risk for transition to psychosis. Thus, it is important to further investigate the determinants of reduced sQoL in ARMS to increase the level of satisfaction with life in these at-risk populations.

Regarding associations between sQoL and psychopathology in ARMS patients, it has been shown that sQoL is related with the severity of positive symptoms and unspecific symptoms, with depressive symptoms being the most important predictor of sQoL in the initial prodromal states (Bechdolf et al., 2005; Ruhrmann et al., 2008). In addition to psychiatric symptoms, functional impairment represents a key feature of psychosis and could be an important determinant of sQoL since it occurs early in the course of illness and has a big impact in daily living. Some studies in schizophrenia and FEP patients have shown that general sQoL has a significant relationship to functioning (Melle et al., 2010; Ritsner et al., 2000, 2012), but it is not well known whether early functional decline is related to sQoL in ARMS patients.

The present study aims to examine associations of symptom severity, functional impairment and Duration of Untreated Illness (DUI) with sQoL in ARMS patients. Based on previous findings, it was hypothesized that positive, negative and depressive symptoms, general psychopathology and functional impairment would be associated with all sQoL domains and overall sQoL. Also, we expected that DUI would be associated with overall sQoL.

2. Methods

2.1. Participants

Patients' inclusion criteria were: a) age between 14 and 35 years old, b) IQ ≥ 75, c) a proper command of Spanish language, and d) meeting criteria for at least one of the ARMS groups based on the *Comprehensive Assessment of At-Risk Mental States* (CAARMS; Yung et al., 2005). Patients were excluded if they met criteria for '*psychosis threshold/anti-psychotic treatment threshold'* as determined by the CAARMS (i.e. severity and frequency score threshold met for longer than one week), if there was presence of organically based psychosis or any previous antipsychotic treatment.

2.2. Measures

Patients were assessed with the CAARMS (Yung et al., 2005) to confirm the fulfilment of the ARMS criteria and to assess prodromal psychopathology. Additionally, depressive symptoms were assessed by the *Calgary Depression Scale* (CDS; Addington et al., 1990; Sarró et al., 2004). Social impairment was assess with the *Social and Role Global Functioning Scales* (GF-S and GF-R; Cornblatt et al., 2007), which were developed to address functioning specifically in the prodromal phases of psychosis and to disentangle the social and role functioning domains. Finally, the *Brief version of the World Health Organization Quality of Life* (WHOQOL-Bref; WHO, 2004), a cross-cultural and widely used measure for assessing health-related QoL, was administered to assess subjective QoL. The WHOQOL-BREF is a 26-item self-report measure widely employed in schizophrenia research to measure subjective assessments of specific aspects of dalily life. It consists of four domains: *physical health* (activities of daily living, dependence on medical treatment, energy and fatigue, mobility, pain and discomfort, sleep, work capacity), *psychological health* (bodily image and appearance, negative feelings, positive feelings, self-esteem, spirituality, concentration), *social relationships* (personal relationships, social support, sexual activity), and *environment* (finances, physical safety, access to health services, home environment,

opportunities to acquire new information, leisure activities, physical environment, transport). In addition, an overall QoL score is calculated using the initial 2 questions of the measure regarding self perception of overall QoL and general health. Domain scores are scaled in a positive direction (i.e. higher scores denote higher quality of life). Finally, DUI was defined as time interval in weeks since onset of prodromal symptoms to receiving the first specialized psychiatric and/or psychotherapeutic treatment. All available information provided by patients, family and clinical history was used to set DUI.

2.3. Procedure

The present study is part of a larger longitudinal study currently being carried out in the Sant Pere Claver - Early Psychosis Program in Barcelona, Spain (Domínguez-Martínez et al., 2011b). The protocol for the research project has been approved by the Ethics Committee of the Catalan health authorities and is being developed in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Written informed consent was obtained from all participants. If the patient was less than 18 years old, consent was given by parents or a legal guardian. All the assessments were conducted by experienced clinical psychologists.

3. RESULTS

3.1. Sample characteristics[1]

A total of 34 ARMS patients were included in the current study. Most of them met criteria for the APS group (94.1%), 3 of them met BLIPS criteria, and 6 for trait and state risk group according to the CAARMS. 8 ARMS belonged to more than one CAARMS group.

[1] For more detail about socio-demographic characteristics see Table 1 of Study 1.

Mean age was 21.2 years (SD= 4.3). Most patients were male (67.6%) and single (88.2%). Most had a high-school diploma, 64.6% were studying, working or performing any daily activity, 32.4% were unemployed/unoccupied and 2.9% had a sick leave. The mean age at onset of unspecific symptoms was 13.6 (SD=4.2) and the mean age at onset of prodromal symptoms was 17.1 (SD=4.1). The mean duration of untreated illness (DUI) was 88.4 weeks (SD=224.4).

3.2. Associations between symptoms and functioning with sQoL

Table 1 presents descriptive data of all clinical, functional and quality of life measures, as well as of mean DUI.

Table 2 presents Pearson's correlations for all WHOQoL domains (WHOQOL-BREF) with CAARMS, CDS, GF:social and GF:role scores and mean of DUI. As shown in Table 2, a large number of significant and negative correlations between several symptom dimensions (especially negative, behavioural and depression) and physical, psychological, social relationships domains of sQoL were found. Notably, all of these correlations had medium-large effect sizes, according to Cohen's guidelines (medium effect: magnitude >.30, large effect: magnitude >.50) despite the relatively small sample size. Furthermore, social functioning was significant positive related with almost all sQoL domains and role functioning show strongly significant positive associations with all sQoL domains with medium-large effect sizes. Nevertheless, DUI was not related with sQoL.

Table 1. Descriptive data[2].

	ARMS N=34		
	Possible range	Range	Mean (SD)
Quality of Life (WHOQOL)			
Physical Health	4-20	4.5-18.7	13.2 (2.9)
Psychological state	4-20	6-18.7	11.9 (3.5)
Social relationship	4-20	4-17.3	11.6 (3.8)
Environment	4-20	7.5-18	12.9 (2.9)
Overall QoL	2-10	2-10	5.7 (2.0)
Symptoms (CAARMS)			
Possitive symptoms	0-24	0-18	9.8 (3.6)
Cognitive change	0-12	1-10	4.6 (1.9)
Emotional disturbance	0-18	0-13	5.7 (2.9)
Negative symptoms	0-18	3-16	8.6 (3.2)
Behavioural change	0-24	3-16	9.4 (3.3)
Motor/physical changes	0-24	0-12	5.2 (3.4)
General psychopathology	0-48	2-26	14.2 (6.1)
Depression (CDS)	0-27	0-17	7.6 (4.8)
Current functioning (GF)			
Social functioning	0-10	2-8	5.6 (1.3)
Role role	0-10	3-7	5.6 (1.2)
Duration of Untreated Illness	-	-	86.4 (224.4)

Abbreviationsn: ARMS: At-Risk Mental State: WHOQoL-BREF: World Organization Quality of Life-Bref version; CAARMS: Comprehensive Assessment of At-Risk Mental States; CDS: Calgary Depression Scale;.GF, Global Functioning.

[2] Descriptive data of Table 1 is the same that in Study 1 and it is shown again because each study of the thesis is written in article format and is prepared to be submitted to publication.

Table 2. Correlations between the different domains of sQoL with severity of symptoms and current functioning in ARMS patients (N= 34).

	Subjective Quality of Life (WHOQoL-BREF)				
	Physical Health	Psychological health	Social Relationships	Environment	Overall sQoL
Symptoms (CAARMS)					
Positive symptoms	-.14	-.38*	-.14	-.24	-.33
Cognitive change	-.08	-.23	.04	-.06	-.08
Emotional disturbance	-.24	-.09	-.04	.01	-.09
Negative symptoms	-.40*	***-.50*** **	-.40*	-.32	-.49**
Behavioural change	-.47**	-.47**	***-.50*** **	-.41*	-.41
Motor/physical changes	-.15	-.11	-.08	-.21	-.27
General psychopathology	-.06	-.29	-.30	-.25	-.38
Depression (CDS)	-.40*	-.41*	-.49**	-.36*	-.48**
Current functioning (GF)					
Social functioning	***.65**** **	.38*	***.62*** **	.33	.31
Role functioning	.43*	.47**	***.60*** **	***.52*** **	***.44*** **
Duration of Untreated Illness	-.74	-.16	*-.04*	*-.16*	-.17

Abbreviations: QoL: Quality of life; WHOQoL-BREF: World Organization Quality of Life-Bref version; CAARMS: Comprehensive Assessment of At-Risk Mental States; CDS: Calgary Depression Scale;.GF: Global Functioning;

*= p<.05, **= p<.01, ***p<.001

Medium effect sizes in bold, large effect sizes in bold and italics.

4. DISCUSSION

Findings show that different domains of sQoL are differentially and meaningfully associated with symptom severity, suggesting that greater symptom severity is associated with decreased sQoL in ARMS stage of psychosis. Furthermore, functional impairment shows to be strongly associated with poor sQoL, with role functioning showing meaningfully associations with all sQoL domains.

Moreover, contrary to previous studies in schizophrenia general psychopathology was not associated with sQoL in ARMS patients. However, it is noteworthy that when depression

was analyzed as independent variable from general psychopathology, it shows to be strongly related with all sQoL domains including overall sQoL. This is consistent with several previous studies on FEP and with one of the two previous studies on ARMS patients suggesting that depression appears to be the most important predictor of sQoL in the initial prodromal states (Ruhrmann et al., 2008). Nevertheless, is important to take with caution these findings, given that previous research has shown that depressed patients tend to overestimate their difficulties (Atkinson et al., 1996), which may also affect their perception of QoL.

Interestingly, behavioral change and negative symptoms was related to most of the sQoL domains, may be because the overlap of this dimension with social functioning. In addition, positive symptoms were only associated with poor psychological health domain. However, DUP was not related with sQoL.

The clear association of sQoL with social and role functioning indicates that functioning in ARMS patients could already be an important determinant of sQoL, so should to be considered in future research about sQoL in the at risk stage of psychosis. These findings underscore the importance of specifically addressing the social and occupational dysfunctions present in early psychosis with psychosocial interventions.

Considering that severity of symptoms and functional impairment are strongly related with a perception of poor QoL in ARMS patients, might be interesting to speculate that many of ARMS individuals seek help not only because they have a range of psychopathology or functional impairment, but because the onset of the syndrome could influence in their own perception of their life satisfaction (Preda et al., 2002). According to Bechdolf et al., (2005), our findings also support the notion that ARMS patients constitute a clinical population for which further intervention is indicated. More research is needed to elucidate which specific factors are determinants of sQoL on these prodromal patients, in order to target early interventions to prevent severity of symptoms, functional and sQoL impairment.

STUDY 3:

Relatives' Expressed Emotion, Attributions and Emotional State in At-Risk Mental State and First-Episode Psychosis.

Abstract

Aim: This study aims to examine associations between relatives' criticism and Emotional Over-Involvement (EOI) with illness attributions and relatives' emotional states in At-Risk Mental States (ARMS) and First-Episode of Psychosis (FEP), as well as to compare these family factors between ARMS and FEP relatives.

Methods: This study comprises 56 relatives in total, from 25 ARMS and from 31 FEP patients. Relatives completed self-administered questionnaires.

Results: Criticism was associated with perception of negative consequences of disorder for both the patient and the relative and attributions of blame toward the patient in both ARMS and FEP relatives. In ARMS, relatives' criticism also related to the perception of a chronic and cyclical pattern of the disorder, attributions of illness coherence and emotional representation. EOI was associated with perception of cyclical pattern of the disorder, attributions of negative consequences for both patient and relatives, and emotional representation in both ARMS and FEP relatives. EOI in ARMS relatives also related to anxiety and perception of chronic disorder. Most FEP relatives showed higher levels of criticism unlike ARMS relatives. ARMS relatives show higher levels of anxiety than FEP relatives. However, no differences were found in any of the illness attributions between ARMS and FEP relatives.

Conclusions: Relatives' illness attributions and emotional state are strongly associated with criticism and EOI even at early stages of psychosis. Family interventions in early psychosis should focus on identifying beliefs about psychosis, to reduce negative appraisal and distress, as well as to prevent the entrenchment of high-EE attitudes over time.

Key words: Criticism, Emotional Over-Involvement, Illness attributions, emotional state, At-Risk Mental States, First Episode Psychosis.

1. INTRODUCTION

Adapting to life with a relative affected by mental disorder is often a stressful experience that creates a sense of subjective burden and distress in family members (Jungbauer and Angermeyer, 2002). There is substantial evidence in the literature which demonstrates that the responsibility of providing care for a family member with psychotic disorder can lead to elevated levels of distress, anxiety and depression in caregivers (Barrowclough et al., 1996; Collins and Addington, 2006), which in turn, may elicit a variety of responses in relatives, including critical and Emotional Over-Involvement (EOI) attitudes (Kavanagh, 1992).

Expressed Emotion (EE) is a measure of the family environment and attitudes expressed by relatives towards an ill family member (Brown et al., 1972; Vaughn and Leff, 1976). High-EE is defined by the presence of elevated levels of criticism, hostility and/or EOI (Vaughn and Leff, 1985). Given that EE has consistently shown to be an important predictor of prognosis in schizophrenia (Butzlaff and Hooley, 1998), much research has focused on trying to understand the psychological factors that underlie this construct. Studies investigating attributions that relatives make about patients' behaviours, have suggested that relatives' emotions would be related to their beliefs about the causes of the disorder (Barrowclough et al., 1994). In the absence of adequate information about the disorder, carers are likely to attribute psychotic symptoms to the patient. In consequence, relatives who blame patient for his behaviour or believe that hi/she has control over their symptoms may react with criticism in an attempt to reduce those behaviours (Hooley and Campbell, 2002; Weisman et al., 1998). Thus, it has been postulated that attributions of control underlie high-EE attitudes (Hooley et al., 2002). On the other hand, it has been suggested that overinvolved relatives tend to believe that they have somehow contributed to the patient's problems, so they usually present self-blaming attributions (Bentsen et al., 1998). Additionally, a recent study has shown that feelings of shame and guilt/self-blaming attributions predict high-EE in relatives of schizophrenia patients (Wasserman et al., 2012).

Most EE studies in the field of psychosis have been carried out with chronic schizophrenia patients (e.g. Kavanagh, 1992; Hooley, 2007). Nevertheless, the recent focus of research on early psychosis has led to an increasing interest in the study of EE at early stages of the psychosis continuum. Some of these studies have shown that high-EE is present, on average, in over half of the relatives of First-Episode Psychosis (FEP) patients (Bachmann et al., 2002; Heikkila et al., 2002), and it seems that caregivers' cognitive representations of psychosis may play an important role in their emotional appraisals even at an early stage of the disorder (Ownmere et al., 2008). McNab et al. (2007) demonstrated that relatives of FEP patients who are highly critical were also more likely to belief that the disorder is controllable by the patient. However, more research is needed to explore relatives' attributions associated with EE in the early stages of psychosis, as well as to examine whether EE, causal attributions and relatives beliefs about the psychotic disorder differ from relatives of patients who are at-risk of psychosis than in FEP relatives.

This study aims to characterize the profile of EE, illness attributions and emotional state in relatives of At-Risk Mental States (ARMS) and FEP patients, as well as to examine how these family factors are associated and how they differ between ARMS and FEP groups. We hypothesized that: a) criticism would be associated with relatives' belief that the patient can control his/her symptoms and with the attribution of blame toward the patient in both ARMS and FEP relatives; b) EOI would be associated with relatives' self-blame attributions and relatives' levels of anxiety in both ARMS and FEP relatives; c) relatives of FEP patients would have higher levels of EOI than those of ARMS patients, while levels of criticism would be higher in ARMS than in FEP relatives.

2. METHOD

2.1. Participants

This study comprises 56 relatives, 25 of ARMS and 31 of FEP patients. They were recruited in the Sant Pere Claver Early Psychosis Program conducted in Barcelona, Spain

(Domínguez-Martínez et al., 2011b). The project is being developed in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) and has been approved by the local ethic committee.

Relatives were selected if they had regular contact and/or the most significant relationship with the patient. In some particular cases we included two relatives per patient, when other relative had regular contact with patient and if they were available to participate in the study. Patients have to meet ARMS criteria assessed by the Comprehensive Assessment of At-Risk Mental States (CAARMS; Yung et al., 2005) or FEP criteria according to DSM-IV (APA, 2002). A total of 73 relatives were initially asked to participate, but only 56 were available and accepted to participate. The main reasons for the refusal to participate were: not interested in the study (n=3); living in another country or city (n=3); relatives not available or difficult to contact (n=10) and lacking fluency in Spanish (n=1). All relatives provided written informed consent to participation.

2.2. Measures

EE status was assessed with the Family Questionnaire (FQ; Wiedemann et al., 2002), which comprises 20 items equally distributed in two subscales (EOI and criticism) scored on a 4-point scale ranging from 'never/very rarely' to 'very often'. Illness Attributions were assessed with the Illness Perceptions Questionnaire for Schizophrenia (IPQS; Lobban et al., 2005), a measure of beliefs that relatives have about schizophrenia. All items are rated from 1 'strongly disagree' to 5 'strongly agree'. For the purposes of this study we used the following subscales of IPQS: cause (personal ideas about the cause of the disorder), timeline acute/chronic and timeline cyclical (perception of the pattern and duration of the disorder), consequences for both patients and relative (the expected effects and outcome of the disorder), 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), treatment control/cure (usefulness of treatment), illness coherence

(understanding of the disorder) and emotional representation (negative emotions about illness). The Depression and Anxiety subscales of the Symptom Checklist (SCL-90-R; Derogatis, 1977; Ruipérez et al., 2001) were used to assess emotional state on relatives.

2.3. Statistical analyses

Chi-square tests, or Fisher's exact test when appropriate, were calculated to test for possible differences between ARMS and FEP relatives on categorical variables. Student's t-test was used to compare mean scores of family factors. Pearson correlations were used to examine the associations between EE indices, illness attributions and emotional states, and Z-Fisher was used to compare differences of these correlations. The effect size of correlations is presented according to Cohen´s guidelines (medium effect: magnitude >.30, large effect: magnitude >.50) (Cohen, 1988).

3. RESULTS

3.1. Characterisation of socio-demographic, EE, attributions and emotional state in ARMS and FEP relatives.

Table 1 shows relatives' socio-demographic characteristics. Most of ARMS relatives were parents who lived with the patient. More than half were working and about half were married. Similarly, relatives of FEP patients were mostly parents and some of them were couple/partner. About half were working, most were married and living with the patient. Significant differences were found on gender between ARMS and FEP relatives, given that most of ARMS relatives were female, unlike FEP relatives.

Table 1. Relatives' socio-demographic characteristics.

	ARMS N=25	FEP N=31	Statistics
	n (%)	n (%)	
Age (mean, SD)	52.4 (8.8)	50.8 (12.2)	t=.55
Gender			X^2=4.857*
Males	5 (20)	15 (48.4)	
Females	20 (80)	16 (51.6)	
Relationship to patient			Fisher=6.916
Parent	24 (96)	26 (83.9)	
Couple/ spouse	-	4 (12.9)	
Sibling	1 (4)	1 (3.2)	
Education			Fisher=5.956
Primary education	5 (20)	6 (19.4)	
Secondary education	15 (60)	17 (54.8)	
University studies	5 (20)	8 (25.8)	
Occupation			Fisher=6.445
Unemployed/unoccupied	2 (8)	4 (12.9)	
Student	-	1 (3.2)	
Worker/Employee	17 (68)	16 (51.7)	
Homemaker	1 (4)	4 (12.9)	
Retired	3 (12)	4 (12.9)	
Sick leave	3 (12)	2 (6.5)	
Marital Status			Fisher=4.624
Single	1 (4)	1 (3.2)	
Married or analogous	13 (52)	24 (77.4)	
Separated/Divorced	8 (32)	5 (16.1)	
Widowed	3 (12)	1 (3.2)	
Living with the patient			Fisher=.821
Yes	23 (92)	26 (83.9)	
No	2 (8)	5 (16.1)	
Nationality			X^2=.777
Spanish	19 (76)	25 (80.6)	
Foreign	6 (24)	6 (19.4)	
Ethnicity			Fisher=4.931
Caucasian-white	19 (76)	26 (83.9)	
Eastern European	-	2 (6.5)	
Arab	-	1 (3.2)	
Sub-Saharan	-	-	
Latino American	6 (24)	2 (6.5)	

Abbreviations: ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; SD: Standard Deviation

* $p<0.05$

Table 2 presents descriptive data for all relatives' measures as well as mean comparisons between ARMS and FEP relatives.

Following Wiedemann et al.'s (2002), relatives were classified as high EE if they scored 23 or more on the criticism subscale of the FQ, or 27 or more on the EOI subscale. Significant differences were found in levels of high and low criticism between groups. Most of FEP relatives show high criticism, whereas less than half of ARMS relatives show high criticism. On the other hand, most of both ARMS and FEP relatives show lower levels of EOI.

In order to explore causal attributions, individual items of the cause-subscale were ranked in terms of strength of belief as indicated by Lobban et al. (2005). Thus, the most strongly held beliefs (median=4) of both ARMS and FEP relatives were that the disorder had been caused by patient stress or worry and, because patients think too much about things. Besides, ARMS relatives believe that patient's problems were caused by patients' personality and mental attitude (e.g. thinking about life negatively). It is interesting to note that, no differences were found in any of the attributions subscales between ARMS and FEP relatives.

Regarding relatives' emotional state, ARMS relatives show significantly higher levels of anxiety than those of FEP relatives.

3.2. Associations between criticism and EOI with illness attributions and emotional state of ARMS and FEP relatives.

Table 3 presents correlations between criticism and EOI with illness attributions and emotional state of relatives of both ARMS and FEP patients.

Several illness attributions were associated with both criticism and EOI. Timeline acute/chronic attributions, which reflect a perception of a more chronic course of the disorder, were associated with EOI in ARMS relatives. Thus, it seems that when relatives believe that ARMS problems would be more chronic over time, they tend to be more overinvolved.

Table 2. Descriptive and mean differences of relatives' measures

		ARMS Relatives N=25		FEP Relatives N=31		Mean Comparison
	Possible range	Range	Mean (SD)	Range	Mean (SD)	t-test
Expressed Emotion (FQ)						
Criticism	10-40	10-33	21.8 (6.1)	10-32	18.7 (6.2)	1.9
EOI	10-40	15-36	24.4 (5.7)	14-35	23.4 (5.7)	.64
High CC (>23), n (%)			11 (44)		25 (80.6)	χ^2=3.976*
Low CC (≤ 23), n (%)			14 (56)		6 (19.4)	
High EOI (>27), n (%)			7 (28)		8 (25.8)	.18
Low EOI (≤ 27), n (%)			18 (72)		23 (74.2)	
Overall high EE n (%)			13 (52)		10 (32.3)	1.5
Overall low EE n (%)			12 (48)		21 (67.7)	
Illness Attributions (IPQS)						
Causes	25-125	32-80	60.4 (12.6)	34-91	61.3 (14.8)	.31
Timeline Acute/Chronic	6-30	6-26	17 (4.3)	7-30	16.6 (5.3)	-.27
Timeline Cyclical	4-20	4-20	13.5 (3.9)	4-20	11.1 (4.5)	-2.1
Consequences-patient	11-55	18-53	34.8 (9.1)	18-47	33.7 (8.3)	-.49
Consequences-relative	9-45	12-38	38 (21.9)	14-40	22.9 (6.5)	.53
Personal control-patient	4-20	8-16	12.9 (2.5)	9-20	14.8 (3.0)	.22
Personal control-relative	4-20	8-16	11.1 (2.6)	6-20	13.7 (3.3)	.97
Personal Blame-patient	3-15	3-15	7.8 (2.7)	3-15	9.3 (2.3)	-1.6
Personal Blame-relative	3-15	3-12	7.8 (2.7)	3-13	6.5 (2.9)	-1.8
Treatment control/cure	5-25	13-25	18.2 (3.4)	11-25	19 (2.8)	.92
Illness coherence	5-25	6-21	13 (4.2)	6-23	12.5 (4.5)	-.65
Emotional representation	9-45	13-40	29 (7.6)	10-41	27.7 (6.3)	-.68
Emotional State (SCL-90-R)						
Anxiety	0-40	0-22	7.2 (6.4)	0-20	5 (4.3)	1.4*
Depression	0-52	0-37	16.5 (10.6)	0-34	11.7 (8.6)	1.8

Abbreviations: ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; SD: Standard Deviation; EOI: Emotional Over-Involvement; SCL-90-R: Symptom Checklist-90-Revised; FQ: Family Questionnaire.

* $p<0.05$

Moreover, attributions of time-line cyclical, which refers to a perception of a more cyclical or episodic pattern of the disorder over time, was highly associated with both criticism and EOI in ARMS relatives, whereas it was only related with EOI in FEP relatives. Attributions of greater negative consequences of the disorder for the patient were significant associated with criticism in ARMS relatives and with EOI in both ARMS and FEP relatives. On the other hand, attributions of greater negative consequences of the disorder for the relatives was highly related with both criticism and EOI in ARMS and FEP relatives, showing larger effect sizes in almost all associations, which suggest that this may be an important kind of attribution in relation to EE at early stages of psychosis.

Neither of the control attributions (nor patient-control or relative-control), nor attributions of self-blame or treatment control/cure (usefulness of treatment) were significantly associated with criticism or EOI.

Attribution of blame toward the patient was related with criticism in both ARMS and FEP relatives. Moreover, attribution of illness coherence, which reflects the sense of having a comprehensive understanding of the disorder, was highly associated with criticism in ARMS relatives. Thus, relatives of ARMS patients who were highly critical seem to have no coherent understanding of the disorder. Furthermore, emotional representation, which reflects negative emotion about the disorder, was significantly associated with EOI in both ARMS and FEP relatives, and with criticism in ARMS relatives. Note that all these associations showed larger effect sizes.

Additionally, significant differences were found on associations between criticism with both attributions of illness coherence and emotional representation in ARMS, unlike FEP relatives. Finally, relatives' levels of anxiety were significantly associated with criticism in both ARMS and FEP relatives, with large effect size in the case of ARMS relatives and with medium effect size in FEP relatives.

Table 3. Differential correlations of EOI and CC with relatives' emotional state and illness attributions.

	ARMS relatives N=26		FEP relatives N=31		Difference of correlation Z-Fisher	
	Criticism	EOI	Criticism	EOI	Criticism	EOI
Illness Attributions (IPQS)						
Cause	.12	*.34*	*.38*	.09	-.88	.83
Timeline Acute/Chronic	*.31*	*.44**	*.30*	*.30*	.12	.41
Timeline Cyclical	***.53****	***.56****	*.36*	*.37**	.74	.87
Consequences-patient	*.47**	***.58****	*.36*	*.38**	.26	.90
Consequences-relative	*.42**	***.52****	***.59****	***.52****	-.74	.70
Personal control-patient	.17	.04	*.36*	.15	-.72	-.41
Personal control-relative	.20	*.34*	-.18	*.46*	1.26	1.09
Personal Blame-patient	*.46**	*.35*	***.48****	.26	-.09	.35
Personal Blame-relative	.20	.14	-.00	.02	.77	.37
Treatment control/cure	-.11	.15	-.07	.00	-.13	.55
Illness coherence	***.52****	.11	.10	.14	1.70*	-.08
Emotional representation	***.65****	***.75****	.17	***.61****	1.99*	.91
Emotional State (SCL-90-R)						
Anxiety	***.53****	***.60****	*.44**	.10	.41	1.95*
Depression	*.46**	*.42**	***.48****	.22	-07	0.7

Abbreviations: ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; EOI: Emotional Over-Involvement; SCL-90-R

* p<0.05; ** p<0.01

Medium effect sizes in bold, large effect sizes in bold and italics.

EOI was strongly and differentially associated with levels of anxiety in ARMS than in FEP relatives. Moreover, relatives' levels of depression were related to both criticism and EOI in ARMS relatives, while it was only associated with criticism in FEP relatives.

4. DISCUSSION

This study shows that even in early stages of psychosis, criticism and EOI are highly associated with several kinds of illness attributions, which supports the idea that relatives' cognitive representations of psychosis are strongly linked to their emotional responses toward the patient's disorder. Furthermore, findings demonstrated that higher levels of

anxiety and depression in relatives are associated with EE, suggesting that relatives' distress and concern about the patients, could provoke negative emotional reactions toward them in form of criticism and EOI.

Regarding prevalence of EE components in our sample, contrary to what was expected, most of ARMS relatives show lower levels of both criticism and EOI, whereas FEP relatives show higher levels of criticism and lower levels of EOI. Nevertheless, the prevalence of high-EE in FEP relatives was consistent with a range of prevalence between 20% and 71%, previously reported in FEP samples (e.g. Bachmann et al., 2002, Heikkilä et al., 2002; Patterson et al., 2005). This wide range of prevalence of EE in FEP samples has led to the hypothesis that EE is not a stable factor but a much more fluid characteristic that changes over time, usually from high to low, as patient exhibit improvement in severity of symptoms (Lenior et al., 2002; Scazufka and Kuipers, 1998). Thus, we could speculate that, in our particular FEP sample, as patients were psychopathologically stable at the moment of the assessment, most relatives presented overall low-EE. On the other hand, prevalence of high-EE in relatives of ARMS patients (52%) was higher than reported in previous studies (O'Brien et al., 2006; Schlooser et al., 2010; McNab et al., 2007). Contrary to McFarlane and Cook (2007), who suggest that EE appears to be secondary to onset and progression toward chronic disability, our findings show that high-EE is already present in at-risk of psychosis phase, in average, on half of the relatives. Therefore, given the important impact of EE on illness prognosis and the vulnerable psychological status of early psychosis patients, family intervention should be a prioritary target of early psychosis programs, in order to prevent the entrenchment of high-EE attitudes over time.

On the other hand, findings show that relatives of this sample tend to belief that the disorder is caused by patient stress or worry, as well as for thinking too much about things. This is consistent with previous findings on FEP, suggesting that relatives attribute the cause of psychosis to stress management difficulties and interpersonal stress (Clarke and Couchman, 2012). Furthermore, ARMS relatives believed that the patients' personality and

mental attitude (e.g. thinking about life negatively) were causes of their problems, which supports the idea that relatives may particularly view prodromal symptoms as related to difficulties in negotiating the normal tasks of adolescence, rather than being symptoms of an emerging psychosis (Lay et al., 2000). Thus, it is important that early psychosis programs and mental health services provide relatives more information about psychosis, in order to improve their understanding of the situation and help them to adequately address the challenges of the disorder.

With respect to the associations between criticism and EOI with relatives' illness attributions and emotional state, as expected, criticism was associated with attributions of blame toward the patient. However, it was also related with attributions of consequences for both patient and relatives in both ARMS and FEP relatives. Therefore, it seems that relatives highly critical, tend to perceive that the disorder is having negative consequences in the patient and in his own life, and therefore, would be likely to blame the patient for the disorder. Nonetheless, criticism in ARMS relatives could also be explained by its associations with negative emotions of the disorder (emotional representation) and their lack of understanding of the disorder (illness coherence). This is consistent with previous studies suggesting that, in absence of adequate information about the disorder, relatives are likely to blame the patient for his behaviour and tend to react with criticism in an attempt to change those behaviours (Weisman et al., 1998). Furthermore, criticism in both ARMS and FEP relatives was also related to higher levels of anxiety and depression, which demonstrated that in these early stages of psychosis, the disorder is having an important impact on relatives' emotional state, provoking feelings of concern and distress (Barrowclough et al., 2001) and, in turn, is influencing their emotional responses, making them more critical (Kavanagh et al., 1992).

On the other hand, contrary to what was expected, EOI was not associated with self-blame attributions (Bentsen et al., 1998), although it was associated with levels of anxiety in ARMS relatives, as was predicted. Furthermore, although several studies on schizophrenia have shown that attributions of control over the disorder are associated with EE

(Barrowclough et al., 1994; Hooley and Campbell, 2002), our findings showed that control attributions were not related with any of EE components, neither in ARMS nor in FEP relatives. Thus, it seems that in early stages of psychosis, unlike in chronic phases of illness, control attributions are not determining high-EE responses. Nevertheless, perception of more negative consequences of the disorder in relatives has emerged as an important kind of attribution that could influence EE in early psychosis, since it was the attribution that most highly associated with both criticism and EOI. However, more research is needed to clarify how relatives' beliefs elicit specific emotional responses in different stages of psychosis.

Besides, comparison between ARMS and FEP groups indicated that there were more females in ARMS group than in FEP group. Nevertheless, more of the FEP relatives showed higher levels of criticism than ARMS relatives. Besides, levels of anxiety were higher and strongly associated with EOI in ARMS than in FEP relatives. Finally, criticism in ARMS was strongly associated with lack of understanding of the disorder (illness coherence) and negative emotions about the disorder (emotional representation), unlike FEP relatives.

In conclusion, findings show that relatives' illness attributions and emotional state are strongly associated with criticism and EOI in early stages of psychosis. Moreover, the relatives' lack of knowledge about the psychotic disorder, especially in ARMS stage, highlights their need to be informed about the nature and course of psychosis, so they can cope and adequately address the challenges of the disorder over time. Furthermore, family intervention needs to focus on identifying beliefs about psychosis in the process of the treatment, especially when relatives are dealing with the emergence of a psychotic disorder, with the purpose to reduce their negative appraisals, distress, anxiety and depression, as well as to prevent the entrenchment of high-EE attitudes over time.

STUDY 4:

Relatives' illness attributions mediate the association of expressed emotion with early psychosis symptoms and functioning

Abstract

Aim: Expressed Emotion (EE), particularly criticism and emotional over-involvement (EOI), is associated with prognosis in psychosis. However, the mechanisms underlying this association are not well understood. The attributional model could be useful for elucidating the developmental pathway through which family stress and early psychotic processes are related. This study investigates: 1) the effect of criticism and EOI on symptoms and functioning of At-Risk Mental State (ARMS) and First-Episode Psychosis (FEP) patients, and 2) whether these associations are mediated by relatives' attributions of control and blame.

Method: 44 patients (20 ARMS and 24 FEP) and their key relatives were included. Relatives completed self-administered measures for EE and illness attributions.

Results: Findings indicated that relatives' criticism predicted all variety of symptoms, while EOI only predicted negative symptoms and general psychopathology. Both indices predicted worse functioning. Most of the relationships between EE indices and illness severity were mediated by relatives' attributions of blaming the patient for their symptoms and difficulties. Conversely, relatives' self-blaming attributions and attributions of control over the disorder by either relatives or patients were not associated with patients' variables or EE. No significant differences emerged between groups (ARMS vs. FEP) on the ratings of relatives' EE or attributions.

Conclusion: Findings highlight the importance of family emotional environment in the very early stages of psychosis, as well as the mediating role that relatives' beliefs can exert in those relationships. Family interventions should be prioritized in order to assist relatives to change attributions that blame patient and to prevent the entrenchment of high-EE.

Keywords: Illness Perceptions, Attributions, Criticism, Emotional Over-involvement, At-Risk Mental States, First-Episode Psychosis.

1. Introduction

An increasing body of evidence indicates that expressed emotion (EE) (Vaughn and Leff, 1985), particularly criticism and Emotional Over-Involvement (EOI), is a strong predictor of prognosis in schizophrenia (Butzlaff and Hooley, 1998; Hooley, 2007). Nevertheless, the mechanisms underlying this association remain unclear.

The attributional model (Barrowclough et al., 1994; Barrowclough and Hooley, 2003) could be useful for elucidating the developmental pathway through which family stress and psychotic processes are related. It postulates that relatives' beliefs about patients' problematic behaviors are related to their emotional attitudes towards them. It seems that critical relatives are more likely to blame patients for their behaviours and view symptoms as controllable by them rather than as a result of the illness. Consequently, they critically attempt to change those behaviours. In contrast, overinvolved relatives tend to attribute symptoms as uncontrollable by the patient. Besides, they believe that they have somehow contributed to the patients' problems, so they usually also present self-blaming attributions.

It has been suggested that those behaviours that more clearly reflect signs of mental disorder, such as positive symptoms, are more likely to elicit attributions of symptoms' uncontrollability in relatives, and therefore, engender EOI attitudes (i.e. exaggerated emotional responses or overprotectiveness) (Brewin et al., 1991). Conversely, disturbance, such as negative symptoms or poor functioning are more probable to be considered under the patient's control, raising more critical attitudes from relatives (Weisman et al., 1998).

The study of EE in the early stages of the psychosis continuum is highly relevant as the specific circumstances of early psychosis differ from those of chronic schizophrenia where the disorder is clearly established and more assumed by relatives. Also, some studies have shown that relatives' EE levels are independent of illness chronicity (Bachmann et al., 2002; Meneghuelli et al., 2011), suggesting the suitability of examining EE in early psychosis. Indeed, the early steges of psychosis are critical to explore associations between EE, symptoms and mediating mechanisms given that both patients' symptoms and relatives'

appraisals and attitudes are emerging and their associations being established. Also, the study of these phenomena without the bias created by chronicity and long term burden is essential to better understand the ontogenesis of the relationship between patients' symptoms and relatives' attitudes, as well as to design early interventions focused on the prevention of entrenchment of high-EE and setting attributional changes.

To date, findings about the differential relationship between EE indices and specific symptoms and functioning in early psychosis are scarce and contradictory. On the one hand, some studies on At-Risk Mental States (ARMS) and First-Episodes Psychosis (FEP) found no association between EE and symptoms/functioning (e.g. Álvarez-Jiménez et al., 2010; McFarlane and Cook, 2007; Meneguelli et al., 2011). On the other hand, some studies on FEP have shown associations between general and negative symptoms with both criticism and EOI (King et al., 2000; Mo et al., 2007). Furthermore, preliminary research on ARMS patients points out the important role that EE seems to play in the outcome of early psychosis. Particularly, attitudes related to positive affect predicted improvement in negative symptoms and functioning (O'Brien et al., 2006, 2008), while negative affect in the form of criticism predicted worsening of positive attenuated psychotic symptoms (Schlooser et al., 2010).

Regarding relatives' illness attributions in early psychosis, McNab et al., (2007) examined the association of attributions with EE in FEP relatives and found support for the attributional model at this stage of the illness, that is, relatives' who were highly critical were more likely to attribute that psychotic disorder was controllable by the patient. Nevertheless, no studies have directly considered the possible mediating role of attributions in the association between EE and illness severity, although it has been demonstrated that caregivers' cognitive representations of psychosis may play an important role in their emotional appraisals, even at an early stage of the disorder (Ownmere et al., 2008).

The present study aims at: 1) examining the effect of relatives' EE (criticism and EOI) on patients' symptoms and functioning and whether this potential association is different in

At-Risk Mental State (ARMS) and FEP patients; and 2) testing whether the association between EE and symptoms/functioning is mediated by relatives' attributions of control and blame. Despite the lack of previous studies, we established hypothesise following the attributional model: (a) EOI would have an effect on positive symptoms, whereas criticism would have an effect on negative symptoms and functioning; (b) considering that, theoretically, signs of illness are more evident in FEP than in ARMS, the association between EOI and positive symptoms would be stronger in the FEP group, while the association between criticism and negative symptoms/functioning would be stronger in the ARMS group; (c) relatives' attributions of self-control and self-blame would mediate the association between EOI and positive symptoms, whereas relatives' attributions of control and blame toward the patient would mediate the association between criticism and negative symptoms and functioning.

2. Methods

2.1. Participants

44 patients (20 ARMS and 24 FEP) and their respective key relatives were included in the study. Key relatives were those who had most contact and/or the most significant relationship with the patient. ARMS criteria were established based on the Comprehensive Assessment of At-Risk Mental States (CAARMS; Yung et al., 2005). FEP patients met DSM-IV (APA, 2002) criteria for any psychotic disorder or affective disorder with psychotic symptoms. Exclusion criteria for patients were: a) evidence of organically based psychosis, b) any previous psychotic episode pharmacologically treated, and c) mental retardation.

2.2. Measures

Relatives completed the Family Questionnaire (FQ; Wiedemann et al., 2002) and the Illness Perceptions Questionnaire for Schizophrenia (IPQS; Lobban et al., 2005). Both are well-established instruments to measure EE and attributions, respectively. The FQ consists

of 20 items equally distributed into two subscales (EOI and criticism) and 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 of .80 for EOI and .87 for criticism. Four subscales of the IPQS were used for the present study: 1) Control–patient; 2) Control–relative; 3) Blame–patient; and 4) Blame–relative. All the IPQS items are rated from 1 'strongly disagree' to 5 'strongly agree'. The Alpha of these subscales was good (from .69 to .88).

Patients were assessed with the Positive and Negative Syndromes Scale (PANSS; Kay et al., 1987), the Calgary Depression Scale (CDS; Addington et al., 1990), the short version of the Social Functioning Scale (SFS; Birchwood et al., 1990), and the Social and Role Global Functioning Scales (GF-S and GF-R; Cornblatt et al., 2007). To confirm the fulfilment of the diagnostic inclusion criteria, the CAARMS (Yung et al., 2005) was administered to ARMS patients and the Structured Clinical Interview for DSM-IV Axis-I Disorders (SCID-I; First et al., 1996) was administered to FEP patients.

2.3. Procedure

The present study is embedded in a larger longitudinal study currently being carried out in three Mental Health Centres of Barcelona (Spain) belonging to the Sant Pere Claver Early Psychosis Program (Domínguez-Martínez et al., 2011b). The project is being developed in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. It has been approved by the local ethic committee. Written informed consent was obtained from all participants.

All the assessments were conducted by experienced clinical psychologists. The time gap between patients and relatives assessments ranged from 3 to 15 days.

2.4. Data analysis

First, the effect of relatives' EE (criticism and EOI), group (ARMS=0 vs. FEP=1) and their interaction (EE x group) on patients' symptoms and functioning was analysed by means of separate multiple linear regression models. The effect size (Cohen's f^2) is also presented and was interpreted following Cohen guidelines (medium effect: magnitude >.30, large effect: magnitude >.50) (Cohen, 1988). Second, in order to investigate whether relatives' illness attributions of control and blame mediated the association between EE (criticism and EOI) and symptoms/functioning, regression analyses were first used to test the association between relatives' beliefs with EE and patients' variables and, secondly, Sobel's test was used to test for partial mediation.

3. Results

3.1. Sample characteristics

Relatives were predominantly woman (65.9%) and patients' mothers (59.1%), with the remaining caregivers being their fathers (27.3%), partners (9.1%) or siblings (4.5%). Mean age was 51.2 years old (SD= 11.9). Most patients were male (65.9%) and lived with their relatives (86.4%). Mean age was 23.7 years old (SD= 5.6). The 59.2% of patients were studying, working or performing any daily activity, the 34.1% were unemployed/unoccupied and the 6.8% had a sick leave.

Descriptive data for all relatives' and patients' measures are presented in Table 1. No significant differences emerged between ARMS and FEP relatives in terms of EE or attributions. Regarding patients' ratings, the only significant differences were that ARMS showed more general psychopathology (t= 2.06; p= .046; Cohen's d=.63) and worse social functioning as assessed by the SFS (t= -3.01; p= .004; Cohen's d=.90) than FEP patients.

Table 1. Descriptive data of ARMS and FEP relatives and patients in all the measures (N= 44)[3].

	ARMS n=20 *Mean (SD)*	FEP n=21 *Mean (SD)*
RELATIVES		
Expressed Emotion (FQ)		
Criticism	21.94 (6.50)	18.20 (6.10)
EOI	24.42 (6.50)	22.52 (4.73)
Attributions (IPQS)		
Control Patient	11.50 (1.82)	11.14 (2.70)
Control Relative	13.00 (2.61)	14.10 (2.94)
Blame Patient	10.80 (2.70)	9.13 (3.33)
Blame Relative	7.84 (2.54)	6.40 (3.02)
PATIENTS		
Symptoms		
Positive symptoms (PANSS)	13.90 (3.24)	13.63 (4.60)
Negative symptoms (PANSS)	19.80 (6.26)	18.50 (6.50)
General symptoms (PANSS)	38.60 (8.20)	33.25 (8.90)
Depression (CDS)	6.70 (4.91)	5.60 (5.20)
Functioning		
Social Functioning (SFS)	19.50 (6.10)	24.50 (4.92)
Social Functioning (GF-S)	6.00 (1.38)	6.17 (1.43)
Role Functioning (GF-R)	5.60 (1.19)	5.46 (1.31)

Abbreviations: ARMS: At-Risk Mental State; FEP: First Episode Psychosis; EE: Expressed Emotion; FQ: Family Questionnaire; EOI: Emotional over-involvement; IPQS: Illness Perceptions Questionnaire for Schizophrenia; PANSS: Positive and Negative Syndrome Scale; CDS: Calgary Depression Scale; SFS: Social Functioning Scale; GF-S: Global Functioning-Social Scale; GF-R: Global Functioning-Role Scale.

[3] Descriptive data of relatives and patients variables are shown again because all studies of the thesis are written in article format and are prepared to be submitted to publication On the other hand, it is important to note that sample of Study 4 is different than those of Study 1 and Study 3, given that in Study 4 we included dyads of one relative by patient, whereas in Study 3 we included in some cases two relatives by patient.

3.2. Effect of relatives' EE on patients' symptoms and functioning and differences between groups (ARMS vs. FEP)

Results of the effect of relatives' levels of criticism and EOI, group (ARMS vs. FEP) and their interaction on patients' measures are provided in Tables 2 and 3. On the one hand, criticism significantly predicted all patients' clinical and functioning variables, except for social functioning as measured with the GF-S (see Table 2). Thus, relatives' criticism had an association with patients' higher symptom severity and worse functioning. No interaction between criticism and group was found. On the other hand, EOI was a significant predictor of negative and general symptoms, as well as of social and role functioning (see Table 3). So, the fact that relatives behaved in a more overinvolved way with patients was also related to worse functioning and more symptom severity, except for positive symptoms and depression. In terms of effect size (f^2), criticism hold a stronger association with positive symptoms and EOI with negative symptoms. Again, no interaction between EOI and group was significant.

Table 2. Linear regressions of the effect of relatives' CRITICISM, group (ARMS vs. FEP) and their interaction on patients' clinical and functional measures (N= 44).

	Step 1 (df= 1, 39) CRITICISM		Step 2 (df= 1, 38) ARMS vs. FEP		Step 3 (df= 1, 37) Criticism x Group INTERACTION	
CRITERION	B	f^2	β	f^2	β	f^2
Clinical measures						
Positive symptoms (PANSS)	.48**	.29	.04	.00	.06	.00
Negative symptoms (PANSS)	.35*	.14	-.08	.00	-.07	.00
General symptoms (PANSS)	.43**	.23	-.25	.08	-.05	.00
Depression (CDS)	.36*	.14	-.02	.00	.05	.00
Functioning						
Social Functioning (SFS)	-.43**	.22	.39**	.20	.02	.00
Social Functioning (GF-S)	-.29	.09	.07	.00	.21	.05
Role Functioning (GF-R)	-.43**	.22	-.19	.04	-.01	.00

Abbreviations: ARMS: At-Risk Mental State; FEP: First Episode of Psychosis; d:f degrees of freedom: β: Beta; *f2*: Effect size coefficient; PANSS: Positive and Negative Syndrome Scale; CDS: Calgary Depression Scale; SFS: Social Functioning Scale; GF-S: Global Functioning-Social Scale; GF-R: Global Functioning-Role Scale.
* p<.05, ** p<.01; Medium effect sizes in bold.

Table 3. Linear regressions of the effect of relatives' EOI, group (ARMS vs. FEP) and their interaction on patients' clinical and functional measures (N= 44).

	Step 1 (df= 1, 40) EOI		Step 2 (df= 1, 39) ARMS vs. FEP		Step 3 (df= 1, 38) EOI x Group INTERACTION	
CRITERION	β	f^2	β	f^2	β	f^2
Clinical measures						
Positive symptoms (PANSS)	.28	.09	.03	.00	-.07	.00
Negative symptoms (PANSS)	.37*	**.16**	-.06	.00	-.14	.02
General symptoms (PANSS)	.40**	**.19**	-.26	.08	-.18	.04
Depression (CDS)	.30	.09	-.02	.00	-.07	.00
Functioning						
Social Functioning (SFS)	-.14	.02	.45**	**.25**	.06	.00
Social Functioning (GF-S)	-.49**	**.31**	.02	.00	.06	.00
Role Functioning (GF-R)	-.43**	**.22**	-.15	.03	-.06	.00

Abbreviations: EOI: Emotional Over-Involvement; ARMS: At-Risk Mental State; FEP: First Episode of Psychosis; df: degrees of freedom; β: Beta; *f*2: Effect size coefficient; PANSS: Positive and Negative Syndrome Scale; CDS: Calgary Depression Scale; SFS: Social Functioning Scale; GF-S: Global Functioning-Social Scale; GF-R: Global Functioning-Role Scale.
*p<.05, **p<.01; Medium effect sizes in bold.

Therefore, it seems that when relatives attributed the disorder and their difficulties to patients they were more likely to express higher levels of EE (especially criticism) and patients were more likely to exhibit higher symptom severity (especially, negative and general symptoms) as well as worse functioning. No significant interaction of relatives' beliefs blaming the patient x group was found. Concerning relatives' attributions of control by the patient, control by relatives themselves and self-blaming attributions, none predicted levels of EE or any of the patients' measures.

Finally, results about relatives' attributions of blaming the patient as mediators of the relationship between EE levels and patients' scores are presented in Table 5.

Table 4. Linear regressions of the effect of relatives' BLAME on PATIENT beliefs, group (ARMS vs. FEP) and their interaction on relatives' EE and patients' clinical and functional measures (N= 44).

	Step 1+		Step 2+		Step 3+	
	BLAME PATIENT		ARMS vs. FEP		Blame patient x Group INTERACTION	
CRITERION	B	f^2	β	f^2	β	f^2
Expressed Emotion (FQ)						
Criticism	.52**	***.37***	-.18	.04	-.12	.02
EOI	.31*	.11	-.11	.01	-.26	.08
Clinical measures						
Positive symptoms (PANSS)	.32*	.12	.02	.00	-.02	.00
Negative symptoms (PANSS)	.49***	.32	-.00	.00	.00	.00
General symptoms (PANSS)	.47**	.29	-.25	.08	-.07	.00
Depression (CDS)	.31*	.11	-.10	.00	-.23	.06
Functioning						
Social Functioning (SFS)	-.45**	.26	.31*	.13	-.05	.00
Social Functioning (GF-S)	-.30*	.10	.02	.00	.10	.01
Role Functioning (GF-R)	-.54***	***.41***	-.19	.05	-.16	.04

Abbreviations: ARMS: At-Risk Mental State; FEP: First Episode of Psychosis; β: Beta; *f* 2:Effect size coefficient; FQ: Family Questionnaire; EOI: Emotional Over-Involvement; PANSS: Positive and Negative Syndrome Scale; CDS: Calgary Depression Scale; SFS: Social Functioning Scale; GF-S: Global Functioning-Social scale; GF-S: Global Functioning - Role Scale;
+NOTE: For the regressions on Criticism, degrees of freedom (df) were (1, 38), (1, 37), and (1, 36) for each step respectively; and for regressions on EOI, df were (1, 39), (1, 38), and (1, 37). For the rest, df were (1, 41), (1, 40), and (1, 39);
*p<.05, ** p<.01,***p<.001; Medium effect sizes in bold; Large effect sizes in bold and italics.

Relatives' attributions of blame toward the patient were a full mediator of the association that criticism showed with negative symptoms, general psychopathology, depression, social functioning (SFS) and role functioning; however, they did not mediated the relationship between criticism and positive symptoms. Moreover, these attributions also fully mediated the relationship that EOI showed with negative and general symptomatology, while it did not mediate the relationship between EOI and social and role functioning. Thus, it seems that relatives' blame to patients believe has to do with the presence of negative and general symptomatology, but not with positive symptoms. Moreover, it appears to be also related to patients' functioning, although this only occurred for criticism.

Table 5. Mediation analyses testing the mediating role of relatives' BLAME on PATIENT beliefs in the association between relatives' EE with patients' symptoms and functioning (N= 44).

DV	IV	Mediator	Zero-Order Correlation	Partial Correlation	Sobel	Mediation?
Positive symptoms (PANSS)	Criticism	Blame Patient	.48**	.36*	0.95 n.s.	None
Negative symptoms (PANSS)	Criticism	Blame Patient	.35*	.11	-	FULL
General symptoms (PANSS)	Criticism	Blame Patient	.43**	.23	-	FULL
Depression (CDS)	Criticism	Blame Patient	.36*	.27	-	FULL
Social Functioning (SFS)	Criticism	Blame Patient	-.44**	-.24	-	FULL
Role Functioning (GF-R)	Criticism	Blame Patient	-.42**	-.19	-	FULL
Negative symptoms (PANSS)	EOI	Blame Patient	.37*	.25	-	FULL
General symptoms (PANSS)	EOI	Blame Patient	.40**	.30	-	FULL
Social Functioning (GF-S)	EOI	Blame Patient	-.49**	-.43**	-1.27 n.s.	None
Role Functioning (GF-R)	EOI	Blame Patient	-.43**	-.32*	-1.79 n.s.	None

Abbreviations: EE: Expressed Emotion; DV: Dependent variable; IV: Independent variable; PANSS: Positive and Negative Syndrome Scale; CDS: Calgary Depression Scale; SFS: Social Functioning Scale; GF-R: Global Functioning - Role Scale; EOI: Emotional Over-Involvement; GF-S: Global Functioning - Social Scale; n.s.non significant

* p<.05, **=p<.01,.

4. Discussion

This study investigated the relationship between relatives' cognitive and emotional appraisals with patients' symptoms and functioning in early psychosis. Findings show important effects of relatives' EE on a wide variety of symptoms and functioning in patients at both the subclinical and onset stages of psychosis. Relatives' attributions of blaming patients for their symptoms and difficulties were found to mediate the relationship between EE and patients' features. Altogether, this highlights the importance of family emotional environment in the very early stages of psychosis, as well as the mediating role that relatives' beliefs can exert in those relationships.

Both criticism and EOI demonstrated to be important predictors of early psychosis symptoms and functioning, although a differential pattern of relationships with positive and negative symptoms emerged. Higher levels of criticism, but not of EOI, were related to the severity of positive symptoms, whereas both EE indices were related to negative symptoms (and general psychopathology). Our first hypothesis, then, was not confirmed, since we expected that EOI would be more strongly related to positive symptoms and criticism to negative symptoms and functioning. This findings seems to suggest that relatives of early psychosis patients, contrary to relatives of patients with longstanding psychosis, express similar levels of EOI and criticism towards negative symptoms and, also, that they react to incipient positive symptoms with a critical attitude instead of overinvolvement, as it is usual in schizophrenia. One plausible explanation to account for these differences is that the attributional model is based on the process of patient relapse in chronic disorders, which implies different forms of interpreting and coping with circumstances than in onset of disorder where symptoms are incipient and relatives' attitudes toward the patient are not yet contaminated by the experience of repeated relapses. Moreover, recent studies suggest that during these early phases of psychosis relatives are more likely to attribute problematic behaviors to factors such as adolescence, patients' personality and/or substance use, rather than as part of an illness process (Clarke and Couchman, 2012). Another interesting and differential of early stages from schizophrenia is that EOI seems to act more as a protective

factor and could have a positive effect in patients' outcome (O'Brien et al., 2006). Thus, it might be that at these stages, relatives still have not developed overprotected or self-sacrificed attitudes, which have been considered the most negative ones for patients within the range of possible EOI attitudes (Vaughn and Leff, 1985), rather, they could be expressing over-concern, distress and/or anxiety towards negative symptoms and poor functioning, but not overprotection and/or self-sacrifice towards positive symptoms, as it has been reported in schizophrenia relatives. Furthermore, our findings are consistent with previous studies showing that EOI is not related to positive symptoms in incipient psychosis (Mo et al., 2007; King et al., 2000) and also support Schlosser et al.'s findings (2010) suggesting that criticism plays a more stressful influence on outcome at these stages than EOI. Given that these kind of attitudes could contribute to precipitate transition to psychosis in prodromal patients and relapse in FEP patients, they should be importantly considered in early family interventions.

Our hypothesis regarding differences in the association between EE and type of symptoms/functioning depending on the group (ARMS vs. FEP) was overall not confirmed. Actually, the groups did not differ in terms of symptom severity, which could be due to the differential pattern and doses of medication. This finding emphasizes the importance of paying attention to psychopathological and family variables even at the at-risk stage, as ARMS and FEP patients are equally dysfunctional and influenced by the family emotional environment.

Concerning the mediating role of relatives' illness attributions in the effect that EE had on patients' features, our findings showed that attributions of blame toward the patient mediated most of the relationships between EE and patients' symptoms and functioning, with the exception that they neither mediated the relationship between criticism and positive symptoms nor the relationship between EOI and functioning. These data lend partial support to the attributional model in the sense that relatives' self-blaming attributions do not seem to be significant at these early stages, as something relevant in chronic schizophrenia (Bentsen et al., 1998). It is possible that relatives' lack of knowledge about the illness at these early

stages (by definition the case in ARMS relatives) enhances beliefs of a stronger controllability by the patient on symptoms, especially the negative ones. According to Brewin (1994), the success of interventions in reducing EE in relatives might lie in part in their ability to promote, an attributional change. Indeed, our findings support the importance of setting attributional changes as an early therapeutic target to help relatives better understand and progressively emotionally accept the new family situation and resolve issues of shame and loss (Patterson et al., 2005; Wasserman et al., 2012). Nevertheless, further research should be conducted to better understand how relatives interpret symptoms prior to the establishment of a mental disorder diagnosis and how these attributions change over the course of the disorder longitudinally.

This study has some limitations. First, the cross-sectional design precludes conclusions about a causal direction. Second, our measure of EE does not consider positive affect (e.g., warmth) of relatives towards patients, which would be very interesting as it has been demonstrated to be importantly related to psychotic symptoms (Medina-Pradas et al, 2012) and it would be informative of family protective factors.

This is the first study, to the best of our knowledge, investigating the mediation of relatives' attributions on the association between EE and patients' symptoms and functioning in early psychosis. In conclusion, this study shows that family negative affect, in form of criticism and EOI, is an important predictor of symptoms and functioning in early stages of psychosis and, that relatives' attributions of blame toward the patient is a strong mediator of the association between EE with clinical and functional features of early psychosis patients. Furthermore, these findings underline important clinical applications. Considering the vulnerable psychological status of early psychosis patients and, given that this is a critical period where patients' symptoms and relatives' appraisals are forming, family interventions should be prioritized in order to assist relatives to change attributions of blame toward the patient and to prevent the entrenchment of high-EE attitudes.

V.GENERAL DISCUSION AND CONCLUSIONS

1. SUMMARY OF MAIN FINDINGS, CLINICAL AND RESEARCH IMPLICATIONS

Overall, this thesis provides highly relevant clinical and research results that can be useful to improve treatment strategies in patients and their families and assist to the design of health policies. Furthermore, findings are consistent and comparable with several programs and studies in early psychosis at different countries. In fact, note that this thesis presents innovative findings, since this is the second national study with the same characteristics and first in Catalonia, which gives it a great add value.

On the one hand, findings justify the importance of early detection and highlight the need of improve treatment, especially in at-risk stages of psychosis, given that patients at this stage show considerable clinical severity, functional impairment and a poor quality of life. On the other hand, findings demonstrate that even in the early stages of psychotic disorder family environment is crucial, since relatives' negative affect in form of criticism and EOI, along with relatives' attributions of blame toward the patient, have an effect on symptoms and functioning of both ARMS and FEP patients. Therefore, family intervention should be a priority target of early psychosis programs, in order to inform relatives about the nature and course of psychosis, to help them to better cope and adequately address the challenges of the disorder over time, as well as to reduce negative appraisals, distress and, therefore, to prevent the entrenchment of high-EE attitudes over time.

1.1. Characterization and differences between At-Risk Mental States and First-Episode stages of the continuum of psychosis

One of the main aims of this thesis was to characterize ARMS and FEP patients, which represent two different stages of the psychosis continuum, and to test the comparability of our sample with international reports. Thus, findings of Study 1 show that socio-demographic, clinical and psychosocial characteristics of the SPC-EPP sample are comparable with those of previous early psychosis studies. However, FEP patients have

shown some differences in comparison with those of some previous studies, maybe because of the heterogeneity of samples across studies.

ARMS stage have been typically characterized as a manifestation of sustained and prolonged period of ill-health including a range of non-specific emotional and behavioural changes such as depressed mood, anxiety, irritability, sleep disturbance, distress, social withdrawal and failure in key areas of relationships, as well as in educational and vocational performance. Besides, ARMS patients usually report mild (or 'attenuated') psychotic-like symptoms such as perceptual changes and suspiciousness (Yung and McGorry, 1996; Yung, 2007). According to this, our findings have shown that ARMS patients were clearly symptomatic and with a marked decline in functional performance. Indeed, psychopathological and functional differences between ARMS and FEP groups were scarce. This suggests that ARMS were almost as ill as FEP patients, and therefore they have to be considered as 'ill' i.e. as 'patients' with a need and right for treatment (Ruhrmann et al., 2010b). Moreover, as has been demonstrated in Study 2, greater symptom severity and functional impairment are strongly related with poor subjective quality of life in ARMS stage of psychosis, which adds one more reason to provide care and specific attention to this at-risk population.

Considering current controversy about the risk/benefit balance of early intervention strategies, critics have argued that some of the patients are falsely identified and treated as if they were at high risk of developing a psychotic disorder, when actually they are never going to develop it. Although it is true that many people attending subthreshold symptoms are not experiencing a current psychotic episode and may never develop one, this does not necessarily mean that they are not experiencing any mental illness. Often they may be experiencing either subthreshold or full threshold symptoms of mood and anxiety disorders (Rosen et al., 2006; Svirskis et al., 2005), and they are all referred to clinical services presenting some form of mental ill health and being usually distressed. Therefore, it is important to consider that most of this population is seeking for help because of their distress

and impaired functioning. So, treatment must be provided to those who require and demand it. According to the staging model, the earlier identification should be associated with safer and less invasive treatments (e.g. psychoeducation and psychosocial treatments rather than medication), focused in alleviate this distress and address their presenting complaints (Yung, 2007). Besides, it is crucial that research at this field should be conducted in an ethical manner and with informed consent.

Furthermore, findings of Study 1 have shown that ARMS and FEP patients present similar illness severity and functional impairment. This suggests that the APS criteria may detect patients at the late prodromal phase who were probably at the edge of their FEP. It is evident that ARMS criteria need improvement in terms of specificity and individual risk assessment to allow for better targeted and earlier interventions. Thus, it is recommendable for the early detection and interventions programs to complement the UHR approach with the COPER and COGDIS risk criteria (Schultze-Lutter et al., 2007), as well as to consider the specific combinations of cognitive, academic and social impairments and disorganization/odd behavior, as has been proposed by RAP program (Cornblatt et al., 2002), in order to improve detection of the 'early psychosis prodrome' instead of the 'late prodrome'.

In conclusion, findings of Study 1 and Study 2 support and justify both the early detection and intervention in psychosis, especially in those ARMS patients who are already ill, distressed and overall unsatisfied with their quality of life. Nevertheless, more research is needed to better characterize the early phases of psychosis, with the purpose of improving the early detection of high-risk populations and deliver treatment as early as possible at the onset of the disorder.

1.2. The importance of relatives' appraisals and the effect of family environment in early psychosis outcome

Considering the compelling evidence in literature demonstrating that family emotional environment can effectively influence the course and outcome of mental disorder and that

the responsibility of providing care for an adolescent or adult child with psychosis can place the caregiver at risk of distress, anxiety, depression, economic strain and stigma (Barrowclough et al., 1996; Szmukler et al., 1996; Addington et al., 2003), another major aim of this thesis was to explore in early stages of psychosis some of the family factors that have been demonstrated to be related with the course and outcome of psychotic disorders. Thus, we developed two different studies at this regard. On the one hand, Study 3 was focused on explore how relatives' expressed emotion, attributions about the disorder and emotional state are associated and how they differ between ARMS and FEP relatives. On the other hand, Study 4 sought to examine the effect of EE' indices on patients' symptoms and functioning, the difference between ARMS and FEP groups on these associations, and finally, the possible mediating role of relatives' attributions in the association between EE and illness severity. It is noteworthy that Study 4 is the first study, as we know, that has investigated the mediation of relatives' attributions on the association between EE and patients' symptoms and functioning in early psychosis.

It is important also to specify that Study 3 was developed with the total of relatives' sample, which include in some cases two relatives by patient, whereas sample in Study 4 was smaller, given that we chose only dyads of one relative by patient, excluding the 'second' relatives.

Overall findings of Study 3 demonstrated that, even in the early stages of psychosis, relatives' expressed emotion is highly associated with relatives' emotional state and with several kinds of illness attributions, supporting the idea that relatives' beliefs about disorder are strongly linked to their emotional responses toward the patient. Moreover, findings show that higher levels of anxiety and depression in relatives are associated with EE, which suggests that relatives' distress and concern about the patients could provoke negative emotional reactions toward them in form of criticism and EOI.

As has been described in Study 3, prevalence of high-EE in FEP relatives was consistent with a range of prevalence between 20% and 71%, previously reported in FEP

samples (e.g. Bachmann et al., 2002, Heikkilä et al., 2002; Patterson et al., 2005). On the other hand, prevalence of high-EE in relatives of ARMS patients (52%) was higher than reported in previous studies (O'Brien et al., 2006; Schlooser et al., 2010; McNab et al., 2007), suggesting that high-EE is already present in at-risk of psychosis phase, in average, on half of the relatives. Moreover, findings of Study 4 highlight the importance of family emotional environment in the very early stages of psychosis, as it has been demonstrated that relatives' EE have an important effect on a wide variety of symptoms and functioning in patients at both the subclinical and onset stages of psychosis. Besides, findings support the idea that criticism plays a more stressful influence on outcome at these stages than EOI (Schlooser et al., 2010). Therefore, considering that high-EE attitudes could contribute to precipitate transition to psychosis in prodromal patients and relapse in FEP patients, they should be a prioritary target in early family interventions, in order to prevent the entrenchment of high-EE attitudes over time.

Furthermore, Study 3 shows that, consistent with previous studies in early psychosis, relatives attribute the cause of patients' problems to stress management (Clarke and Couchman, 2012), whereas ARMS relatives, in particular, view prodromal symptoms as related to difficulties in negotiating the normal tasks of adolescence. Another important finding supported by Study 3 and Study 4 was that, in early stages of psychosis, unlike the chronic phases of illness, it seems that control attributions are not determining high-EE responses and that self-blame attributions were not associated with EOI. Nevertheless, perception of more negative consequences of the disorder in relatives has emerged as an important kind of attribution that could influence EE in early psychosis, since it was the attribution that was most strongly associated with both criticism and EOI (in Study 3). Furthermore, in Study 4, relatives' attributions of blame toward the patient show to be a strong mediator of most of the associations between EE' indices with clinical and functional features of early psychosis patients. Therefore, it can be said that the perception of negative impact of the disorder in relatives' life seems to provoke negative emotional reactions and

blame appraisals toward the patient. Considering that this is a critical period where patients' symptoms and relatives' appraisals are forming, all this findings support the importance of setting attributional changes as an early therapeutic target, in order to help relatives better understand and progressively emotionally accept the new family situation and resolve issues of shame and loss (Patterson et al., 2005; Wasserman et al., 2012). In addition, findings emphasizes the importance of paying attention to psychopathological and family variables even at the at-risk stage, as ARMS and FEP patients are equally dysfunctional and influenced by the family emotional environment.

1.3. Clinical and research implication of early detection and intervention in psychosis

The field of early detection and intervention in psychotic disorders is promising as it offers the possibility of prevention of full-blown disorder and its related negative consequences. However, there are many issues that need to be dealt with in order to achieve this goal, and ongoing evaluation of methods to identify and treat such individuals is needed.

Although bringing treatment as soon as possible to a person who has become psychotic is in itself enough to justify early detection efforts (McGlashan and Johannessen, 1996), the highlighted ethical issues need to be considered seriously when working with young people thought to be at risk of developing psychosis. The establishment of first contact with young psychotic patients requires a high level of experience and professionalism. Thus the task of detection and assessment should preferably be performed by a specialized team (Jorgensen et al., 2000). Moreover, ethical issues about where, when and who to treat preemptively present challenges that will not be erased by the outcome of research (Yung, 2007). In addition, further work is needed to investigate and improve intervention options and it is also important do not to forget those patients with a poorer prognosis in need of a long and continuous attention. Another set of issues is the ethical considerations of early

intervention such as stigma and avoiding iatrogenic harms, particularly in intervention during a pre-psychotic phase (McGlashan, 2005).

Furthermore, is important to consider that no single type of therapeutic activity is ideal for all patients. Different subgroups of patients require different approaches within a broad spectrum of psychotherapeutic models. Thus, there is a clear need for a broader theoretical foundation of a set of therapeutic techniques, as well as an ability of greater depth and duration of therapy (McGorry, 2009).

The best practical approach at present is to engage the patient and the family, treat what is there, especially depression, anxiety and interpersonal issues, advice strongly against substance abuse, especially cannabis and stimulants, and monitor progress proactively (Yung, 2007). Nevertheless, given the complex etiology and clinical manifestation of psychosis, treatment need to be individually tailored to specific needs rather than applied homogenously across early psychosis patients (Haddock and Lewis, 2005). Thus, some challenges for psychological interventions in early psychosis are to adapt treatment modalities that have been proven effective in stable and residual stages of the disease to early psychosis, and to develop new forms of therapy tailored to the very specific characteristics of the early stages of psychosis (Vallina et al., 2007).

Furthermore, interventions should be aimed not only at improving patients' symptomatic outcome, but also the quality of life of the whole family (Scazufka and Kuipers, 1998). In the initial stages of psychosis family members are clearly stressed and have numerous concerns. So, they are willing to be involved in a family intervention program. Potentially, family work could address their individual needs and concerns particularly when relatives are dealing with the emergence of a psychotic disorder, with the hope of reducing their anxiety, depression, stress, and distress. Moreover, family intervention in at-risk stage should consider providing enough and adequate information with the purpose of reducing long-term levels of high EE and avoid the blame toward the patient. Nevertheless, information should be handled with great caution, considering that some patients are not going to develop a

psychotic disorder. Thus, families could be informed of the importance of maintaining positive communication with the patient to avoid stress and subsequent worsening of symptoms.

2. SHORTCOMINGS AND FUTURE DIRECTIONS

This thesis has some shortcomings. 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 design precludes conclusions about causal direction. We hope that the currently longitudinal follow-up studies that are being carried out by our group will enable us to elucidate the possible changes of EE and illness attributions over time in our sample, as well as to disentangle the causal influences among the different studied variables in the next future. Third, our measure of EE does not consider positive affect (e.g., warmth) of relatives towards patients, which would be very interesting as it has been demonstrated to be importantly related to psychotic symptoms and it would be informative of family protective factors. Furthermore, it would be interesting to explore a dyadic view of EE with the Brief Dyadic Scale of Expressed Emotion (BDSEE, Medina-Pradas et al., 2011) that we have incorporated recently in the assessment protocol, in order to compare the patients' perception of EE with those expressed by their relatives. On the other hand, it would be important to include the stress-coping model as a complement of the framework of attributional model, to investigate the role of relatives' coping strategies in relation with illness attributions and EE in early psychosis. In addition, considering that relatives of our sample perceived a negative impact of patient situation on his life, and given that their levels of anxiety and depression were related with EE (in Study 3), it would be also interesting to explore difference on family burden between ARMS and FEP relatives and its associations with patients' clinical and functional severity. Indeed, all these future lines of research that will complement the results obtained in the studies of this thesis are currently being developed by our group of research.

Regarding clinical and psychosocial features of early psychosis patients, future research should include cognitive impairment, given that it represents a core feature of psychotic disorder and it has been shown to be present in our ARMS sample as moderately severe symptom. Furthermore, as has been suggest by the Study 1, including COPER and COGDIS criteria as a complement of UHR criteria would be essential to improve the detection of early prodrome symptoms in our sample. Finally, further research is needed to evaluate the effectiveness of SPC-EPP intervention.

REFERENCES

1. Addington, D., Addington J., Schissel, B., (1990). A depression rating scale for schizophrenics. Schizophr. Res. 3: 247-251.
2. Addington, J., Addington, D., (2001). Early Intervention for Psychosis: The Calgary Early Psychosis Treatment and Prevention Program. CPA Bulletin de L'APC 2001: 11-16 (Fall).
3. Addington, J., Zipursky, R., Perkins, D.,Woods, S.W., Miller, T.J., McGlashan, T.H., (2004). Decline in social functioning for those with an "at risk mental state". Schizophr. Res. 70 (1), 37-37.
4. Addington, J., Collins, A., McCleery, A., Addington, D., (2005). The role of family work in early psychosis. Schizophr. Res. 79: 77-83.
5. Addington J, Epstein I, Liu L, French P, Boydell KM, Zipursky RB. (2010) A randomized controlled trial of cognitive behavioral therapy for individuals at clinical high risk of psychosis. Schizophr Res. 125:54-61.
6. Addington, J., Epstein, I., French, P., Boydell, K.M., Zipursky, R.B., (2011). A randomized controlled trial of cognitive therapy for individuals at clinical high risk of psychosis. Schizophr. Res. 125: 54-61.
7. Addington, J., Cadenhead, K., Cannon, T., Cornblatt, B., McGlashan, T., Perkins, D.O., Seidman, L.J., Tsuang, M., Walker, E.F., Woods, S.W., Heinssen, R. (2007). North American Prodrome Longitudinal Study: A collaborative multisite approach to prodromal schizophrenia research. Schizophr. Bull. 33: 665-672.
8. Alanen, Y., (1997). Schizophrenia. Its origins and need-adapted treatment. Karnac Books, London.
9. Alanen, Y.O., Räkköläinen, V., Aaltonen, J. (1991). Need-adapted treatment of new schizophrenic patients: experiences and results of the Turku Project. Acta Psychiatr. Scand. 83: 363-372.

10. Alanen, Y.O., Lehtinen, V., Lehtinen, K., Aaltonen, J., Räkköläinen, V., (2009). El modelo finlandés integrado para el tratamiento precoz de la esquizofrenia y psicosis afines, in: Martindale, B.V., Bateman, A., Crowe, M., Margison, F. (Eds). Las psicosis. Los tratamientos psicológicos y su eficacia. Editorial Herder, Barcelona.
11. Allardyce, J., Boydell, J., (2006). Review: The Wider Social Environment and Schizophrenia. Schizophr. Bull. 32: 592-598.
12. Alonso, J., Olivares, J.M., Ciudad, A., Manresa, J.M., Casado, A., Gilaberte, I. (2008). Desarrollo y validación de la versión corta de la Escala de Funcionamiento Social en esquizofrenia para su uso en la práctica clínica. Actas. Esp. Psiquiatr. 36: 102-110.
13. Álvarez, E. (2002). Intervenciones psicosociales en el tratamiento de la esquizofrenia. Anales de Psiquiatría 18(1):18-26.
14. Álvarez-Jiménez, M., Gleeson, J.F., Cotton, S.M., Wade, D., Yap, M.B.H. McGorry, P., (2010). Differential predictors of critical comments and emotional over-involvement in first episode psychosis. Psychol. Med. 40: 63-72.
15. American Psychiatric Association, (2000). Diagnostic and statistical manual of mental disorders, fourth ed., text rev. Author, Washington, DC.
16. American Psychiatric Association. (2002). DSM-IV-TR: Manual diagnóstico y estadístico de los trastornos mentales. Masson, Barcelona. American Psychiatric Association., (2010). Proposed Criteria for DSM-V Attenuated Psychotic Symptoms Syndrome. Retrieved on April 20, 2010, from http://www.dsm5.org/ProposedRevisions/Pages/proposedrevision.aspx?rid=412#
17. Anglin, D. M.; Cohen, P. R.; Chen, H. (2008). Duration of early maternal separation and prediction of schizotypal symptoms from early adolescence to midlife. Schizophr. Res. 103: 143–150.
18. Bachmann, S., Bottmer, C., Jacob, S., Kronmüller, K.T., Backenstrass, M., Mundt, C., Renneberg, B., Fiedler, P., Schröder, J. (2002). Expressed emotion in relatives of

first-episode and chronic patients with schizophrenia and major depressive disorder-a comparison. Psychiat. Res. 112: 239-250.

19. Bachmann, S., Bottmer, C., Jacob, S., Schröder, J. (2006). Perceived criticism in schizophrenia: A comparison of instruments for the assessment of the patient's perspective and its relation to relatives' expressed emotion. Psychiat. Res. 142: 167-175.
20. Barrantes-Vidal, N., Fañanás, L., Rosa, A., Caparrós, B., Dolors Riba, M., Obiols, J.E. (2003). Neurocognitive, behavioural and neurodevelopmental correlates of schizotypy clusters in adolescents from the general population. Schizophr. Res., 61: 293-302.
21. Barrantes-Vidal, N.; Ros-Morente, A.; Kwapil, T. R. (2009). An examination of neuroticism as a moderating factor in the association of positive and negative schizotypy with psychopathology in a nonclinical simple. Schizophr. Res., 115: 303-309.
22. Barrantes-Vidal, N.; Lewandowski, K.E.; Kwapil, T. R. (2010). Psychopathology, social adjustment and personality correlates of schizotypy clusters in a large nonclinical sample. Schizophr. Res., 122: 219-225.
23. Barrowclough, C. Tarrier, N., (1990). Social functioning in schizophrenic patients. I. The effects of expressed emotion and family intervention. Soc. Psych. Psych. Epid. 25: 125-129.
24. Barrowclough, C., Johnson, M., Tarrier, N. (1994). Attributions, Expressed Emotion and Patient Relapse: An Attrbutional Model of Relatives' Response to Schizophrenic Illness. Behav. Ther. 25: 67-88
25. Barrowclough, C., Tarrier, N., Johnson, M. (1996). Distress, expressed emotion and attributions in relatives of schizophrenia patients. Schizophr. Bull. 22: 691-702.

26. Barrowclough, C. Parle, M. (1997). Appraisal, psychological adjustment and expressed emotion in relatives of patients suffering from schizophrenia. Br. J. Psychiatry. 171: 26-30.
27. Barrowclough, C., Lobban, F., Hatton, C., Quinn, J. (2001). An investigation of models of illness in carers of schizophrenia patients using the Illness Perception Questionnaire. Br. J. Clin. Psychol. 40: 371–385.
28. Barrowclough, C., Hooley, J.M. (2003). Attributions and expressed emotion: A review. Clin. Psychol. Rev. 23: 849-880.
29. Bäuml, J., Froböse, T., Kraemer, S., Rentrop, M., Pitschel-Walz, G. (2006). Psychoeducation: A basic psychotherapeutic intervention for patients with schizophrenia and their families. Schizophr. Bull. 32: 1-9.
30. Bechdolf, A., Rurhmann, S., Wagner, M., Kühn, K.U., Janssen, B., Bottlender, R., Wieneke, A., Schultze-Lutter, F., Maier, W., Klosterköter, J. (2005). Interventions in the prodromal states of psychosis in Germany: concept and recruitment. Br. J. Psychiatry 187 suppl.: 45-48.
31. Beiser, M., Erikson, D., Fleming. J.A., Iacono, W.G. (1993). Establishing the onset of psychotic illness. Am. J. Psychiatry 150: 1349-1354.
32. Bendall, S., Jackson, H.J., Hulbert, C.A., McGorry, P.D. (2008). Childhood trauma and psychotic disorders: a systematic, critical review of the evidence. Schizophr. Bull. 34: 568-579.
33. Bentsen, H., Boye, B., Munkvold, O. G., Notland, T. H., Lersbryggen, A. B., Oskarsson, K., Ulstein, I., Uren, G., Bjørge, H., Berg-Larsen, R., Lingjærde, O., Malt, U. F. (1996). Emotional Overinvolvement in Parents of Patients with Schizophrenia or Related Psychosis: Demographic and Clinical Predictors. Br. J. Psychiatry 169, 22-630.
34. Bentsen, H., Notland, T.H., Munkvold, O., Boye, B., Ultstein, I., Biørge, H., Uren, G., Lerbryggen, A.B., Oskarsson, K.H., Berg-Larsen, R., Lingjærde, Malt, U.F. (1998).

Guilt proneness and expressed emotion in relatives of patients with schizophrenia or related psychosis. Br. J. Med. Psychol. 71, 125-138.

35. Bertelsen, M., Jeppesen, P., Petersen, L., Thorup, A., Øhlenschlæger, J., Le Quach, P., Østergaard, T., Krarup, G., Jørgensen, P. Nordentoft M. (2008). Five-year follow-up of a randomized Multicenter Trial of Intensive Early Intervention vs Standard Treatment for Patients with a First Episode of Psychotic Illness. The Opus Trial. Arch. Gen. Psychiatry 65: 762-771.
36. Bhangoo, R.K., Carter, C.S. (2009). Very early intervention in psychotic disorders. Psychiatr. Clin. N. Am. 32: 81-94.
37. Bilder, R. M., Mukherjee, S., Rieder, R. O., Pandurangi, A. K. (1985). Symptomatic and neuropsychological components of defect states. Schizophr. Bull. 11, 409–419.
38. Birchwood, M., Smith, J., Cochrane, R., Wetton, S. (1990). The Social Functioning Scale: The development and validation of a new scale of social adjustment for use in family intervention programmes with schizophrenic patients. Br. J. Psychiatry 157: 853-859.
39. Bion, W. (1976). Experiences in Groups. Basic Books, New York.
40. Birchwood, M, Smith. Schizophrenia and the family (1987). In: Orford, J. ed. Coping with disorder in the Family. Kent: Croom Helm.
41. Birchwood, M., Smith, J., Cochrane, R., Wetton, S. (1990). The Social Functioning Scale: The development and validation of a new scale of social adjustment for use in family intervention programmes with schizophrenic patients. Brit. J. Psychiat. 157, 853-859.
42. Birchwood, M., McGorry, P., Jackson, H., (1997). Early intervention in schizophrenia. Br. J. Psychiatry 170: 2-5.
43. Birchwood, M., Todd, P. Jackson, C. (1998). Early intervention in psychosis.The critical period hypothesis. Br. J. Psychiatry 172 suppl. 33: s53-s59.

44. Birchwood, M., Fowler, D., Jackson, C., (2002). Early Intervention in Psychosis. A guide to concepts, evidence and interventions. Wiley, Chichester.
45. Bowlby, J. (1980). Loss: Sadness and Depression. Basic Books: New York.
46. Bowlby, J. (1988). A Secure Base: Clinical Applications of Attachment Theory. Routledge: London.
47. Breitborde, N., Woods, S., Srihari, V., (2009). Multifamily psychoeducation for first-episode psychosis: A cost-effectiveness analysis. Psychiatr. Serv. 60: 1477-1483.
48. Brewin, C.R., MacCarthy, B., Duda, K., Vaughn, C.E. (1991). Attribution and Expressed Emotion in the Relatives of Patients with Schizophrenia. J. Abnorm. Psychol. 4, 546-554.
49. Brewin, C.R., (1994). Changes in attribution and expressed emotion among relatives of patients with schizophrenia. Psychol. Med. 24: 905-911.
50. Broome, R.M., Wooley, J.B., Johns, L.C., Valmaggia, L.R., Tabraham, P., Gafoor, R et al. (2005) Outreach and support in south London (OASIS): implementation of a clinical service for prodromal psychosis and at the risk mental state. Eur. Psychiatry, 20:372-378.
51. Brown, G. W., Carstairs, G. M. Topping, G. (1958). Post-hospital adjustment of chronic mental patients. The Lancet*, 2,* 685-689.
52. Brown, G.W., Birley, J.L.T., Wing, J.K. (1972). Influence of family life on the course of schizophrenic disorders: A replication. Br. J. Psychiatry 121: 241-258.
53. Butzlaff, R., Hooley, J.M. (1998). Expressed Emotion and Psychiatric Relapse. A Meta-analysis. Arch. Gen. Psychiatry 55: 547-552.
54. Caqueo, A., Lemos, S. (2008).Calidad de vida y funcionamiento familiar de pacientes con esquizofrenia en una comunidad latinoamericana. Psycothema, 20: 577-582.
55. Canoon-Spoor, H.E., Potkin, S.G., Wyatt, R.J. (1982). Measurement of premorbid adjustment in chronic schizophrenia. Schizophr. Bull. 8, 470-484

56. Cannon, T., Cornblatt, B. McGorry, P. (2007). Editor´s Introduction: the empirical status of the Uktra High Risk (Prodromal) Research Paradigm. Schizophr. Bull., 33: 661-664.
57. Cannon, T.D., Cadenhead, K., Cornblatt, B., Woods, S.W., Addington, J., Walker, E., Seidman, L.J., Perkins, D., Tsuang, M., McGlashan, T., Heinssen, R. (2008). Prediction of psychosis in youth at high clinical risk: a multisite longitudinal study in North America. Arch. Gen. Psychiatry 65: 28–37.
58. Cantor-Graae, E. (2007). The contribution of social factors to the development of schizophrenia: a review of recent findings. Can. J. Psychiatry 52: 277-286.
59. Carpenter, W. (2009). Anticipating DSM-V: Should psychosis risk become a diagnostic class? Schizophr. Bull. 35: 841-843.
60. Caspi, A., Reichenberg, A., Weiser, M., Rabinowitz, J., Kaplan, Z., Knobler, H., Davidson-Sergi N., Davidson, M. (2003). Cognitive performance in schizophrenia patients assessed before and following the first psychotic episode. Schizophr. Res. 65: 87-94.
61. Chapman, L.J., Chapman, J.P., Raulin, M.L. (1976). Scales for physical and social anhedonia. Journal of Abnormal Psychology, 85: 374-382.
62. Chok, J.T., Kwapil, T.R., Scheuermann, A., (2005). Dermatoglyphic anomalies in psycho-metrically identified schizotypic young adults. Schizophr. Res. 72: 205-214.
63. Claridge, G., McCreery, C., Mason, O., Bentall, R., Boyle, G., Popplewell, D. (1996). The factor structure of 'schizotypal' traits: a large replication study. Br. J. Clin. Psychol. 35:103–115.
64. Claridge, G., 1997. Theoretical background and issues. In: Claridge, G. (Ed.), Schizotypy: Implications for Illness and Health. Oxford University Press, Oxford.
65. Clarke, K., Couchman, G. (2012) Caregiver causal attributions in youth psychosis. Early Interv. Psychiatry doi: 10.1111/j.1751-7893.2011.00335.x

66. Cohen, J. (1988). Statistical power analysis for the behavioral sciences, second (Ed.) Hilllsdale, NJ, Erlbaum.
67. Cole, J.D., Kazarian, S.S. (1998).The Level of Expressed Emotion Scale: a new measure of expressed emotion. J. clin. Psychol. 44: 392-397.
68. Colom, F., Vieta, E., Martínez-Arán, A., García-García, M., Reinares, M., Torrent, C., Goikolea, J.M., Banús, S., Salamero, M. (2002). Spanish versión of a scale for the assessment of mania: validity and reliability of the Young Mania Rating Scale. Med. Clin (Barc).119: 366-371.
69. Collins, A. and Addington, J. "Working with families following the diagnosis of an at risk mental state" (p.p.153-168). In: Addington, J., Francey, S. M. & Morrison, A. (Eds.) (2006) Working with People at high risk of developing psychosis. A treatment handbook. Chichester, John Wiley & Sons, Ltd.
70. Corcoran, C., Davidson, L., Sills-Shahar, R., Nickou, C., Malaspina, D., Miller, T. & McGlashan, T. (2003) A qualitative research study of the evolution of symptoms in individuals identified as prodromal to psychosis. Psychiat. Quart. 74: 313-332.
71. Corcoran, C., Malaspina, D., Hercher, L. (2005). Prodromal interventions for schizophrenia vulnerability: the risks of being "at-risk". Scizophr. Res, 73:173-184.
72. Corcoran, C., First, M., Cornblatt, B., (2010). The psychosis risk syndrome and its proposed inclusion in the DSM-V: A risk–benefit analysis. Schizophr. Res. 120 (1-3): 16-22.
73. Corell C.U., Hauser M., Auther A.M., Cornblatt B.A., (2010). Research in people with psychosis risk syndrome: a review of the current evidence and future directions. J. Child Psychol. Psychiatry 51: 390-431.
74. Cornblatt, B.A., (2002) The New York High Risk Project to the Hillside Recognition and Prevention (RAP) Program. Am. J. Med. Genet. (Neuropsychtr. Genet.) 114: 956-966.

75. Cornblatt, B.A., Lencz, T., Smith, C.W., Corell, C.U., Auther, A.M., Nakayama, E. (2003). The schizophrenia prodrome revisted: a neurodevelopmental perspective. Schizophr. Bull. 29: 633-651.

76. Cornblatt, B.A., Auther, A.M., Niendam, T., Smith, C.W., Zinberg, J., Bearden, C.E., Cannon, T.D., (2007). Preliminary findings for two new measures of social and role functioning in the prodromal phase of schizophrenia. Schizophr. Bull. 33: 688-702.

77. Cuesta, M.J., Peralta, V. (1995) Psychopathological Dimensions in Schizophrenia. Schizophr. Bull. 21: 473-482.

78. Cullberg, J., Johannessen, J.O., (2005). La dinámica de la psicosis aguda y el papel de la psicoterapia dinámica, in: Gleeson, J., McGorry, P.D Eds., Intervenciones psicológicas en la psicosis temprana. Un manual de tratamiento. Desclée de Brouwer; Bilbao.

79. Cutting, L. P., Aakre, J. M. Docherty, N. M. (2006). Schizophrenic patients perception of Stress, Expressed Emotion, and Sensivity to criticism. Schizophr. Bull. 32:743-750.

80. Davis, L.M., Drummond, M.F. (1994) Economics and schizophrenia: the real cost. Br. J. Psychiatry Suppl. 25:18–21

81. Derogatis, L.R., Cleary, P.A. (1977). Factorial invariance across gender for the primary symptom dimensions of the SCL-90. Br. J. Clin. Psychol. 16:347-356.

82. Dominguez, M.D., Saka, M.C., Lieb, R., Wittchen, H.U., van Os, J. (2010). Early expression of negative/disorganized symptoms predicting psychotic experiences and subsequent clinical psychosis: a 10-year study. Am. J. Psychiatry. 167: 1075–1082.

83. Domínguez-Martínez T, Vilagrà R, Blanqué JM, Vainer E, Berni R, Montoro M, Mauri L, Bedoya E, Kwapil TR, Barrantes-Vidal N. (2010a). Levels of Emotional Over-involvement (EOI) and Critical Comments (CC) in relatives of First Episode Psychosis and At Risk Mental State patients. Presented at: 7th International Conference on Early Psychosis (Amsterdam, NL), November 2010. *Abstract publication:* Early Interv in Psychiatry 4:55.

84. Domínguez-Martínez, T., Vilagrà, R., Blanqué, J.M., Vainer, E., Berni, R., Montoro, M., Mauri, L., Bedoya, E., Kwapil, T.R., Barrantes-Vidal, N., (2010b). The association between relatives' Expressed Emotion with clinical and functional features of early-psychosis patients. Presented at: 7th International Conference on Early Psychosis (Amsterdam, NL), November 2010. *Abstract publication:* Early Interv in Psychiatry 4: 55.

85. Domínguez-Martínez T, Blanqué JM , Codina J, Montoro M, Mauri L, Barrantes-Vidal N. (2011a) Rationale and state of the art in early detection and intervention in psychosis, Salud Ment. 34: 341-350.

86. Domínguez-Martínez, T., Vainer, E., Massanet, M.A., Torices, I., Jané, M., Barrantes-Vidal, N., (2011b). The need-adapted integrated treatment in Sant Pere Claver-Early Psychosis Program (SPC-EPP) in Barcelona, Spain. Salud Ment. 34: 517-524.

87. Erikson, D., (2010). Cognitive-behaviour therapy for medication-resistant positive symptoms in early psychosis: a case series, Early. Interv. Psychiatry 4: 251-256.

88. Espinoza, I., Osorio, P., Torrejón, M.J., Lucas-Carrasco, R., Bunot, R. (2011) Validación del cuestionario de calidad de vida (WHOQOL-BREF) en adultos. Rev. Med. Chile 139: 579-586.

89. Esterberg, M.L., Goulding, S.M., Walker, E.F., (2010). Cluster A Personality Disorder: Schizotypal, Schizoid and Paranoid Personality Disorders in Childhood and Adolescence, J Psychopatol. Behav. 32: 515-528.

90. Fallon, I.R., Coverdale, J.H., Laidlaw, T.M., Merry, S., Kydd, R.R., Morosini, P., (1998). Early intervention for schizophrenic disorders. Implementing optimal treatment strategies in routine clinical services. OPT Collaborative Group. Br. J. Psychiat. Suppl. 72: 33-38.

91. Fallon, I.R., Kydd, R.R., Coverdale, J.H., Laidlaw, T.M., (1996). Early detection and intervention for episodes of schizophrenia. Schizophr. Bull. 22: 271–282.

92. First, M..B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., (1996). Structured Clinical Interview for DSM-IV Axis I Disorders. American Psychiatric Press, Washington. D.C.

93. First, M.B., Spitzer, R.L., Gibbon, M. & Williams, J.B.W. (1999) Entrevista clínica estructurada para los trastornos de personalidad del eje II del DSM-IV (versión clínica) SCID-II. Barcelona: Masson.

94. Flaum, M.A., Andreasen, N.C., Arndt, S. (1992). The Iowa prospective longitudinal study of recent-onset-psychosis. Schizophr. Bull. 18: 481–90.

95. Folkman, S., Lazarus, R.S. (1980). An analysis of coping in a middle-aged community sample. J. Health. Soc. Behav. 21:219-239.

96. Folkman, S., Lazarus, R. S. (1985). If it changes it must be a process: A study of emotion and coping during three stages of a college examination.J. Pers. Soc. Psychol. 48*:*150-170.

97. Fòrum de Salut Mental, (2006). Proposta de desenvolupament d'un model d'atenció als trastorns psicòtics incipients, «Document de treball». Fòrum de Salut Mental, Barcelona.

98. Foulkes, S.H., Anthony, E.J., 1964. Psicoterapia psicoanalítica de grupo. Paidós, Buenos Aires.

99. Galdos M, Simons C, Fernandez-Rivas A, et al. (2011). Affectively salient meaning in random noise: a task sensitive to psychosis liability. Schizophr. Bull. 37:1179–1186.

100. Gerson, R., Wong, C., Davidson, L., Malaspina, D., McGlashan, T. Corcoran, C. (2011). Self-reported coping strategies in families of patients in early stages of psychotic disorder: an exploratory study. Early. Interv. Psychiatry 5: 76-80.

101. Gafoor, R., Nitsch, D., McCrone, P., Craig, T.K.J., Garety, P.A., Power, P., McGuire, P., (2010). Effect of early intervention on 5-year outcome in non-affective psychosis. Br. J. Psychiatry 196: 372-376.

102. García Badaracco, J. (2000). Psicoanálisis Multifamiliar. Los otros en nosotros y el descubrimiento de sí mismo. Paidós, Buenos Aires.

103. García-Portilla, M.P., Saiz, P.A., Bousoño, M., Bascaran, M.T., Guzmán-Quilo, C., Bobes, J. (2011) Validación de la versión española de la escala de Funcionamiento Personal y Social en pacientes ambulatorios con esquizofrenia estable o inestable. Rev. Psiquiatr. Salud Ment. (Barc.) 4: 9-18.

104. Garland, E.L., Fredrickson, B., Kring, A.M., Johnson, D.P, Meyer, P.S., Penn, D.L., (2010). Upward spirals of positive emotions counter downward spirals of negativity: Insights from the broaden-and-build theory and affective neuroscience on the treatment of emotion dysfunctions and deficits in psychopathology. Clin. Psychol. Rev., 30: 849-64.

105. Gleeson, J., Jackson, H. J., Stavely, H., & Burnett, P. (1999). Family intervention in early psychosis. In P. D. McGorry, H. J. Jackson (Eds.). Recognition and management of early psychosis Cambridge: Cambridge University Press.

106. Gleeson, J., McGorry, P. (2005). Intervenciones psicológicas en la psicosis temprana. Un manual de tratamiento. Desclée de Brouwer, Bilbao.

107. Glynn, S.M., Randolph, E.T., Eth, S., Paz, G.G., Leong, G.B., Shaner, A.L., Strachan, A. (1990). Patient Psychopathology and Expressed Emotion in Schizophrenia. Br. J. Psychiatry 157, 877.880.

108. Grandón, P., Jenaro, C., Lemos, S. (2008). Primary caregivers of schizophrenia outpatients: Burden and predictor variables. Psychiatr. Res. 158: 335-343.

109. Goldman HH, Skodol AF, Lave TR, (1992) Revising Axis V for DSM-IV: A Review of Measures of Social Functioning. Am.J Psychiatry 149; 1148-1156.

110. Guía de Práctica Clínica sobre la Esquizofrenia y el Trastorno Psicótico Incipiente. Madrid: Plan de Calidad para el Sistema Nacional de Salud del Ministerio de Sanidad y Consumo. Agència d'Avaluació de Tecnologia i Recerca Mèdiques. (2009) .http://www.gencat.cat/salut/depsan/units/aatrm/html/ca/dir303/doc13319.html

111. Gumley, A., Schwannauer, M. (2008). Volver a la normalidad después de un trastorno psicótico: Un modelo cognitivo-relacional para la recuperación y la prevención de recaídas. Desclée de Brouwer, Bilbao.

112. Guthrie, E., Moorey, J., Margison, F., McGrath, G. (1998). Psychodinamic-interpersonal psychotherapy in patients with treatment resistance psychiatric symptoms. Br. J. Psychother. 15: 155-166.

113. Haddock, G., Lewis, S. (2005). Psychological Intervention in Early Psychosis. Br. J. Psychiatry 31: 667-704.

114. Häfner, H., Riecher-Rössler, A., Hambrecht, M., Maurer, K., Meissner, S., Schmidtke, A., Fätkenheuer, B., Löffler, W., vander Heiden, W. (1992). IRAOS: an instrument for the assessment of onset and early course of schizophrenia. Schizophr. Res. 6: 209–223.

115. Häfner, H., Maurer, K., Löffler, W., Riecher-Rössler, A. (1993). The influence of age and sex on the onset and early course of schizophrenia. Br. J. Psychiatry. 62:80-86

116. Hafner, H., Maurer, K., Loffier, W., Heiden, W., Hambrecht, M., Schultze-Lutter, F. (2003). Modeling the early course of schizophrenia. Schizophr. Bull. 29: 325-340.

117. Häfner, H., Maurer, K., Ruhrmann, S., Bechdolf, A., Klosterkötter, J., Wagner, M., Maier, W., Bottlender, R., Möller, H.J., Gaebel, W., Wölwer, W. (2004). Early detection and secondary prevention of psychosis: facts and visions. Eur. Arch. Psychiatry Clin. Neurosci. 254(2): 117-28.

118. Haroun,N., Dunn, L.,Haroun, A., et al (2006) Risk and protection in prodromal schizophrenia: ethical implications for clinical practice and future research. Schizophr. Bull. 32,166-178.

119. Hegarty JD, Baldessarini RJ, Tohen M, Waternaux C, Oepen G., (1994). One hundred years of schizophrenia: a meta-analysis of the outcome literature. Am J. Psychiatryry 151: 1409-1416.

120. Hahlweg, K., Feinstein, E., Muller, U., dose, M. (1989). Family management programmes for schizophrenic patients- Prevention of relapse and modification of familial communication patterns. Br. J. Psychiatry 155, 112-116

121. Hanssen, M., Bak, M., Vollebergh, W., van Os, J. (2005). The incidence an outcome of subclinical psychotic expereinces in the general population. Br. J. Psychol. 44: 181-191.

122. Hatfield. A. B. Coping and adaptation: a conceptual framework for understanding families. In: Hatfield. A. B., Lefley, H.P., ed. (1987). Families of the mentally ill: coping and adaptation. New York Guilford Press.

123. Heikkilä, J., Karlsson, H., Taiminen, T., Lauerma, H., Ilonen, T., Leinonen, K. M., Wallenius, E., Virtanen, H., Heinimaa, M., Koponen, S., Jalo, P., Kaljonen, A., Salakangas, R., (2002). Expressed emotion is not associated with disorder severity in first-episode mental disorder. Psychiat. Res. 111: 155-165.

124. Heinimaa, M., Larsen, T.K., (2002). Psychosis: conceptual and ethical aspects of early diagnosis and intervention. Curr. Opin. Psychiatr. 15: 533-541.

125. Henry, L.P., Harris, M.G., Amminger, P., Yuen, H.P., Harrigan, S.M., Lambert, M., Conus, P., Schwartz, O.S., Prosser, A., Farelly, S.E., Purcell, R., Herrman, H., Jackson, H.J., McGorry, P.D. (2007). Early Psychosis Prevention and Intervention Centre long-term follow-up study of first-episode psychosis: methodology and baseline characteristics. Early Interv. Psychiatry 1: 49-60.

126. Henry, L.P., Amminger, P., Harris, M.G., Yuen, H.P., Harrigan, S.M., Prosser, A-L., Schwartz, O.S., Farelly, S.E., Herrman, H., Jackson, H.J., McGorry, P.D. (2010). The EPPIC Follow-Up Study of First-Episode Psychosis: Longer term Clinical and functional Outcome 7 years After Index Admission. J. Clin. Psychiatry, 71:716-728.

127. Hinrichsen, G.A., Lieverman, J.A. (1999). Family attributions and coping in the prediction of emotional adjustment in family members of patients with first-episode schizophrenia. Acta. Psychiatr. Scand. 100: 359-366.

128. Hooley, J.M., Teasdale, J.D. (1989). Predictors of relapse in unipolar depressives: expressed emotion, marital distress, and perceived criticism. J. Abnorm Psychol. 98: 229-235.

129. Hooley, J.M., Campbell, C., (2002). Control and controllability: beliefs and behaviour in high and low expressed emotion relatives. Psychol. Med. 32: 1091-1099.

130. Hooley, J.M., (2007). Expressed emotion and relapse of psychopathology. Annu. Rev. Clin. Psychol. 3: 329-352.

131. Insel, T.R. (2007). The arrival of preemptive psychiatry. Early. Interv. Psychiatry 1: 5-6.

132. Jansson, L.B., Pamas, J. (2007). Competing definitions of schizophrenia: what can be learned from polydiagnostic studies? Schizophr. Bull. 33: 178-1200.

133. Johannessen, J. O., McGlashan, T. H., Larsen, T. K., et al (2001). Early detection strategies for untreated first episode psychosis. Schizophr. Res. 51, 39-46.

134. Johns, L.C., van Os, J. (2001). The continuity of psychotic experiences in the general population. Clin. Psychol. Rev. 21: 1125-1141

135. Jørgensen, P., Nordentoft, M., Abel, M.B., Gouliaev, G., Jeppesen, P., Kassow, P., (2000). Early detection and assertive community treatment of young psychotics: The OPUS Study. Rationale and design of the trial. Soc. Psych. Psych. Epid. 35: 283-287.

136. Jungbauer, J., Angermeyer, M. C. (2002). Living with a schizophrenic patient: A comparative study of burden as it affects parents and spouses. Psychiatry, 65, 110-123.

137. Kaczorowski, J.A., Barrantes-Vidal, N., Kwapil, T.R., (2009). Neurological soft signs in psychometrically identified schizotypy. Schizophr. Res. 115: 293-302.

138. Kavanagh, D.J. (1992). Recent Developments in Expressed Emotion and Schizophrenia. Br. J. Psychiatry. 160: 601-620.

139. Kavanagh, D.J., O'Halloran, P., Manicavasagar, V., Clark, D., Piatkowska, O., Tennat, C., Rosen, A. (1997). The Family Attitude Scale: reliability and validity of a

new scale for measuring the emotional climate of families. Psychiatry Res. 70: 185.195.

140. Kay, S. R., Fiszbein, A., Opler, L.A., (1987). The Possitive and Negative Syndrome Scale for Schizophrenia. Schizophr. Bull. 13: 261-276.

141. Kaymaz, N., van Os, J. (2010). Extended psychosis phenotype—yes: single continuum—unlikely. Psychol. Med. 40: 1963-1966.

142. Kazarian, S.S., Malla, A.K., Cole, J.D., Baker, B. (1990). Comparisons of two expressed emotion scales with the Camberwell Family Interview. J. Clin. Psychol. 46: 306-309Kerr, I.B., Crowley, V., Beard, H., (2008). Una aproximación cognitivo-analítica al trastorno psicótico, in: Johannessen JO, Martindale BV, Cullberg J. (Eds.), Evolución de las Psicosis. Heder, Barcelona.

143. Kelley, M.E., Gilbertson, M., Mouton, A., van Kammen, D.P. (1992) Deterioration in premorbid functioning in schizophrenia: A developmental model of negative symptoms in drug-free patients. Am. J. Psychiatry 149(11):1543-1548.

144. Kerr, A., McClelland, H. (Eds). (1991*).* Concepts of Mental Disorder. Gaskell, London.

145. Keshavan, M.S., Schooler, N.R. (1992). First-episode studies in schizophrenia: criteria and characterization. Schizophr. Bull. 18: 491–513.

146. Keshavan, M.S., Amirsadri, A., (2007). Early intervention in schizophrenia: current and future perspectives. Curr. Psychiat. 9: 325-328.

147. Kety, S.S., Rosenthal, D., Wender, P.H., Schulsinguer, F. (1968). The types and prevalence of mental illness in the biological and adoptive families of adopted schizophrenics. In: D. Rosenthal and S.S. Kety (Eds). The transmission of schizophrenia (pp. 345-362). Pergamon, Press,Oxford.

148. King, S., (2000). Is expressed emotion cause or effect in the mothers of schizophrenic young adults? Schizophr. Res. 45: 65-78.

149. Kirrane, R. M., Siever, L. J. (2000). New perspectives on schizotypal personality disorder. Curr. Psychiatry Rep. 2: 62–66.

150. Klosterkotter, J., Schultze-Lutter, F.,Gross,G., Huber, G., Steinmeyer, E.M. (1997) Early self-experienced neuropsychological deficits and subsequent schizophrenic diseases: an 8-year average follow-up prospective study. Acta Psychiatr. Scand. 95, 396-404.

151. Klosterkötter, J., Hellmich, M., Steinmeyer, E.M., Schultze-Lutter, F., (2001). Diagnosing schizophrenia in the initial prodrome phase. Arch. Gen. Psychiatry 58: 158-164.

152. Klosterkötter, J., Ruhrmann, S., Schultze-Lutter, F., Salokangas, R.K., Linszen, D., Birchwood, M., Juckel, G., Morrison, A., Vázquez-Barquero, J.L., Hambrecht, M., Reventlow, H., on behalf of the EPOS group. (2005). The European prediction of psychosis study (EPOS): integrating early recognition and intervention in Europe. World Psychiatry 4: 161-167.

153. Koplewicz, A., Zarate, R., González, V., López, S.R., Ortega, P., Obregón, N., Mintz, J. (2002). Evaluation of expressed emotion in schizophrenia: a comparison of Caucasians and Mexican-Americans. Schizophr. Res. 55: 179-186.

154. Krabbendam L, Myin-Germeys I, Hanssen M, et al. (2004) Hallucinatory experiences and onset of psychotic disorder: evidence that the risk is mediated by delusion formation. Acta Psychiatr. Scand. 110:264–272.

155. Krabbendam L, Myin-Germeys I, Hanssen M, et al. (2005) Development of depressed mood predicts onset of psychotic disorder in individuals who report hallucinatory experiences. Br. J. Clin. Psychol. 44:113–125.

156. Kreisman, D.E., Simmens, S.J., Joy, V.D. (1979). Rejecting the patient: preliminary validation of a self-report scale. Schizophr Bull. 5: 220-222.

157. Kuipers, L., Bebbington, P. (1985). Relatives as a resource in the management of functional disease. Br. J. Psychiatry. 147: 465-470.

158. Kuipers, S.L. Bebbington, P. (1988). Expressed emotion research in schizophrenia: theoretical and clinical implications. Psychol. Med .18: 893-909.

159. Kuipers, E., (2005). Evaluating Cognitive Behavior Therapy for psychosis. Clin. Psychol. Sci. Pract. 12: 65-67.

160. Kuipers, E., Bebbington, P., Dunn, G., Fowler, D., Freeman, D., Watson, P., Hardy, A. Garety, P. (2006). Influence of carer expressed emotion and affect on relapse in non-affective psychosis. Br. J. Psychatry 188: 173: 179.

161. Kwapil, T.R., (1998). Social anhedonia as a predictor of the development of schizophrenia-spectrum disorders. J. Abnorm. Psychol. 107: 558-565.

162. Kwapil, T.R., Barantes-Vidal, N., Silvia, P.J., (2008). The dimensional structure of the Wisconsin Schizotypy Scales: Factor identification and construct validity. Schizophr. Bull. 34: 444-457.

163. Kwapil, T.R., Barrantes-Vidal, N. (2012). Schizotypal Personality Disorder: An Integrative Review, in: Widiger, T.A. (Ed.), The Oxford Handbook of Personality Disorders. Oxford University Press, New York.

164. Kwapil, T.R., Ros-Morente, A., Silvia, P.J., Barrantes-Vidal, N. (2012). Factor invariance of Psychometric Schizotypy in Spanish and American Samples. J. Psychopathol. Behav. Assess. 34: 145-152.

165. Lahti, J., Raïkkönen, K., Sovio, U., Miettunen, J., Hartikainen, A.L., Pouta, A., Taanila, A., Joukamaa, M., Järvelin, M.R., Veijola, J. (2009). Early-life origins of schizotypal traits in adulthood. Br. J. Psychiatry 195: 132-137.

166. Larsen, T.K., Joa, I., (1999). Identifying persons prodromal to first episode schizophrenia: the TOPP-project. Curr. Opin. Psychiat. 12: 207.

167. Larsen, T.K., Melle, I., Auestad, B., Friis, S., Haahr, U., Johannessen, J.O., Opjordsmoen, S., Rund, B.R., Simonsen, E., Vaglum, P., McGlashan, T., (2006). Early Detection of First-Episode Psychosis: The Effect on 1 Year Outcome. Schizophr. Bull. 32: 758-764.

168. Lay, B., Blanz, B., Hartmann, M., Schmidt, M.H. (2000). The psychosocial outcome of adolescent-onset schizophrenia: a 12-year follow-up. Schizophr. Bull. 26: 801-816.

169. Lazarus, R. S., Folkman, S. (1984). Stress, appraisal, and coping. New York: Springer.

170. Lazarus, R. S. (1993). Coping theory and research: Past, present, and future. Psychosom. Med. 55, 234-247.

171. Leff, J., Vaughn, C., (1985). Expressed Emotion in Families. Its significance for Mental Illness. The Guilford Press, London.

172. Lenior, M.E., Dingemans, P, Schene, A.H., Hart, A, Linszen, D.H., (2002). The course of parental expressed emotion and psychotic episodes after family intervention in recent-onset schizophrenia. A longitudinal study. Schizophr. Res. 57: 183-190.

173. Lenzenweger, M.F., Korfine, L. (1995). Tracking the taxon: o the latent structure and base rate of schizotypy. In A. Raine, T. Lencz and S.A. Mednick (Eds.) Schizotypal personality (pp. 135-167). United States of America: Cambridge University Press.

174. Lenzenweger, M.F., 2006. The longitudinal study of personality disorders: history, design considerations, and initial findings. J. Pers. Disord. 20 (6), 645–670.

175. Lester, H., Birchwood, M., Bryan, S., Jones-Morris, J., Kaambwa, B. *et al*., (2007). Evaluating the development and impact of Early Intervention Services (EIS) in the West Midlands. Report for the NIHR Service Delivery and Organization Programme. NCCSDO, London.

176. Lewis, S., (2006). Introduction. At Risk Mental states in psychosis: an introduction, in: Addington, J., Francey S.M, Morrison A (eds). Working with People at high risk of developing psychosis. A treatment handbook. John Wiley & Sons, Ltd., Chichester.

177. Lieberman, J.A., (1996). Atypical antipsychotic drugs as a first-line treatment of schizophrenia: a rationale and hypotheses. J. Clin. Psychiat. 57:68-71.

178. Lieberman, J.A., Perkins, D., Belger, A., Chakos, M., Jarskog, F., Boteva, K., Gilmore, J. (2001) The early stages of schizophrenia: Speculations on pathogenesis, pathophysiology, and therapeutic approaches. Biol. Psychiatry 50:884-897.

179. Liddle, P. F. (1987). The symptoms of chronic schizophrenia: a reexamination of the positive-negative dichotomy. Br. J. Psychiatry 151: 145–151.

180. Lincoln, C., Harrigan, S., McGorry, P.D. (1998). Understanding the topography of the early psychosis pathways. An opportunity to reduce delays in treatment. Br.J. Psychiatry. Suppl. 172: 21-25.

181. Linscott RJ, Van Os J. (2010) Systematic reviews of categorical versus continuum models in psychosis: evidence for discontinuous subpopulations underlying a psychometric continuum. Implications for DSM-V, DSM-VI, and DSM-VII. Annu Rev Clin Psychol. 6:391–419.

182. Liu, P., Parker, A.G., Hetrick, S.E., Callahan, P., De Silva, S., Purcell, R., (2010). An evidence map of interventions across premorbid, ultra-high risk and first episode phases of psychosis. Schizophr. Res. 123: 37-44.

183. Lobban, F., Barrowclough, C. Jones, S., (2005). Assessing cognitive representations of mental health problems. II. The illness perception questionnaire for schizophrenia: Relatives' version. Brit. J. Clin. Psychol. 44: 163-179.

184. Loebel, A.D., Lieberman, J.A., Alvir, J.M.J., Mayerhoff, D.I., Geisler, S.H., Szymanski, S.R. (1992) Duration of psychosis and outcome in first-episode schizophrenia. Am. J. Psychiatry 149:1183–1188.

185. López M., Rodríguez, S., Apiquian, R., Paez, F., Nicolini, H. (1996) Translation study and validation of the Premorbid Adjustment Scale for Schizophrenia [Spanish] Salud Mental, 19: 24-29.

186. Lua, P.L., Bakar, Z.A. (2011) Health-related quality of life profiles among family caregivers of patients with schizophrenia. Fam. Community Health 34:331-339.

187. Maier, W., Falkai, P., Wagner, M. Schizophrenia-spectrum disorders. (1999) M. Maj, N. Startorius (Eds.) WPA Series: Evidence and Experience in Psychiatry, Wiley, Chichester.

188. Machón, R.A., Huttunen, M.O., Mednick, S.A., Sinivuo, J., Tanskanen, A., Bunn Watson, J., Henriksson, M., Phyhälä, R. (2002). Adult schizotypal personality characteristics and prenatal influenza in a Finnish birth cohort. Schizophr. Res. 54 (1–2): 7–16.

189. Magaña, a.B., Goldstein, J.M., Karno, M., Miklowitz, D.J., Jenkins, J., Fallon, I.T. (1986). A brief method for assessing expressed emotion in relatives of psychiatric patients. Psychiatry Res. 17: 203-212.

190. Magliano, L., Guarneri, M., Marasco, C., Tosini, P., Morosini, P.L., Maj, M. (1996). A new questionnaire assessing coping strategies in relatives of patients with schizophrenia: development and factor analysis. Acta. Psychiatr. Scand. 94: 224-228.

191. Malla A, Norman R,McLean T, Scholten D, Townsend L. (2003) A Canadian programme for early intervention in nonaffective psychotic disorders. Aust NZ J Psychiat. 37:407–413.

192. Malla, A., Norman, R., Scholten, D., Manchanda, R. & McLean, T. (2005) A community intervention for early identification of first episode Psychosis. Impact on duration of untreated psychosis (DUP) and patient characteristics. Soc. Psychiatry Psychiatr. Epidemiol. 40:337-344.

193. Marom, S., Munitz, H., Jones, P.B., Weizman, A., Hermesh, H. (2005). Expressed Emotion: Relevance to Rehospitalization in Schizophrenia Over 7 Years. Schizophr Bull. 31: 751-758.

194. Marshall, M., Lewis, S., Lockwood, A., Drake, R., Jones, P., & Croudace, T (2005) Association between duration of untreated psychosis and outcome in cohorts of first-episode patients: A systematic review. Arch. Gen.Psychiatry. 62: 975-983.

195. Martindale, B.V., Bateman, A., Crowe, M., Margison, F., (2009). Las psicosis. Los tratamientos psicológicos y su eficacia. Editorial Herder, Barcelona.

196. Mason, O., Startup, M., Halpin, S., Schall, U., Conrad, A., Carr, V., (2004). Risk factors for transition to first episode psychosis among individuals with 'at-risk mental states'. Schizophr. Res. 71: 227-237

197. Maurer, K., Hörrmann, F., Schmidt, G., (2004). The early recognition inventory ERIraos: a two-step procedure for detection of ‘at-risk mental states’. Schizophr. Res. 70 (suppl): 76.

198. McFarlane, W.R. (2002). Multifamily groups in the treatment of severe psychiatric disorders. New York: Guilford Press.

199. McFarlane, W.R., Cook, W.L. (2007). Family Expressed Emotion Prior to Onset of Psychosis. Fam. Process. 46: 185-197.

200. McGlashan, T.H., Johannessen, J.O., (1996). Early detection and intervention with schizophrenia: Rationale. Schizophr. Bull. 22: 201-222.

201. McGlashan, T.H. (1998). The profiles of clinical deterioration in schizophrenia. J. Psychiatr. Res. 32: 133-141.

202. McGlashan, T.H., (1999). Duration of untreated psychosis in first-episode schizophrenia: marker or determinant of course? Biol. Psychiatry, 46:899-907.

203. McGlashan, T.H., Zipursky, R.B., Perkins, D., Addington, J., Miller, T.J., Woods, S.W., Hawkins, K.A., Hoffman, S., Lindborg, S., Tohen, M., Breier, A., (2003). The PRIME North America randomized double-blind clinical trial of olanzapine versus placebo in patients at risk of being prodromally symptomatic for psychosis. I. Study rationale and design. Schizophr. Res. 61: 7-18.

204. McGlashan, T.H., Zipursky, R.B., Perkins, M.D., Addington, J., Miller, T., Woods, S.W., Hawkins, K.A., Hoffman, R.E., Preda, A., Epstein, I., Addington, D., Lindborg, S., Traskoma, Q., Tohen, M., Breier, A., (2006). Randomized double-blind trial of

olanzapine versus placebo in patients prodromally symptomatic for psychosis. Am J. Psychiatryry 163: 790-9.

205. McGorry, P.D., and Singh, B.S. (1995) Schizophrenia: Risk and possibility. In: Raphael, B., and Burrows, G.D., (eds.) Handbook of Studies on Preventive Psychiatry. Elsevier, Amsterdam. pp. 491-514.

206. McGorry, P.D., Edwards, J., Mihalopoulos, C., Harrigan, S.M., Jackson, J.J., (1996). EPPIC: An envolving system of early detection and optimal management. Schizophr. Bull. 22: 305-326.

207. McGorry, P.D., (1998). Preventive strategies in early psychosis: verging on reality. Br. J. Psychiat., 172,1-2.

208. McGorry PD. (2002a). Implementing Early Intervention in Psychosis: A Guide to Establishing Early Psychosis Services. Martin Dunitz Ltd., London.

209. McGorry, P.D., (2002b). The recognition and optimal management of early psychosis: an evidence-based reform. World Psychiatry 1: 76-83.

210. McGorry PD, Purcell R, Hickie IB, Yung AR, Pantelis C, Jackson HJ. (2007). Clinical staging: a heuristic model for psychiatry and youth mental health. MJA. 187:S40–S42.

211. McGorry, P.D., Yung, A.R., Bechdolf, A., Amminger, P. (2008). Back to the future: predicting and reshaping the course of psychotic disorder. Arch. Gen. Psychiatry. 65: 25-27.

212. McGorry, P.D., (2009). Un resumen de los antecedentes y del alcance de las intervenciones psicológicas en psicosis temprana, in: Martindale, B.V., Bateman, A., Crowe, M., Margison, F. Las psicosis. Los tratamientos psicológicos y su eficacia. Editorial Herder, Barcelona.

213. McGorry, P.D., Nelson, B., Goldstone, S., Yung, A., (2010). Clinical Staging. A heuristic and practical strategy for new research and better health and social outcomes for psychotic and related mood disorders. Can. J. Psychiatry 55: 486-497.

214. McGorry P.D., Yung A, Phillips L., (2003). The “Close-in” or Ultra High-Risk Model: A safe and effective strategy for research and clinical Intervention in prepsychotic mental disorder. Schizophr. Bull. 29: 771-790.

215. McGorry, P.D., Barnaby, N., Sherilyn, G., Yung, A.R. (2010). Clinical staging: A heuristic and practical strategy for new research and better health and social outcomes for psychotic and related mood disorders. La Revue canadienne de psychiatry, 55:486-497.

216. McNab, C., Haslam, N., Burnett, P., (2007). Expressed emotion, attributions, utility beliefs, and distress in parents of young people with first episode psychosis. Psychiat. Res. 151: 97-106.

217. Medina-Pradas, C., Navarro, J.B., López, S.R., Grau, A., Obiols, J.E. (2011). Further development of a scale of perceived expressed emotion and its evaluation in a simple of patients with eating disorders. Psychiatry. Re. 190: 291-296.

218. Meehl, P.E. (1962). Schizotaxia, schizotypy, schizophrenia. American Psychologist, 17:827

219. Meehl, P.E., 1999. Clarifications about taxometric method. Appl. Prev. Psychol. 8: 165–174.

220. Medina-Pradas, C. Sheimbaum, T., Barrantes-Vidal, N. (2012). Instrumento de Vulnerabilidad a la Esquizofrenia, Versión para Adultos (SPI-A). Giovanni Fioriti Editore, Roma.

221. Meneguelli, A., Alpi, A., Patelli, G., Preti, A., Cocchi, A., (2011). Expressed emotion in first-episode schizophrenia and in ultra high-risk patients: results from the Programma 2000 (Milan, Italy). Psychiat. Res. 189: 331-338.

222. Mihalopoulos, C., Harris, M., Henry, L., Harrigan, S., McGorry, P., (2009). Is early intervention in psychosis cost-effective over the long term? Schizophr. Bull. 35: 909-918.

223. Miklowitz, D.J., Goldstein, M.J., Fallon, I.R., (1983). Premorbid and symptomatic characteristics of schizophrenics from families with high and low levels of expressed emotion. J. Abnorm. Psychol. 92, 359-367.

224. Miklowitz, D.J. (2004). The role of family systems in severe and recurrent psychiatric disorders: A developmental psychopathology view. Dev. Psychopatol. 16: 667-688.

225. Miller., F., Dworkin, J., Ward, M. & Barone, D. (1990) A preliminary Study of Unresolved Grief in Families of Seriously Mentally Ill Patients. Hospital and Community Psychiatry, 41: 1321-1325.

226. Miller, R., Mason, S.E. (1999). Phase-specific psychosocial interventions for first-episode schizophrenia. Bull. Menninger Clin. 63: 499–519.

227. Miller, P., Byrne, M., Hodges, A., Lawrie, S., Owens, D., Johnstone, E., (2002). Schizotypal components in people at high risk of developing schizophrenia: Early findings from the Edinburgh high-risk study. Br. J. Psychiatry, 180: 179-184.

228. Miller, T., McGlashan, T., Rosen, J., Cadenhead, K., Ventura, J., McFarlane, W., Perkins, D.O., Pearlson, G.D., Woods, S.W. (2003a). Prodromal Assessment with the Structured Interview for Prodromal Syndromes and the Scale of Prodromal Symptoms: Predictive Validity, Interrater Reliability, and Training to Reliability. Schizophr. Bull., 29: 703-715.

229. Miller, T.J., Zipursky, R.B., Perkins, D., Addington, J., Woods, S.W., Hawkins, K.A., Hoffman,, R., Preda, A., Epstein, I., Addington, D., Lindborg, S., Márquez, E., Tohen, M., Breier, A., McGlashan, T.H. (2003b). The PRIME North America randomized double-blind clinical trial of olanzapine versus placebo in patients at risk of being prodromally symptomatic for psychosis. II. Baseline characteristics of the "prodromal" sample. Schizophr. Res. 61:19-30.

230. Miller, T.J., McGlashan, T.H., Rosen, J.L., Somjee, J., Markovich, P.J., Stein, K., Woods, S.W., (2002). Prospective diagnosis of the initial prodrome for schizophrenia

based on the Struetured Interview for Prodromal Syndromes: preliminary evidenee of interrater reliability and predictive validity. Am J. Psychiatry 159: 863-865

231. Myin-Germeys I, Marcelis M, Krabbendam L, Delespaul P, van Os J. (2005). Subtle fluctuations in psychotic phenomena as functional states of abnormal dopamine reactivity in individuals at risk. Biol. Psychiatry 58:105–110.

232. Mo, F.M.Y., Chung, W.S., Chun, D.Y.Y., Wong, K.S., (2007). Expressed Emotion in Relatives of Chinese Patients with First-episode Psychosis in Hong Kong. Hong Kong J. Psychiat. 17: 38-44.

233. Morgan, C., Fisher, H., (2007). Environment and schizophrenia: Environmental factors in schizophrenia: Childhood trauma—A critical review. Schizophr. Bull. 33: 3-10.

234. Morrison, A.P., Bentall, R.P., French, P., Walford, L., Kilcommons, A., Knight, A., Kreus, M., Lewis, S.W., (2002). Randomized controlled trial of early detection and cognitive therapy for preventing transition to psychosis in high-risk individuals. Study design and interim analysis of transition rate and psychological risk factors. Br. J. Psychiatry 181: 78-84.

235. Morrison, A.P., French, P., Parker, S., Roberts, M., Stevens, H., Bentall, R.P., Lewis, S.W., (2007). Three-year Follow-up of a Randomized Controlled Trial of Cognitive Therapy for the Prevention of Psychosis in People at Ultrahigh Risk. Schizophr. Bull. 33: 682-687.

236. Morrison, A., Stewart, S.L.K., French, P., Bentall, R.P., Birchwood, M., Byrne, R., Davies, L.M., Fowler, D., Gumley, A.I., Jones, P.B., Lewis, S.W., Murray, G.K., Patterson, P., Dunn, G. (2011) Early detection and intervention evaluation for people at high-risk of psychosis-2 (EDIE): trial rationale, design and baseline characteristics. Early Interv. Psychiatry. 5:24-32.

237. Myin-Germeys, I., Van Os, J., (2007). Stress-reactivity in psychosis: Evidence for an affective pathway to psychosis. Clin. Psychol. Rev. 27: 409-424.

238. Norman, R.M., and Malla, A.K. (2001) Duration of untreated psychosis: A critical examination of the concept and its importance. Psychol. Med. 31:381-400.

239. Nuevhterlein, K.H., Dawson, M.E. (1984). A heuristic vulnerability/stress model of schizophrenic episodes. Schizophr. Bull. 10: 300-312.

240. O´Brien, M. P, Gordon, J. L., Bearden, C. E., López., S. R., Kopelowicz, A., Cannon, T.D. (2006). Positive family environment predicts improvement in symptoms and social functioning among adolescents at imminent risk for onset of psychosis. Schizophr. Res. 81: 269-275.

241. O´Brien, M.P., Zinberg, J.L., Bearden, C.E., López, S.R., Kopelowicz, M.D., Cannon. T. D. (2008). Parent attitudes and parent adolescent interaction in families of youth at risk for psychosis and with recent-onset psychotic symptoms. Early Interv. Psychiatry 2: 268-276.

242. O´Brien, M., Zinberg, J.L., Ho, L., Rudd, A., Kopelowicz, A., Daley, M., Bearden, C.E., Cannon, T.D., (2009). Family problem solving interactions and 6 month symptomatic and functional outcomes in youth at ultra-high risk for psychosis and with recent psychotic symptoms: A longitudinal study. Schizophr. Res. 107: 198-205.

243. O'Flynn, K., Gruzelier, J.H., Bergman, A., Siever, L.J., (2003). The schizophrenia spectrum personality disorders, in: Hirsch S.R., Weinberger, D. Eds. Schizophrenia. Chichester, Blackwell, pp. 80-100.

244. Olsen, K.A., Rosenbaum, B. (2006). Prospective investigations of the prodromal state of schizophrenia: review of studies. Acta. Psychiatr. Scand. 113: 247-272.

245. Onwumere, J., Kuipers, E., Bebbington, P., Dunn, G., Fowler, D., Freeman, D., Watson, P., Garety, P. (2008). Caregiving and Illness Beliefs in the Course of Psychotic Illness. Can. J. Psychiat. 53, 460-468.

246. Patterson, P., Birchwood, M., Cochrane, R., (2000). Preventing the entrenchment of high expressed emotion in first episode psychosis: early developmental attachment pathways. Aust. Nz. J. Psychiat. 34: S191-S197.

247. Patterson, P., Birchwood, M. & Cochrane, R. (2005). Expressed emotion as an adaptation to loss. Prospective study in first-episode psychosis. Br. J. Psychiatry 187: 559-564.

248. Peralta V, Cuesta MJ. (1994) Validación de la escala de los síndromes positivo y negativo (PANSS) en una muestra de esquizofrénicos españoles. Actas Luso-Españolas de Neurología, Psiquiatría y Ciencias Afines, 22: 171-177.

249. Peralta, V., Cuesta, M. J., & de Leon, J. (1992). Positive versus negative schizophrenia and basic symptoms. Compr. Psychiatry 33: 202–206.

250. Peralta, V., Cuesta, M.J. (2005).The underlying structure of diagnostic systems of schizophrenia: A comprehensive polydiagnostic approach. Schizophr. Res. 79: 217-229.

251. Peralta, V., Cuesta, M.J., (2001). Motor features in psychotic disorders. II Development of diagnostic criteria for catatonia. Schizophr. Res. 47, 117–126.

252. Perkins, D., Gu, H., Boteva, K., Lieberman, J., (2005). Relationships between duration of Untreated Psychosis and Outcome in First-Episode Schizophrenia: A critical Review and Meta-Analysis. Am J. Psychiatry. 162: 1785-1804.

253. Phillips, L.J., Francey, S.M., Edwards, J., McMurray, N. (2007). Stress and psychosis: Towards the development of new models of investigation. Clin. Psychol. Rev. 27:307-317.

254. Poulton, R., Caspi, A., Moffitt, T., Cannon, M., Murray, R., Harlins, J.N., (2000). Children's self-reported psychotic symptoms and adult schizophreniform disorder. Arch. Gen. Psychiatry 57: 1053–1058.

255. Piskulic, D., Addington, J., Auther, A., Cornblatt, B. (2011). Using the global functioning social and role scales in a first-episode sample. Early Interv. Psychiatry 5: 219-223.

256. Rado, S. (1953). Dynamics and classification of disordered behavior. Am. J. Psychiatry 110: 406-416.

257. Raine, A., Reynolds, C., Lencz, T., Scerbo, A., Triphon, N., Kim, D. (1994) Cognitive-perceptual, interpersonal and disorganized features of schizotypal personality. Schizophr Bull. 20:191–201.

258. Raune, D., Kuipers, E. & Bebbington, P.E. (2004). Expressed emotion at first-episode psychosis: investigating a carer appraisal model. Br. J. Psychiatry 184: 321-326.

259. Regier, D.A., Narrow, W.E., Kuhl, E.A. Kupfer, D. J. (2009). The conceptual development of DSM-V. Am. J. Psychiatry. 166:645-650.

260. Riecher-Rössler, A., Gschwandtner, U., Aston, J., Borgwardt, S., Drewe, M., Fuhr, P., Pfluger, M., Radu, W., Schindler, C., Stieglitz, R.D., (2007). The Basel early-detection-of-psychosis (FEPSY)-study — design and preliminary results. Acta Psychiat. Scand. 115 (2), 114–125.

261. Ruhrmann, S., Schultze-Lutter, F., Klosterkötter, J. (2003). Early detection and intervention in the initial prodromal phase of schizophrenia. Psychopharmacopsychiatry, 36 suppl. 162-167.

262. Ruhrmann, S., Paruch, J., Bechdolf, A., Pukrop, R., Wagner, M., Berning, J., Shultze-Lutter, F., Janssen, B., Gaebel, W., Möller, H-J., Maier, W. (2008). Reduced subjective quality of life in persons at risk for psychosis. Acta Psychiatr Scan, 117:357-368.

263. Ruhrmann, S., Schultze-Lutter, F., & Klosterkötter, J. (2009). Intervention in the at-risk state to prevent transition to psychosis. Curr. Opin. Psychiatr. 22*:* 177–183.

264. Ruhrmann, S., Schultze-Lutter, F., Salokangas, R.K., Heinimaa, M., Linszen, D., Dingemans, P.M., Birchwood, M., Patterson, P., Juckel, G., Heinz, A., Morrison, A., Lewis, S., Graf von Reventlow, H., Klosterkötter, J., (2010a). Prediction of psychosis in adolescents and young adults at high risk: results from the prosepective European Prediction of Psychosis Study (EPOS). Arch. Gen. Psychiatry 67 (3), 241–251.

265. Ruhrmann, S., Schultze-Lutter, F., Klosterkötter, J. (2010b). Probably at-risk, but certainly ill--Advocating the introduction of a psychosis spectrum disorder DSM-V. Schizophr.Res. 120: 23-37.

266. Ruipérez, M.A., Ibáñez, M.I., Lorente, E., Moro, M., Ortet, G. (2001). Psychometric Properties of the Spanish Version of the BSI. Contributions to the Relationship between Personality and Psychopathology. E.J.P.A. 17: 241-250.

267. Power, P., McGuire, P., Iacoponi, E., Gatery, P., Morris, E., Valmaggia, L., Grafton, D., Craig, T., (2007). Lambeth Early Onset (LEO) and Outreach & Support in south London (OASIS) service. Early Interv. Psychiatry 1: 97-103.

268. Powers, A.D., Thomas, K.M., Ressler, K.J., Bradley, B., (2011). The differential effects of child abuse and posttraumatic stress disorder on schizotypal personality disorder. Compr. Psychiat. 52, 438-445.

269. Räkköläinen, V., Lehtinen, K., Alanen, Y.O., (1991). Need-adapted treatment of schizophrenic processes: the essential role of family-centered therapy meetings. Contemp. Fam. Treat. 13: 573-582.

270. Raune, D., Kuipers, E., Bebbington, P.E., (2004). Expressed emotion at first-episode psychosis: investigating a career appraisal model. Br. J. Psychiatry 184: 321-326.

271. Read, J., Fink, P.J., Rudegeair, T., Felitti, V., Whitfield, C.L., (2008). Child maltreatment and psychosis: A return to a genuinely integrated bio-psycho-social model. Clin. Schizophr. Relat. Psychoses 2: 235–254.

272. Rosa, A., Van Os, J., Fañanás, L., Barrantes-Vidal, N., Caparrós, B., Gutiérrez, B., Obiols, J., (2000). Developmental instability and schizotypy. Schizophr. Res. 43 (2–3): 125–134.

273. Rurhmann, S., Schultze-Lutter, F., Salokangas, R., Heinimaa, M., Linszen, D., Dingemans, P., Birchwood, M., Patterson, P., Juckel, G., Heinz, A., Morrison, A., Lewis, S., Von Reventlow, H., Klosterkötter, J., (2010). Prediction of Psychosis in

Adolescents and Young Adults at High Risk. Results from the Prospective European Prediction of Psychosis Study. Arch. Gen. Psychiatry 67: 241-251.

274. Ruhrmann, S., Schultze-Lutter, F., Klosterkötter, J., (2009). Intervention in the at-risk state to prevent transition to psychosis. Curr. Opin. Psychiatr., 22: 177-183.

275. Saksa, J.R., Cohen, S.J., Srihari, V.H., Woods, S.W., (2009). Cognitive Behavior Therapy for Early Psychosis: A comprehensive review of individual vs. group treatment studies. Int. J. Group Psychother. 59: 357-383.

276. Salokangas, R.K.R., Heinimaa, M., Ilonen, T., Suomela, T., Korkeila, J., Plathin, M., *et al*. (2004). Vulnerability to and current risk of psychosis. Description, experiences and preliminary results of the Detection of Early Psychosis or DEEP project. Neurol. Psychiat. B. R. 11: 37-44.

277. Sarró, S. Dueñas, R.M., Galve, L., Mediavilla, R., Mensa, I., Solé, J., Sotelo, C., Pomarol-Clotet, E., Cebamanos, J.M. (2006) Validación de la escala de Calgary en pacientes con esquizofrenia crónica. Informaciones psiquiátricas. 182: 203-13.

278. Scazufca, M., Kuipers, E., (1996). Links between Expressed Emotion and Burden of care in Relatives of Patients with Schizophrenia. Br. J. Psychiatry 168: 580-587.

279. Scazufca,.M., Kuipers, E. (1998). Stability of expressed emotion in relatives of those with schizophrenia and its relationship with burden of care perception of patients' social functioning. Psychol. Med. 28: 453-461.

280. Schlooser, D.A., Zinberg, J.L., Loewy, R.L., Casey-Cannon, S., O´Brien, M.P., Bearden, C.E., Vinogradov, S., Cannon, T.D., (2010). Predicting the longitudinal effects of the family environment on prodromal symptoms and functioning in patients at-risk for psychosis. Schizophr. Res. 118: 69-75.

281. Schultze-Lutter, F., Ruhrmann, S., Klosterkötter, J. (2006). Can schizophrenia be predicted phenomenologically? In: Johannessen JO, Martindale B, Cullberg J, eds. Evolving Psychosis. Different Stages, Different Treatments. London, UK: Routledge:104–123.

282. Schultze-Lutter, F., Addington, J., Ruhrmann, S., & Klosterkötter, J (2007) Schizophrenia Pronness Instrument. Adult Version (SPI-A) Roma: Giovanni Fioriti Editore. pp. 91.

283. Schultze-Lutter, F., (2009). Subjective symptoms in schizophrenia in research and the clinic: The Basic Symptoms Concept. Schizophr. Bull. 35: 5-8.

284. Schultze-Lutter, F., Addington, J., Ruhrmann, S., Klosterkötter, J., (2007). Schizophrenia Proneness Instrument. Adult Version (SPI-A). Giovanni Fioriti Editore, Roma.

285. Schultze-Lutter, F., Koch, E., (2010a). Schizophrenia Proneness Instrument, Child & Youth version (SPI-CY). Giovanni Fioriti Editore, Roma.

286. Schultze-Lutter, F., Ruhrmann, S., Berning, J., Maier, W., Klosterkötter, J., (2010b). Basic symptoms and Ultrahigh Risk Criteria: Symptom development in the initial prodromal state. Schizophr. Bull. 36: 182-191.

287. Shapiro, D.I., Cubells, J.F., Ouslay, O.Y., Rockers, K.; Walker, E.E., (2011). Prodromal symptoms in adolescents with 22q11.2 deletion syndrome and schizotypal personality disorder. Schizophr. Res. 129: 20-28.

288. Simons, C.J., Wichers, M,. Derom, C., Thiery, E., Myn-Germeys, I., Krabbendam, L., van Os, J. (2009). Subtle gene-environment interactions driving paranoia in daily life. Genes Brain. Behav. 8: 5–12.

289. Skodol, A.E., Pagano, M.E., Bender, D.S., Shea, M.T., Gunderson, J.G., Yen, S., Stout, R.L., Morey, L.C., Sanislow, C.A., Grilo, C.M., Zanarini, M.C., McGlashan, T.H. (2005). Stability of functional impairment in patients with schizotypal, borderline, avoidant, or obsessive-compulsive personality disorder over two years. Psychol. Med. 35: 443-451.

290. Skodol, A.E., (2008). Longitudinal course and outcome of personality disorders, Psychiat. Clin. N. Am., 31: 496-503.

291. Smeets, F., Lataster, T., Dominguez, M.D., Hommes, J., Lieb, R., Wittchen, H.U., van Os, J. (2012). Evidence that onset of psychosis in the population reflects early hallucinatory experiences that through environmental risks and affective dysregulation become complicated by delusions. Schizophr. Bull. 38: 531-542.

292. Smith, J., Birchwood, M., Cochrane, R., George, S., (1993). The needs of high and low expressed emotion families: a normative approach. Soc. Psych. Psych. Epid. 28: 11-16.

293. Spauwen, J., Krabbendam, L., Lieb, R., Wittchen, H.U., Van Os, J., (2006). Impact of psychological trauma on the development of psychotic symptoms: relationship with psychosis proneness. Br. J. Psychiatry, 188: 527-533.

294. Stanton AL, Kirk SB, Cameron CL, Danoff-Burg S. (2000). Coping through emotional approach: scale construction and validation. J. Pers. Soc. Psychol. 78: 1150–69.

295. Stefanis, N., Hanssen, M., Smirnis, N.K., Avramopoulos, D.A., Evdokimidis, I.K., Stefanis, C.N., Verdoux, H., Van Os, J., (2002). Evidence that three dimensions of psychosis have a distribution in the general population. Psychol. Med. 32: 347–358.

296. Stefanis NC, Smyrnis N, Avramopoulos D, Evdokimidis I, Ntzoufras I, Stefanis CN. (2004) Factorial composition of self-rated schizotypal traits among young males undergoing military training. Schizophr. Bull. 30:335–350.

297. Stirling, J., Tantam., D., Thomas, P., Newby, D., Montague, L., Ring, N., Rowe, S. (1993). Expressed emotion and schizophrenia: the ontogeny of EE during an 18-month follow-up. Psychol. Med. 32: 771-8.

298. Tang, Y., Wong, G., Hui, C., Lam, M., Chiu, C., Chan, S., Chung, D., Tso, S., Chan, K., Yip, K., Hung, S., Chen, E., (2010). Early intervention for psychosis in Hong Kong the EASY program. Early Interv. Psychatry 3: 214-219.

299. Tennakoon, L., Fannon, D., Doku, V., O´Ceallaigh, S., Soni, W., Santamaria, M., Kuipers, E., Sharma, T. (2000). Experience of caregiving: relatives of people experiencing a first episode of psychosis. Br. J. Psychiatry 177: 529-533.

300. Tessner, K.D., Mittal, V., Walker, E. F., (2011). Longitudinal Study of Stressful Life Events and Daily Stressors Among Adolescents at High Risk for Psychotic Disorder. Schizophr. Bull. 37: 432-441.

301. Thompson, A., Nelson, B., Yung, A. (2011) Predictive validity of clinical variables in the "at-risk" for psychosis population: International comparison with results from the North American Prdorome Longitudinal Study. Schizophr. Res. 126:51-57.

302. Tien, A., (1991). Distributions of hallucinations in the population. Soc. Psychiatry Psychiatr. Epidemiol. 26, 287–292.

303. Tienari, P., Wynne, L.C., Läksy, K., Moring, J., Nieminen, P., Sorri, A., Lahti, I., Wahlberg, K.E. (2003). Genetic boundaries of the schizophrenia spectrum: evidence from the Finnish adoptive family study of schizophrenia. Am J Psychiat. 160: 1587–1594.

304. Torgersen, S., Kringlen, E., Cramer, V., (2001). The prevalence of personality disorders in a community sample. Arch. Gen. Psychiatry 58: 590-596.

305. Trotman, H., McMillan, A., Walker, E., (2006). Cognitive function and symptoms in adolescents with schizotypal personality disorder. Schizophr. Bull. 32: 489-497.

306. Trull, T., Durrett, C., (2005). Categorical and Dimensional Models of Personality Disorder. An. Rev. Clin. Psychol. 1: 355-380.

307. Vallina, O., Alonso, M., Gutierrez, A., Ortega, J.A., García, A., Fernández, P., Lemos, S., (2003). Aplicación de un programa de intervención temprana en psicosis. Un nuevo desarrollo para las unidades de salud mental. Av. Salud Ment. Relac. 2. http://bibliopsiquis.com/asmr/0203/

308. Vallina, O., Lemos, S., Fernández, P., (2007). Early detection and intervention in psychosis: the state of the art. Psychology in Spain 11: 1-23.

309. van Os, J., Hanssen, M., Bijl, R.V., Vollebergh, W. (2001). Prevalence of psychotic disorder and community level of psychotic symptoms: an urban–rural comparison. Archives of General Psychiatry 58, 663–668.

310. Van Os, J., Kapur, S. (2009) Schizophrenia. Lancet, 374: 635-645.

311. Van Os, J., Linscott, R.J., Myin-Germeys, I., Delespaul, P., Krabbendam, L., (2009). A systematic review and meta-analysis of the psychosis continuum: evidence for a psychosis proneness-persistence-impairment model of psychotic disorder. Psychol. Med. 39 (2), 179–195.

312. Van Os, J., Kenis, G., Rutten, B.P.F. (2010). The environment and schizophrenia. Nature, 468: 203-212.

313. van Os, J., Linscott, R.J. (2012). Introduction: The Extended Psychosis Phenotype- Relationship with Schizophrenia and Whith Ultrahigh Risk Status for Psychosis. Schizophr. Bull. 38: 227-230.

314. van Rossum, I., Dominguez, M.D., Lieb, R., Wittchen, H.U., van Os, J. (2011). Affective dysregulation and reality distortion: a 10-year prospective study of their association and clinical relevance. Schizophr. Bull. 37:561–571.Vaughn, C.E., Leff, J.P. (1976). The influence of family and social factors on the course of psychiatric illness. A comparison of schizophrenic and depressed neurotic patients. Br. J. Psychiatry129:125-137.

315. Vaughn, C., Leff, J. (1985). Expressed emotion in families: its significance for mental illness, Guilford Press, New York.

316. Velthorst E, Nieman DH, Becker HE, et al. (2009) Baseline differences in clinical symptomatology between ultra high risk subjects with and without a transition to psychosis. Schizophr Res. 109:60–65.

317. Verdoux, H., Cougnard, A., (2003). The early detection and treatment controversy in schizophrenia research. Curr. Opin. Psychiatr. 16: 175-179.

318. Verdoux, H., van Os, J. (2002). Psychotic symptoms in non-clinical populations and the continuum of psychosis. Schizophr. Res. 54: 59-65.

319. Vilagrà, R., Domínguez-Martínez, T., Blanqué, J.M., Vainer, E., Berni, R., Montoro, M., Mauri, L., Bedoya, E., Kwapil, T.R, Barrantes-Vidal, N., (2010). Impact of depression on psychotic symptoms in At Risk Mental State and First Episode Psychosis patients. Presented at: 7th International Conference on Early Psychosis (Amsterdam, NL), November 2010. *Abstract publication:* Early Interv in Psychiatry 4:83.

320. Vollema, M.G., Hoijtink, H. (2000). The multidimensionality of self-report schizotypy in a psychiatric population: an analysis using multidimensional Rasch models. Schizophr. Bull. 26:565-575.

321. Walder, D.J., Andersson, T.L., McMillan, A.L., Breedlove, S.M., Walker, E.F., (2006). Sex differences in digit ratio (2D:4D) are disrupted in adolescents with schizotypal personality disorder: altered prenatal gonadal hormone levels as a risk factor. Schizophr. Res. 86: 118-122.

322. Wasserman, S., Weisman de Mamani, A., Suro, G. (2012). Shame and guilt/self-blame as predictors of expressed emotion in family members of patients with schizophrenia. Psychiat. Res. 196: 27-31.

323. Wearden, A.J., Tarrier, N., Barrowclough, C., Zastowny, T.R., Rahill. A. A., (2000). A review of expressed emotion research in health care. Clin. Psychol. Rev. 20: 633-666.

324. Weisman, A.G., Nuechterlein, K.H., Goldstein, M.J., Snyder, K.S., (1998). Expressed emotion, Attributions, and Schizophrenia Symptoms Dimentions. J. Abnorm. Psychol. 107: 355-359.

325. Werker, A.K., Long, J.D., Haas, G.L., Bellack, A.S. (2002). Interpersonal control, expressed emotion, and change in symptoms in families of persons with schizophrenia. Schizophr. Res. 58: 281-292.

326. Wiedemann, G., Rayky, O., Feisnstein, E., Hahlweg, K., (2002). The family Questionnaire: Development and validation of a new self-report scale for assessing expressed emotion. Psychiat. Res. 109: 265-279.

327. Widiger, T.A., Frances, A.J. and Sweeney, M., (1988). Schizophrenia spectrum disorders. Curr. Opin. Psychiatry 1: 13-18.

328. Wigman, J.T. W., van Nierop, M., Vollebergh, W.A.M., Lieb, R., Beesdo-Baum, K., Wittchen, H.U. van Os, J. (2012). Evidence That Psychotic Symptoms Are Prevalent in Disorders of Anxiety and Depression, Impacting on Illness Onset, Risk, and Severity- Implications for Diagnosis and Ultra-High Risk Research. Schizophr. Bull. 38: 247-257.

329. Woods, S.W., Breier, A., Zipursky, R.B., (2003). Randomized trial of olanzapine versus placebo in the symptomatic acute treatment of the schizophrenic prodrome. Biol. Psychiat. 54: 453-64.

330. Woods, S., Addington, J., Cadenhead, K., Cannon, T., Cornblatt, B., Heinssen, R., Perkins, D.O., Seidman, L.J., Tsuang, M.Y., Walker, E.F., McGlashan, T.H. (2009). Validity of the prodromal risk syndrome for first psychosis: Findings from the North American Prodrome Longitudinal Study. Schizophr. Bull. 35: 894-908.

331. World Helath Organization (WHO) (1992). ICD: The ICD-10 classification of mental and behavioural disorders- clinical descriptions and diagnostic guideline. Geneva: WHO.

332. World Health Organization. (1994). International Statistical Classification of Diseases and Related Health Problems, 10th Rev. Author, Geneva

333. World Health Organization (2004).The World Health Organization Quality of Life (WHOQOL)-BREF. WHO: Geneve.

334. Wynne, L.C. (1981). Current concepts about schizophrenics and family relationships. J. Nerv. Ment. Dis. 169: 82–89.

335. Young. R.C., Biggs, J.T., Ziegler, V.E. & Meyer, D.A. (1978). A rating scale for mania: reliability, validity and sensitivity. Br. J. Psychiatry 133: 429-435.

336. Yung, A.R., McGorry, P.D., McFarlane, C.A., Jackson, H.J., Patton, G.C., Rakkar, A. (1996). Monitoring and care of young people at incipient risk of psychosis. Schizophr. Bull. 22: 283-303.

337. Yung, A.R., McGorry, P.D. (1996). The initial prodrome in psychosis: descriptive and qualitative aspects. Aust. N. Z. J. Psychiatry 30: 587-599.

338. Yung, A.R., Phillips, L.J., Yuen, H.P., Francey, S.M., McFarlane, C.A., Hallgren, M., McGorry, P.D. (2003a). Psychosis prediction: 12-month follow up of a high-risk ("prodromal") group. Schizophr. Res. 60: 21-32.

339. Yung A.R. (2003b). The schizophrenia prodrome: a high-risk concept. Schizophr Bull. 29:859-865.

340. Yung, A.R., Phillips, L.J., McGorry, P.D. (2004a) Treating Schizophrenia in the Prodromal Phase. Taylor and Francis, London.

341. Yung, A.R., Phillips, L.J., Yuen, H.P, MCGorry, P.D (2004b). Risk factors for psychosis in an ultra high-risk group: psychopathology and clinical features. Schizophr. Res. 67:131-142.

342. Yung, A.R., Pan Yuen, H., McGorry, P.D., Phillips, L.J., Kelly, D., Dell'ollio, M., Francey, S.M., Cosgrave, E.M., Killackey, E., Standford, C., Godfrey, K., Buckby, J., (2005). Mapping the onset of psychosis: the Comprehensive Assessment of At-Risk Mental States. Aust. NZ. J. Psychiat. 39: 964-971.

343. Yung, A.R., Stanford, C., Cosgrave, E., Killackey, E., Phillips, L., Nelson, B., McGorry, P.D., (2006). Testing the Ultra High Risk (prodromal) criteria for the prediction of psychosis in a clinical sample of young people. Schizophr. Res. 84 (1), 57–66.

344. Yung, A.R., McGorry, P.D., Francey, S.M., Nelson, B., Baker, K., Phillips, L.J., Berger, G., Amminger, G.P., (2007a). PACE: a specialized service for young people at risk of psychotic disorders. Med. J. Australia 187: 43-46.

345. Yung, A.R., Yuen, H.P., Berger, G., Francey, S., Hung, T., Nelson, B., Phillips, L., McGorry, P. (2007b). Declining Transition Rate in Ultra High Risk (Prodromal) Services: Dilution or Reduction of Risk? Schizophr. Bull, 33:673-681.

346. Yung, A., McGorry, P.D., (2007) Prediction of psychosis: setting the stage. Br. J. Psychiatry 191 suppl. s1-s8.

347. Yung, A., Nelson, B., Thompson, A., Wood, S., (2010). Should a “risk syndrome for psychosis” be included in the DSM-V? Schizophr. Res. 120(1-3): 7-15.

348. Yung, A.R., Pan Yuen, H., McGorry, P.D., Phillips, L.J., Kelly, D., Dell’ollio, M., Francey, S.M., Cosgrave, E.M., Killackey, E., Standford, C., Godfrey, K., Buckby, J., (2005). Mapping the onset of psychosis: the Comprehensive Assessment of At-Risk Mental States. Aust. NZ. J. Psychiat. 39: 964-971.

349. Zubin, J., Spring, B. (1977). Vulnerability- a new view of schizophrenia. J. Abnorm. Psychol. 86: 103-126.

350. Zubin, J., Steinhauer, S.R., Condray.R. (1992). Vulnerability to relapse in schizophrenia. Br. J. Psychiatry Suppl: 13-18.

ACKNOWLEDGEMENTS

La realización de esta tesis ha sido gracias a mucha gente que me ha acompañado durante estos años y al apoyo de diversas instituciones que han permitido el desarrollo de este trabajo.

Agradezco al Ministerio de Asuntos Exteriores y de Cooperación y a la Agencia Española de Cooperación Internacional para el Desarrollo (MAEC-AECID) por haberme otorgado la beca doctoral sin la cual no hubiera sido posible la realización de esta tesis.

Agradezco a Neus Barrantes por dirigirme la tesis y por haberme dado la oportunidad de trabajar de cerca con ella durante estos años. Gracias por compartir conmigo tus conocimientos y experiencia clínica, investigadora, profesional y personal. Gracias por confiar en mí y por reconocer mi trabajo, por apoyarme, por promoverme profesionalmente y por darme la oportunidad de continuar trabajando en este gran proyecto que hemos ido edificando juntas a base de mucho esfuerzo y que ahora empieza a dar los primeros frutos. Siempre estaré agradecida contigo por todo el aprendizaje que he adquirido de ti, por todo lo que has hecho por mí y sobretodo porque ha sido un enorme placer compartir contigo la pasión por el estudio de la psicosis.

Agradezco a todos los psiquiatras, psicólogos y al personal administrativo del CSMA de Sants, del CSMA de Montjuïc, del CSMIJ y del Hospital de Día para adolescentes de la Fundació Sanitaria Sant Pere Claver por haberme proporcionado todos los recursos necesarios y por haberme brindado todas las facilidades para realizar el muestreo de la tesis.

Agradezco especialmente a todos los pacientes y familiares que compartieron su experiencia conmigo y que aceptaron participar en este estudio, porque sin ellos no hubiera sido posible la realización de esta tesis, pero también por todo el conocimiento y la experiencia que he adquirido gracias a ellos.

Agradezco a todos mis amigos y colegas del grupo de investigación Persona-Gen Ambiente de la UAB con los que he trabajado estos años: Agnès, Erika, Sergi, Mercè, Tamara, Erika y Raül. Ha sido un gusto trabajar con ustedes y formar parte de un mismo equipo.

Thanks to Prof.Thomas Kwapil for helping me with statistical analyzes, for solve all the problems that have arisen, and for having always the best disposition to help.

Agradezco a Josep Ma. Blanch porque gracias a él pude venir a Barcelona a estudiar el máster y porque me dio todo su apoyo para empezar el doctorado y para solicitar la beca MAEC-AECID.

Agradezco a Tamara porque me ha mostrado un apoyo incondicional, porque siempre me ha ayudado en todo lo que he necesitado y porque me ha enseñado prácticamente todo lo que sé de estadística, pero sobretodo agradezco haber encontrado en ella a una gran amiga en la que puedo confiar plenamente y con quien sé que puedo contar siempre.

Agradezco a Cristina por haberme entrenado en la *Camberwell Family Interview* y por transmitirme la pasión por el estudio de la emoción expresada. Cris, ha sido un verdadero gusto haberte conocido y haber trabajado contigo este último año porque he aprendido muchas cosas sobre la investigación que me servirán para mejorar mi trabajo de aquí en adelante.

Agradezco a Paz Flores por darme la oportunidad de colaborar con ella en el proyecto EMILIA, no sólo porque resultó ser una de las mejores experiencias en mi vida profesional y porque aprendí mucho trabajando con ella, sino porque pude descubrir a una gran persona, una gran profesional, una gran amiga y una madre adoptiva que me ha abierto los brazos y me ha mostrado un gran apoyo todos estos años en Barcelona.

Agradezco a todos los pacientes y profesionales de la Asociació Septimania por la experiencia y el aprendizaje que adquirí trabajando con ellos.

Agradezco a mis papás y a mi hermano por todo su cariño, por su apoyo incondicional y por todo lo que han hecho por mí. Papá, gracias por ayudarme con las correcciones del inglés, gracias por haberme enseñado tantas cosas y por apoyarme siempre en mis decisiones. Mamá, quién iba a pensar que cuando empezaste tu doctorado y nos trajiste a vivir a Barcelona hace casi 18 años, iba a terminar yo haciendo también el doctorado en la misma ciudad y en la misma universidad. Yo creo que no es ninguna casualidad porque siempre has sido mi mayor inspiración y mi ejemplo a seguir.
¡Gracias por todo a los tres!

Agradezco a Ber por compartir casi media vida juntos, pero sobretodo por haber estado a mi lado en estos últimos cinco años, por haberme tenido tanta paciencia y soportarme en los momentos de mayor estrés, por ayudarme y apoyarme siempre en los momentos difíciles y por hacerme tan feliz.

Agradezco a Jesus y a Esther por haberme recibido cuando llegué y por haberme apoyado desde el principio.

Agradezco a todos los amigos que he conocido durante mi estancia en Barcelona por compartir momentos de diversión y alegría, y por ayudarme a desconectar del estrés constante en el que he vivido estos años, gracias a Olalla, Noelia, Esther, Sandra, Miriam, Marta, Leonardo, Susana y Aina.

Finalmente, agradezco a toda mi familia y amigos de México que a pesar de la distancia han estado presentes y me han apoyado siempre.

CURRICULUM VITAE

Address:
C/ Entença 116 6º 3ª
C.P.08015
Barcelona, Spain

DNI: 49324715L

Telephone:
930040634
622817593
e-mail:
tecelli.dominguez@uab.cat
tecelli.dominguez@gmail.com

Tecelli Domínguez Martínez

PERSONAL INFORMATION

- Date of birth: 27 septiembre 1983
- Place of birth: México City, México
- Age:28
- Nationalities: Mexican and Spanish

PRESENT PROFESIONAL POSITION

Researcher Clinical Psychologist

Departament de Psicologia Clínica i de la Salut

B5/158.28
Facultat de Psicologia
Universitat Autònoma de Barcelona
08193 Bellaterra (Barcelona), Spain.

EDUCATION

2008-2012
PhD in Clinical and Health Psychology. Departament de Psicologia Clínica i de la Salut. Universitat Autònoma de Barcelona (UAB). Barcelona, Spain.
Supervisor: Dr. Prof. Neus Barrantes-Vidal
2007-2008
MSc in Psychosocial Rehabilitation in Mental Health. Departament de Psicologia Social, Psicología Clínica i de la Salut. Universitat Autònoma de Barcelona (UAB). Barcelona, Spain.
Supervisor: Dr. Josep Ma. Blanch

2002-2006
Degree of Psychology. División de Ciencias Sociales y Humanidades. Universidad Autónoma Metropolitana Unidad Xochimilco (UAM-X). México City, México.
Psychology Degree homologated by the Spanish Education Ministry,
Number: 0846037 /2011/H22309.

PREFESIONAL EXPERIENCE

2011
Psychologist-Monitor in the Centro de Día *Septimània* Associació per a la Salut Mental (Barcelona, Spain), from February 2009 to May 2011.
Activities: conducting several psychosocial rehabilitation workshop and activities for patients with psychotic disorders.

Substitution as Psychologist-Monitor in the Centro de Día *Septimània* Associació per a la Salut Mental (Barcelona, Spain), from 18 to 22 de April; from 6 to 10 de June; and from 28 July to 6 de August 2011.
Activities: conducting several psychosocial rehabilitation workshop and activities for patients with psychotic disorders.

2010
Substitution as Psychologist-Monitor in the Centro de Día *Septimània* Associació *per a la Salut Mental* (Barcelona, Spain), from 23 August to 6 September 2010.
Activities: conducting several psychosocial rehabilitation workshop and activities for patients with psychotic disorders.

Substitution as Psychologist-Monitor in the Centro de Día *Septimània* Associació *per a la Salut Mental* (Barcelona, Spain), from 29 March to 9 Abril de 2010.
Activities: conducting several psychosocial rehabilitation workshop and activities for patients with psychotic disorders.

2009
Substitution as Psychologist-Monitor in the Centro de Día *Septimània Associació per a la Salut Mental* (Barcelona, Spain), from 6 to 17 April 2009 and from 27 July to 7 September 2009.
Activities: conducting several psychosocial rehabilitation workshop and activities for patients with psychotic disorders.

2008
Psicologist-Monitor of therapeutic apartments for patients with Several Mental disorders, in the *Fundació Malalts Mentals de Catalunya* (FAMMCA) (Barcelona, Spain). From May 2008 to October 2008.
Activities: Therapeutic support and supervision

Substitution as Psychologist-Monitor in the Centro de Día *Septimània Associació per a la Salut Mental* (Barcelona, Spain), from 17 to 28 March 2008; from 24 July to 10 September 2008.
Activities: conducting several psychosocial rehabilitation workshop and activities for patients with psychotic disorders.

Professional practices in the Servicio de Rehabilitación Comunitaria Sants-Monjüic (Barcelona), from Asociación JOIA (Barcelona, Spain). From Febrary to April 2008.

2007
Resarcher Asistant in the colaboration in the organization of the training for relatives of patients with several mental disorders "*Familia a Familia de NAMI*" organized by Voz Pro Salud Mental. From 7 March to 30 May 2007 (Mexico City, Mexico).

2006
Researcher Psychologist in the Instituto Nacional de Psiquiatría Ramón de la Fuente, Dirección de Investigaciones Epidemiológicas y Psicosociales, in the project: "*Creencias, estigma, necesidades y apoyo para personas con esquizofrenia, familiares, cuidadores y profesionales"* (Mexico City, Mexico)
Supervisor: Dra. Ma. Luisa Rascón Gasca.
From January 2006 to Febrary 2008.
Project number: EP09.
Finantial institution: CONACyT: 4317.0. 46569

Research Assistant in the collaboration of the Project of Assessment and Educational Diagnostic of the Fase Básica of the Universidad Intercultural de Chiapas, Tabasco y Veracruz (Mexico).
From August to November 2006.
Supervisor: Dra. Dolores Martínez Guzmán

Social service in the Instituto Nacional de Psiquiatría Ramón de la Fuente, Dirección de Investigaciones Epidemiológicas y Psicosociales (Mexico City, Mexico).
Supervisor: Dra. Ma. Luisa Rascón Gasca.
Project: "*Funcionamiento familiar y esquizofrenia*"
From Septiembre 2005 to March 2006.
Total of hours: 480

Professional practices in the "Comunidad Terapéutica Casa Azul" giving therapeutic support to patients with chronic psychotic disorders (Mexico City, Mexico). From August 2005 to January 2006.

2005
Professional practices in the Instituto Nacional de Psiquiatría Ramón de la Fuente, Dirección de Investigaciones Epidemiológicas y Psicosociales (Mexico City, Mexico).
Project: "*Funcionamiento familia y esquizofrenia*"
Supervisor: Dra. Ma. Luisa Rascón Gasca
From March to September 2005.
Finantial institution: CONACyT: 3335-H9308

2004
Professional practices in the Instituto Mexicano de la Audición y el Lenguaje (IMAL).
Activity: Disegn learning activities for deaf children (Mexico City, Mexico)
From September 2003 to March 2004.

Research Assistant, collaboration in the sampling of the Situational Diagnostic of the Education System of the Nuevo León State (México). August 2003.

PARTICIPATION IN RESEARCH PROJECTS

Participation as Research Clinical Psychologist in the European Network of National Schizophrenia Networks Studying Gene-Environment Interactions (EU-GEI)
Granting agency: European Community's Seventh Framework Program under grant agreement No. HEALTH-F2-2010-241909 (Project EU-GEI)
General Project Coordinator: Prof. Jim van Os
Duration: March 2010 - March 2015
UAB-SPC is an Affiliated Center of the WorkPackage 5 (Prodromal participants)
Principal Investigators: Prof. Phillip McGuire and Prof. Luccia Valmaggia (Institute of Psychiatry, London, UK)
Barcelona Site Coordinator: Prof. Dra. Neus Barrantes-Vidal
Incoporated to the project on November 2011

Researcher Psychologist if the Reseaarch Group *"Interacción Persona-Ambiente en Psicopatología",* from the Departamento de Psicología Clínica y de la Salud, Facultad de Psicología, Universidad Autónoma de Barcelona (UAB) (Barcelona, Spain).
Principal Investigator: Prof. Dra. Neus Barrantes-Vidal
Finantial Institution: Agència de Gestió d'ajuts Universitaris i de Recerca (AGAUR)-Generalitat de Catalunya: (2009SGR672.
Financing: 41.600€
Duration: 2009-2014
Incorporation: 2011

Researcher Psychologist of the Research Project: "*The Interaction between Daily-Life Stressors and Subjective Appraisals of Psychotic-Like Symptoms in the Psychosis Prodrome during One Year Follow-up: Ecological and Dynamic Evaluation with the Experience Sampling Methodology and Analysis of Gene-Environment (Stress) Interactions"* (ATTRM059, duración 2009-2013).
Principal Investigator: Prof. Neus Barrantes-Vidal
Finantial Institution: Fundació La Marató TV3
Financing: 136.256,98€
Duration: 2009-2013
Incorporation: 2009

Collaboration as Researcher Psychologist in the European Project: *Empowerment of Mental Illness Service Users: Lifelong Learning, Integration and Action (EMILIA*)
Project Number: 513435
Principal Investigator: Prof. Peter Rayan
Finantial Institution: 6to Framework Program of the European Union
Duration: 2005-2010
Incorporation: 2007

Researcher in Medical Sciences category "A" according to the criteria and procedures established by the Comisión Coordinadora de los Institutos Nacionales de Salud y Hospitales de Alta Especialidad de México.

Researcher Psychologist of the Research Project: "*Creencias, estigma, necesidades y apoyo para personas con esquizofrenia, familiares, cuidadores y profesionales*". Instituto Nacional de Psiquiatría Ramón de la Fuente, Dirección de Investigaciones Epidemiológicas Psicosociales.

Principal Investigator: Dra. Ma. Luisa Rascón Gasca.
Project number: EP09.
Finantial Institution: CONACyT: 4317.0. 46569
Duration: 2006-2010
Incorporation: 2008.

TEACHING EXPERIENCE

Theaching in the Master de Danza MovimientoTerapia en la Universidad Autónoma de Barcelona (UAB), Barcelona, Spain. 5 of Febrary 2011 (4hours).

Teaching in the seminary about the research Project "Empowerment of Mental Illness Service Users: Lifelong Learning, Integration and Action (EMILIA)". In the Escola Bonanova Formació Profesional Sanitària, Barcelona, Spain. 20 of May 2008.

PUBLICATIONS

SCIENTIFIC ARTICLES

2011
Domínguez-Martínez, T., Blanqué, J.M., Codina, J., Montoro, M., Mauri, L., Barrantes-Vidal, N. (2011) Rationale and state of the art in early detection and intervention in psychosis, Salud Mental, 34 (4): 341-350.

Domínguez-Martínez, T., Vainer, E., Massanet, M.A., Torices, I., Jané, M., Barrantes-Vidal, N. (2011) The need-adapted integrated treatment in Sant Pere Claver-Early Psychosis Program (SPC-EPP) in Barcelona, Spain. Salud Mental 34(6), 517-524.

Domínguez-Martínes, T, Kwapil, T.R., Barrantes-Vidal, N. (2011) Actualización sobre la investigación del Trastorno Esquizotípico de la Personalidad (TEP) en la Adolescencia. Revista de Psicopatología y Salud Mental del niño y del adolescente, 18 (Noviembre):99-104.

2010
Flores, P., Roquer, A., Masferrer, C. Domínguez, T. (2010) Experiencia de un taller Multifamiliar en un hospital de día de psiquiatría" MOSAICO Revista de la Federación Española de Asociaciones de Terapia Familiar, 46:25-30.

2008
Flores, P., Palomer, E., Domínguez, T., Rosado, S., Castaño, J., Izquierdo, R., Leahy Ni Laocha, E., Masferrer, C. (2008) "Proyecto EMILIA: Formación de usuarios de salud mental para la inclusión social". Interpsiquis (-1).

BOOK CHAPTERS

2010
Rascón-Gasca, M.L. Alcántara, A., Domínguez-Martínez, T. Casanova, L. (2010) "Las necesidades clínicas y sociales de los familiares de personas con esquizofrenia". En: Saint Martí & León (Coords) La medicina social en México I. Experiencia, subjetividad y salud. México: Ediciones EÓN. pp. 89-103.

ABSTRACTS PUBLISHED

2010

1. Domínguez, T., Vilagrà, R., Blanqué, J.M., Vainer, E., Berni, R., Montoro, M., Mauri, L., Bedoya, E., Kwapil, T.R., Barrantes-Vidal, N. (2010). The association between relatives' Expressed Emotion with clinical and functional features of early-psychosis patients. Presented at: 7th International Conference on Early Psychosis (Amsterdam, NL), November 2010. *Abstract publication: Early Intervention in Psychiatry*, 4(Suppl. 1), p.55.
2. Domínguez, T., Vilagrà, R., Blanqué, J.M., Vainer, E., Berni, R., Montoro, M., Mauri, L., Bedoya, E., Kwapil, T.R., Barrantes-Vidal, N. (2010). Levels of Emotional Over-involvement (EOI) and Critical Comments (CC) in relatives of First Episode Psychosis and At Risk Mental State patients. Presented at: 7th International Conference on Early Psychosis (Amsterdam, NL), November 2010. Presented at: 7th International Conference on Early Psychosis (Amsterdam, NL), November 2010. *Abstract publication: Early Intervention in Psychiatry*, 4(Suppl. 1), p.128.
3. Vilagrà, R., Domínguez, T., Blanqué, J.M., Vainer, E., Berni, R., Montoro, M., Mauri, L., Bedoya, E., Kwapil, T.R., Barrantes-Vidal, N. (2010). Impact of depression on psychotic symptoms in At Risk Mental State and First Episode Psychosis patients. Presented at: 7th International Conference on Early Psychosis (Amsterdam, NL), November 2010. *Abstract publication: Early Intervention in Psychiatry*, 4(Suppl. 1), p.83.

ARTÍCLES SUBMITED FOR PUBLICATION

Domínguez-Martínez, T., Medina-Pradas, C., Kwapil, T.R., Barrantes-Vidal, N. Relatives' illness attributions mediate the association of expressed emotion with early psychosis symptoms and functioning.

Domínguez-Martínez, T., Barrantes-Vidal, N. Clinical and Psychosocial Characterization of At-Risk Mental State and First-Episode of Psychosis patients from the Sant Pere Claver Early Psychosis Program in Barcelona (Spain): Preliminary Baseline Results.

Domínguez-Martínez, T., Medina-Pradas, C., Barrantes-Vidal, N. Determinants of Subjective Quality of Life in the At-Risk Mental State

Domínguez-Martínez, T., Barrantes-Vidal, N. Relatives' Expressed Emotion, Attributions and Emotional State in At-Risk Mental State and First-Episode Psychosis.

BOOK CHAPTERS IN PRESS

Rascón, M.L., Valencia, M., Domínguez-Martínez, T. "El estudio de la carga familiar, su expresión emocional y las creencias acerca de la esquizofrenia". En: Psicología y salud: Las aportaciones en México. Red de Psicología Clínica, Editorial Thompson (En prensa)

CONGRESS PARTICIPATION

2012

Participation in the IPRN-Schizophrenia International Research Society Conference "Prodromal" satellite. 14 April 2012 in Florence:

1. Domínguez-Martínez, T., Medina-Pradas, C., Vainer, E., Fuentenebro, S., Torices, I., Kwapil, T.R., Barrantes-Vidal, N. Quality of Life in the prodromal stage of psychosis is associated with symptoms, functioning and premorbid adjustment.

2. Medina-Pradas, C., Domínguez-Martínez, T., Blanqué, J.M., Montoro, M., Peruzzi, S., Kwapil, T.R., Barrantes-Vidal, N. How do clinical, social and role functioning of At-Risk Mental States and First-Episode of Psychosis related to their relatives' Expressed Emotion?

Participation on the 3rd Biennal Schizophrenia International Research Society (SIRS) Conference. 14-18 april 2012 in Florence:

1. Medina-Prades, C., Domínguez-Martínez, T., Blanqué, J.M., Montoro, M., Peruzzi, S., Kwapil, T.R., Barrantes-Vidal, N. How do clinical, social and role functioning of At-Risk Mental States and First-Episode of Psychosis related to their relatives' Expressed Emotion?
2. Kwapil, T.R., Domínguez-Martínez, T., Bedoya, E., Barrantes-Vidal, N. Interpersonal Appraisals and Subjective Stress Predict Psychotic Symptoms in Daily Life.

2011

Participation on the Meeting of the Society for Research on Psychopathology. 22-25 September 2011 in Boston. MA. Oral presentation: Kwapil, TR., Barrantes-Vidal, N., Domínguez, T., Bedoya, E. Interpersonal Appraisals and Subjective Stress in the Moment Predict Psychotic Symptoms in Daily Life in Patients with Early Psychosis.

Participación en la 7ª Reunión Anual de la Sociedad Catalana de Psiquiatría Infanto-Juvenil. De los pródromos a la psicosis en niños y adolescentes. El 20 de mayo de 2011 en el Hospital Sant Joan de Déu, Barcelona con los siguientes posters:

1. Domínguez, T., Vilagrà, R., Blanqué, J.M., Vainer, E., Berni, R., Montoro, M., Mauri, L., Bedoya, E., Kwapil, T.R., Barrantes-Vidal, N. (2011). The association between relatives' Expressed Emotion with clinical and functional features of early-psychosis patients.
2. Domínguez, T., Vilagrà, R., Blanqué, J.M., Vainer, E., Berni, R., Montoro, M., Mauri, L., Bedoya, E., Kwapil, T.R., Barrantes-Vidal, N. (2011) Levels of Emotional Over-involvement (EOI) and Critical Comments (CC) in relatives of First Episode Psychosis and At Risk Mental State patients.
3. Vilagrà, R., Domínguez, T., Blanqué, J.M., Vainer, E., Berni, R., Montoro, M., Mauri, L., Bedoya, E., Kwapil, T.R., Barrantes-Vidal, N. (2011) Impact of depression on psychotic symptoms in At Risk Mental State and First Episode Psychosis patients.

2010

Participación en la "7th International Conference on Early Psychosis of the International Early Psychosis Association" con los siguientes posters:

1. Domínguez, T., Vilagrà, R., Blanqué, J.M., Vainer, E., Berni, R., Montoro, M., Mauri, L., Bedoya, E., Kwapil, T.R., Barrantes-Vidal, N. (2010). The association between relatives' Expressed Emotion with clinical and functional features of early-psychosis patients. Presented at: 7th International Conference on Early Psychosis (Amsterdam, NL), November 2010. *Abstract publication: Early Intervention in Psychiatry*, 4(Suppl. 1), p.55.
2. Domínguez, T., Vilagrà, R., Blanqué, J.M., Vainer, E., Berni, R., Montoro, M., Mauri, L., Bedoya, E., Kwapil, T.R., Barrantes-Vidal, N. (2010). Levels of Emotional Over-involvement (EOI) and Critical Comments (CC) in relatives of First Episode Psychosis and At Risk Mental State patients. Presented at: 7th International Conference on Early Psychosis (Amsterdam, NL), November 2010. *Abstract publication: Early Intervention in Psychiatry*, 4(Suppl. 1), p.128.
3. Vilagrà, R., Domínguez, T., Blanqué, J.M., Vainer, E., Berni, R., Montoro, M., Mauri, L., Bedoya, E., Kwapil, T.R., Barrantes-Vidal, N. (2010). Impact of depression on psychotic symptoms in At Risk Mental State and First Episode Psychosis patients. Presented at: 7th International Conference on Early Psychosis (Amsterdam, NL), November 2010. *Abstract publication: Early Intervention in Psychiatry*, 4(Suppl. 1), p.83.

2009
Oral participation in the I Congreso Ibérico de Terapia Familiar y XXX Jornadas Españolas de Terapia Familiar con el Taller: "Experiencia de un Taller de Formación Multifamiliar en Hospital de Día de Psiquiatría". 30 October 2009 in Barcelona, Spain.

Participation in the XXIV Congreso de la Asociación Española de Neuropsiquiatría (AEN). *Nuevas Expresiones Clínicas en una Sociedad Cambiante* y las XXVI Jornadas AAN Asociación Andaluza de Profesionales de Salud Mental-AEN, From 3 to 6 Juny 2009 in Cadiz, Spain.
with the following posters:

1. Experiencia de un grupo multifamiliar en un Hospital de Día de Psiquiatría". Autores: Paz Flores, Tecelli Domínguez, Aurelia Ortells, Roser Izquierdo, Eduard Palomer, Eithene Ní Laocha y Carmen Masferrer

2. La introducción del experto por experiencia en salud mental: descripción de una propuesta". Autores: Paz Flores, Roser Izquierdo, Silvia Rosado, Tecelli Domínguez, Eduard Palomer, Carmen Masferrer, y Eithne Leahy.

Participation in the IV Congrès Català de Salut Mental "Salut Mental i Comunitat", con el poster: "Projecte EMILIA: l´autoorganització i la legitimació del coneixement d´expert com resultat dels processos de coparticipació". Autors: Eduard Palomer, Carmen Masferrer, Roser Izquierdo, Tecelli Domínguez, Eithne Leanhy y Paz Flores. 3-6 Juny in Barcelona, Spain.

Participation in the Public Health Practices Around the Globe Program, 12th World Congress on Public Health con el poster "The Introduction of Experts by Experience in a Barcelona Psychiatric Hospital due to the implementation of the EMILIA (Empowerment of Mental Illness Service Users: Lifelong Learning, Integration and Action) Project". Authors: Paz Flores, Montserrat Sorro, Eithne Leahy, Tecelli Domínguez, Roser Izquierdo and Carmen Masferrer. 27 Abril to 1 May 2009 in Istambul, Turkey.

Participation in the IV Congrès de la Societat Catalano Balear de Psicología de L´Academia de Ciències Mèdiques i de la Salut de Catalunya i de Balears, con el poster: "Avaluació d´un taller multifamiliar en un Hospital de Día: Atenció a Familiars y Pacients amb trastorn mental des d´una perspectiva formativa. Autores: Masferrer, c., Muñoz, A., Domínguez, T., Ortells, A y Flores, P. 24 and 25 Abril 2009 in Tortosa (Tarragona, Spain).

Participation in the XII Congress of the International Federation of Psychiatric Epidemiology (IFPE), with the poster "The introduction of experts by experience in a Barcelona psychiatric hospital due to the implantation of the EMILIA (Empowerment of Mental Illness Service Users: Lifelong Learning, Integration and Action) Project. Autores: Paz Flores, Eithne, Leanhy, Carmen Masferrer, Roser Izquierdo y Tecelli Domínguez. Del 16 al 19 de abril de 2009 en Vienna.

Participación en The WPA Congress- Treatments in Psychiatry: A new Update con el poster: "The EMILIA Project, the story so far…" Autores: Flores, P., Izquierdo, R., MAsferrer, C., Domínguez, T., Palomer, E y Dawson, I. Del 1 al 4 de abril de 2009 en Florencia.

Paticipación en el 10° Congreso Virtual de Psiquiatría Interpsiquis 2009, con el artículo: "Grupo de formación multifamiliar en un Hospital de Día de Psiquiatría". Autores: Paz Flores; Tecelli Domínguez; Aurelia Ortells; Roser Izquierdo; Eduard Palomer; Eithene Ní Laocha; Carmen Masferrer. Del 1 al 28 de febrero de 2009.

2008

Participación en el XII Congreso Nacional de Psiquiatría con los posters: 1) "Proyecto EMILIA. La formación continua de personas con trastorno mental grave como vía de inserción social y laboral. Autores: Paz Flores, Tecelli Domínguez, Roser Izquierdo, Eithne Ni Laocha, Eduard Palomer, Silvia Rosado y Carmen Masferrer; 2) "Propuesta de formación para familias y pacientes en un Hospital de Día. Proyecto EMILIA". Autores: Paz Flores, Tecelli Domínguez, Aurelia Orells, Roser Izquierdo, Eduard Palomer y Carmen Masferrer. Del 3 al 7 de noviembre de 2008, en Valencia.

Participación en el XIII Curso Anual de Esquizofrenia: "Psicosis: cultura psicoterapia e integración social" con el poster: "Formación para pacientes y familias en un Hospital de Día. Proyecto EMILIA". Autores: Paz Flores, Tecelli Domínguez, Aurelia Ortells, Roser Izquierdo, Eithne Ní Laocha, Eduard Palomer y Carmen Masferrer. Hospital de Día de Psiquiatria del Centre Fòrum de l'Hospital del Mar. Centre de Salut Mental. Sant Martí Sud. IAPS-IMAS-FIMIM. Barcelona. Del 9 al 11 de octubre de 2008 en Madrid.

Participación en el XIV Congreso Mundial de Psiquiatría, con el poster: "The Challenge of changing the relationship between patients with sever mental illness and mental Health professionals". Autores: Paz Flores, Eduard Palomer, Carmen Masferrer, Eithne Leany, Juan R. Castaño, Tecelli Domínguez, Silvia Rosado y Roser Izquierdo. IAPS, IMAS, IAS. Del 20 al 25 de septiembre de 2008 en Praga.

Participación en el XXIX Internacional Congress of Psychology (ICP2008), con el Poster: "Mental Health Service Users, Empowerment through Training, The EMILIA Project". Autores: Carmen MAsferrer, Roser Izquierdo, Tecelli Domínguez, Eithne Ni Laocha y Paz Flores. Hospital de Día de Psiquiatría del Centre Fórum del Hospital del Mar. Centre de Salut Mental Sant Martí Sud. IAPS-FIMIM. Barcelona. Del 20 al 25 de julio de 2008, en el ICC de Berlín.

Presentación de "Mobilising Community Resources for Mental Health. A Family Based Support Program-from hospital to home". En *ENTER* Annual Conference Paros, Greece. El 4 de Junio 2008.

Participación en WPA & WONCA Thematic Conference: Depression and other Common Mental Disorders in Primary Care, con el poster: "Rehabilitation, training of professionals can the relationship between mental health service users and profesionals be changed? Autores: Paz Flores, Ma. Carmen Masferrer, Eduard Palomer, Tecelli Domínguez, Eithne Ní Laocha, Roser Izquierdo. Hospital de Día de Psiquiatría del Centre Fòrum del Hospital del Mar. IAPS-FIMIM. En Granada, del 18 al 21 de junio de 2008.

Participación en el 3er Congreso Iberoamericano de Investigación Cualitativa en Salud. Con el trabajo: "Las necesidades de familiares de pacientes con esquizofrenia en situaciones de crisis" Del 6 al 9 de mayo de 2008 en el recinto de Ciencias Médicas y en el Hotel Holiday Inn en Isla Verde, Carolina, Puerto Rico.

Participación en el 9º Congreso Virtual de Psiquiatría Interpsiquis 2008 con el artículo: "Proyecto EMILIA: Formación de usuarios de salud mental para la inclusión social". Autores: Paz Flores, Eduard Palomer, Tecelli Domínguez, Silvia Rosado, Juan Castaño, Roser Izquierdo, Eithene Leahy Ni Laocha y Carmen Masferrer del 1 al 20 de febrero de 2008.

Participación en el congreso ¿bioingeniería o medicina? Jornadas estatales de estudio y debate sobre el futuro de la formación integral del médico, con el cartel: "Proyecto EMILIA: Formación de profesionales para la mejora de los servicios de salud mental en colaboración con los usuarios como expertos". Autores: Paz Flores, Carmen

Masferrer, Tecelli Domínguez, Eduard Palomer, Silvia Rosado, Eithene Leía Ni Laocha, Roser Izquierdo. El 8 y 9 de febrero de 2008 en Barcelona.

2007
Participación en el 6º concurso de carteles "Experiencia de estigma, discriminación y falta de integración social en pacientes con esquizofrenia". Autores: Tecelli Domínguez, Ma. Luisa Rascón, Humberto Alcántara y Leticia Casanova. En el marco de la XXII Reunión de Investigación del Instituto Nacional de Psiquiatría Ramón de la Fuente. Del 5 al 7 de septiembre de 2007.

Participación en el 6º concurso de carteles con la temática "Atribución de los familiares respecto al comportamiento problemático de pacientes con esquizofrenia". Autores: Leticia Casanova, Ma. Luisa Rascón, Tecelli Domínguez, Humberto Alcántara y Marcelo Valencia. En el marco de la XXII Reunión de Investigación del Instituto Nacional de Psiquiatría Ramón de la Fuente. Del 5 al 7 de septiembre de 2007

Participación en el 6º concurso de carteles con la temática "El prejuicio en los pacientes con esquizofrenia. Resultado de dos grupos de discusión". Autores: Humberto Alcántara, Ma. Luisa Rascón, Tecelli Domínguez y Leticia Casanova. En el marco de la XXII Reunión de Investigación del Instituto Nacional de Psiquiatría Ramón de la Fuente. Del 5 al 7 de septiembre de 2007.

2006
Participación en el 5to concurso de carteles: "Estilos de afrontamiento en cuidadores de pacientes con esquizofrenia". Autores: Madián Fragoso, Ma. Luisa Rascón, Tecelli Domínguez, Marcelo Valencia y Ester Mourow. En el marco de la XXI Reunión de Investigación del Instituto Nacional de Psiquiatría Ramón de la Fuente. Del 4 al 6 de Octubre de 2006.

SCHOLARSHIPS

Becaria de Ministerio de Asuntos Exteriores y de Cooperación y la Agencia Española de Cooperación Internacional (MAEC-AECID) (Méx./0314/08) para realizar los estudios de Doctorado en Psicología Clínica y de la Salud en la Universidad Autónoma de Barcelona. De septiembre de 2008 a Septiembre de 2012.

Becaria de CONACYT (Consejo Nacional de Ciencia y tecnología) Clave: 46569-H. Para participar en el proyecto de investigación "Creencias, estigma, necesidades y apoyo para personas con esquizofrenia, familiares, cuidadores y profesionales" y para realizar la tesis de Licenciatura "El sujeto con esquizofrenia a partir de la relación psiquiatra-familia en un hospital psiquiátrico ambulatorio". De enero a Octubre de 2006.

PROFESIONAL AND ACADEMIC TRAINING

2012
IV Jornada dels programes d'atenció específica al transtorn psicótic incipient (PAE-TPI). Barcelona 22 de febrero 2012.

2011
Curso de entrenamiento en la *Camberwell Family Interview* (CFI) y otras escalas de Emoción Expresada. Impartido por Cristina Medina-Prades y Adrián Montesano del Campo, ambos están formados y acreditados por la Dra. Christine Vaughn, autora de la CFI. El curso se llevó a cabo en el Centro de Salud Mental de Sants de la

Fundació Sant Pere Claver, Barcelona, España. Del 7 de septiembre al 10 de octubre de 2011, con una duración de 70 horas (40 horas presenciales y 30 horas no presenciales).

7ª Reunió Anual organitzada per la societat Catalana de Psiquiatria Infanto Juvenil. De los pródromos a la psicosis en niños y adolescentes, celebrada a Barcelona el dia 20 de mayo de 2011. Duración total 6,5 horas.

Training PAE-TPI for learn to use the following measures: The Comprehensive Assessment of At-Risk Mental States (CAARMS), Positive and Negative Syndrome Scale (PANSS), Hamilton Rating Sclae for Depression (HRSD), Young Mania Rating Scale (YMRS) and the Social Functioning Scale (SFS). Total duration 15 hours.

Jornadas Neurosciencias y psicoanálisis. La construcción de un paradigma científico e interdisciplinar. 18 febrero de 2011, Barcelona.

Jornadas Internacionales BAETUALE. La Atención Integral a las Psicosis. Segundas Jornadas: el trabajo cotidiano atendiendo a los pacientes en riesgo de psicosis. 4 y 5 de febrero de 2011. Badalona (Barcelona). Con el reconocimiento sanitario por parte del Institut d'Estudis de la Salut.

2010

Jornada Científica "El projecte EMILIA 4 anys després" el 14 de mayo de 2010, con una duración total de 5 horas. En el Hospital del Mar de Barcelona.

2009

Conferencias del I Congrès Ibèric- XXX Jornades espanyoles de teràpia familiar: "Cambios familiares: nuevas relaciones, nuevas jerarquías" Organizades per la Societat Catalana de Terapia Familiar Celebradas en Barcelona del 29 al 31 de octubre de 2009. Activitad acreditada por el Consell de la Formació Médica Continuada-Comisión de Formación Continuada del Sistema Nacional de Salud: 0,8 créditos.

Seminario sobre "Psychanalitic Diagnostic Scale On Basic Psychological Positions (PDSBP), impartido por el Dr. Jaume Aguilar y organizado por el Departamento de Salud de la Fundaciò Hospital Sant Pere Claver, con una duración total de 4 horas. 18 de septiembre de 2009.

2008

Congreso Internacional "Familia y Crisis: Modalidades de intervención para el siglo XXI". En Castellón, los días 27, 28 y 29 de noviembre de 2008. Con una duración de 25 horas.

Jornada "Ciuadania, drets i salut mental: protecció jurídica i atenció integral" 7 de noviembre de 2008. Barcelona, Auditori ONCE Catalunya.

XIII Curso Anual de Esquizofrenia: "Psicosis: cultura psicoterapia e integración social" Del 9 al 11 de octubre de 2008 en Madrid.

1ª Jornada "Llocs de Vida i Recuperació" 2 de octubre de 2008, Caixa Fórum, Barcelona.

XXII Jornadas Estatales de la Asociación Española de Neuropsiquiatría (AEN) "Innovar, integrar y cuestionar en Salud Mental", de 20 horas de duración, celebradas en Girona los días 22,23 y 24 de mayo de 2008.

2007

Jornada de Presentación Proyecto EMILIA. 30 de noviembre de 2007 en la Sala Joseph Marull del Hospital del Mar de Barcelona.

XXII Reunión Anual de Investigación del Instituto Nacional de psiquiatría Ramón de la Fuente Muñiz, del 5 al 7 de septiembre de 2007.

Seminario: "Meta psicología de Freud" impartido por el Dr. Roberto Castro. Del 13 de junio al 13 de octubre de 2007
Curso: Actualidad y futuro del psicoanálisis del 13 al 15 de abril de 2007 impartido por el Dr. André Green. Valor curricular 30 horas
Supervisión de casos a cargo del Dr. Andrée Green (valor curricular 6 horas). 11 de abril.
Diálogos con los psicoanalistas (valor curricular 16 horas) Presidente Dr. André Green. 9 y 10 de abril de 2007.
Seminario: "La memoria del uno y la memoria del Otro" impartido por el Dr. Nestor Braunstein en la Facultad de Filosofía y Letras de la UNAM. De febrero a junio de 2007.
2006
Seminario: "Ficciones de la memoria" Impartido por el Dr. Nestor Braunstein en la Facultad de Filosofía y Letras de la UNAM. De agosto a diciembre de 2006.

Seminario mensual: "Representaciones Sociales: Epistemología y Género. Efectuado en las instalaciones del CRIM y del CEIICH, del 18 de enero al 15 de noviembre de 2006, con una duración de 44 horas.
Seminario: "Teoría de las representaciones sociales: Epistemología y método", impartido por el Dr. Wolfang Wagner en el auditorio del CRIM los días 11 y 12 de octubre de 2006, con una duración de 10 horas.
Asistencia a la XXI Reunión Anual de Investigación del 4 al 6 de octubre 2006, en el Instituto Nacional de Psiquiatría Ramón de la Fuente Muñiz.
Seminario: "La clínica psicoanalítica de la Psicosis" del 20 de abril de 2006 al 5 de abril de 2007. En el Centro psicoanalítico Monte Albán.
Curso-Taller: "Continuidad de Cuidados en la Comunidad" impartido por el Dr Ramón Blasi. Sede en la Escuela Nacional de Enfermería y Obstetricia de la UNAM los días 20 y 21 de junio de 2006, con una duración de 15 horas.
Curso: "La vida de hoy: aspectos psicoanalíticos, impartido por el Dr. Nestor Braunstein, con una duración de 30 horas, en el marco de las actividades de la Cátedra Extraordinaria Maestros del exilio Español, correspondiente al semestre 2006-1. En la Facultad de Filosofía y Letras de la UNAM.
2005
Curso "Salud mental comunitaria y reforma psiquiátrica" impartido por la Doctora Graciela Natella, los días 25 y 26 de noviembre de 2005 en la Universidad Autónoma Metropolitana y en el Centro Psicoanalítico Monte Albán.
Seminario: "Elementos de aprehensión clínica en la psicosis ordinaria. ¿Cómo identificar la estructura psicótica en sujetos que no presenten ni delirios ni alucinaciones?" Impartido por el Dr. Jean-Claude Maleval 22 y 23 de abril de 2005, en el Centro de Investigaciones y Estudios Psicoanalíticos de la Fundación Mexicana de Psicoanálisis. Con una duración de 14 horas.
Seminario 8 Lacan: Transferencia. Del 13 de Mayo de 2005 al 20 de Febrero de 2006, tres horas semanales (125 horas en total) a cargo de Virginia Poo Gaxiola.
Segundas Jornadas Internacionales: Un siglo de sexualidad. A cien años de la publicación de teoría sexual de Sigmund Freud. 18 al 20 de febrero de 2005, con una duración de 22 horas.

Curso: (Père) versiones del padre y desamparo- Nuevos giros de la paternidad en tiempos de tecnociencia. Impartido por la Dra. Martha Gerez Ambertín. UAM- Xochimilco. 3 al 5 de Febrero del 2005, con una duración de 20 horas

Curso: Introducción a los fundamentos de la clínica psicoanalítica: Freud y Lacan. UAM- Xochimilco, Educación Continua. 8 de noviembre de 2004 al 15 de marzo de 2005. Con una duración de 48 horas.

2004
Coloquio: Consistencias del cuerpo. Asociación de la escuela Lacaniana de Psicoanálisis y el Ateneo Psicoanalítico de la Asociación Psicoanalítica Mexicana. 6 de noviembre 2004.

Seminario: Psicoanálisis y Filosofía. Impartido por Alain Jurnaville. Fundación Mexicana de Psicoanálisis, I. A. P (FMP) 14, 15 y 16 de octubre de 2004. Con una duración de 16 horas.

VII Congreso al Encuentro de la Psicología Mexicana y III Congreso Latinoamericano de Alternativas en Psicología. Acapulco, México. 22 al 25 de septiembre de 2004.

"2do simposio El Mal, Diálogo entre Filosofía, Psicoanálisis y Literatura. Universidad Nacional Autónoma de México. Facultad de Filosofía y Letras. 8 y 9 de septiembre de 2004.

XII Foro Psicoanalítico de la Psicosis, "Una cínica de la escucha" Historia y evolución de la relación con el paciente. UAM- Xochimilco. 26 y 27 de marzo de 2004.

Congreso "El Psicoanálisis en la Psicosis". Infierno (Acerca de los delirios demoníacos). Círculo Psicoanalítico Mexicano A. C. y Federación Mexicana de Salud Mental. Sede: Colegio de Ingenieros Civiles. 20 al 22 de febrero de 2004.

Seminario: Filosofía y Psicoanálisis. Universidad Nacional Autónoma de México Facultad de Filosofía y Letras. 15 de marzo al 6 de septiembre de 2004.

2003
Seminario Michel Foucault (Historia de la sexualidad). UAM- Xochimilco. Septiembre 2003.

LANGUAGES

Spanish: Native Language

English: Fluent (TOEFL-Institutional)

French: Appropriate (DELF B1)

Catalan: Fluent