



# **UNIVERSIDAD DE DEUSTO**

**Facultad de Psicología y Educación  
Departamento de Fundamentos y Métodos de la Psicología**

**Programa de Doctorado Psicología Clínica y de la Salud**

**Insight in First Episode Psychosis;  
Role of Time and Cognitive Reserve**

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Bilbao, Octubre 2012**

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Este trabajo se ha realizado gracias a las ayudas (2008111010) concedidas por el Departamento de Sanidad y Consumo del Gobierno Vasco y la ayuda concedida por la Fundación Vasca de Ciencia e Innovación (BIO 09/EM/015), para la realización del primer proyecto sobre enfermedades mentales graves realizado con la participación de los 3 hospitales principales del País Vasco, e involucrando a las 3 provincias.

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This project has been carried out thanks to the funding conceded by the Health and Consume Department of the Basque Government (2008111010) and by The Basque Foundation for Health Innovation and Research (BIO 09/EM/015), to the first research project carried out by the three main hospitals in Basque Country, and comprising the three Basque Provinces.

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Dr Natalia Ojeda del Pozo, Department of Fundamental and Methods of Psychology manager, as advisor of the present work; and Dr Javier Peña Lasa, Department of Fundamental and Methods of Psychology professor, as co-advisor of the present work, certify that this dissertation, entitle: INSIGHT IN FIRST EPISODE PSYCHOSIS: ROLE OF TIME AND COGNITIVE RESERVE, is an original and unprecedented research work, which is introduce by MRS. M<sup>a</sup> ACEBO GARCIA GUERRERO, to apply for PhD.

La Dra. Natalia Ojeda del Pozo, directora del Dpto. de Fundamentos y Métodos de la Psicología de la Universidad de Deusto, como directora del presente trabajo; y el Dr. Javier Peña Lasa, profesor del Dpto. de fundamentos y Métodos de la Psicología de la Universidad de Deusto, como c-o-director de este trabajo certifican esta tesis doctoral, titulada: INSIGHT IN FIRST EPISODE PSYCHOSIS: ROLE OF TIME AND COGNITIVE RESERVE, constituye un trabajo de investigación original e inédito, el cual es presentado por D<sup>ña</sup>. M<sup>a</sup> ACEBO GARCIA GUERRERO para optar al grado de doctor.

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Para que así conste,

Bilbao, 2nd october 2012  
En Bilbao, 2 de octubre de 2012





A la gente que más quiero:  
A mis padres,  
Alberto y Mavi.  
A mis hermanos,  
David (& Saman), Pablo, Patricia y Diego.  
A Alejandro.



## **Agradecimientos**

En primer lugar querría agradecer a mi directora de Tesis, la Dra. Natalia Ojeda, todo el esfuerzo y empeño que me ha dedicado. Gracias no sólo por apostar por mí, sino también por animarme a mejorar y a seguir aprendiendo. Y sobre todo, gracias por apoyarme y pelar por mí. Sin lugar a dudas, hoy no estaría aquí si no fuese por tu ímpetu y dedicación.

Otro gran gracias a Javier Peña, por su paciencia, entusiasmo y perseverancia. Por estar ahí en todo momento. Con orgullo nombro a las personas que me han dirigido la tesis, gracias a los dos.

Debo agradecer enormemente a Miguel Gutiérrez Fraile su apoyo durante los últimos 3 años, si hay algo que le engrandece en su apuesta por un futuro de calidad apoyando la formación continua y crecimiento científico. Gracias Miguel.

Este trabajo ha sido posible gracias a la colaboración de mucha gente, a todos ellos le agradezco su participación. Entre ellos debo nombrar a los servicios de psiquiatría del Hospital Universitario Donostia, Hospital de Cruces y Hospital Universitario de Álava-sede Santiago.

Gracias al apoyo institucional que me ha brindado el Departamento de Fundamentos y Métodos de la Psicología, perteneciente a la Facultad de Psicología de la Universidad de Deusto; a DeustoPsych; y al Departamento de Sanidad y Consumo de Gobierno Vasco.

I would like to thank Paul Lysaker and his team in the Roudebush VA Medical Center in Indianapolis. They made me feel at home and showed me how kind people can be. Thanks Paul for taking care of me as you did, and you are still doing.

Un trabajo como esté conlleva mucho esfuerzo y tiempo, y durante todo ese tiempo ha habido personas que han estado ahí en todo momento y a los cuales no puedo más que agradecer eternamente su apoyo, ánimo y cariño. Especialmente quiero agradecerle a Eneritz el haber estado ahí hora tras hora, día tras día... A todos mis compañeros de Deusto-Psych, de todos me llevo lo mejor. A Laura, por su infinita dulzura y bondad.

A Alejandro, por todo su apoyo y cariño, y por haberse involucrado en este trabajo más de lo que te tocaba. A mi familia y amigos, por haber tenido la paciencia de soportar la distancia y la ausencia, por cada momento que este trabajo no nos ha dejado compartir, y por seguir ahí como siempre a pesar de ello. Gracias.

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**Glossary of abbreviations**

**AS:** Attributional style

**ASQ:** Attributional style questionnaire

**CN:** Control for negative events

**CP:** Control for positive events

**DAI:** Drug Assessment Inventory

**EN:** Externality for negative events

**EP:** Externality for positive events

**FEP:** First Episode Psychosis

**GAF:** Global assessment Inventory

**GN:** Globallity for negative events

**GP:** Globallity for positive events

**ICD:** Insight into the consequence of their disorder

**IEM:** Insight into the effects of medication

**IMD:** Insight into mental disorder

**IN:** Internality for negative events

**IP:** Internality for positive events

**IQ:** Intelligence quotient

**MADRS:** Montgomery Asberg depression rating scale

**MMAS-4:** Morisky Medication Adherence Scale.

**NCI:** Neurocognitive insight

**Non-SSD:** Non Schizophrenic spectrum disorders

**SSB-C:** Self Serving Bias for controllability

**SSB-I:** Self Serving Bias for internality

**SSD:** Schizophrenic spectrum disorders

**SUMD:** Schedule unawareness of mental disorders

**TMT:** Trail Making Test

**YMRS:** Young mania rating scale

**WCST:** Wisconsin Card Sorting Test

## **SUMMARY**

Insight is broadly understood as a dimensional concept including: the awareness of one's illness, its symptoms and consequences, but insight has mainly been studied as a general construct. Moreover insight has been related to outcome, and it changes over time but the moment in which insight's stability starts is not clear. Etiology of insight has been explored by different theories but none have been fully supported by experimental data, the integration of these theories could explain better insight. The main objectives of the present work were the following: to explore change of insight and its dimensions over time, to explore an explanatory model of insight integrating the main etiology theories, and finding out the role of insight, among cognitive and clinical variables, in the prediction of functional outcome. 75 patients with First-Episode-Psychosis were recruited in three hospitals of the Basque Country, with two and six-month of follow-up. T-students were used to analyze insight change over time, step-wise-hierarchical-regressions were used to create the explanatory model of insight and mediational analysis were used to clarify the role of insight in the prediction of functionality. Results showed how insight dimensions were stable from two months on, while general insight improved until six months. Mania and cognitive reserve arose as the explanatory variables of insight and its dimensions. And finally, the relationship among functionality and its predictors was mediated by insight. This study supports the relevance of the moment in which insight is measured, and highlights the possible relevant role of cognitive reserve on insight.

## **RESUMEN**

Insight es generalmente entendido como la conciencia de enfermedad, de sus consecuencias y los efectos del tratamiento. Además, en psicosis, está relacionado con el outcome de la enfermedad. El nivel insight y sus dimensiones cambia a lo largo de la enfermedad, pero el momento en el cual empieza a ser estable no está claro. Diferentes teorías abordan su etiología, pero ninguna ha sido capaz de explicarlo por sí misma. Los objetivos del presente trabajo consistieron en analizar el cambio del insight a lo largo de la etapa temprana de la enfermedad, explorar qué modelo explicativo define mejor el insight desde un punto de vista integrador, y averiguar qué rol tiene el insight en la predicción de la funcionalidad. 75 primeros episodios psicóticos fueron reclutados en 3 hospitales principales del País Vasco, y evaluados en el momento basal, a los dos y 6 meses. Las diferencias entre los tiempos de seguimiento fueron evaluadas mediante T-Student, se utilizó una regresión por pasos jerarquizada para extraer el mejor modelo explicativo de insight y se usaron análisis mediacionales para explorar el rol del insight al predecir funcionalidad. Los resultados mostraron que en la muestra analizada las dimensiones de insight fueron estables a partir de los dos meses, en cambio, el insight general continuó mejorando al menos hasta los 6 meses. Síntomas maníacos y reserva cognitiva surgieron como los predictores de insight. Y, por último, la relación entre funcionalidad y sus predictores resultó estar mediada por el insight del paciente. Este estudio destaca la relevancia del momento en el que insight es medido, y la necesidad de abordar de manera integradora la etiología del insight en pacientes con psicosis. Perspectiva en la cual ha surgido el posible papel relevante de la reserva cognitiva.

## **1. INTRODUCTION**

### 1.1. PSYCHOSIS

Psychosis is considered a mental state often described as involving a "loss of contact with reality" (American Psychiatric Association, 1994). People suffering from psychosis are described as psychotic. This means, in a narrow sense, the presence of hallucinations and/or delusions (Semple, Smyth, Burns, Darjee, & McIntosh, 2005), occurring in the absence of insight into their pathological nature (American Psychiatric Association, 1994). Therefore, lack of insight can be considered a core symptom of the illness with about 50% and 80% of patients showing lack of insight (Amador & Gorman, 1998).

Several disorders can present psychotic symptoms (Lewis Corpus dementia, Creutzfeldt-Jakob disease or some patients with a brain injury). However, psychosis is not the core feature on each of them, and not all of these disorders share etiological models (American Psychiatric Association, 1994). Additionally, lack of insight is not an exclusive sign of psychosis either, but the combination of hallucinations and delusions plus the absence of insight are considered core symptoms of the illness. This combination is what gives psychosis its unique nature.

Psychosis has a serious impact on patients' lives by interfering with their lives. The illness causes enormous burden for individuals who suffer from it, for their cares, and for society at large (Knapp, Mangalore, & Simon, 2004). People with psychosis have always endured very poor social outcomes including 80% unemployment and poorer global functioning

(Marwaha & Johnson, 2004; Pyne, Bean, & Sullivan, 2001; Thornicroft et al., 2004); even worse, they have been stigmatized and misunderstood (Thirthalli & Kumar, 2012).

### 1.1.1. The onset

Several disorders can present psychotic symptoms. Therefore, the DSM-IV diagnosis requires the illness's course to be followed-up during a minimum of 6 months before a clinician confirms the diagnosis (American Psychiatric Association, 1994). Until then, patients who have entered the emergency room with psychotic symptoms are distinguished as suffering a First Episode Psychosis (FEP). First Episode Psychosis usually runs from the first-ever intervention by the psychiatrist, due to psychotic symptoms to the final confirmation of the diagnosis which usually varies among schizoaffective, bipolar disorder, or schizophrenia.

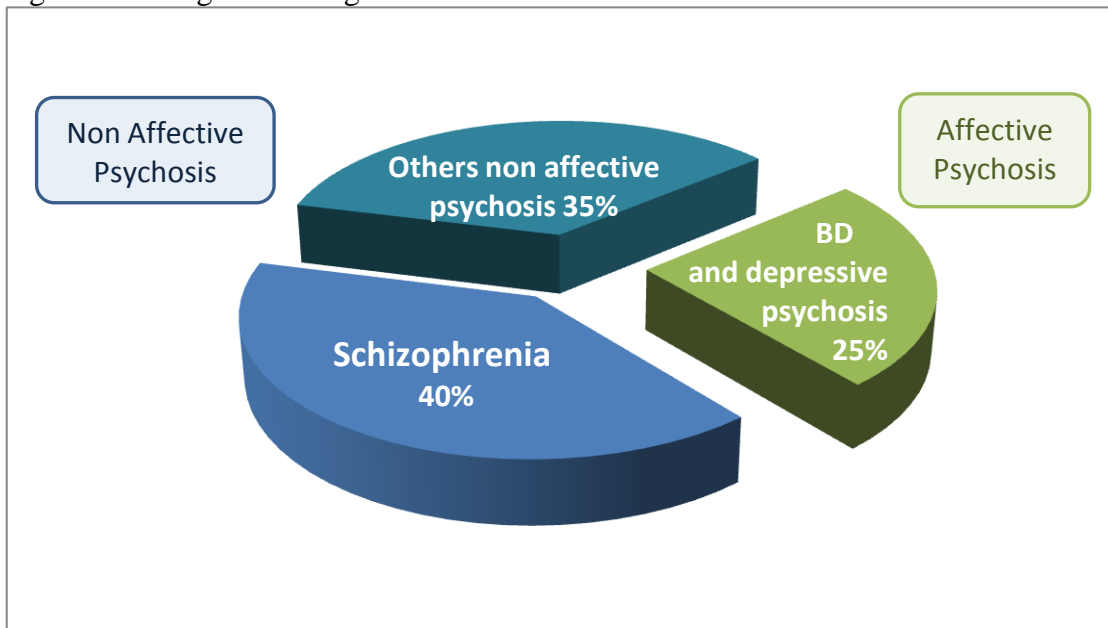
Epidemiological studies estimate the average age at onset in men and women to be about 25/29 years respectively (Hafner et al., 1998; Jablensky & Cole, 1997). Onset occurs for most individuals (around 75%) between ages 15 and 30 (van der Heiden & Hafner, 2000). The incidence of FEP's in 15 to 29 year-old individuals is 16.7 per 10,000 person-years in males, and 8.1 per 10,000 person-years in females, for the 25-29 year-old group the rates are significantly lower than the 15-29 year-old (Amminger et al., 2006).

In Spain, up to a 56% (CI 95%: 46-66%) of FEP in patients between 22 to 28 years is related to the use of cannabis (Gonzalez-Pinto et al., 2011). This does not mean that drug use/abuse may be the cause of a FEP, but acts increasing the probability of the FEP in people with a predisposition (Leeson, Harrison, Ron, Barnes, & Joyce, 2011).

### 1.1.2. Classification

After a FEP the follow-up brings us the diagnosis. A first classification can be made in two diagnostic categories. It is possible to distinguish between Non-Affective Psychosis and Affective Psychosis. The first group (7.9 to 75.5% of FEPs) includes Schizophrenic Spectrum Disorders (Schizophrenia, Schizophreniform Disorder), Schizoaffective Disorder, and Delusional Disorder, Psychotic disorder Not Otherwise Specified and Brief Psychotic Disorder. Affective Psychosis' diagnostic category (24.5 to 28.1% of FEPs) includes Bipolar disorder (BD) and Depressive Psychosis (Alvarez-Jimenez et al., 2011).

Figure 1.1. Diagram of diagnoses



Specifically, schizophrenia is largely known as the most common disease in psychosis, 40% of FEPs follow this diagnosis (Canuso, Kosik-Gonzalez, Sheehan, Mao, & Kalali, 2010), with a lifetime prevalence of 0.3–2.0%, and an average of approximately of 0.7% (Saha, Chant,



& McGrath, 2007). This condition is one of the major contributors to the global burden of the disease (American Psychiatric Association, 1994).

## 1.2. PSYCHOTIC SYMPTOMATOLOGY

The psychotic symptoms are commonly classified into positive and negative symptoms, two distinct yet overlapping symptom clusters. The positive symptoms consist of the hallucinations, delusions, positive thought disorder, bizarre or disorganized behavior and catatonic motor behavior. The negative symptoms include affective blunting, impoverished thinking, anhedonia and avolition-apathy (Kay, Fiszbein, & Opler, 1987).

Apart from the traditional positive and negative symptoms, it is currently known that deficits in memory, attention, working memory, problem solving, processing speed, and social cognition (Nuechterlein et al., 2004) are a core component of psychosis, and they are referred to as neurocognitive impairment. This impairment has been shown to be associated with impaired functional and social outcome (Green, 1996; Green, Kern, Braff, & Mintz, 2000; Ojeda, Peña, Sanchez, Elizagarate, & Ezcurra, 2008; Ojeda et al., 2010; Sánchez et al., 2009). The severity of neurocognitive impairment predicts poorer treatment adherence (Burton, 2005; Prouteau et al., 2005), poorer outcome, and increased relapse risk in first-episode patients (Chen et al., 2005). Moreover, decreased performance in all main cognitive domains has been identified in people at risk of psychosis, despite not having developed yet positive symptoms of the illness, however a differential pattern of impaired performance is shown in people at ultra high risk (pre-onset periods of psychosis) (Giuliano et al., 2012).

Lastly, insight is an essential feature of the psychotic illnesses. Early clinical descriptions of psychosis identified lack of insight as a characteristic symptom of the illness (Freudenreich, Deckersbach, & Goff, 2004). And the seminal WHO International Pilot Study of Schizophrenia confirmed this clinical impression in a large epidemiological cohort (Carpenter, Strauss, & Bartko, 1973). In spite of this fact, insight is not yet included in the diagnostic criteria from DSM-IV (American Psychiatric Association, 1994) for this disease.

### 1.3. INSIGHT

The concept of insight is clinically relevant because poor insight is associated with relapse (Saravanan et al., 2010), symptom severity (Segarra et al., 2012), poorer treatment adherence (Goff, Hill, & Freudenreich, 2011), functional and psychosocial dysfunction (Segarra et al., 2012), and poor outcome in general (McEvoy et al., 2006). Therefore, researching which factors are specifically related to poor insight at very early stages of the illness is of decisive relevance for understanding psychotic disorders and for further development of treatment strategies in early phases.

There was very little mention on insight as a concept (*insightlessness* at the time) in the clinical literature before the first half of the 19<sup>th</sup> century. After that, two new ideas allowed to arise the term insight. On the one hand, the concept of *partial insanity* and, on the other hand, concepts such as consciousness (awareness), introspection, and self, without which, the notion of insight would be difficult to understand. During the nineteenth century, the concept of consciousness was coached in terms of perception (an inner eye), comprehension (*verstehen*), and later of self-consciousness (Amador & David, 2004).

All these terms generated an appropriate conceptual setting to the development of a new concept: *insight*, which makes reference to the self consciousness. With the concept creation came the first definitions and its meaning was defined across the time. In 1934, Lewis first provided a temporary definition of the term insight: "A correct attitude to morbid change in oneself." Jaspers (1913/1963) focused specifically on the concept of insight into mental illness. He combined both clinical and psychological/philosophical perspectives to explore the concept of insight in several ways, awareness of mental process (consciousness in a narrow sense), awareness of the sense and activities of the self and attitudes toward mental illness (Markova, 2005). Carpenter et al. (1973), on the other hand, described insight as a symptom of schizophrenia which was evaluated as merely present or absent.

Later, David (1990) arose with a concept of insight which had at least three dimensions: awareness of illness, the capacity to re-label psychotic experiences as abnormal, and treatment compliance. Markova and Berrios (1992) broadened the definition of insight to view "insight as a process allowing the longitudinal and dynamic aspects of insight to be examined".

In spite of the variability of definitions, most of the authors and researchers in psychotic disorders follow the multidimensional concept of insight provided by Amador and David (Amador & Gorman, 1998; Amador & David, 2004) which includes: (1) Awareness of mental disorder, (2) understanding of the social consequences of disorder, (3) awareness of the need of treatment, (4) awareness of specific signs and symptoms of the disorder, (5) the attribution of symptoms to a disorder. The definition given by Amador and David is the most extended in the literature, and insight is mostly understood as the patient disagreement with their clinicians, friends and families about whether they have a mental illness, whether their unusual experiences and behaviors are abnormal, and whether they are in need of clinical treatment.

These disagreements are traditionally held by clinicians to reflect a lack of clinical insight on the part of the individual with psychosis (Cooke, Peters, Kuipers, & Kumari, 2005a). In the framework of this dissertation, insight will be understood under Amador and David's proposal.

Although, as Carpenter et al. (1973) stated, insight has been defined for a very long time as a dichotomous phenomenon (McEvoy, Apperson, Appelbaum et al. 1989; McEvoy, Freter, Everett, & Geller, 1989b), the recent clinical modeling of this concept in psychosis (Amador, Strauss, Yale, & Gorman, 1991; Beck, Baruch, Balter, Steer, & Warman, 2004) and the development of tools for its clinical evaluation (Amador et al., 1993; Beck et al., 2004; Sanz, Constable, Lopez-Ibor, Kemp, & David, 1998) has stressed its multidimensional nature.

In spite of the obvious importance of insight in psychosis, its research has not been a core of the studies until late twenty century. From this moment, the new developed tools for its evaluation had made increase the interest and research on this topic, and in consequence new aspects and dimensions of insight have emerged. In the next section a new possible dimension of insight is addressed.

### 1.3.1. Insight about the neurocognitive impairment

Despite a huge well-documented literature on neurocognitive deficits in psychosis, little is known about the own perception of patients regarding their neurocognitive functioning (Johnson et al., 2009). Neurocognitive insight refers to the unawareness of the cognitive impairment associated with the disorder, also called insight into the neuropsychological symptoms (Gonzalez-Suarez et al., 2011; Medalia & Thysen, 2008).

This insight dimension is usually quantified by questionnaires which measure neurocognitive complaints of patients, sometimes compared with caregivers complaints about the patient's cognitive performance in daily life (Keefe, Poe, Walker, Kang, & Harvey, 2006; Medalia & Thysen, 2008; Medalia, Thysen, & Freilich, 2008; Stip, Caron, Renaud, Pampoulova, & Lecomte, 2003). Patients with psychosis demonstrated partial to poor neurocognitive insight (Johnson, Tabbane, Dellagi, & Kebir, 2011; Medalia & Thysen, 2010), and previous findings indicate that patients' own evaluations of their neurocognitive function correlate poorly with objective measures of their cognitive performance (Chan et al., 2008; Keefe et al., 2006; Medalia & Lim, 2004; Medalia & Thysen, 2008; Stip et al., 2003; van den Bosch & Rombouts, 1998; Moritz, Ferafli, & Naber, 2004).

Recently, evidence for the lack of association between traditional insight and insight into neurocognitive performance has begun to be accumulated (Gonzalez-Suarez et al., 2011; Johnson et al., 2011; Medalia & Thysen, 2010). This evidence supports the idea that insight into neurocognitive performance is independent of traditional insight in psychosis (Gonzalez-Suarez et al., 2011; Medalia & Thysen, 2008). Donohoe et al. (2009) studied this topic in depth; in a sample of 51 patients with schizophrenia they found that patients lacking insight did not necessarily also lack cognitive insight. However, they found that self-rating of cognitive difficulties only correlated with actual cognitive performance within the patients with intact insight (Donohoe et al., 2009), that is to say, while good cognitive insight may not be necessary for good clinical insight, good cognitive awareness is at least partly reliant on the processes involved in clinical insight. These findings support the idea that these two concepts are different in their nature, and are, at the same extent, overlapped. Moreover, it seemed that neurocognitive insight, since it did not just take the form of lack of clinical insight, sometimes patients underestimated their cognitive performance, and sometimes they over-estimated it (Donohoe et al.,

2009). Additionally, the level of neurocognitive insight depends on the neurocognitive performance of each patient and on the specific cognitive domain analyzed (Gonzalez-Suarez et al., 2011; Medalia & Thysen, 2008). Subjective unawareness of neurocognitive deficits was most frequent in relation to memory impairment and executive impairment. In contrast, more patients overestimated their attentional difficulties (Gonzalez-Suarez et al., 2011; Medalia & Thysen, 2008). Patients without neurocognitive impairment do not recognize neurocognitive difficulties, and 34.2 to 52% of patients with impairment in one or more cognitive areas recognize moderate to frequent cognitive difficulties (Donohoe et al., 2009; Gonzalez-Suarez et al., 2011; Medalia & Thysen, 2008).

In short, a FEP (First Episode Psychosis) is characterized by the presence of positive symptoms, negative symptoms, neurocognitive impairment and lack of insight. Currently, insight is understood as a continuous and multidimensional concept which includes: insight of illness, insight about the treatment effects, and insight about the illness consequences. There is a recent interest on a new possible dimension of insight, insight about the cognitive impairment. Although the small amount in literature about this new dimension suggests it is independent from the traditional insight dimensions.

### 1.3.2. Clinical insight across the time

Only 3-5% of Spanish patients with a FEP have insight into mental disorder (IMD), the effects of medication (IEM), and/or the consequence of their disorder (ICD) (Aspiazu et al., 2010). These are the 3 of the most explored dimensions from clinical insight. Separately, IMD is the most impaired dimension (70% of patients are unaware) compared to IEM (47%), or ICD (42%) (Aspiazu et al., 2010; Ayesa-Arriola et al., 2011).

The different dimensions of insight (SUMD dimensions) improve over time during the first year, and both patients with schizophrenic spectrum disorder (SSD) and non-schizophrenic spectrum disorder (Non-SSD) improve significantly over this period of time. After the first year, the insight about the mental illness and the insight about treatment consequences of SSD patients still improves until the second year, the period when it starts stabilizing. In contrast, all insight dimensions of the Non-SSD starts to be stable since the first year (Parellada et al., 2011).

Some studies have reported a significant improvement in insight over the first year after the FEP, with long term stabilization at 2 or 3 years (Parellada et al., 2011; Saeedi, Addington, & Addington, 2007). During this first year the greatest improvements in clinical insight are reported to occur in the first 6 months of the longitudinal course of the FEP (Saravanan et al., 2010), another study delimited the period of significant improvement to the first 3 months (Mintz, Addington, & Addington, 2004). Clinical changes during this period are of great interest since the final diagnosis is confirmed after the first 6 months of the illness in most cases.

Insight is not a static condition and it may be influenced by neurobiological, clinical, therapeutic, and social circumstances (Lappin et al., 2007); and in the long term, differences among the possible diagnosis can be made. Lack of clinical insight (IMD) is a well-recognized and common clinical characteristic of both affective and non-affective psychosis (Amador et al., 1993; Amador, Flaum, Andreasen, & Strauss, 1994; Peralta & Cuesta, 1994a). However, specifically, schizophrenic patients demonstrate significantly less clinical insight than schizoaffective psychosis (Wiffen, Rabinowitz, Fleischhacker, & David, 2010). A review of insight in mood disorders (Ghaemi & Rosenquist, 2004) suggests that people with a bipolar

disorder or depressive disorder (both psychotic and non psychotic) show better insight than those with schizophrenia; though bipolar disorder is closer to schizophrenia (Amador et al., 1994). In fact, it has been suggested that clinical insight in schizophrenic patients in remission and Bipolar Disorder patients in remission are comparable (Yen et al., 2008). This data may add some support to the conceptualization of psychiatric disorders as a continuum. Impaired clinical insight is frequently observed in patients with bipolar disorder, particularly during pure manic episodes (Cassidy, Rabinovitch, Schmitz, Jooper, & Malla, 2010). Insight decreased during the manic period in patients with only a single manic episode as well as in those with repeated manic episodes. However, insight returned to the pre-episode level for patients with only a single manic episode, but did not so for most of the patients with repeated episodes. No changes in insight were observed during depressive episodes for neither patients with a single nor those with repeated depressive episodes (Yen, Chen, Ko, Yen, & Huang, 2007).

Therefore, insight levels seem not to be constant across time, and they depend on the patient's diagnosis and the phase of illness.

#### 1.4. ETIOLOGICAL MODELS

Although a number of different theories of the etiology of insight have been forwarded, three main etiological models of poor insight in psychosis dominate the current literature. The first model, which can be grouped under the name of clinical models, considers insight either as a primary symptom of a disease process in its own right (Peralta & Cuesta, 1994a) or propose it to be related to how a particular symptom is formed (Markova & Berrios, 1995). The second model, the neuropsychological model, proposes poor insight could be the product of deficits in neurocognition that are secondary to brain deficits (Drake & Lewis, 2003; Lysaker & Bell,



1994). The third model, the defensive model (Moore, Cassidy, Carr, & O'Callaghan, 1999), contends that poor insight reflects the use of cognitive strategies in an attempt to protect the individual person against distress. Finally, some authors have made arose a fourth etiological model which would actually be a combination of two or more of the above models with the objective of achieve an integrative model which contains, for example, neurocognitive and denial aspects in a overall explanatory model (Cooke et al., 2005a). Each model will be at a great length explained in the following sections.

#### 1.4.2. Clinical models

This group of models consider insight as a “delusion of health”- a specific type of delusion wherein the individual with schizophrenia forcibly denies the presence of a mental illness even in the face of obvious evidence of interference with daily functioning (Amador & David, 2004). Within this psychopathological perspective, some authors consider lack of insight as a negative symptom, a “mental withdrawal” from attempting to understand one's own phenomenological experience of the world (Mintz, Dobson, & Romney, 2003). Lack of insight has also been linked to disorganized symptoms or symptoms of formal thought disorder. The cognitive disorganization in schizophrenia may preclude the capacity to engage in abstract thinking needed to compared one's current to premorbid functioning, or one's own functioning to that of an average healthy other, leaving the schizophrenic individual without a coherent concept of normality (Osatuke, Ciesla, Kasckow, Zisook, & Mohamed, 2008).

The possible association between insight and symptoms severity was first meta-analyzed by Mintz et al. in 2003. These authors found that the relationship between insight and symptom domains (global symptoms, positive symptoms, negative symptoms and depression) were

significant, but merely 3-7% of the variance in insight was accounted for by the severity symptomatology. Affective symptoms have also been explored in their relations to insight. Depression and suicidal ideation have been linked to better insight. Mania symptoms have been less studied; there is one recent study which found that higher mania in first episode psychosis (FEP) was related to less insight (Ayesa-Arriola et al., 2011).

Most of the previous studies were carried out in chronic patients. Studying insight in FEP can therefore allow us to better explore the potential etiological factors in a relatively homogeneous group without influence from illness chronicity. Recently, Chan et al. (2012) explored 79 FEPs six months after starting medication, and they used a five factors PANSS model to assess the patients. The authors found that higher positive, negative, disorganization and excitement (not for emotional distress) scores on PANSS 5-model dimensions were related to poor clinical insight dimensions: awareness of a mental disorder, of the medication effect (except with excitement) and of social consequences. These results are consistent with a previous study by Hwang, Chang, Lee, Ahn, & Kim (2009), which however was carried out with chronic patients, and where they used structural equation modeling and a general measure of insight (item G12 from PANSS). They found that positive, negative and cognitive factors from PANSS were the primary predictors of insight. Even though, Nieto et al. (2012) do not find relation between negative traditional dimension from PANSS and insight dimensions (SUMD) in a sample of chronic patients, whereas they do find SUMD dimensions are related to positive and general dimensions.

Cross-sectional studies report small but significant relationships, indicating that greater insight may concur with lower levels of global psychopathology and positive negative symptoms (Mintz et al., 2004; Mutsatsa et al., 2003; Mutsatsa, Joyce, Hutton, & Barnes, 2006).

However, longitudinal analyses have shown less consistent findings (Carroll et al., 1999; McEvoy et al., 1989b).

### 1.4.3. Neurocognitive models

First described by Babinski in relation to unawareness of left-side hemiplegia, anosognosia refers to the unawareness of deficits in individuals with organic neurological disorders. The intuitive parallel between awareness deficits in neurological disorders and poor insight in psychosis may suggest similar mechanisms are involved, which may be cognitive (Amador et al., 1991) or neuroanatomical (Shad, Eshavan, Tamminga, Cullum, & David, 2007). The suggestion that impaired insight in psychosis may have a neurological basis (Amador et al., 1991; McGlynn, 1997) could be reflected on cognitive impairment, secondary to brain abnormalities (Lysaker & Bell, 1994; Young, Davila, & Scher, 1993). This hypothesis has been investigated by examining the correlations between measures of insight and performance on neuropsychological tests that index different domains of cognition (Cooke, Apperson, Appelbaum et al., 2005).

The main domains of cognition that have been explored in relation to insight have been attention, memory, executive function and intelligence quotient. Different relational theories have been developed for each domain; it has been stated that failures in the attentional system could result in impaired insight (Kinsbourne, 1998), due to the fact that deficits in attention may contribute to the inability to attribute psychotic thoughts and hallucinatory experiences to a mental illness (Subotnik et al., 2005). In a similar way, memory impairment could limit the past information to contrast with the current one, which would impede patients to contrast them and realize about the new aspects in their life, i.e. the illness' symptoms. Researches in frontal

function are based in the similarity between symptoms observed in schizophrenia and those seen in neurological patients with frontal lobe dysfunction (Amador & David, 2004), moreover neuroimaging studies support these similarities (Flashman, McAllister, Andreasen, & Saykin, 2000; Shad, Muddasani, Prasad, Sweeney, & Keshavan, 2004; Shad, Tamminga, Cullum, Haas, & Keshavan, 2006) and therefore, the theory that due to a frontal dysfunction patients are not able to be cognitive flexible, being unable 'to hold an abstract representation related to an actual situation, but different from it, at the same time as the more obvious immediate representation' (Drake & Lewis, 2003). This capacity would difficult patients to evaluate their own perceptions, thoughts and behavior in relation to knowledge of symptoms of mental illness (Aleman, Agrawal, Morgan, & David, 2006).

Only Aleman et al. (2006) have carried out a meta-analysis about the relation of insight and neurocognition. It showed that poor insight is weakly associated with poor functioning in a range of cognitive domains, including intelligence quotient (IQ), memory and executive function. Specifically, they found that Wisconsin Card Sorting Test performance and insight had a stronger association than insight and IQ in samples of patients with psychotic disorders in general. This difference between the two associations disappeared when analyses were limited to samples of patients with a diagnosis of schizophrenia. After that, Osatuke et al. (2008) have made a review in which they concluded that the findings in this area are discrepant, and nonspecific results are predominant.

It seems that frontal function is the most relevant domain in relation to insight in psychosis. Executive function is the neuropsychological variable most commonly related to insight (Aleman et al., 2006; Wiffen et al., 2012). With the aim of clarifying this general conclusion, a brief summary of each domain explored is showed in the next section.

#### 1.4.4. Neurocognition and insight

##### **1.4.4.1. Attention**

It can be speculated that deficits in attention might bias capacities to properly integrate and organize information, producing systematic errors in the evaluation of evidence of suffering from a mental disorder (Ayesa-Arriola et al., 2011). Overall, the studies about attention and clinical insight are not conclusive, with studies that support this relation (Lysaker, Bell, Bryson, & Kaplan, 1998; Marks, Fastenau, Lysaker, & Bond, 2000), and studies that do not (Keshavan, Rabinowitz, DeSmedt, Harvey, & Schooler, 2004; Mintz et al., 2004). In the last years, new studies that deal with attention and clinical insight showed that this relation may depend on the dimension of insight explored (Raffard et al., 2009; Ritsner & Blumenkrantz, 2007). In spite of the last advances, new studies measuring the clinical insight dimensions in different patients' samples are needed.

##### **1.4.4.2. Memory**

Despite memory was a focus of interest as one of the possible determinants of clinical insight, the results have been mixed. Taking into account a review made by Cooke et al. (2005a) and the following published articles on the topic; there are at least twenty studies that have examined this relationship, with six finding an association between poorer memory and poorer insight (Keshavan et al., 2004; Lysaker, Bryson, Lancaster, Evans, & Bell, 2003; Ritsner & Blumenkrantz, 2007; Saeedi et al., 2007; Upthegrove, Oyebode, George, & Haque, 2002; Voruganti, Heslegrave, & Awad, 1997). One study found the unexpected result of better performance on memory tasks (immediate verbal and delayed visual) relating to poorer insight

(Peralta & Cuesta, 1994a) and the remaining 14 studies found no significant relationships (Cooke et al., 2005a).

Again, there are inconclusive results, so studies analyzing in different psychotic samples and the possible relations among clinical insight dimensions and memory are needed.

#### **1.4.4.3. Frontal function**

Several models and theoretical frameworks of executive functions have emerged in the past two decades. These models have stressed the complex relationships that exist between executive functioning and other cognitive areas such as working memory (Baddeley, 1992) and attention (Norman & Shallice, 1986). In a fractionated approach to executive functioning, Miyake et al. (2000) proposed the identification of three separate executive components which are (1) inhibition of prepotent responses (“Inhibition”), (2) information updating and monitoring (“Updating”), and (3) mental set shifting (“Shifting”). Of note that a fourth process, dual task coordination (“Divided Attention”), not primarily hypothesized by Miyake et al. (2000), was found to be independent of the three afore mentioned executive processes (Raffard et al., 2009).

Moreover, attention deficits have been related to a neuronal circuitry involving the frontal lobes (Cohen, Nordahl, Semple, Andreason, & Pickar, 1998; Riccio, Reynolds, Lowe, & Moore, 2002). The association between attention deficit (Rodriguez-Sanchez et al., 2008), frontal lobe dysfunction (Winterer et al., 2006) and schizophrenia has been reported in a considerable number of studies, which have found that poor insight in FEP patients is mainly mediated by prefrontal dysfunctions (Drake & Lewis, 2003; Keshavan et al., 2004; McCabe,

Quayle, Beirne, Anne, & Margaret, 2002). All these facts support the idea that insight is more related to frontal functions than other cognitive domains, and it has made research focus on this topic. Despite the obvious complexity of executive function, a single test, the Wisconsin Card Sorting Test (WCST, (Heaton et al., 1993)), is often held to be its defining measure and is by far the most popular test examined in relation to insight.

A key question is how deficits in executive function lead to poor insight in psychosis. It has been suggested that a failure to detect errors may be particularly important in the apparent unawareness of the incorrectness of symptoms in individuals with psychosis (Laroi et al., 2000). It follows that poor insight should show a relationship with perseveration on the WCST, as individuals with poor insight would be expected to fail to alter their responses in the light of negative feedback. The studies offer some support for a relationship between perseveration on the WCST and insight, although the number failing to replicate the relationship is considerable (Aleman et al., 2006; Cooke et al., 2005a; Osatuke et al., 2008).

#### **1.4.4.4. Global neurocognition or intelligence**

An alternative formulation of the relationship between insight and neuropsychological measures is that poor insight is related to generalized cognitive deficit (Keshavan et al., 2004), rather than a specific impairment of, for example, executive function. Intelligent Quotient (IQ) tests provide an index of global cognitive function, since it is known there is a neurocognitive decline after the onset of the illness (Seidman et al., 2010) two different measures of IQ can be made depending on the moment of assessment, before or after the onset. Current IQ (after the onset) provide an index about the actual cognitive function of the patients, while premorbid IQ

has been designed to provide an index about the cognitive function of the patients before the onset of the illness.

In general, studies who have used an IQ measure found that lower scores are correlated with poorer insight (Donohoe, Donnell, Owens, & O'Callaghan, 2004; Drake & Lewis, 2003; Koren et al., 2004; Lysaker & Bell, 1994). But the number of studies that did not find this relation is numerous too (Cuesta, Peralta, Zarzuela, & Zandio, 2006; Laroi et al., 2000; Monteiro, Silva, & Louzã, 2008). Results suggest a relation between insight and IQ, but the characteristics and the intensity of the relationship is not clear. Sometimes IQ plays an intermediate role between insight and other variables, the most explored have been the neurocognitives. The necessity of controlling IQ when analyzing the relationship between insight and neurocognition has been pointed out by Cooke, Peters, Kuipers, & Kumari (2005b). After that, authors as Jovanovsky et al. found that the relation between executive deficits and insight changed when they controlled for IQ (Jovanovski, Zakzanis, Young, & Campbell, 2007).

#### **1.4.4.5. Cognitive reserve**

The concept of cognitive reserve (CR) has been proposed to account for the disfunction between the degree of brain damage or pathology and its clinical manifestations (Stern, 2009). Cognitive reserve is the ability to optimize and maximize performance through two mechanisms: recruitment of brain networks and/or compensation by alternative cognitive strategies (Nucci, Mapelli, & Mondini, 2011). Barnett, Salmond, Jones, & Sahakian, (2006) suggested the hypothesis that cognitive reserve is also important in neuropsychiatric disorders including schizophrenic, bipolar disorder and depression. They considered that cognitive



reserve may improve our understanding of individual differences in the causes, consequences of neuropsychiatric disorders, and the fluctuations that similar lesions have in different individuals.

Education is one of the first and most commonly used proxies in studies on CR (Gatz et al., 2001; McDowell, Xi, Lindsay, & Tierney, 2007; Ngandu et al., 2007; Pernecky et al., 2006; Stern, Alexander, Prohovnik, & Mayeux, 1992). Individuals with more years of formal education have greater brain weight, larger neurons and increased arborization of neurons (Katzman et al., 1988). Moreover, the structure of the central nervous system is clearly sensitive to functional factors such as occupation and practice, for example, as demonstrated by changes in the topographical organization of the hippocampus in taxi drivers (Maguire et al., 2000).

Intelligence is another frequently used index of CR (Alexander et al., 1997; Scarmeas et al., 2003) where IQ in healthy population or pre-morbid IQ in patients are the most common measures used to estimate CR. Some of the most common instruments that have been used to evaluate IQ are the Vocabulary Subtest of the Wechsler Adult Intelligence Scale (Wechsler, 2001) and the National Adult Reading Test (NART,(Russell et al., 2000)).

The influential effect of one of the above measures are rather difficult to isolate from other protective factors such as a successful job, the awareness of health risks, and quality of the social environment, amongst others. Therefore, a measure which takes into account more than one of these indexes will measure more accurately the cognitive reserve of a person (Nucci et al., 2011).

Cognitive reserve measure, as described above, has barely been studied in psychosis population (Barnett et al., 2006). Instead of it, a wide number of research studies have used premorbid IQ measures. Since clinicians usually have no information about the patient's IQ prior to the entrance to the emergency room and IQ measures are slanted by the neurocognitive impairment, premorbid IQ is the only one which can be an indirect measure of cognitive reserve.

Premorbid IQ in relation with insight has been used to control relationship with other variables as verbal memory (Mysore et al., 2007; Wiffen et al., 2012) or executive function (Jovanovski et al., 2007). The studies which have focused on the relation between premorbid IQ and insight have shown significant results with some of its items (Ayesa-Arriola et al., 2011), but many of them have not found significant correlations (Drake & Lewis, 2003; Monteiro et al., 2008; Raffard et al., 2009).

The relation between premorbid IQ and insight still needs to be elucidated (Aleman et al., 2006; Osatuke et al., 2008; Cooke et al., 2005b). This, together with the fact that there are studies which have not found relation between neurocognition and insight when controlling for IQ (Wiffen et al., 2012), supports the idea that IQ could be an intermediate variable between insight and other variables. A first approach to this possible role was done by our team, and CR was found to be a moderator variable on the relationship between insight and neurocognition (García et al., 2011).

#### 1.4.5. Cognitive models and defensive mechanism

Beck et al., (2004) formulated an alternative approach to understanding insight based on the cognitive processes that involve patients' ability to evaluate or distance them from anomalous. Cognitive biases reflect deviations in the style of information acquisition, processing, and appraisal, rather than poor cognitive performance as such. Impairment in the capacity to evaluate misinterpretations and alter appraisals despite feedback from others, may lead an individual with schizophrenia to disagree with others who call their experiences symptoms of illness; what would be what the traditional insight measures (Greenberger & Serper, 2010). This means that cognitive insight is a set of cognitive internal processes and the traditional clinical insight would be its expression.

As an example, there are response styles strongly associated with paranoid patients: jumping to conclusions (i.e., little evidence is gathered for decisions); and a bias against disconfirmatory evidence (i.e., neglect of counterarguments for decision making). Also deviations in attributional style have been repeatedly associated with psychosis (Jolley et al., 2006; Langdon, Ward, & Coltheart, 2010; Lincoln, Mehl, Exner, Lindenmeyer, & Rief, 2010; Mehl et al., 2010).

The dysfunctional cognitive processes could help patients to deal with the personal consequences of the illness and its stigmatization (Bassman, 2000; Cooke, Peters, Fannon et al., 2007; Tait, Birchwood, & Trower, 2003), as low self-esteem and distress (Cooke, Peters, Fannon et al., 2007; Cooke, Peters, Greenwood et al., 2007). The idea that poor insight represents an individual's response to a diagnosis of schizophrenia is supported by the results of

several studies revealing that patients with less insight into their illness demonstrate a smaller risk of depression and suicide (Mintz et al., 2003; Schwartz & Smith, 2004). Therefore, these dysfunctional cognitive processes could be the result of psychological defenses or coping mechanisms (defensive model) developed to combat the social consequences of the illness and its stigmatization.

Research has indicated that patients with schizophrenia are not flexible in their use of coping strategies or styles (Wilder-Willis, Shear, Steffen, & Borkin, 2002), tend to use maladaptive or emotion-oriented coping style (Higgins & Endler, 1995), and rely more on passive avoidant strategies and less on active problem solving (Lysaker, Bell, Bryson, & Kaplan, 1999; Lysaker, Lancaster, Nees, & Davis, 2004).

#### **1.4.5.2. Attributional Style**

Some of the dysfunctional cognitive processes are the deviations in attributional style; attributions are the causal explanations that individuals use to understand why things happen to them (Addington, Addington, & Robinson, 1999). Individuals attribute causality through several dimensions: internal/external, global/specific, stable/unstable, control/uncontrol; Attributional style is the tendency to use the same pattern of causal attributions (Fraguas et al., 2008).

Abnormal attributional processes are implicated in many disorders, particularly depression and paranoia (Kinderman & Bentall, 1997). According to Abramson's reformulated learned-helplessness model of depression, the tendency to attribute negative or bad events to

internal, stable, and global causes plays a causal role in predisposing people to depression (Abramson, Seligman, & Teasdale, 1978).

Bentall, Kinderman, and Kaney (1994) have proposed a detailed attributional model of paranoid ideation based on Higgins's (1987) self-discrepancy theory. It is argued that externalizing causal attributions are evoked for negative events that might otherwise increase the accessibility of underlying or implicit negative self-representations. External attributions reduce the accessibility of potential actual self-ideal and self discrepancies but increase the accessibility of discrepancies between self-perceptions and representations of others' views of oneself.

Conversely, source-monitoring is a complex set of cognitive processes that involves discriminating the source of an event. These events may be internally generated (such as in imagination) or externally generated (such as something seen or heard) (Johnson, Hashtroudi, & Lindsay, 1993). A comprehensive review by Ditman and Kuperberg concluded that people with psychosis have difficulties with many aspects of source-monitoring (Ditman & Kuperberg, 2005). An external misattribution bias is one form of source monitoring error and has been postulated as a cognitive mechanism that may underlie hallucinations (Bentall, Baker, & Havers, 1991). According to this theory, hallucinations are internal events (such as imagined or remembered voices) attributed to an external source (such as another person). While external misattribution is theorized as a cognitive correlate of hallucinations, in that imagined events or memories are mistakenly attributed to external sources, the data are mixed as to whether the external source attribution bias is specific to hallucinators (Donohoe et al., 2008; Jolley et al., 2006; Mehl et al., 2010; Moritz, Burlon, Braus, & Andresen, 2007).

The possible role of attributional style on clinical insight has been explored only in 2 studies (Donohoe et al. 2004; Fraguas, et al. 2008). Only Donohoe et al. (2004) found a relation between insight and two attributional style dimensions´ (internal and chance), which suggests a possible association between insight and attributional style. Nevertheless, Fraguas et al. (2008) did not found association between insight and the attributional style dimension explored (Internal/external). New studies with these measures and including more attributional style dimensions are needed to clarify this possible relation.

#### 1.4.6. Integrative Approach

Insight in psychosis has been conceptualized in a number of ways but none of them was found to be self-explanatory, and studies are incongruent between them. None of the previous models has been able to fully explain the lack of insight in psychosis. As a result, some authors have started to analyze the possible interaction of two or more explanatory models in the insight etiology (Osatuke et al., 2008). Positive results in these studies could suggest that more than one etiology may explain insight.

Results from studies using both the coping and the neurocognitive models suggest that both factors may be involved, and may, in fact, interact with each other (Amador et al., 1991; Cooke, Peters, Greenwood et al., 2007; Lysaker, Bryson, Lancaster, Evans, & Bell, 2002). Therefore, neuropsychological and defense theories of insight apparently warrant an integrative approach, rather than being used as competing models (Lysaker, France, Hunter, & Davis, 2005; Mohamed, Fleming, Penn, & Spaulding, 1999). The studies which empirically analyzed this approach support the possibility of multiple etiologies, although the domains of specific etiological influences have not been firmly established so far (Lysaker et al., 2005; Mohamed et

al., 1999). For example, Startup (1996) found that poor insight was caused by neurocognitive skills in patients with neurocognitive impairment, but that was caused by coping strategies in patients with a non impaired neurocognition. Another approach to an integrative model was carried out by Lysaker et al. (2003) by performing a cluster analysis on 64 patients with schizophrenic spectrum disorders; cluster showed that the poor insight-average executive function group endorsed a significantly greater preference for denial as a coping strategy than the poor insight-poor executive function group, suggesting that denial may play a role in the unawareness of illness in some schizophrenic patients who have maintained average executive function.

Several studies have done an approach to this integrative idea by including in a regression analysis of clinical and neurocognitive variables with the aim to predict or explain insight. Results in part of the studies were negative and the model did not improve after adding neurocognitive variables (Freudenreich et al., 2004; Monteiro et al., 2008; Rossell, Coakes, Shapleske, Woodruff, & David, 2003). Conversely, in the study by Ritsner and Blumenkrantz (2007), neurocognitive variables, among others, played a main role in the models while clinical symptoms had a minority role. Quee et al. (2011) have used a regression analysis to explain insight in a general psychosis population. They found that clinical symptoms, neurocognition and social cognition together explained insight significantly. But they tested the same model on FEP and it resulted non significant (Quee et al., 2011). Moreover, Chan et al. (2012) carried out similar analyses to explain insight, and they found that the percentage of variance explained by the clinical symptoms always arose after adding neurocognitive measures to the model.

Summarizing, three main perspectives have been trying to explain insight: clinical models, neurocognitive models and denial, or cognitive models. These perspectives separately

have had positive but weak results. And none has been able to explain insight. Recently, several authors have become to suggest that the combination of more than one explanatory model of insight could define it more accurately than taking them separately.

#### 1.4.7. Role of insight dimensions in etiological models

Generally, studies try to find the explanatory model on insight as a general concept, and there are fewer ones that explore these models separately by each of the insight dimension. Results suggest a different underlying mechanism within each dimension of insight and they may have specific etiological models. Therefore, studying insight with a focus on these different dimensions may allow a better understanding of the etiology of poor insight (Ayesa-Arriola et al., 2011).

In the study carried out by Ritsner and Blumenkrantz (2007) with chronic patients, they introduce several predictive variables in a regression analysis and perform one analysis per each insight dimension as the dependent factor. They used, among other neurocognitive scales, self-scales and a five-factorial structure of the PANSS (positive, negative, activation, dysphoric mood and autistic preoccupations), recommended by White, Harvey, Opler, and Lindenmayer (1997). As a result, each insight dimension obtained its own explanatory model, being the three of them different. The models obtained by Ritsner and Blumenkrantz (2007) are displayed in table 1.1. Of note, contrary to the item 2 (SUMD) model, item 1 and 3 (SUMD) models included among the predictors: years of education and one dimension for the PANSS. However, neurocognitive variables had a bigger role on item 2 (SUMD) model. As common characteristics, all models included temperament variables.



Table 1.1. Insight dimensions models found by Ritsner and Blumenkrantz (2007).

Insight dimension explored	Model obtained
<b>Insight of illness (Item 1 SUMD)</b> Adj. $R^2 = 0.29$	Years of education Illness duration Positive symptoms Temperament (novelty seeking and reward dependence) Coping style (task orienting) Self-esteem Visual/motor movements skills Executive functions
<b>Insight about treatment effects (Item 2 SUMD)</b> Adj. $R^2 = 0.27$	Years of education Autistic preoccupations Temperament (novelty seeking and reward dependence) Coping style (task orienting and avoidance coping) Self-efficacy Visual/motor movements skills Attention/memory
<b>Insight about illness consequences (Item 3 SUMD)</b> Adj. $R^2 = 0.29$	Temperament (reward dependence) Coping style (task orienting and emotion orienting) Visual/motor movements skills Attention/memory Executive functions

A more recent study from Chan et al. (2012) with 79 six-months into treatment first-episode psychosis found that the relationship among cognition, clinical symptoms and insight depends on the insight dimension analyzed. And they suggest that different neurocognitive functions and hence, possibly different neural networks, may be involved in different dimensions of insight. Chan et al. (2012) results revealed that a combination of clinical variables and neurocognitive factors explain the overall insight and the insight of the effects of

medication, but only clinical variables explained significant insight of mental illness and insight of the social consequences of the illness. They concluded that at early stages of the illness, other factors, such as acute symptoms, might determine awareness of mental disorder more than cognitive functions (Chan et al., 2012).

So, when the insight dimensions are analyzed separately instead of as a general factor, different patterns of relationships with other variables are found.

### 1.5. PREDICTIVE VALUE OF INSIGHT

It is known that poor insight is associated with relapse (Saravanan et al., 2010), symptom severity (Ayasa-Arriola et al., 2011), poorer treatment adherence (Goff et al., 2011), functional and psychosocial dysfunction, and outcome in general (JMcEvoy et al., 2006). But the evidence in the relation between insight and outcome was mostly done in cross-sectional studies.

Functional outcome has been predicted by duration of psychosis untreated, clinical symptomatology and neurocognition. Although, neurocognitive dysfunction has been found to be one of the predictors of functional outcome in psychosis (Allott, Liu, Proffitt, & Killackey, 2011; Mancuso, Horan, Kern, & Green, 2011), Carlsson Nyman, Ganse, and Cullberg (2006) found that all the intelligence subscales for the WAIS were related to functionality, after that similar results have been found in FEP (Leeson, Sharma, Harrison et al., 2011; Leeson, Barnes, Hutton, Ron, & Joyce, 2009). The current literature is inconsistent with how well initial insight can predict long-term outcome measures (Wiffen et al., 2010). Some studies have started to define the predictive capacity of insight on outcome. Nevertheless, the specific relation between

insight and long-term functionality is not clear. Segarra et al. (2012) found that functionality was predicted by: lack of judgment and insight, lack of insight about the treatment effect (item 2 for the SUMD scale), social withdrawal and anhedonia, and education in a FEP sample. In another study with FEP patients, only change during the first six months of insight and a global measure of clinical symptomatology predicted functional outcome at 12 months (Saravanan et al., 2010). But none of these studies did include neurocognitive variables.

Crumlish et al. (2007) explored the relationship among insight, psychopathology and functionality; they found both insight and psychopathology variables explain 64% of the functionality variance. However this study used chronic patients and did not comprises cognitive variables.

Differences among diagnosis groups have not been found in FEP (Parellada et al., 2011; Segarra et al., 2012); but Varga et al. found in a sample of chronic patients that the group with Bipolar Disorder had a significant better functionality than the schizophrenic group (Varga, Magnusson, Flekkøy, David, & Opjordsmoen, 2007), though Carlsson et al. (2006) did not found differences between groups in a chronic sample either.

So, it seems that insight is related to functional outcome; but the role of clinical insight dimensions, taking into account clinical symptoms, cognition, attributional style and controlling for a measure of intelligence on the predictive value of outcome, has not been explored in a longitudinal study with first episode psychosis.

#### 1.5.1. Relation between Neurocognitive insight and outcome.

Neurocognitive insight (NCI) is a new topic of interest and, therefore, few studies have explored the relation of this insight domain with clinical variables, outcome, and prognosis. Table 1.2 includes the studies which have analyzed the relation between NCI with clinical and outcome measures so far.

All the same, it has been found that cognitive complaint is informative of the patient's point of view about their quality of life and informative of the patient's well being (Prouteau et al., 2004). This fact increases the interest on studying NCI.

In several studies, the cognitive factors from PANSS and INC were related (Bengochea Seco et al., 2010; Lecardeur, Briand, Prouteau et al. 2009; Voruganti et al., 2007). And, results suggest that affective symptoms are related to NCI (Bayard, Capdevielle, Boulenger, & Raffard, 2009; Lecardeur, Stip, Giguere et al., 2009; Medalia & Thysen, 2008). On the other hand, the association with outcome was only explored in 3 studies (Bayard et al., 2009; Lecardeur, Stip, Giguere et al., 2009; Medalia & Thysen, 2008; Voruganti et al., 2007); the studies did not find significant associations between the variables explored. Only Bayard et al. (2009) found an association with number of hospitalizations. Nevertheless, all these results are inconsistent and represent a very limited set of data. The different scales used to measure INC, differences in samples' characteristics, and the diversity aims of the studies could be some of the causes for the inconsistencies of the data. The role of INC on the psychopathology of psychosis remains therefore unclear and new studies are needed to clarify these relationship. Furthermore, no longitudinal studies have so far analyzed if these interactions remain stable in the pathology or are modified with the course of illness, as other clinical and cognitive symptoms do.

Only two follow-up studies have been carried out. One study evaluated chronic patients and followed them up for up to 2 years. Authors concluded that NCI predicts the probability of being employed (Verdoux, Monello, Goumilloux, Cougnard, & Prouteau, 2010). Only Moritz et al. (2000) analyzed the relationships among NCI, clinical symptoms, and insight in a longitudinal study of FEP. The authors studied 53 schizophrenia spectrum disorder patients which were followed up for 12 months. They concluded that self-perceived cognitive deficits at baseline significantly predicted symptomatic worsening at follow-up (S. Moritz et al., 2000). The results are isolated since there are no more studies that have explored these associations and these findings have not been replicated.

Table 1.2. Relation between neurocognitive insight with clinical variables and outcome.

<b>Authors</b>	<b>Patients</b>	<b>Insight Ncog</b>	<b>Clinical Scales</b>	<b>Results</b>
(Voruganti et al., 2007)	85 Sz	SSTICS	PANSS, SIP, GAF	Cognitive Factor from PANSS was associated with PANSS.
(Medalia & Thysen, 2008)	75 Sz	MIC-CR	PANSS, ILS-PS	Anxiety (item G2 from PANSS) and depression (item G9 from PANSS) were associated with MIC-RC. Duration of Illness was not correlated with MIC-CR.
(Johnson et al., 2009)	105 Sz	SSTICS	PANSS	No correlation.
(Lecardeur et al., 2009)	54 NAP 17 AP	SSTICS	PANSS	Negative, cognitive and Depression factors from PANSS were associated with SSTICS.
(Bayard et al., 2009)	92 NAP, 9 AP, 60 controls	SSTICS	PANSS, BDI, STAI	No correlation with PANSS. Anxiety (STAI) and Depression (BDI) were associated with SSTICS. DUP and hospitalizations were correlated with SSTICS.
(Bengochea Seco et al., 2010)	46 NAP	SSTICS	PANSS	Cognitive factor from PANSS was associated with SSTICS.
(Medalia & Thysen, 2010)	75 Sz	MIC-CR	PANSS	No correlation.

Sz: schizophrenia. NAP: Non-affective Psychosis. AP: Affective Psychosis. MIC-CR: Measure of Insight into Cognition-Clinical Rated (Medalia & Thysen, 2008). SSTICS: Subjective Scale to Investigate Cognition in Schizophrenia (Stip et al., 2003b). PANSS: Positive and Negative Symptoms Scale. BDI: Beck Depression

*Inventory. STAI: State-Trait anxiety Inventory. ILS-PS: Independent Living Scale-Problem Solving. SIP: sickness Impact Profile. GAF: Global assessment of Functioning. DUP: Duration of Untreated Psychosis.*

Summarizing, from this literature review, the following conclusions can be raised:

- 1) Lack of insight is highly common in psychosis with up to 80% of patients presenting poor insight. Despite of the general consensus about its dimensionality, studies generally analyze it as a global concept.
- 2) The stability of the insight after the first episode of psychosis is very vulnerable with significant changes across time. This variability seems to be higher during the first 6 months of the illness, although, very few longitudinal studies have been published, and findings are inconclusive. Moreover, different diagnoses are related to different levels of insight.
- 3) A wide agreement exists about insight being composed by three main dimensions: insight of having a mental illness, insight about treatment effects, and insight about illness consequences.
- 4) A new possible dimension of insight has arisen: insight about the cognitive impairment, and research tried to figure out whether it can be considered another dimension of the clinical insight. Early results suggest this new dimension is independent from clinical insight.
- 5) None of the traditional explanatory models of insight have been fully supported by experimental data in clinical samples. More recent studies suggest that insight is a complex concept including clinical, cognitive and maybe dynamic concepts. And a comprehensive and integrative model of insight in psychosis would benefit from including all these dimensions.

6) Lack of insight influence significantly the prognosis and course of the disease. But the relation with a long-term functional outcome when the cognitive reserve is controlled has not been explored yet. Only one study has analyzed so far the longitudinal interactions among lack of insight, clinical variables, and functional outcome in early phases of psychosis and findings therefore need to be replicated.

## **2. OBJECTIVES AND HYPOTHESIS**

### 2.1. OBJECTIVES

The general goal of this study is to explore insight across the first months after the FEP and across its different dimensions: insight about the illness, insight about the treatment effects, insights about consequences of the illness and insight about cognitive impairment.

Concrete Objectives:

- 2.1.1. To explore the level of the different dimensions of insight over the first months of illness in FEP, and to compare it to the clinical symptoms changes over the same period of time.
- 2.1.2. To select the variables which better define each insight dimension taking into account the time of illness evolution.
- 2.1.3. To define the role and value of insight in a predictive model of the functionality taking into account the clinical and cognitive variables.

### 2.2. HYPOTHESIS

1) The insight scores in FEP are different depending on the follow-up time. The baseline insight scores are the highest, and they decrease over time suggesting improvement of the insight ability.



- 2) Insight about cognitive impairment does not correlated with insight about the illness or insight about the treatment effects and insights about consequences of the illness. And they do not share etiological models.
  
- 3) Insight levels differ depending on the diagnosis group. Schizophrenic Spectrum disorder has higher insight scores than Non-Schizophrenic Spectrum Disorder.
  
- 4) Cognitive measures, cognitive reserve, clinical measures and attributional style measures together are included in an explanatory model of insight and its dimensions.
  
- 5) Insight measures are related to functional outcome. The predictive model of functional outcome includes at least insight, cognitive measures and clinical measures.

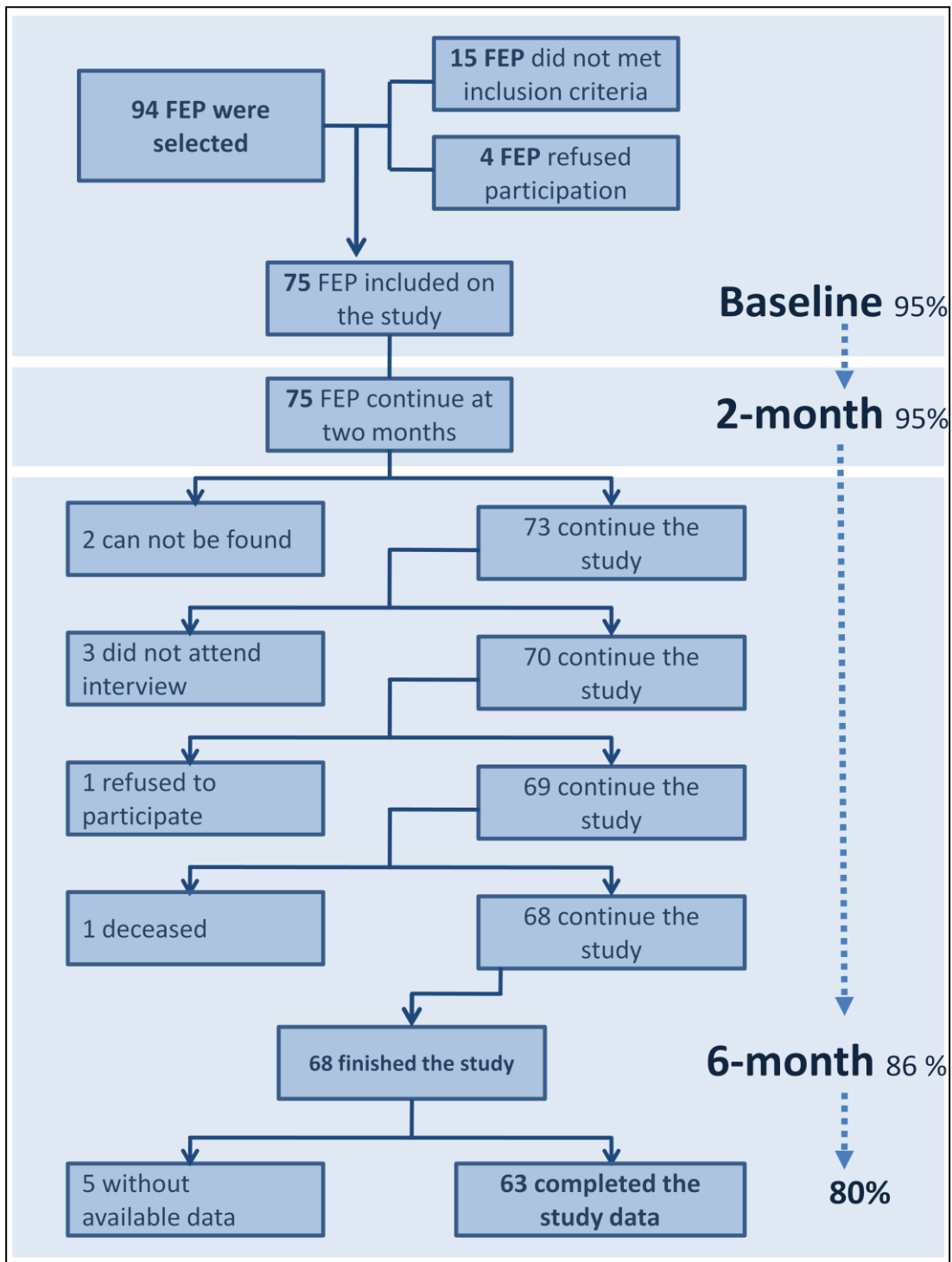
### **3. METHOD**

The present work is a prospective and multisite study with a first episode psychosis (FEP) sample, representative of the FEP community in Spain. The length of follow-up was 6 months according to the length of duration of the FEP, as after that they usually receive another diagnosis.

The sample was composed of 75 FEP who were admitted in the adult psychiatry service of three main hospitals located in the Basque Country: Donostia Hospital, which has a catchment area population of around 700.000 people in Guipuzkoa region; Santiago Apostol Hospital, which has a catchment area population of around 300,000 people in Araba region; and Cruces Hospital, which has a catchment area population of around 370.000 people in Bizkaia region. These 3 hospitals are the biggest main hospitals in each of the 3 Basque provinces and their psychiatric services cover up to 93% of the services offered to patients with a first onset of psychosis. The recruitment process lasted for 18 months, from September of 2009 to February of 2012. This study was officially funded by the Health and Consume Department of the Basque Government (research code: 2008111010) and The Basque Foundation for Health Innovation and Research (research code: BIO 09/EM/015).

**Inclusion criteria:** In order to participate in the current study, subjects needed to be between 18 and 45 years old, present at least one positive symptom (hallucinations and/or delusions) for no longer than one year, not to have previous history of organic disease of the central nervous system neither additional developmental disorders, not to have a diagnosis of substance dependence (DSM-IV criteria), and be willing and able to give informed consent.

Figure 3.1. Diagram of withdrawals.



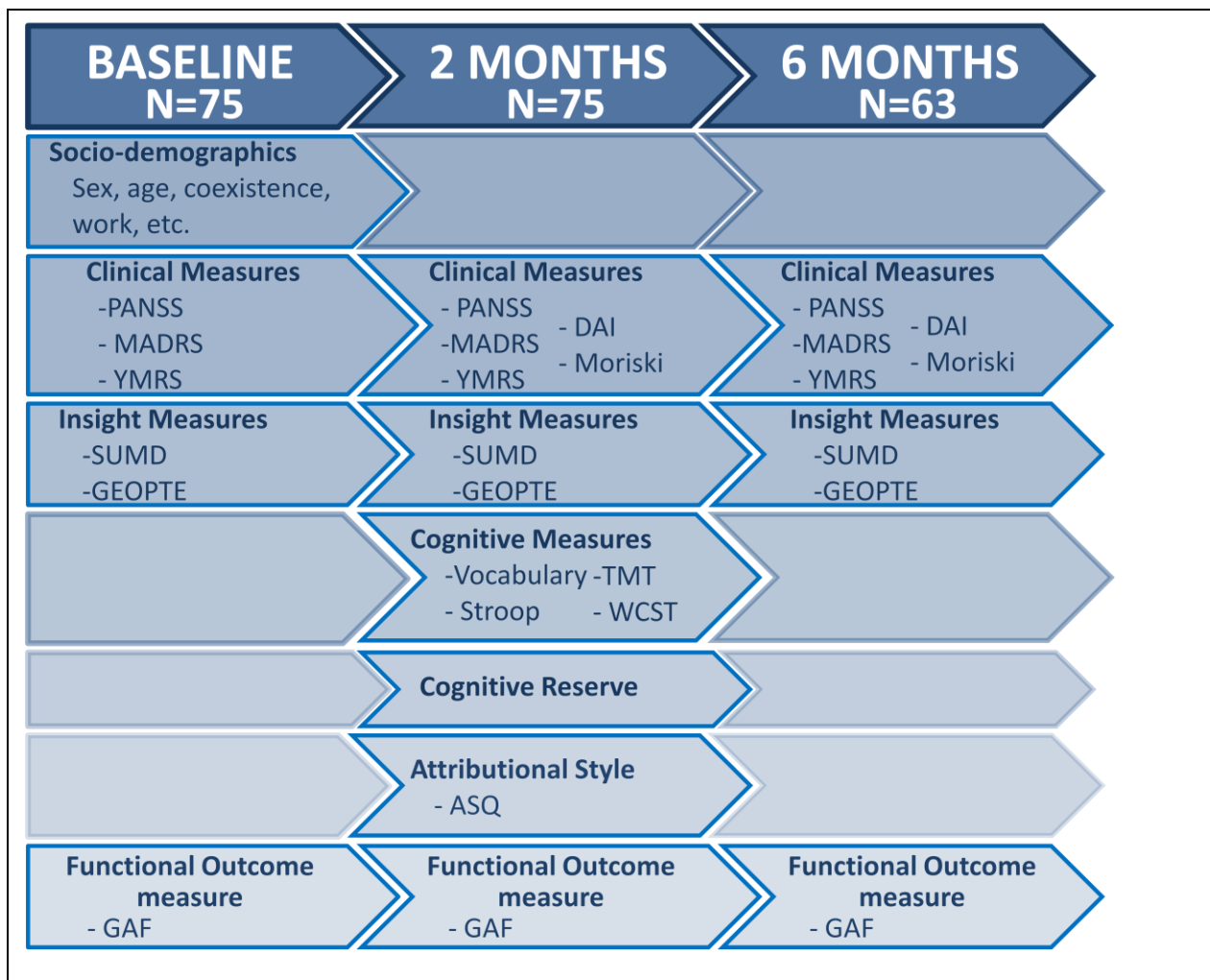
Initially, 94 patients were identified as good candidates to participate in the study. Out of these 94, 15 did not meet the inclusions criteria, and 4 did not give their consent to

participate on the study. Finally, 75 completed baseline assessment, 75 completed the 2 months follow-up and 68 the 6 months follow-up with a resulting retention rate of 86%.

Of the 94 patients with a first psychotic episode, 19 did not meet the inclusion criteria: They were excluded due to organic diseases ( $n = 3$ ), a diagnosis of drug abuse ( $n = 5$ ), having a foreign mother tongue and not speaking Spanish properly (4) and not giving informed consent ( $n = 7$ ). Therefore the sample was composed by 75 FEP, 49,3% admitted in Donostia Hospital, 24,3% admitted in Santiago Apostol Hospital, and 24,3% admitted in Cruces Hospital. Of the 75 patients enrolled at baseline, 68 (90%) were followed up at 6 months. Two patients voluntarily refused to maintain the participation on the study, another two patients did not attend to the interviews repeatedly, one patient could not be contacted, one patient moved to another country and one patient deceased. A diagram about withdrawal circumstances and final sample is shown in Figure 3.1. Clinical data after a six-month follow-up of 5 patients were not available due to the uncompleted data picked up by the clinicians, and 63 (84%) data were available at 6 months follow-up and comprise the total study sample.

The patients underwent an assessment at base line and at 2, and 6 months of follow-up. In order to maximize cooperation of the data, cognitive and attributional style measures were assessed at two-month follow-up. This time make sure that the patient's clinical status permitted a reliable performance on the tasks.

Figure 3.2. Assessment diagram including scales in the protocol for each assessment.



All participants gave written informed consent, and the study was approved by the Committee for Medical Research Ethics from the three participating hospitals; Santiago Apostol Hospital, Cruces Hospital, Donostia Hospital, and The Basque Foundation for Health Innovation and Research. Figure 3.1 provides information about the protocol scales, including clinical interview and clinical scales. A record-book with the written informed and all the scales used in the procedure was designed before starting the recruitment process (shown in Appendix 1). The full clinical assessments were performed by 3 trained psychiatrics, one at each of the participating hospitals. Inter-rates reliability was calculated at the beginning of the study, before training (0.74) and after training (0.83). Further details about each measure included can be read below:

### 3.1. CLINICAL ASSESSMENT

A general clinical interview and the scale for clinical symptoms were performed at each of the 3 moments of the study. In addition, at baseline and 6 months follow-up, participants were diagnosed based on a Structured Clinical Interview for Diagnostic (SCID) and Statistical Manual of Mental Disorders (DSM-IV), conducted by trained interviewers. The FEP was understood as the first ever manifestation of psychotic symptoms in a person's life.

1) Positive and Negative Symptoms Scale (PANSS); Spanish version from Peralta and Cuesta (1994b). The PANSS assesses the severity of symptoms and consists of 30 items rated on a 7-point scale, and it's a well known scale, broadly used to measure psychopathology. Several factor-analytic studies have suggested that a five-factor model better captures PANSS structure in schizophrenic samples (Wallwork, Fortgang, Hashimoto, Weinberger, & Dickinson, 2012). Versions of the five-factor model have been used in diverse schizophrenia research areas including insight (Monteiro et al., 2008). Wallwork et al. (2012) pointed out that this model has revealed associations in instances when the original three subscales have not. This study examined factors from a pentagonal model of the PANSS which includes positive, negative, disorganization, excitement, and emotional distress symptom dimensions (van der Gaag et al., 2006). Items used to create these dimensions are showed in table 3.1. The internal consistency coefficient (Chronbach's alpha) was 0.87 to 0.91.

Table 3.1. Items used to create the pentagonal model of the Positive and Negative Syndromes Scale.

Dimensions	Items used	Possible range of scores
Positive	P1 + P3 + P5 + P6 + G1 + G9 + G12 + G16 - N5	1 to 55
Negative	N1 + N2 + N3 + N4 + N6 + G7 + G8 + G13 + G16 - P2	2 to 62
Disorganization	P2 + N5 + N7 + G5 + G9 + G10 + G11 + G12 + G13 + G15	10 to 70
Excitement	P4 + P5 + P7 + N3 + G4 + G8 + G14 + G16	8 to 56
Emotional Distress	P6 + G1 + G2 + G3 + G4 + G6 + G15 + G16	8 to 56

P1 = Delusions; P2 = Concept disorganization; P3 = Hallucinations; P4 = Excitement; P5 = Grandiosity; P6 = Suspiciousness/Persecution; P7 = Hostility; N1 = Blunted Affect; N2 = Emotional withdrawal; N3 = Poor rapport; N4 = Passive/apathetic social withdrawal; N5 = Abstract thinking; N6 = Lack of spontaneity and flow of conversation; N7 = Stereotype thinking; G1 = Somatic concern; G2 = Anxiety; G3 = Guilt feelings; G4 = Tension; G5 = Mannerism and posturing; G6 = Depression; G7 = Motor retardation; G8 = Uncooperativeness; G9 = Unusual thought content; G10 = Disorientation; G11 = Poor attention; G12 = Lack of insight; G13 = Disturbance of volition; G14 = Poor impulse control; G15 = Preoccupation; G16 = Active social avoidance.

### 3.1.1. Affective symptoms

Scales which measure affective symptoms were performed at baseline, two and six-month follow-up by the psychiatrists.

2) Montgomery-Åsberg Depression Rating Scale (MADRS) (Montgomery & Asberg, 1979); The MADRS is a ten-item diagnostic questionnaire used to measure the severity of mood (apparent sadness, reported sadness, pessimistic thoughts, suicidal thoughts), anxiety (inner tension, concentration difficulties), somatic symptoms (reduced sleep, reduced appetite, lassitude), and inability to feel.

3) Young Mania Rating Scale (YMRS) (Colom et al., 2002); The YMRS is a rating scale used by clinicians to evaluate manic symptoms as elevated mood, sexual interest, hyperactivity, irritability, speech and sleep.

### 3.1.2. Medication Measures

The type and dosage of antipsychotic medication taken at each clinical assessment were recorded and registered by the clinician. Doses of antipsychotic medic were transformed into chlorpromazine equivalents following Andreasen, Pressler, Nopolous, Miller, and Ho's (2010) recommendations, so a direct comparison among them is facilitated. Selecting comparable doses of antipsychotic medications is an important challenge in the studies that compare efficacy and side effects of two or more antipsychotic. Andreasen et al. (2010) designed an objective and quantitative measure that can be used to make equivalent doses of clozapine, olanzapine, quetiapine, ziprasidone and aripiprazole into chlorpromazine. Davis (2006) designed a bioequivalence of amisulpride into chlorpromazine (Davis, 2006). And Castberget and Spigset (2004) designed a bioequivalence of risperidona into chlorpromazine. No bioequivalence has been found in the literature for paliperidona and clotiapine. In addition two of the measures related to medication intake were administered:

4) Drug Attitude Inventory (DAI) (Hogan, Awad & Eastwood, 1983); This is an established, reliable self-report instrument that evaluates patients' perceived effects and benefits of maintenance antipsychotic drug therapy. DAI is a 10-item dichotomous (true or false) answer scale that enables classification of patients based upon their attitudes towards medication. The final score is the sum of all partial scores, a resulting punctuation between 10 and 20. Higher scores mean a positive subjective response (compliant).

5) Morisky Medication Adherence Scale (MMAS-4) (Morisky, Green & Levine, 1986); The MMAS-4 is a self-report scale for identifying medication non-adherence. The scale is



constructed of four items answered by 'yes' or 'no'. Four 'no' responses signifies perfect adherence. Any 'yes' responses indicates some degree of non-adherence with medication.

### 3.1.3. Insight measures

Insight measures were performed at baseline, two and six-month follow-up by the psychiatrists.

6) Scale to Assess Unawareness of Mental Disorders (SUMD) (Amador & Strauss, 1990); The SUMD is a semi-structured interview rating for schizophrenic patients measuring their clinical insight items on a 5-point likert scale. SUMD ratings are made on the basis of direct patient interview. The scale assesses current clinical insight in three dimensions: insight of having a mental disorder (IMD), insight of the need for medication (INM) and insight of the social consequences of having a mental disorder (ISC). Scores for each dimension ranged from 1 to 5, with higher scores indicating poorer awareness (1=aware; 2= partially aware; 3= somewhat aware; 4= scarcely aware; 5=unaware). The total SUMD score is obtained summarizing the 3 main dimensions (IMD + INM + ISC). The Crombach's alpha obtained for the SUMD considered in this study was  $\alpha=0.91$  to  $0.94$  (items 1 to 3 were included, with each of them having a possible response range of from 1 to 5).

7) Scale for the Subjective Perception of Cognitive Deficit (Geopte) (Sanjuan et al., 2003); The Geopte is an original scale designed and validated in Spain (has no international equivalence) consists of a self-report scale of 15 items. It was designed to evaluate subjective perception of cognitive deficits, the patient's perception. The items are formulated as short questions that are answered using a scale with five possible answers (1, no; 2, a little; 3, to a fair degree; 4, quite a bit; 5, a lot). The items included in the scale are shown in Appendix 1. These

15 items collect two types of information: items 1 through 7 refer to questions about basic cognitive functions, and items 8 through 15 are questions about aspects of cognition and social functioning. The Cronbach's alpha obtained for the baseline, two months and six months of the Cognitive-Geopte-measure considered in this study was  $\alpha=0.89$  to  $0.92$  (items 1 to 7 were included, with each of them having a possible response range of from 1 to 7).

Table 3.2. Classification of insight scales.

Scale		Author	Year	Aspects of insight measured
SUMD	Scale of Unawareness of Mental Diseases	Amador	1991	3 dimensions of awareness of illness: - awareness of mental illness - awareness of treatment effect - awareness of illness consequences & a global score
G12 item (PANSS)	Positive and Negative Symptoms Scale	Peralta & Cuesta	1994	Lack of judgment and insight
Geopte-1	Scale for the Subjective Perception of Cognitive Deficit	San Juan et al.	2003	Insight about neurocognitive impairment

#### 3.1.4. Functional Outcome Measures

The scale which measure functionality was performed at baseline, two and six-month follow-up by the psychiatrists.

#### 8) Global Assessment of Functioning (GAF) (Endicott, Spitzer, Fleiss, & Cohen, 1976);

The GAF measures general activity (psychological, social, and work) of patient rated on wealthy-pathological continuum though a 0 to 100 punctuation.

### 3.2. NEUROCOGNITIVE ASSESSMENT

The neurocognitive evaluation was conducted by the same trained neuropsychologist at the 3 settings enrolled in this study. This person was blinded to the results of the psychiatric interviews and insight ratings, and was performed at two-month follow-up. The study's protocol was designed to assess mainly frontal performance and included the following:

1) Trail Making Test (TMT) (Reitan & Wolfson 1985); This test is a classic neuropsychological test originally part of the Halstead Reitan Battery that has been extensively used in the assessment of visual scanning, attention and speed. The best known and used part of the test is divided into two parts: TMT-A and TMT-B. In TMT-A the subject must first draw lines to connect consecutively numbered circles on one work sheet. In TMT-B, he/she is asked to alternatively connect numbers and letters circled alternating between the two sequences. In both TMT-A and B, the subject is urged to connect the circles "as far as he/she can" without raising the pencil from the paper. Total time in seconds to complete the task and number of errors are registered (Lezak, 2004).

2) Stroop Test (Golden, 2001); The Stroop tests a timed neuropsychological task divided into 3 trials. Each one contains 100 of items, which are organized in 5 columns of 20 items requesting the subject to complete different task in 45 seconds for each trial as fast as they can. The first trial presents randomly the words: "azul" (blue), "rojo" (red) and "verde" (green). The subject has to read them aloud. The performance of this first trial measures speed of reading (W). The second trial presents sets of "xxx" printed with blue, red or green ink. The subject has to say aloud the ink's color as quick as possible. Performance on this second trial is an estimation of chromatognosia and speed of identification of colors (C). In the last trial the

words “azul” (blue), “verde” (green), “rojo” (red) are presented again randomly, but the color of the ink does not match the color name (WC). This is an incongruent cognitive task. The subject has to say aloud the ink’s color and he/she is corrected if any errors are made. The total number of correct items performed is registered for each trial. In addition, the test permits to calculate an interference index ( $WC - [(W * C) / (W + C)]$ ) which is an estimation of the subject’s ability to avoid the influence of non relevant but competitive cognitive stimuli when searching another cognitive goal.

3) Wisconsin Card Sorting Test (WCST) (Heaton et al., 1993); The WCST consists of four key cards and 128 response cards with geometric figures that vary according to three perceptual dimensions (color, form, or number). The task requires subjects to find the correct classification principle by trial and error and examiner feedback. Once the subject chooses the correct rule, they must maintain this sorting principle (or set) across changing stimulus conditions while ignoring the other – now irrelevant – stimulus dimensions. After ten consecutive correct matches, the classification principle changes without warning, demanding a flexible shift in set. The WCST is not timed and sorting continues until all cards are sorted or a maximum of six correct sorting criteria have been reached. Despite the fact that Heaton’s correction norms offer sixteen different scores, due to the internal structure of the test, many authors normally rely on no more than two or three scores as an index of subject’s performance, including: number of categories completed, number of perseverative errors, and number of non-perseverative errors.

To create the cognitive factors all the cognitive measures, in which lower scores indicated better performance, were reversed. So that, all higher scores of the cognitive measures

indicated better performance. After the conversion, all the cognitive measures were standardized to typically scores. The cognitive factors were created with the typically scores:

4) Executive functioning; a composite measure of executive function was based on the mean of the z-scores from the WCST scores: Perseverative responses, perseverative errors, number of completed categories, and number of conceptual responses. The internal consistency of the measure was good ( $\alpha = 0.76$ ).

### 3.3. COGNITIVE RESERVE MEASURE

1) Vocabulary subtest from the Wechsler Adult Intelligent Scale -Third edition (WAIS-III) (Wechsler, 2001); Vocabulary is one of the WAIS-III's subtests, and it assesses the degree to which one has learned, is able to comprehend and verbally express the lexicon. The subject must provide an as acute as possible definition of up to 33 words in progressive order of difficulty: from more frequently used to less frequently used words. Total score on Vocabulary subtest, either alone or together with additional measures, has been used in the neuropsychology literature as an adequate estimation of the person's premorbid IQ. Vocabulary seems to be less affected by potential negative changes in the brain and therefore becomes a reflection of the person's crystallized intelligence (Barona, Reynolds, & Chastain, 1984).

Cognitive reserve; cognitive reserve score was estimated using Vocabulary subtest from WAIS-III and years of formal education completed by each subject. This method has been employed in other past studies about dementia (Alexander et al., 1997; Garrett, Grady, & Hasher, 2010), high performing adults (Daffner et al., 2005), healthy young and old adults (Stern et al., 2005) and Bipolar Disorder (Martino et al., 2008). And it has become one of the

common ways to calculate cognitive reserve in the neuropsychological literature. For the purpose of this study, the arithmetic mean of z-scores was extracted. *Crombach's alpha* was used as a measure of the internal consistency, and the internal consistency obtained in this factor in our study was ( $\alpha = 0.56$ ).

### 3.4. ATTRIBUTIONAL STYLE MEASURE

Attributional Style Questionnaire Spanish version (ASQ) (Sanjuán & Magallanes, 2006); this is a self-report measure of the attributions people make. The ASQ asks participants to consider the causes of six positive and six negative hypothetical events. Subjects rate on a 7-point scale:

- a) Whether the cause of a hypothetical event is due to the context or to the individual (external versus internal dimension). A rating of “1” on the internality/externality index indicates the event is totally due to other people or circumstances (externality), while at the other extreme, a “7” reflects an event caused by the patient himself (internality).
- b) Whether it is likely to be present in the future or not (unstable versus stable dimension). A rating of “1” on the unstable/stable index indicates the cause will never be presented (unstable), while at the other extreme, a “7” reflects the cause will be present in all circumstances (stable).
- c) Whether it applies to other areas in their lives (specific versus global dimension). A rating of “1” on the specific/global index indicates only this event is influenced by the cause (specific), while at the other extreme, a “7” reflects all events are influenced by the cause selected by the patient (global).
- d) Whether it is under patient’s control (uncontrolled versus controlled dimension). A rating of “1” on the uncontrolled/controlled index indicates the cause of an event is fully under patient’s control (controlled), while at the other extreme, a “7” reflects that the cause of an event is

absolutely not controlled by the patient (uncontrolled). Attributional-style scores are calculated for each dimension and for positive and negative events.

Self-serving Bias (SSB) is a score which indicates rating for internality (SSB-I). It is calculated by subtracting the internality mean score for negative events from the mean score for positive items (Kaney & Bentall, 1989). When the obtained score is negative, it suggests a trend to internalize positive events that is to say, a tendency to attribute to internal personal factors the origin/cause of a positive event and, at the same time, externalize negative events. With positives scores in SSB-I the opposite profile arise. These trends are more exaggerated when the total scores in SSB (positive or negative) are higher. Following the same methodology, we calculated a new score labeled SSB for controllability (SSB-C) by subtracting the controllability mean score for negative events from that for positive items. Although this procedure has not been described in the literature before, its rationality carefully follows the same principles that Kaney & Bentall (1989) published for SSB-I. In our group's opinion, this new index provide an additional score that could provide the results on the ASQ a wider scope to analyze the controllability dimension in relation to the rest of variables included in our protocol. Internal reliability of the positive and negative scores was moderate (Crombach's  $\alpha=0.61$  and  $0.68$ , respectively).

A summary of the scales used by each professional is displayed in table 3.3.

Table 3.3. Scales performed by the psychiatrists and the neuropsychologist.

<b>Psychiatrists</b>	<b>Neuropsychologist</b>
Baseline, 2 and 6 month:	2 month:
PANSS	Vocabulary (WAIS-III)
MADRS	TMT
YMRS	Stroop test
SUMD	WCST
Geopte	ASQ
Morisky	
DAI	
GAF	

PANSS = Positive and Negative Symptoms Scale; MADRS = Montgomery-Asberg Depression Rating Scale; YMRS = Young Mania Rating Scale; Morisky = Morisky Medication Adherence Scale; DAI = Drug Attitude Inventory; SUMD = Scale for Unawareness of Mental Illness; Geopte = Scale for the Subjective Perception of Cognitive Deficit; GAF = Global Assessment of Functioning; TMT = trail Making Test; WCST = Wisconsin Card Sorting Test; ASQ = Attributional Style Questionnaire.

#### **4. DATA ANALYSIS**

Statistical analyses were carried out using Statistical Package for social Science (SPSS) version 18.0. All tests were two tailed with a significance level of  $p < .05$ . Categorical and ordinal variables were summarized using counts and percentages, while continuous variables were summarized using the mean or median with the measures of dispersion, standard deviation (SD) and confidence interval (CI). The Kolmogorov-Sminorv test and D'Agostiono test inspected the normality of variables; the not normality variables were transformed. Standardized transformation, square root, squaring and log-transformation were used depending on the level and the valence of asymmetry.

Paired t-tests and U-Mann-Whitney-test were used to analyze any differences between baseline and follow-up scores or diagnosis groups.



Data were analyzed using Pearson Product Moment correlations and multiple regressions in order to determine the relationships among variables. A linear regression with step-wise forward selection was used to determine a parsimonious set of factors that predict the variable of interest from independent variables selected in the correlation analysis.

Mediational analyses were tested using multiple regressions. This approach involves testing three equations. First, the outcome variable is regressed on the predictor to establish that there is an effect to mediate. Second, the mediator is regressed on the predictor variable. In the third equation, the outcome variable is regressed on both the predictor and the mediator. This method provides a test of whether the mediator is related to the outcome as well as an estimate of the relation between the predictor and the outcome controlling for the mediator.

## **5. RESULTS**

### 5.1 DESCRIPTION OF THE FINAL SAMPLE OBTAINED

The resulting sample consisted of 75 first-episode-psychosis patients. Six-month follow-up data were available for 63 patients (84% of the total sample). To ensure that the final sample was representative of the total sample differences between the final sample and the ones who withdrew were tested. Non parametric test for independent samples were used due to the size of the group of patients who finally withdrew the study (12). There were no significant differences in socio-demographic and clinical scores between patients who completed the study and the group who withdrew it; results are presented in table 5.1.

Table 5.1. Socio-demographic and clinical differences between the group who finished the study and the group who withdrew the study.

	Patients who completed the study N=63	Patients who withdrew the study N=12	test	<i>p</i>
	Median (QD) / N(%)	Median (QD) / N(%)		
<b>Age (years)</b>	26.3 (5.6)	25.9 (5.9)	<i>U</i> = -0.22	0.823
<b>Years of formal education</b>	12 (2.5)	12 (3.5)	<i>U</i> = -1.20	0.229
<b>Gender</b>				
Male	37 (60%)	10 (77%)	$\chi^2 = 1.37$	0.242
Female	25 (40%)	3 (23%)		
<b>PANSS</b>				
Positive	27 (7.5)	28.5 (4.4)	<i>U</i> = -0.39	0.694
Negative	24 (7)	15 (5.5)	<i>U</i> = -2.02	0.044
Excitement	24 (7.5)	22.5 (4.4)	<i>U</i> = -0.01	0.993
Disorganization	33 (9.5)	31 (6.3)	<i>U</i> = -0.05	0.062
Emotional distress	27 (6.0)	26 (5.4)	<i>U</i> = -0.20	0.841
<b>Mania</b>	16 (7.5)	23 (6.9)	<i>U</i> = -1.36	0.174
<b>MADRS</b>	23 (9.0)	19.5 (11.4)	<i>U</i> = -0.54	0.593

QD: Quartile Deviation; *U*: U Mann-Whitney test;  $\chi^2$ : Pearson Chi-Square.

Only negative symptoms were significantly different between the two groups. The group who withdrew from the study had significantly less negative symptoms than the group who completed the study. The dispersion measures, quartile deviations, show higher deviations in the group of patients who completed the study which contains 63 patients. In contrast, the group who withdrew the study contains 12 patients, and its dispersion was lower.

The descriptive and demographic characteristics of the total sample who participate in the follow ups are provided in table 5.2.

Table 5.2. Socio-demographic characteristics of the patients.

	N=75		
	Mean / %		CI (95%)
<b>Age (years)</b>	27.78 (SD 6.73)		26.23 to 29.32
<b>Years of education (years)</b>	12.37 (SD 3.59)		11.55 to 13.19
<b>Gender</b>			
Male	62.3 %	47	51.17 to 72.33
Female	37.7 %	28	27.67 to 48.83
<b>Work Situation</b>			
Full/part-time employed/Student	48 %	36	37.07 to 59.13
Unemployed/disabled	52 %	39	40.87 to 62.93
<b>Marital Status</b>			
Single	85.3 %	64	75.62 to 91.61
Married	9.3 %	7	4.59 to 18.03
Separated/divorced	5.3 %	4	2.09 to 12.93
<b>Coexistence</b>			
Alone	9.3 %	7	4.59 to 18.03
Family (couple or sons)	16 %	12	9.40 to 25.92
Family of origin	70.7 %	53	59.56 to 79.76
Others	4 %	3	1.37 to 11.11

CI: Confidence Interval; Alone: patients who live alone, without company or family. Others: patients who live with someone that is not family or couple (i.e., shelter).

At the moment of the inclusion on the study most patients had completed secondary school, were single, and lived with their families of origin. The resulting sample was

representative of two well defined and different occupational situations; about half of the patients were full/part-time employed or were studying and the resting half were unemployed or disabled at time of onset.

### 5.1.2. Clinical characterization of the sample

All patients were offered to be treated with atypical antipsychotics after admission. Pharmacological treatments are specified in table 5.3. The number of patients who did not receive antipsychotic treatment was 1 from baseline on (the patient rejected the antipsychotic medication), 1 patient from the two-month follow-up and on, and 3 patients at the six month follow-up. With the exception of the patient who rejected the medication from the baseline and on, the others four were only receiving not-antipsychotic medication (antidepressant, anxiolytics or mood stabilizers) by the psychiatrist consideration. Finally, 5 patients were not receiving antipsychotic medication at six-month follow-up. Moreover, 7, 9 and 8 at base line, two-month follow-up, and 6 months follow-up respectively were taking two kinds of antipsychotics simultaneously. Therefore, 67, 64 and 40 were taking only one kind of antipsychotics at baseline, two months and six months respectively. Bioequivalence of chlorpromazine were calculated for each antipsychotic except for paliperidona and clotiapine. As result, dosages in milligrams per day were obtained and are showed in table 5.3. Nevertheless, the mean dosage were 381.7 (SD = 192.1), 309.9 (SD = 151.3) and 278.9 (SD = 166.2) at baseline, two months and six months respectively.

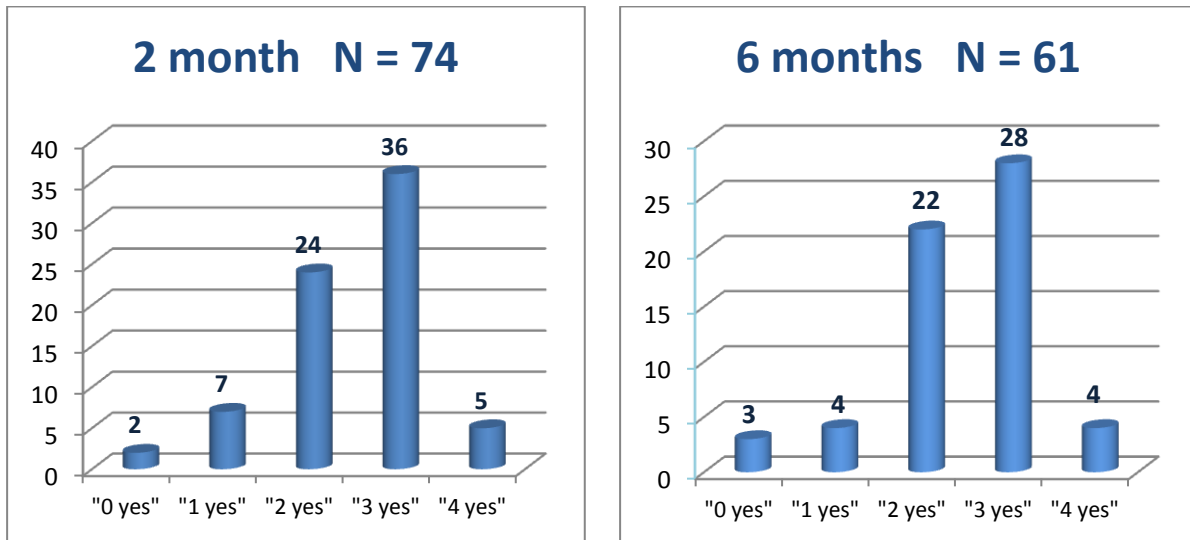
Table 5.3. Description of the pharmaceutical treatment at each follow up assessment: number of patients which are taken each antipsychotic with its percentage in the whole sample, and the mean of the bioequivalence of chlorpromazine from each antipsychotic.

	Base line		2 months		6 months	
	N (%)	CPZ mg/day	N (%)	CPZ mg/day	N (%)	CPZ mg/day
Clozapine	3 (4%)	162.8	5 (6.7%)	155.8	4 (6.5%)	383.6
Risperidone	27 (36%)	463.3	24 (32%)	348.7	15 (24.2%)	305.9
Olanzapine	36 (48%)	320,1	28 (37.3%)	297.0	20 (32.3%)	218.4
Quetiapine	2 (2.7%)	245.0	4 (5.3%)	113.8	4 (6.5%)	131.3
Ziprasidone	0	0	0	0	1 (1.6%)	79.2
Aripiprazole	9 (12%)	268.3	15 (20%)	212.9	9 (12%)	198.6
Sertindole	0	0	0	0	0	0
Amisulpride	0	0	0	0	0	0
Paliperidone	7 (9.3%)	1.0*	7 (9.7%)	0.8*	3 (4.8%)	0.3*
Clotiapine	2 (2.75%)	40**	0	0	0	0

CPZ mg/day: miligrams of chlorpromazine per day; \*miligrams of paliperidone per day; \*\*miligrams of clotiapine per day.

The Medication Adherence Scale (MMAS-4) includes four questions about attitude towards treatment. A larger number of affirmative responses indicate a worse attitude towards treatment. In this sample most of the patients gave a positive answer in 2 or 3 questions which indicates a fair or bad attitude towards treatment at (at two and six-month follow-up). Data from de MMAS-4 scale were available only for those patients who were taking a pharmacological treatment; therefore data were available for 74 patients at base line and 61 patients at 6 months follow-up.

Figure 5.1. Classification of patients depending on the number of “yes” responses in the Medication Adherence Scale scale at two and 6 months follow-up.



According to the results obtained in the MMAS-4, only 2 patients at two months, and 3 patients at six months, expressed a correct medication adherence. As it is shown in figure 5.1, more than 80% of patients expressed that they were having a poor adherence towards medication as measured by the MMAS-4, which affect their treatment effectiveness.

Attitude towards treatment was measured by the Drug Attitude Inventory. Results obtained were similar for the two moments of assessment. At two months patients obtained an average score of 16.55 (SD = 2.12; CI 95% = 16.23 to 17.31). Whereas at six months the average score was 17.00 (SD = 2.44; CI 95% = 16.37 to 17.63). This scores show a positive attitude towards in both moments medication.

Patients were diagnosis with a FEP at baseline, after that, at six-month follow-up the course of the illness allowed the psychiatrist to do a second diagnosis. Diagnoses received at six-month follow-up are specified on table 5.4. Sixty diagnoses were available after six-month follow-up, 3 patients maintained the FEP diagnosis because the psychiatrist referred more time

of follow-up would be needed to assign a new clinical diagnosis. Therefore, at 6 months follow-up 47.54% of the patients received a schizophrenic spectrum disorder diagnosis (N=29), and 52.46% received a non-schizophrenic spectrum diagnosis (N=31). The group of schizophrenic spectrum disorders is assembled in paranoid and schizophreniform types. None of the patients received a disorganized, residual or undifferentiated type diagnosis. Whereas the non schizophrenic group is distributed in several diagnoses, the larger groups are unspecified psychosis and bipolar disorders.

Table 5.4. Diagnosis at six-month follow-up.

	%*	N = 63	CI (95%)
<b>First Episode Psychosis</b>	4.70%**	3	
<b>Schizophrenic spectrum</b>			
Paranoid type	27.87%	17	18.19 to 40.17
Disorganized type	0 %	0	-----
Residual type	0 %	0	-----
Undifferentiated type	0 %	0	-----
Schizophreniform	19.67 %	12	11.62 to 31.31
<b>Non schizophrenic spectrum</b>			
Brief psychotic disorder	9.84%	6	4.59 to 19.85
Schizoaffective disorder	3.29%	2	0.90 to 11.19
Unspecified psychosis	19.67%	12	11.62 to 31.31
Bipolar disorder	16.39%	10	9.16 to 27.61
Substance-induced psychosis	1.64%	1	0.29 to 8.72

CI: Confidence Interval. \* Percentages of diagnoses are based on the 60 patients who receive a new diagnosis. \*\* Percentage based on the total sample, 63 patients.

Clinical data are showed in table 5.5. This table contains the mean, standard deviation and confidence interval for the clinical (clinical and affective) and functional scales over time. The significant differences among assessments are showed in table 5.6. It can be observed that all the clinical scores show higher averages at baseline than after six months including negative and affective symptoms. Moreover, the functionality (GAF) average score shows that patients

at baseline have a major impairment in several areas, such as work, school or family. Taking into account the range of possible scores resulting from each PANSS dimension (table 3.1.), at baseline, the dimensions with higher averages scores are positive, disorganization and emotional distress symptoms ( $p < 0.001$ ). At two and six-month follow-ups, disorganization and emotional distress remain being the clinical symptoms with high presence in the sample. Both, positive and negative symptoms improve significantly ( $p < 0.001$ ) along the follow-up periods. However, the gaining in negative symptoms is shorter compared with positive symptoms and arrives later on the course of the illness; mainly after the two month follow up period. As the previous scales, MADRS and YMRS average scores are higher at baseline, but both of them significantly diminishes over time ( $p < 0.001$ ). Depression scores show that patients at baseline have a severe depression, while after 6 months the levels decrease and they present a mild depression. In turn, mania symptoms also diminishes significantly over time ( $p < 0.001$ ), and the average scores at 6 month are clinically not significant.



Table 5.5. Descriptive data of clinical and affective symptoms and functional outcome over time.

	Base line		2 months		6 months	
	Mean (SD)	CI (95%)	Mean (SD)	CI (95%)	Mean (SD)	CI (95%)
<b>PANSS</b>						
Positive	27.29 (8.7)	25.27 to 29.31	14.73 (7.1)	13.08 to 16.40	11.40 (4.99)	10.18 to 12.74
Negative	22.84 (9.9)	20.53 to 25.14	20.14 (8.2)	18.23 to 22.05	17.81 (7.2)	15.96 to 19.68
Disorganization	31.88 (11.0)	29.28 to 34.47	20.75 (8.6)	18.74 to 22.76	17.60 (5.9)	16.18 to 19.17
Excitement	23.99 (9.2)	21.84 to 26.14	14.47 (5.3)	13.23 to 15.72	12.68 (4.0)	11.69 to 13.75
Emotional distress	26.42 (8.6)	24.41 to 28.44	18.60 (6.14)	17.17 to 20.04	15.00 (5.2)	13.76 to 16.41
<b>MADRS</b>	21.24 (11.0)	18.71 to 23.77	15.31 (9.6)	13.11 to 17.51	10.14 (6.6)	8.61 to 16.94
<b>YMRS</b>	17.0 (11.2)	14.40 to 19.57	4.25 (4.8)	3.15 to 5.35	3.29 (4.42)	2.21 to 4.46

SD: Standard Deviation; CI: Confidence Interval; \*  $p < 0.001$ ; ns = non significant. PANSS = Positive and Negative Symptoms Scale; MADRS = Montgomery-Asberg Depression Rating Scale; YMRS = Young Mania Rating Scale; GAF = Global Assessment of Functioning;

Table 5.6. Change of clinical, affective and functional measures over time: t-test differences among times.

	Diff. T1-T2 $t^{\text{sig}}$	Diff. T1-T3 $t^{\text{sig}}$	Diff. T2-T3 $t^{\text{sig}}$
<b>PANSS</b>			
Positive	12.57 <sup>***</sup>	13.84 <sup>***</sup>	5,29 <sup>***</sup>
Negative	2.56 <sup>*</sup>	4.41 <sup>***</sup>	2,94 <sup>**</sup>
Disorganization	9.45 <sup>***</sup>	10.85 <sup>***</sup>	4,06 <sup>***</sup>
Excitement	9.18 <sup>***</sup>	9.11 <sup>***</sup>	3,91 <sup>***</sup>
Emotional distress	8.92 <sup>***</sup>	10.16 <sup>***</sup>	5,55 <sup>***</sup>
<b>MADRS</b>	4.45 <sup>***</sup>	7.99 <sup>***</sup>	4,56 <sup>***</sup>
<b>YMRS</b>	9.73 <sup>***</sup>	9.49 <sup>***</sup>	1,94 <sup>0.057</sup>
<b>GAF</b>	-9.99 <sup>***</sup>	-12.41 <sup>***</sup>	-5,54 <sup>***</sup>

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ ; 1 DAI scores were taken at 2 and 6 months follow-up. PANSS = Positive and Negative Symptoms Scale; MADRS = Montgomery-Asberg Depression Rating Scale; YMRS = Young Mania Rating Scale; GAF = Global Assessment of Functioning; Diff. T1-T2 = Differences between insight score at baseline and insight score at 2 months follow-up; Diff. T1-T3 = Differences between insight score at baseline and insight score at 6 months follow-up; Diff. T2-T3 = Differences between insight score at 2 months follow-up insight score at 6 months follow-up.

### 5.1.3. Insight

Six different insight scores were obtained in this study. On the one hand, the SUMD scale offers 3 dimensional scores from insight (insight of mental disorders, insight about the treatment effects and insight of the consequences of the illness) and a total score. A second insight score was obtained from the PANSS's G12 item. And finally, the Geopte scale offers an insight measure about neurocognitive performance. Data over time of each insight score are showed in table 5.6. All insight scores obtained from SUMD, PANSS and Geopte decrease over time suggesting an improvement on the overall ability and the specific dimensions of insight in this sample. To analyze whether this change was significant, direct scores from SUMD and non parametric tests were used due to the not normal distribution of the insight scores. Table 5.7

shows that insight dimensions scores significant decrease (it means that improves) from baseline to two or six-month follow-up. But not all the scores significant change from two to six-month follow-up.

SUMD dimensions scores show that, at baseline, patients have a fair to null awareness about having a mental disorder, insight of the need for medication, and insight of the social consequences of having a mental disorder. Consequently, the SUMD total insight score suggest that the general insight is very deficient in the sample. The other general measure of insight, G12 item, suggest that patients at baseline show only a vague or shallow recognition of illness, with possible fluctuations about awareness of being ill or having major symptoms. As it will be shown in section 1.5.1, patients had low neurocognitive performance, however Geopte scores show that patients referred few complains about cognitive impairment at baseline. Nevertheless, at two months SUMD scores show that patients have improved their insight and are close to be aware of having a mental disorder, insight of the need for medication, insight of the social consequences of having a mental disorder, but they have not a fully insight. G12 item average score show that patients recognize having a psychiatric disorder but clearly underestimate its seriousness, the implications for treatment, or the importance of taking measures to avoid relapse. And, Geopte subscale shows that patients at this moment complain few to null about cognitive impairment. Results in table 5.7 show all the scores significantly change from baseline to two-month follow up.

Afterwards, six-month follow-up SUMD insight average scores are again reduced compared with the ones at baseline and two months. Scores at six months show that patients awareness about having a mental disorder, insight of the need for medication, and insight of the social consequences of having a mental disorder is questionable, being at the boundary between

awareness and unawareness. In a similar way, the G12 item average score show that patients are in the upper extreme of normal limits, although still not having a fully normal insight. Finally, complains about cognitive impairment at six-month follow-up (Geopte) remain clinically comparable to the ones obtained at two-month follow-up.

Table 5.7. Mean, standard deviation, and interval coefficient of insight dimensions over time.

	Baseline	2 months	6 months
	Mean (SD)	Mean (SD)	Mean (SD)
	CI (95%)	CI (95%)	CI (95%)
Item 1 SUMD	3.58 (1.47) 3.23 to 3.92	2.43 (1.50) 2.08 to 2.78	2.23 (1.32) 1.89 to 2.57
Item 2 SUMD	3.32 (1.41) 2.99 to 3.64	2.36 (1.33) 2.05 to 2.67	2.15 (1.34) 1.80 to 2.50
Item 3 SUMD	3.38 (1.55) 3.02 to 3.75	2.44 (1.37) 2.12 to 2.77	2.24 (1.79) 1.90 to 2.59
SUMD Total	10.27 (4.18) 9.30 to 11.25	7.24 (3.88) 6.33 to 8.15	6.63 (3.79) 5.65 to 7.60
G12 PANSS	4.62 (1.96) 4.12 to 5.11	2.97 (1.68) 2.55 to 3.39	2.21 (1.42) 1.85 to 2.56
Geopte-1	15.91 (5.5) 13.99 to 17.84	12.44 (4.3) 11.03 to 13.84	12.57 (5.0) 10.64 to 14.50

SD: Standard Deviation; CI: Confidence Interval; Item 1 SUMD= insight of mental disorders; Item 2 SUMD = insight of the treatment effects; Item 3 SUMD = insight of the social consequences; SUMD total = Scale Unawareness of mental disorders total score; G12 PANSS = Lack of judgment and insight from PANSS; Geopte-1 = Neurocognitive insight dimension from Geopte Scale.

Table 5.8 show that these change are significant when considering the insight general scores SUMD total and G12 change. But, the 4 insight dimensions scores explored remain stable and do not significantly change from two to six-month follow-up: insight of mental disorders ( $p = 0.075$ ), insight of the treatment effects ( $p = 0.187$ ), insight of the social consequences ( $p = 0.072$ ) and insight about neurocognitive performance ( $p = 0.169$ ).

Table 5.8. Change of insight over time: t-test differences among times.

	Diff. T1-T2 $t^{\text{sig}}$	Diff. T1-T3 $t^{\text{sig}}$	Diff. T2-T3 $t^{\text{sig}}$
Item 1 SUMD	6.32 *	7.03 *	1.81 <sup>0.075</sup>
Item 2 SUMD	5.73 *	6.04 *	1.33 <sup>0.187</sup>
Item 3 SUMD	5.41 *	6.27 *	1.83 <sup>0.072</sup>
SUMD total	6.48 *	6.82 *	2.01 *
G12	6.76 *	9.02 *	5.28 *
Geopte-1	-2.91 *	-2.62 **	-1.38 <sup>0.169</sup>

\*  $p < 0.001$ ; \*\*  $p < 0.01$ ; Item 1 SUMD= insight of mental disorders; Item 2 SUMD= insight of the treatment effects; Item 3 SUMD= insight of the social consequences; SUMD total = Scale Unawareness of mental disorders total punctuation; Geopte-1 = NeuroCognitive dimension from Geopte Scale; Diff. T1-T2 = Differences between insight score at baseline and insight score at 2 months follow-up; Diff. T1-T3 = Differences between insight score at baseline and insight score at 6 months follow-up; Diff. T2-T3 = Differences between insight score at 2 months follow-up insight score at 6 months follow-up.

In short, as measured by the SUMD scale, insight dimensions in this sample improve significantly over the first two months of the illness and remain stable from two months until 6 months. Neurocognitive complaints measured by Geopte scale show a significant decreasing of the complaints from baseline to two-month follow-up. But the scores do not differ significantly from two-months to six-month follow-up. General insight measures as SUMD total score and G12 item significantly change from baseline to two-month, and to six-month follow-up.

Regarding to consider patients as having or not insight, Amador et al. (1994) recommended using stringent criteria for FEP when assess whether they have good or poor insight, for that reason they defined poor insight as SUMD scores greater than 1 (Amador et al., 1994). Following this criteria, patients were categorically classified in two groups (good and poor insight) in each of the three dimensions and the total score of the SUMD scale, where a score of two or higher in the SUMD implies lack of insight in some degree. When the G12 is used to select patients with good insight, literature also recommend stringent classification insight criteria for FEP, and poor insight is defined as G12 score greater than 3 (Mintz et al.,

2004; Saeedi et al., 2007). When patients of this sample are classified following these criteria, results show that most patients at baseline were unaware of their illness, the treatment effects and the social consequences of the illness. The percentages of patients with lack of insight are shown in table 5.9. However, the percentages obtained with G12 at baseline are comparable to the ones obtained with the SUMD scale, but at two and six-month follow-up the scores among the two scales diverged.

Table 5.9. Percentages of patients with lack of insight when categorized into Good and Bad insight according to Amador et al (1994) criteria.

	<b>Baseline</b>	<b>2 months</b>	<b>6 months</b>
Item 1 SUMD	82.2%	56.9%	53.3%
Item 2 SUMD	82.2%	58.3%	50.0%
Item 3 SUMD	78.1%	61.1%	54.2%
SUMD total	83.6%	66.7%	61.7%
G12 PANSS	83.6%	50.7%	34.9%

Item 1 SUMD= insight of mental disorders; Item 2 SUMD = insight of the treatment effects; Item 3 SUMD = insight of the social consequences; SUMD total = Scale Unawareness of mental disorders total score; G12 PANSS = Lack of judgment and insight from PANSS.

With the aim of exploring whether insight levels depend on the specific type of psychosis, two groups were created based on the diagnosis that patients received after six-month follow-up. Mean differences were used to compare insight scores between the group of schizophrenic spectrum disorder (SQ) and the group of non-schizophrenic spectrum disorder (Non SQ). As shown in table 5.10, all the SUMD insight scores and G12 score from PANSS differed significantly between groups at base line, and at two-month follow-up. Nevertheless, after six-month follow-up two of the SUMD dimensions were no longer significantly different. Only differences between groups in insight about having a mental illness, general insight (total SUMD score) and G12 from PANSS were significant after six months follow-up. Even though, these differences were significant, the p-values were higher than the previous assessments

(baseline and two-month). By contrast, insight about neurocognitive impairment (Geopte-1) was not significantly different between the groups in none of the three times assessed.

Table 5.10. Differences on insight scores depending on the diagnosis group over time.

	Mean		Mean differences	
	SQ	Non SQ	<i>t</i>	<i>p</i>
<b>Baseline</b>				
Item 1 SUMD	4.03	3.16	2.36	0.022
Item 2 SUMD	3.93	2.84	3.16	0.003
Item 3 SUMD	3.86	3.06	2.07	0.043
Total SUMD	11.83	9.06	2.60	0.012
G12 PANSS	5.50	3.75	3.88	0.000
Geopte-1*	16.38	15.81	-0.56	0.583
<b>2 months</b>				
Item 1 SUMD	2.93	2.00	2.49	0.016
Item 2 SUMD	2.90	1.84	3.42	0.001
Item 3 SUMD	3.00	1.97	3.14	0.003
Total SUMD	8.83	5.81	3.28	0.002
G12 PANSS	3.64	2.41	3.01	0.004
Geopte-1*	13.50	11.88	-1.03	0.302
<b>6 months</b>				
Item 1 SUMD	2.69	1.90	2.32	0.024
Item 2 SUMD	2.50	1.87	1.73	0.089
Item 3 SUMD	2.58	1.98	1.67	0.101
Total SUMD	7.77	5.76	2.02	0.048
G12 PANSS	2.64	1.84	2.16	0.035
Geopte-1*	12.83	12.38	-0.33	0.744

\* = U Mann Witney test.; SQ = patients with a schizophrenic spectrum disorder; Non SQ = patients with a non schizophrenic spectrum disorder; Item 1 SUMD= insight of mental disorders; Item 2 SUMD = insight of the treatment effects; Item 3 SUMD = insight of the social consequences; SUMD total = Scale Unawareness of mental disorders total score; G12 PANSS = Lack of judgment and insight from PANSS; Geopte-1 = NeuroCognitive dimension from Geopte Scale.

#### 5.1.4. Attributional style

Data from Attributional Style (AS) measured by Attributional Style Questionnaire Spanish version (ASQ-E) were available for 66 patients. Means and confident interval for each dimension are specified in table 5.11.

Table 5.11. Descriptive data for Attributional Style Questionnaire scores. Means, standard deviation and confident interval for each dimensions and kind of event.

		N= 66		
	Events	Mean	(SD)	CI (95%)
<b>Internality</b>	Positive	4.99	0.78	4.80 to 5.18
	Negative	4.24	1.13	3.97 to 4.52
<b>Specificity</b>	Positive	4.95	0.85	4.74 to 5.16
	Negative	4.22	0.80	4.03 to 4.42
<b>Globality</b>	Positive	5.32	2.96	4.60 to 6.05
	Negative	4.11	1.06	3.85 to 4.37
<b>Control</b>	Positive	4.75	1.14	4.47 to 5.03
	Negative	4.11	1.10	3.84 to 4.38
<b>SSB-I</b>		0.75	1.17	0.46 to 1.04
<b>SSB-C</b>		0.64	1.13	0.37 to 0.92

SD: Standard Deviation; CI: Confidence Interval; SSB-I = Self-Serving Bias for internality; SSB-C = Self-Serving Bias for controllability.

Six patients refused to specifically collaborate in completing this questionnaire, as the task was valued as too difficult in their opinion. Despite the collaboration and help from the clinician, they offered no reliable data as their level of collaboration was very limited so finally that data were excluded from the analyses. Patients needed an average time of 15-20 minutes to complete the questionnaire. And the most repeated complaints were that they were not able to understand the task of the questionnaire, and difficulties with abstract thinking. Patients had difficulties on imagine the situation and think on what they would have done in that situation. ASQ dimensions are dimensional, and scores close to the middle point (4) show that the



dimensions are not an exaggerated or diminish trait. The available data showed a tendency of patients to believe that the causes of positive and negative events occurring in their life were internal, stable, global and under their control. But the pattern for negative symptoms is not as exaggerated as the one for positive symptoms. The SSB of the sample was close to the central score (0) meaning that patients have not an exaggerated or diminishes SSB for both internality and controllability.

#### 5.1.5. Neurocognitive performance

Neurocognition data were obtained at two-month follow-up and all the scores are displayed in table 5.12. Again neurocognitive assessment was only carried out at two months to ensure the validity of the scores obtained. A cognitive assessment at baseline is usually significantly affected by the clinical instability of the FEP patients since high levels of clinical symptoms (both positive and negative) could dull the neurocognitive performance during the assessment. In addition, a second cognitive assessment at 6 month follow up could only be recommended if alternative equivalent test format would be available for the neuropsychological tools, and that is not the case for most of the cognitive tests available into Spanish.

The neurocognitive average scores show that patients have a high premorbid IQ (vocabulary = 39.75), nevertheless the measures which reflect the current neurocognitive performance show a moderate to severe impairment. The average score obtained in TMT-A, Stroop color and word show suggest a moderate impairment on processing speed. The only index of attention show this area is severely impaired (pc TMT-B <10). Executive function is also impaired but scores on Stroop interference and WCST suggest mild-moderate impairment on this area. Neurocognitive tests show that patients had a very low performance in TMT, with percentile punctuations of 20 and <10 in TMT A and B respectively. However, the percentiles

obtained for the whole sample on the Stroop test were between 40 and 48 which merely reflect a low performance. This level of performance is similar to the one on the WCST, although there are some scores which reflect a lower performance as perseverative responses, perseverative errors and percentage of conceptual level responses with percentiles of 19, 19 and 27 respectively.

Table 5.12 Description of the scores obtained on the neurocognitive measures.

	Mean	CI	SD
<b>Vocabulary</b>	39.75	37.27 to 42.24	10.66
<b>TMT</b>			
Part A	34.30	30.77 to 37.84	14.38
Part B	96.08	78.37 to 113.78	72.01
<b>Stroop</b>			
Words	101.15	96.09 to 106.21	20.59
Color	65.48	61.27 to 69.70	17.15
Words-color	40.56	37.54 to 43.58	12.29
Interference	1.24	-0.55 to 3.02	7.26
<b>WCST</b>			
Total trials	105.91	100.81 to 111.01	20.76
Total Correct	73.58	71.24 to 75.91	9.49
Total errors	32.38	27.78 to 36.98	18.72
Perseverative responses	21.44	17.91 to 24.97	14.37
Perseverative errors	18.47	15.48 to 21.46	12.18
Non perseverative errors	13.23	11.20 to 15.26	8.26
% Concept level responses	62.80	59.66 to 65.95	12.81
Categories completed	5.18	4.90 to 5.46	1.15
Trials to 1 <sup>st</sup> category	13.70	11.72 to 15.68	8.06
Failure-to-maintain.set	0.86	0.59 to 1.14	1.12
Learning to learn score	-2.00	-3.97 to -0.04	8.00

CI: Confidence Interval; SD: Standard Deviation; Vocabulary subtest from WAIS-III (Wechsler, 2001); TMT: Trail Making Test (Reitan & Wolfson, 1985); Stroop test (Golden, 2001); WCST: Wisconsin Card Sorting Test (Heaton et al., 1993).

Moreover the average score of total trials obtained at WCST reveal that patients needed at least 80% of the set of trials (128) to finish the test, but the average of completed categories reveals that at least 5 (out of 6) categories were obtained correctly by the patients which can be considered average compared to general normal population. Around 70 % of the responses were correct, 30% were incorrect and 21% were perseverative responses.

#### 5.1.6. Cognitive Reserve

Cognitive reserve is an average score which include the score obtained in vocabulary (WAIS-III) and the number of formal years of education. Both of them, vocabulary and education, are high in the sample (an average of 39.75 and 12.37 years respectively), therefore the level of cognitive reserve on the sample is high too.

## 5.2. TESTING THE EXPLANATORY MODELS OF INSIGHT

Once analyzed the clinical, cognitive and functional status of the FEP across the longitudinal course of the study, a following aim of this research was to explore the variables which contribute best to explain the level of insight in the sample, the change of the insight over time, and the type of interaction among the variables.

For that purpose the variables obtained in the two-month assessment were analyzed since they include all the variables of this study (for more details, see figure 3.1), including sociodemographics, clinical, neurocognitive, cognitive reserve, functional outcome and attributional style).

Therefore the predictive value of two months variables was explored to search for explanations for the levels of insight at two but also at six-month follow-up. A first cross-sectional set of analysis were carried out to explore which variables explain better two-month follow-up insight dimensions. A second set of analyses were carried out to explore which variables predict six-month follow-up insight dimensions, that is to say, longitudinal analysis.

### 5.2.1. Cross-sectional models

With the goal of finding out which variables have an explanatory role on the different insight dimensions, several regression analyses were carried out. Five different models in total were created, one per each insight dimensions explored. The statistical methodology consisted of a regression analysis carried out with the variables that showed significant correlations on a previous analysis.

First, a bivariate correlation showed which variables at two-month are related to the two-month insight dimensions. Correlations between potential variables and insight dimensions are displayed in table 5.13. The variables which were significantly correlated or had a tendency to correlation were selected to be entered into the regression analysis. No additional control of potential confusion variables was considered since they are already controlled at the regression analyses per se.

Hierarchical regression models were built to examine the relationship between the dependent variable (each insight dimension) and blocks of intervenient variables such as: 1) Socio-demographics variables (age, gender, etc), 2) Cognitive variables (cognitive reserve, executive function factor, cognitive measures, etc), 3) Clinical variables (PANSS dimensions,

depression, mania), and 4) Attributional style dimensions. Thus, a model was created for each of the dependent variables: insight dimensions from SUMD (item 1, item 2, item 3 and total score) and Geopte-1 (insight about cognitive impairment) were introduced as dependent variables. G12 item from PANSS was not taken into account for these analyses because it is an item included on the PANSS dimensions, and troubles from co-linearity would have been obtained.

After selecting the independent variables, the regression analyses were carried out with two-month independent variables distribute on four steps and two months insight as dependent variables. As a result of the linear regression analysis, four best-fitted models were obtained and are presented in table 5.14.

As a result of the first set of regression analyses four models were obtained. All of them included cognitive reserve and mania among the variables which significantly contributed to explain insight. Each model was significant and explained 42% to 64% of the insight variance. Nevertheless, when the individual contribution of the variables is considered, some of the variables that were included in the models did not significantly explain insight. But their inclusion in the model increases significantly the percentage of explained variance. Among the sociodemographics variables, only gender was introduced into the models that explained insight of illness and global insight. Only two models included neurocognitive measures, the model which explains insight of the effects of medication included TMT-B and WCST conceptual responses. The second was the model which explains insight about neurocognitive performance, which included Stroop-interference and negative symptoms.

Table 5.13. Pearson correlation among 2 months variables and 2 months insight dimensions:

	Item1 SUMD $\beta$	Item 2 SUMD $\beta$	Item 3 SUMD $\beta$	SUMD Total $\beta$	Geopte-1 $\beta$
<b>Socio-demographics</b>					
Gender	0.26*	0.17	0.15	0.21	0.00
Age	-0.08	-0.18	-0.05	-0.11	0.15
<b>PANSS dimensions</b>					
Positive	0.34**	0.30*	0.37**	0.36**	0.51**
Negative	0.31**	0.32**	0.31**	0.34**	0.63***
Disorganization	0.27*	0.29*	0.38**	0.33**	0.70***
Excitement	0.43***	0.38**	0.44**	0.45***	0.51**
Emotional Distress	0.06	0.13	0.18	0.13	0.65***
<b>Clinical measures</b>					
MADRS	-0.05	0.08	0.05	0.03	0.51**
YMRS	0.47***	0.44***	0.55***	0.52***	0.51**
<b>Cognitive measures</b>					
TMT A	-0.03	-0.12	-0.02	-0.06	0.28
TMT B	-0.15	-0.20	-0.11	-0.17	0.03
Stroop word	-0.10	-0.04	-0.10	-0.09	-0.13
Stroop color	-0.05	0.00	-0.03	-0.03	0.01
Stroop interference	-0.02	-0.15	-0.04	-0.07	-0.40*
<b>WCST</b>					
Correct responses	-0.12	-0.16	-0.16	-0.16	0.11
Errors	0.11	0.26*	0.05	0.15	0.18
% Perseverative responses	0.04	0.10	-0.05	0.03	0.34*
% Perseverative errors	0.02	0.13	-0.03	0.04	0.31
% No perseverative errors	0.10	0.17	0.01	0.10	0.15
% Conceptual level resp.	0.05	0.33*	-0.02	0.12	0.10
Number of completed	-0.15	-0.04	-0.22	-0.15	0.11
Trials to complete 1 <sup>st</sup>	0.12	0.01	0.20	0.12	0.08
Learn to learn	0.08	0.07	0.06	0.08	-0.16
Executive function	-0.15	-0.04	-0.22	-0.15	0.11
<b>Cognitive reserve</b>	-0.34**	-0.39**	-0.37**	-0.40**	-0.30
<b>Attributional Style</b>					
<b>Positive</b> Internal	-0.10	0.03	-0.00	-0.03	-0.31
<b>Events</b> Stable	-0.01	0.16	0.00	0.05	0.04
Global	-0.10	-0.14	-0.11	-0.13	-0.28
Control	-0.06	0.23	0.08	0.08	-0.27
<b>Negative</b> Internal	-0.11	-0.14	-0.11	-0.13	-0.00
<b>Events</b> Stable	0.27*	0.13	0.20	0.22	-0.17
Global	0.12	-0.04	0.15	0.09	0.10
Control	-0.06	0.23	0.08	0.08	-0.27
SSB-I	0.04	0.15	0.10	0.10	-0.27
SSB-C	-0.09	0.11	-0.10	-0.03	-0.27

\*\* Correlation is significant at the 0.01 level. \* Correlation is significant at the 0.05 level; Item 1 SUMD= insight of mental disorders; Item 2 SUMD= insight of the treatment effects; Item 3 SUMD= insight of the social consequences; SUMDtotal = Scale Unawareness of mental disorders total punctuation; Geopte-1 = NeuroCognitive dimension from Geopte Scale; WCST = Wisconsin Card Sorting Test; TMT A= Trail Making Test part A; TMT B = Trail Making Test part B; PANSS = Positive and Negative Symptoms Scale; MADRS = Montgomery-Asberg Depression Rating Scale; YMRS = Young Mania Rating Scale; CGI = Clinical Global Impression; GAF = Global Assessment of Functioning; DAI = Drug Attitude Inventory. SSB-I = Self-Serving Bias for internality; SSB-C = Self-Serving Bias for controllability.

Table 5.14. Models obtained in the regression analyses to explain insight at two-month follow-up from two-month clinical, functional, neurocognitive, cognitive reserve and attributional style variables.

Two months Dependent Variables and model's properties	Two months Independent Variables	$\beta$	T	P	Partial $R^2$ (%; adjusted for rest)
<b>Insight of illness</b> Model: $R^2=0.51$ , Adj. $R^2=0.46$ , $F=10.08$ , $df=4$ , $P<0.001$	Gender	0.26	2.3	0.030	0.34
	Cognitive reserve	-0.23	2.0	0.055	-0.30
	Mania	0.49	4.2	0.000	0.56
	Stable/unstable AS	0.25	2.2	0.034	0.33
<b>Insight of the effects of medication</b> Model: $R^2=0.48$ , Adj. $R^2=0.42$ , $F=8.20$ , $df=4$ , $P<0.001$	Cognitive reserve	-0.53	-3.8	0.000	-0.54
	Mania	0.23	1.7	0.094	0.28
	TMT B	-0.31	-2.5	0.018	-0.38
	WCST conceptual Responses	0.28	2.2	0.035	0.34
<b>Insight of the consequences of illness</b> Model: $R^2=0.44$ , Adj. $R^2=0.41$ , $F=17.71$ , $df=2$ , $P<0.001$	Cognitive reserve	-0.19	-1.7	0.103	-0.24
	Mania	0.59	5.2	0.000	0.61
<b>Global Insight</b> Model: $R^2=0.50$ , Adj. $R^2=0.47$ , $F=13.54$ , $df=3$ , $P<0.001$	Gender	0.25	2.2	0.034	0.33
	Cognitive reserve	-0.24	-2.1	0.044	-0.31
	Mania	0.54	4.7	0.000	0.60
<b>Geopte -1</b> Model: $R^2=0.66$ , Adj. $R^2=0.64$ , $F=22.63$ , $df=2$ , $P>0.001$	Stroop interference	-0.45	-3.7	0.001	-0.61
	Negative PANSS	0.70	5.8	0.000	0.77

### 5.2.2. Longitudinal models

Secondly, the purpose was longitudinal and consisted on determining which of the two-month independent variables predicted insight dimensions at 6 months since onset. Following the same methodology than above (section 5.3.1), correlations among variables and insight results are displayed on table 5.15. After, the independent variables were selected, and a hierarchical step-wise linear regression analysis was performed to analyze the predictive role of the socio-demographics and two-month clinical, affective, neurocognitive, cognitive reserve and AS variables on insight dimensions at 6 months: SUMD (item 1, item 2, item 3 and total score) and Geopte-1.

After selecting the variables on the correlation analysis, a hierarchical regression models were built to examine the relationship between the dependent variable (insight) and blocks of intervenient variables such as: 1) Socio-demographic variables (age, gender, etc); 2) Cognitive variables (cognitive reserve, executive function factor, cognitive measures, etc); 3) Clinical variables (PANSS dimensions, depression, mania, premorbid adjustment); a fourth step with the attributional style scores was not included due none of the AS scores were correlated with insight scores at six-month follow-up.

The models obtained with the step-wise linear regression are showed in table 5.16. Similar to the cross-sectional analyses (table 5.14), all the longitudinal models obtained included cognitive reserve and mania, except for the model which explains 6-month insight of the effects of medication. In this occasion, all the variables included in the models had a significant contribution on insight when they are individually considered.



Table 5.15. Pearson correlation among 2 months variables and 6 months insight

	Item 1 $\beta$	Item 2 $\beta$	Item 3 $\beta$	Total $\beta$	Geopte $\beta$
<b>Socio-demographics</b>					
Gender	0.25*	0.15	0.22	0.22	-0.01
Age	-0.10	-0.00	-0.07	-0.06	0.45*
<b>PANSS dimensions</b>					
Positive	0.29*	0.16	0.14	0.21	0.38*
Negative	0.26*	0.29*	0.24	0.28*	0.33
Disorganization	0.25	0.21	0.16	0.22	0.38*
Excitement	0.34**	0.30*	0.26*	0.32*	0.29
Emotional Distress	0.07	0.07	0.01	0.06	0.43*
<b>Clinical measures</b>					
MADRS	-0.07	-0.01	-0.10	-0.06	0.27
YMRS	0.37**	0.37**	0.32(*)	0.37**	0.30
<b>Cognitive measures</b>					
TMT A	0.11	0.13	0.09	0.12	0.46*
TMT B	-0.06	-0.00	-0.07	-0.05	0.27
Stroop word	0.12	0.09	0.11	0.11	-0.14
Stroop color	0.21	0.22*	0.15	0.20	-0.16
Stroop interference	-0.17	-0.20	-0.16	-0.19	-0.44*
<b>WCST</b>					
Correct responses	0.08	0.19	0.11	0.13	0.17
Errors	0.05	0.07	0.11	0.08	-0.03
Perseverative responses	-0.01	0.02	0.05	0.02	0.14
Perseverative errors	-0.011	0.00	0.04	0.01	0.07
No perseverative errors	0.04	0.00	0.14	0.06	-0.21
Conceptual level resp., %	0.03	0.13	0.06	0.08	0.16
Number of completed	-0.06	-0.03	-0.01	-0.04	-0.18
Trials to complete 1 <sup>st</sup>	-0.07	-0.19	-0.21	-0.17	0.21
Learn to learn	-0.08	-0.03	-0.12	-0.08	0.31
<b>Cognitive factors</b>					
Executive function	-0.06	-0.03	-0.01	-0.04	-0.18
<b>Cognitive reserve</b>	-0.40**	-0.46***	-0.41**	-0.44***	-0.27
<b>Attributional Style</b>					
<b>Positive events</b>					
Internal	-0.12	-0.20	-0.21	-0.19	-0.26
Stable	-0.18	-0.09	-0.22	-0.18	-0.01
Global	-0.16	-0.13	-0.13	-0.15	-0.24
Control	-0.15	-0.17	-0.21	-0.19	-0.08
<b>Negative Events</b>					
Internal	-0.19	-0.17	-0.19	-0.19	-0.00
Stable	0.06	-0.02	0.17	0.08	0.03
Global	0.06	0.04	0.13	0.08	0.28
Control	-0.06	0.03	-0.00	-0.01	0.30
SSB-I	0.11	0.04	0.05	0.07	-0.23
SSB-C	-0.08	-0.20	-0.21	-0.17	-0.30

\*\* Correlation is significant at the 0.01 level (2-tailed). \* Correlation is significant at the 0.05 level (2-tailed). WCST = Wisconsin Card Sorting Test; TMT A = Trail Making Test part A; TMT B = Trail Making Test part B; PANSS = Positive and Negative Symptoms Scale; MADRS = Montgomery-Asberg Depression Rating Scale; YMRS = Young Mania Rating Scale; CGI = Clinical Global Impression; GAF = Global Assessment of Functioning; DAI = Drug Attitude Inventory; SSB-I = Self-Serving Bias for internality; SSB-C = Self-Serving Bias for controllability

Table 5.16. Longitudinal models obtained in the regression analysis to explain insight after six months from two-month clinical, functional, neurocognitive, cognitive reserve and attributional style variables.

Six months Dependent Variables and model's properties	Two months Independent Variables	B	T	P	Partial R <sup>2</sup> (%; adjusted for rest)
<b>Insight of illness</b> Model: $R^2=0.37$ , $Adj.R2=0.34$ , $F=12.82$ , $df=2$ , $P>0.001$	Cognitive reserve	-0.39	-3.1	0.003	-0.43
	Mania	0.37	3.0	0.005	0.42
<b>Insight of the effects of medication</b> Model: $R^2=0.39$ , $Adj.R2=0.36$ , $F=13.16$ , $df=2$ , $P>0.001$	Cognitive reserve	-0.57	-4.7	0.000	-0.59
	Stroop color	0.25	2.1	0.047	0.31
<b>Insight of the consequences of illness</b> Model: $R^2=0.35$ , $Adj.R2=0.32$ , $F=11.41$ , $df=$ , $P>0.001$	Cognitive reserve	-0.41	-3.2	0.002	-0.44
	Mania	0.32	2.5	0.015	0.36
<b>Global Insight</b> Model: $R^2=0.52$ , $Adj.R2=0.47$ , $F=11.03$ , $df=4$ , $P>0.001$	Cognitive reserve	-0.57	-4.8	0.000	-0.60
	Mania	0.52	3.6	0.001	0.50
	Disorganization	-0.61	-3.1	0.003	-0.44
	Negative symptoms	0.37	2.2	0.032	0.33
<b>Geopte-1</b> Model: $R^2=0.51$ , $Adj.R2=0.44$ , $F=7.18$ , $df=3$ , $P=0.002$	Age	0.36	2.3	0.031	0.45
	Stroop interference	-0.15	-0.8	0.438	-0.17

The model that predicts insight of the effects of the medication was the only one which included a neurocognitive measure, Stroop color, index of processing speed. Moreover, the model obtained for the SUMD total score was the only one that included other clinical (disorganization and negative symptoms) measures out of mania symptoms. Finally, results in Geopte -1 revealed different significant predictors for Geopte-1 than the ones obtained for SUMD measures. Moreover, the model differed to the cross-sectional model for Geopte-1 (table 5.14)

### 5.2.3. Explanatory role of the longitudinal variables

Following the previous methodology, the next step would be testing whether or not similar models arise when six-month variables are taken to explain six-month insight. Since this study does not include neurocognitive variables at six-month, it is not possible to test this analysis. Nevertheless, it is possible to test whether cognitive reserve and six-month mania significantly explain six-month insight about illness, insight about the effects of medication, insight about the illness consequences and insight total score. It was not possible to explore a cross-sectional model of Geopte-1 because the only variable included in both models (5.14 and 5.16) was one of the neurocognitive scores (Stroop-interference).

For this new purpose four models were tested, cognitive reserve and six-month mania were entered in several regression analyses to explain insight dimensions. Results are displayed in table 5.17; all the models tested were significant.

Table 5.17. Role of mania and cognitive reserve on the prediction of six-month insight.

Six months Dependent Variables and model's properties	Six months Independent Variables	B	t	P	Partial R <sup>2</sup> (%; adjusted for rest)
<b>Insight of illness</b> Model: $R^2=0.43$ , Adj. $R^2=0.41$ , $F=21.19$ , $df=2$ , $P<0.001$	Cognitive reserve	-0.24	-2.3	0.028	-0.29
	Mania	0.54	5.2	0.000	0.56
<b>Insight of the effects of medication</b> Model: $R^2=0.40$ , Adj. $R^2=0.37$ , $F=18.46$ , $df=2$ , $P<0.001$	Cognitive reserve	-0.34	-3.2	0.002	-0.39
	Mania	0.44	4.0	0.000	0.47
<b>Insight of the consequences of illness</b> Model: $R^2=0.35$ , Adj. $R^2=0.33$ , $F=15.16$ , $df=2$ , $P<0.001$	Cognitive reserve	-0.27	-2.5	0.017	-0.31
	Mania	0.45	4.1	0.000	0.47
<b>Global Insight</b> Model: $R^2=0.43$ , Adj. $R^2=0.42$ , $F=21.90$ , $df=2$ , $P<0.001$	Cognitive reserve	-0.32	-3.1	0.003	-0.35
	Mania	0.49	4.7	0.000	0.55

### 5.3. ROLE OF INSIGHT ON THE PREDICTION OF THE FUNCTIONALITY

The main goal of this section was to accurately define the relationship between insight and functionality. And moreover, to explore whether this relationship varies depending on the insight dimension considered.

Among all the measures obtained in the study, scores at two months follow up were taken into account as predictive variables for these analyses. Variables at baseline do not allow exploring the predictive value of neurocognitive measures.

Firstly, the goal was to find out which specific variables predict functional outcome when socio-demographics, insight, clinical and neurocognitive data are considered. And moreover, we aimed to determine the role or weight of each specific variable of insight in the model. For that purpose the methodology employed was similar to the one used in the 5.3 section.

To explore whether or not each insight scores are longitudinally related to functional outcome taking into account clinical and neurocognitive variables, four regression analyses were carried out, one per each insight score. The regression analyses were performed entering, on the one hand, the score of the GAF (functional outcome) as dependent variable. On the other hand, the variables that significantly correlated with functional outcome were entered as independent variables in a step wise regression.

The correlations were bivariate and no control variables were included waiting for the control effect of the regression analysis. Results of the correlation analysis are displayed in

table 5.18. Data showed that all insight scores but Geopte-1 were significantly correlated with functionality at long term.

Table 5.18. Pearson correlation among 2 months variables and six-month functionality.

	GAF Pearson's <i>r</i>		GAF Pearson's <i>r</i>
<b>Socio-demographics</b>		<b>WCST</b>	
Gender	-0.06	Correct responses	0.03
Age	0.05	Number of Errors	0.25
Years of formal Education	0.20	Perseverative responses	-0.25
<b>PANSS dimensions</b>		Perseverative errors	-0.23
Positive	-0.06	Nonperseverative errors	-0.21
Negative	-0.45***	Conceptual level responses	0.04
Disorganization	-0.30*	Number of categories	0.28*
Excitement	-0.20	Trials to complete 1 <sup>st</sup> category	-0.14
Emotional Distress	-0.16	Learning to learn	-0.06
<b>Insight</b>		Failure to maintain Set	-0.27*
Item 1 SUMD	-0.39**	<b>Stroop</b>	
Item 2 SUMD	-0.32*	Stroop word	0.14
Item 3 SUMD	-0.43**	Stroop color	0.18
Total SUMD	-0.41**	Stroop interference	0.22
<b>G12 PANSS</b>		<b>Attributional Style</b>	
<b>Geopte-1</b>	-0.18	<b>Positive</b>	Internal
<b>Clinical measures</b>		<b>Events</b>	Stable
MADRS	-0.19		Global
YMRS	-0.24		Control
<b>Cognitive factors</b>		<b>Negative</b>	Internal
Executive function	-0.12	<b>Events</b>	Stable
Cognitive reserve	0.25*		Global
<b>Cognitive measures</b>			Control
TMT A	-0.13	SSB-I	0.02
TMT B	-0.31	SSB-C	0.21

\*\*\* Correlation is significant at the 0.001 level; \*\* Correlation is significant at the 0.01 level; \* Correlation is significant at the 0.05 level. WCST = Wisconsin Card Sorting Test; TMT A= Trail Making Test part ; TMT B = Trail Making Test part B; PANSS = Positive and Negative Symptoms Scale; MADRS = Montgomery-Asberg Depression Rating Scale; YMRS = Young Mania Rating Scale; CGI = Clinical Global Impression; GAF = Global Assessment of Functioning; DAI =Drug Attitude Inventory; SSB-I = Self-Serving Bias for internality; SSB-C = Self-Serving Bias for controllability

Although, four step-wise regression analysis were performed (one per each insight dimension and the total score), none of the insight dimensions arose on the predictive model obtained. Therefore, same model was obtained in the four step-wise regression analyses. This

unique model is presented in table 5.19. In spite of all insight dimension but Geopte-1 were correlated with functional outcome, any insight dimension was included in the predictor model when other variables are taken into account.

Table 5.19. Longitudinal model obtained in the regression analysis to explain functional outcome after six months from two months clinical, affective, insight, neurocognitive, cognitive reserve and attributional style variables.

Dependent Variables and model's properties	Independent Variables entered in the model	$\beta$	t	P	Partial $R^2$ (%;adjusted for rest)
GAF Model: $R^2=0.40$ , Adj. $R^2=0.36$ , $F=11.17$ , $df=3$ , $P>0.001$	Nº Categories	0.36	3.3	0.002	0.42
	Failure to maint. set	-0.20	-1.8	0.072	-0.25
	Negative symptoms	-0.46	-4.2	0.000	-0.51

Due to the fact that cognitive reserve significantly correlated with functionality and it is one of the central variables on this study, an added goal was explored. The new goal consisted on exploring which variables predict functionality when cognitive reserve is controlled. Another set of regression analyses were performed following a similar methodology than the one used in 5.3 section. The difference consisted on the addition of the potential effect of cognitive reserve as a covariable. The step-wise linear regression analyses were carried out controlling cognitive reserve.

Table 5.20. Longitudinal models obtained in the regression analysis to explain functional outcome after six months from two months clinical, cognitive and attributional style variables when cognitive reserve is controlled.

Dependent Variables and model's properties	Insight dimension used among independent variables	Independent variables finally entered in the model	$\beta$	t	P	Partil R <sup>2</sup> (%;adjusted for rest)
<b>GAF</b> Model: $R^2=0.25$ , Adj. $R^2=0.22$ , $F=8.66$ , $df=2$ , $P>0.01$	<b>Insight about illness</b>	Cognitive reserve	0.16	1.32	0.191	0.18
		Negative sym.	-0.45	-3.68	0.001	-0.46
<b>GAF</b> Model: $R^2=0.25$ , Adj. $R^2=0.22$ , $F=8.66$ , $df=2$ , $P>0.01$	<b>Insight of the effects of medication</b>	Cognitive reserve	0.16	1.32	0.191	0.18
		Negative sym.	-0.45	-3.68	0.001	-0.46
<b>GAF</b> Model: $R^2=0.31$ , Adj. $R^2=0.27$ , $F=7.52$ , $df=3$ , $P>0.001$	<b>Insight of the consequences of illness</b>	Cognitive reserve	0.07	0.53	0.598	0.074
		Negative sym.	-0.39	-3.17	0.003	-0.41
		SUMD Item 3	-0.27	-2.04	0.046	-0.28
<b>GAF</b> Model: $R^2=0.25$ , Adj. $R^2=0.22$ , $F=8.66$ , $df=2$ , $P>0.01$	<b>Global Insight</b>	Cognitive reserve	0.16	1.32	0.191	0.18
		Negative sym.	-0.45	-3.68	0.001	-0.46

SUMD Item 3 = Insight of the consequences of illness



Results of the models obtained controlling cognitive reserve are showed in table 5.20. Compared with the model obtained without controlling cognitive reserve (table 5.19); when the effect of cognitive reserve was controlled, the neurocognitive measures were no longer significant and were excluded from the models. Only the severity of negative symptoms arose as a significant predictive variable in the models. Insight dimensions were not included in the models with the exception of the insight of the consequences of illness (SUMD item 3), which was significant entered in the model

The original objective was to analyze the role of insight on the prediction of functionality which (insight and functionality) were significantly correlated (table 5.18). But finally, insight had not enough weight in the prediction of the functionality to be included on the regression models. Therefore, the following purpose was to explore if insight plays some intermediate role in the relationship between the predictive variables (negative symptoms and cognitive reserve) and the functionality. A set of mediational analyses were tested with the insight scores as the mediator variable.

According to the method developed by Baron and Kenny for testing mediation in psychology (Baron & Kenny, 1986), there are four steps (performed with three regression equations) in analyzing if a defined variable (e.g., insight) mediates the relation between a predictor variable (e.g., cognitive reserve or negative symptoms) and an outcome variable (functionality).

The first step is to show a significant relation between the predictor and the outcome. The second step is to show that the predictor is significantly related to the mediator. The third step is to show that the mediator is significantly related to the outcome variable controlling for

the effects of the predictor on the outcome. The final step is to show that the strength of the relation between the predictor and the outcome is significantly reduced when the mediator is added to the model (Frazier, Tix, & Barron, 2004).

### 5.3.1. EXPLORING THE INTERMEDIATE ROLE OF INSIGHT IN THE PREDICTION OF FUNCTIONALITY

Following this methodology two sets of mediations were explored. The first set included the negative symptoms as a predictive variable. And a mediation model was tested with each insight dimensions as the mediator variable. Results of these analyses are displayed in table 5.21. The first step of the mediational analysis (the significant relation between negative symptoms and functionality) is common for all the mediations tested in this first set, so it is showed on the first line, as “Step 1”. After the first step, a set of seconds and thirds steps specifics for each mediation are displayed. Each one corresponds to the model created with each SUMD dimension and total score, as a result the table show four mediational models.

Results showed that all the analyzed models but the model 2 were significant. Therefore insight dimensions (with the exception of insight of the treatment effect) explain the observed relationship between negative symptoms and functionality. In other words, the insight dimensions are the mechanism by which negative symptoms influence functionality at six-month follow-up. An illustration of the model is displayed in the figure 5.2, with illustration in line 1 showing the model before the influence of insight, and line 2 showing the changed model after including the influence of insight. The Baron & Kenny formula was used (Baron & Kenny, 1986; Kenny, Kashy, & Bolger, 1998) to assess whether the unstandardized regression coefficient of the model's before the mediation (-1.058) drops significantly until the

unstandardized regression coefficient of negative symptoms after the mediation (-0.838, -0.820 or -0.818; respectively at models 1, 3 and 4) are significant.

Table 5.21. Two months insight dimensions as mediators of the relationship between Cognitive Reserve and Functional outcome after a six-month follow-up.

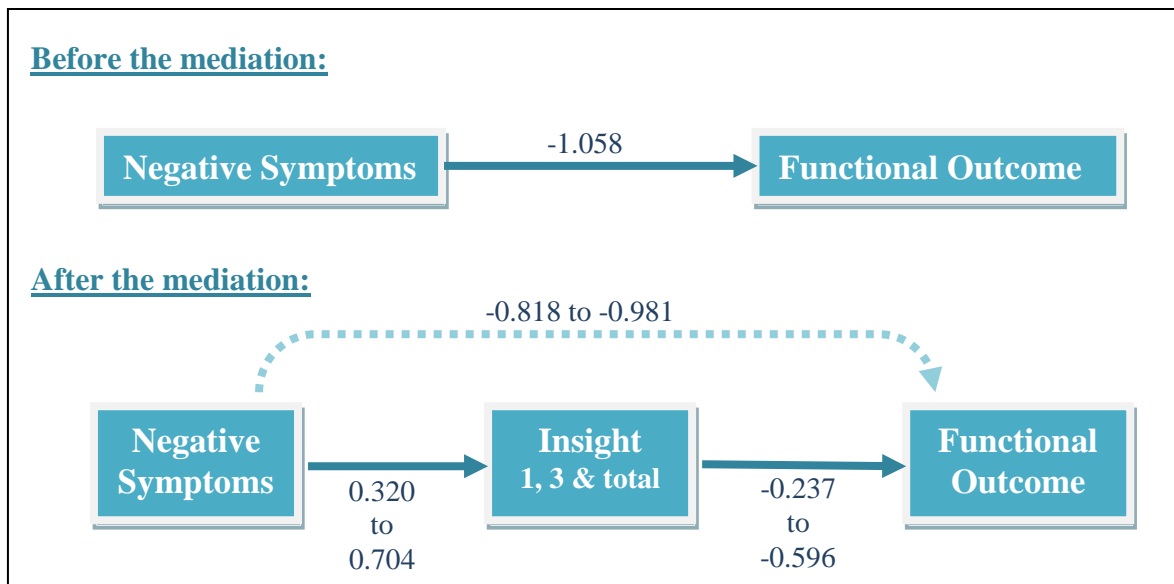
	Predictive variables	B	Std. Error	B	T	Dependent variable
	<b>Step 1</b>					
	Neg	-1.058	0.277	-0.442	-3.818***	GAF
<b>Model 1. Awareness of having a mental illness</b>	<b>Step 2</b>					
	Neg	0.320	0.134	0.277	2.393*	SUMD item1
	<b>Step 3</b>					
	Neg	-0.838	0.280	-0.350	-2.987**	GAF
	SUMD item1	-0.596	0.241	-0.290	-2.473*	GAF
<b>Model 2. Awareness of the treatment effect</b>	<b>Step 2</b>					
	Neg	0.648	0.272	0.276	2.385*	SUMD item2
	<b>Step 3</b>					
	Neg	-0.891	0.285	-0.372	-3.129**	GAF
	SUMD item2	-0.237	0.124	-0.228	-1.912 <sup>0.061</sup>	GAF
<b>Model 3. Awareness of the illness consequences</b>	<b>Step 2</b>					
	Neg	0.656	0.280	0.271	2.342*	SUMD item3
	<b>Step 3</b>					
	Neg	-0.820	0.272	-0.342	-3.016**	GAF
	SUMD item3	-0.340	0.112	-0.343	-3.023**	GAF
<b>Model 4. Total awareness</b>	<b>Step 2</b>					
	Neg	0.704	0.277	0.293	2.544*	SUMD total
	<b>Step 3</b>					
	Neg	-0.818	0.278	-0.342	-2.937**	GAF
	SUMD total	-0.312	0.116	-0.313	-2.693**	GAF

\*\* p < 0.01; \* p < 0.05; Item 1 SUMD= insight of mental disorders; Item 2 SUMD= insight of the treatment effects; Item 3 SUMD= insight of the social consequences; SUMDtotal = Scale Unawareness of mental disorders total punctuation; CR = Cognitive reserve; Mania= Young Mania Rating scale; GAF = Global Assessment of Functioning.

The results showed that the change from the original model (seen in line 1 of the figure 5.2) to the one which includes the mediator (insight) is significant at the 0.05 level on each

model (Model 1:  $Z=1.65$ ; Model 3:  $Z= 180$ ; Model 4:  $Z=1.78$ ). The proportion of the total effect that is mediated by insight (Shrout & Bolger, 2002) was 18.03%, 21.08% and 20.76% respectively for models 1, 3 and 4. In summary, the results of the mediational analyses suggest that between 18.03% and 21.08% of the total effect of negative symptoms on functional outcome is mediated by insight. Nevertheless, after controlling this influence of insight, the coefficient of negative symptoms still is significant, therefore the mediation was partial and not total.

Figure 5.1. Mediational effect of insight over the relation between negative symptoms and functional outcome.



A second set of mediations were tested to explore the possible mediator effect of insight on the predictive value of cognitive reserve on functional outcome. These mediation models were tested again with each insight dimensions as the mediator variables. Results of these analyses are displayed in table 5.22. Following the structure of the above section (5.4.1), the first step (the significant relation between cognitive reserve and functionality) is common to all the mediations, so it is showed on the first line of the table 5.22. Second and third steps of the

four models are displayed on the table separated by the name of the insight dimension used as mediator.

Table 5.22. Two-month Insight of having a mental disease as mediator of the relationship between Cognitive Reserve and functional outcome at six-month follow-up.

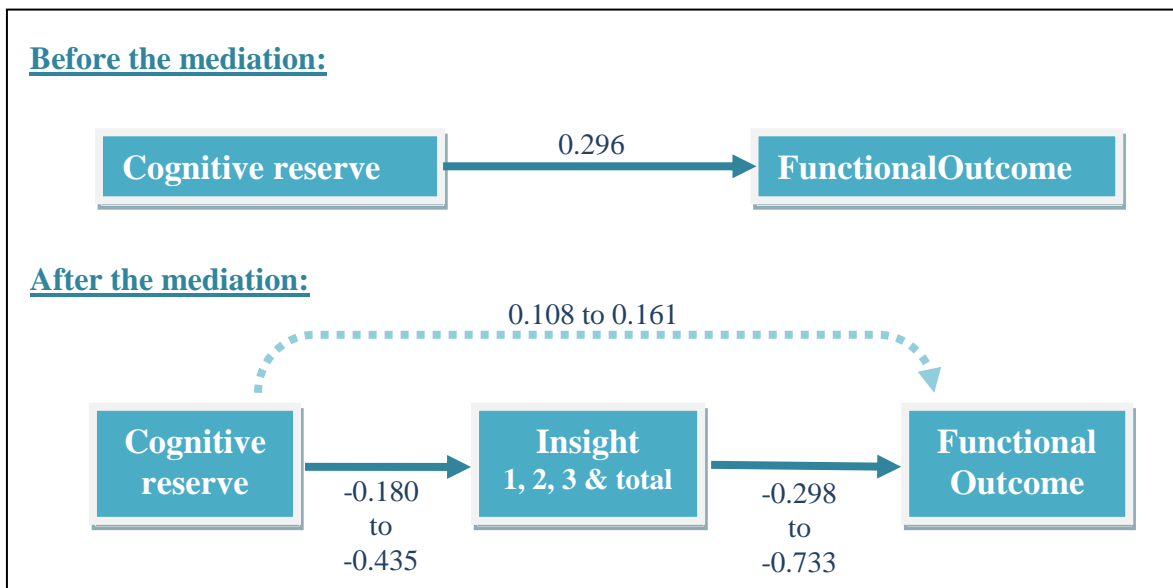
Mediator	Predictive variables	B	Std. Error	$\beta$	T	Dependent variable
	<b>Step 1</b>					
	CR	0.296	0.147	0.251	2.011*	GAF
<b>Model 1. Awareness of having a mental illness</b>	<b>Step 2</b>					
	CR	-0.180	0.064	-0.322	-2.825**	SUMD item1
	<b>Step 3</b>					
	CR	0.146	0.149	0.124	0.981	GAF
	SUMD item1	-0.733	0.260	-0.357	-2817**	GAF
<b>Model 2. Awareness of the treatment effect</b>	<b>Step 2</b>					
	CR	-0.409	0.131	-0.51	-3.114**	SUMD item2
	<b>Step 3</b>					
	CR	0.161	0.156	0.137	1.036	GAF
	SUMD item2	-0.298	0.137	-0.287	-2.171*	GAF
<b>Model 3. Awareness of the illness consequences</b>	<b>Step 2</b>					
	CR	-0.423	0.131	-0.363	-3.233**	SUMD item3
	<b>Step 3</b>					
	CR	0.108	0.149	0.092	0.727	GAF
	SUMD item3	-0.402	0.125	-0.407	-3.218**	GAF
<b>Model 4. Total awareness</b>	<b>Step 2</b>					
	CR	-0.435	0.130	-0.373	-3.336**	SUMD total
	<b>Step 3</b>					
	CR	0.111	0.151	0.094	0.734	GAF
	SUMD total	-0.383	0.128	-0.384	-2.987**	GAF

\*\* p < 0.01; \* p < 0.05; Item 1 SUMD= insight of mental disorders; Item 2 SUMD= insight of the treatment effects; Item 3 SUMD= insight of the social consequences; SUMDtotal = Scale Unawareness of mental disorders total punctuation; CR = Cognitive reserve; Mania= Young Mania Rating scale; GAF = Global Assessment of Functioning.

Results showed that all the models were significant. In other words, insight dimensions are the mechanism by which cognitive reserve influences functional outcome at six-month follow-up. Unstandardized  $\beta$  drops from 0.296 to 0.146, 0.161, 0.108 and 0.111 (respectively for 1 to 4).

These changes are significant at 0.05 level (Model 1:  $Z=1.93$ ; Model 2:  $Z=1.73$ ; Model 3:  $Z=2.23$ ; Model 4:  $Z=2.18$ ) (Baron & Kenny, 1986; Kenny et al., 1998). Finally, the proportion of the total effect that is mediated by insight (Shrout & Bolger, 2002) was 44.57%, 41.18%, 57.45% and 56.29% respectively for models 1, 2, 3 and 4. Thus, between 41.18% and 56.29% of the total effect of cognitive reserve on functional outcome is mediated by insight. After controlling the influence of insight, the coefficient of cognitive reserve stopped be significant, therefore these mediation are total. An illustration of the total mediational model is showed in the figure 5.2.

Figure 5.2. Mediation effect of insight over the relation between cognitive reserve and functional outcome.



## **6. DISCUSSION**

One of the main objectives of the present study was to explore the different insight dimensions over time analyzing which variables of the illness explain insight in a more comprehensive way, testing potential explanatory models to define the best one. Also we aimed to determine the role of insight and insight dimensions in the prediction of functionality in FEP, as autonomy is one of the determinants of the person's final quality of life and level of competence.

Among the major contributions of this research was to analyze the mentioned relationship with a major inclusion of variables, from sociodemographics to clinical variables such as symptoms, affective status, and additional relevance factors revealed by the literature such as cognition, attributional style, and cognitive reserve. This combination of variables was an effort to overcome some of the limitations identified in the literature review of previous studies and research projects that partially contributed to the analysis of insight with limited explanation of the statistical variance. Combining a vast group of variables allowed exploring integrative models that explain insight, which has been demonstrated to be complex and multidimensional.

The time frame chosen for this study was focused on the 6 months of course of psychosis right after the FEP onset. Although longer follow-up periods are always recommended, the reason to proceed with this longitudinal approach was based on two main clinical reasons/thoughts. The first one is that six months is the average period of time recommended by the international scientific community for a FEP to be supervised before the clinicians' final judgment for a later diagnosis is done (American Psychiatric Association,

1994). After the first 6 months, most patients present a change in diagnosis (Zhang-Wong, Beiser, Bean, & Iacono, 1995) that in the case of our sample, was concentrated in two big diagnostic groups: squizophrenic spectrum disorders, non squizophrenic spectrum disorders. The second thought was related with the fact that the first 6 months of the illness seem to present the highest variability in terms of symptoms manifestation (Addington & Addington, 2008), and therefore, the identification of the key factors/variables contributing to the course of the illness during that period seems a clinical priority. The appendix III includes the clinical conclusions that can be reached from this work.

The most important finding of this study is the change of insight during the first months after the onset of the illness, and how this change could influence the pattern of relationship between the illness variables and insight. Due to this process of change, the specific moment in which insight is assessed could affect the findings of significant relationship with the resting variables. This study adds support to the literature of insight in presenting insight in psychosis as a concept explained by multiple variables needed to define its etiology. Another relevant aspect is that not all the insight dimensions share the same pattern of interaction with the illness variables, and the idea of considering some of them separately might be needed.

Moreover, the present results highlight the importance of the patient's cognitive reserve as a key variable when explaining insight in FEP and the relationship among insight and additional variables. To our knowledge, this is the first study that has analyzed the role of insight on the long-term functional outcome while controlling for a measure of cognitive reserve.



### 6.1. SAMPLE CHARACTERISTICS.

Of the 79 selected for the study, 75 were finally enrolled in the present study, and 69 completed assessment at six-month follow-up, resulting in a retention rate of 92%. Most longitudinal studies have at least one-year follow-up, and reported rates of drop up are overall lower, from 60% to 68% (Leeson, Sharma, Harrison et al., 2011; Mintz et al., 2004; Saeedi et al., 2007). Nevertheless, studies with a similar length of follow-up informed of better rates of retention (88%) closer to the one obtained in this study (Saravanan et al., 2010). A study with FEP in our area obtained a six-month retention rate of 77%, but the sample was composed by drug-naïve patients (Cuesta, Peralta, Campos, & Garcia-Jalon, 2011).

The sociodemographic characterization of the resulting sample is comparable to the ones in previous studies with the same population (Ayesa-Arriola et al., 2011; Pelayo-Terán et al., 2008). A larger proportion of the sample were males with sex rates similar to the ones reported in past studies (Pelayo-Terán et al., 2008). An average age of 27.78 years old in FEP is again in accordance to the literature, where other studies show an average age in FEP from 24.5 to 29.4 (Leeson et al., 2009; Mintz et al., 2003; Thompson, McGorry, & Harrigan, 2001; Wiffen et al., 2012). Due to the fact that this sample comprises the entire FEP spectrum, the average age is higher than in other studies which only included first episode schizophrenic spectrum disorder (Cotton et al., 2012; Johnson et al., 2009). Patients' coexistence is mostly settled with their family of origin (70.7%), which could be partially related to the higher average age of emancipation in Spain, 29.2 years old; (Instituto Nacional de Estadística, 2012). A Spanish epidemiological study on FEP showed a rate of single patients in the marital status data of

83.91% (Pelayo-Terán et al., 2008), which is close to the sample of the present study (85.3%). International rates are also similar 87.9% (Saeedi et al., 2007). Again national statistics have shown a high average age of marriage, 33.92 (Instituto Nacional de Estadística, 2012), which is higher than the average age of the study sample, and emphasizes that FEP patients influenced by their sociocultural context. However, the rate of employment at time of first onset at the Pelayo et al. (2008) study was 34%, slightly lower than the one obtained in this study. However, they did not consider students as active population, as it was the case in terms of this research (Pelayo-Terán et al., 2008). The main reason to proceed this way is the youth of the FEP samples, since onset usually comes when most patients are just finishing studying or beginning their professional careers. Moreover, the average years of education (12.37 years) shows that most of patients besides having finished the Spanish secondary obligatory school (from 12 to 16 years old), they have also completed the preparatory courses for the university (2 years) or a vocational training (2 years for most of the sample). This rate is again similar to other recent studies with FEP (Chan et al., 2012; Leeson, Harrison, Ron et al., 2011).

In short, the sociodemographics data obtained from the sample show a population with a high rate of unemployment or disability, most of which are single and live with their family of origin. This profile, which is not uncommon for the general normal population of that age in Spain, has been related in other cultures, such as USA, as an expression of some level of premorbid impairment of this particular population group (Giuliano et al., 2012; Seidman et al., 2010). However, in our study nearly half of the sample was employed or a full time student at the moment of the breakdown. This rate is higher than the usually found in schizophrenic population. But it has probably been arisen by the presence of other diagnosis groups as the non-schizophrenic spectrum disorder patients (Varga et al., 2007), which usually present higher rates of employment than patients with a SSD.

All patients that accepted to be treated with atypical antipsychotics were receiving so. Although the percentage of patients that were treated with more than one antipsychotic increased over time, the final rate was inferior to the 8% of the sample. These data are comparable to the ones in other studies in FEP (Leeson, Harrison, Ron et al., 2011). This pattern could reflect a clinical observation in the psychiatrics' habit to proceed with medication which has been reported in other longitudinal studies in FEP. Clinicians tend to start treatment with atypical antipsychotic medication which usually implies lower side effects (Crossley, Constante, McGuire, & Power, 2010). Atypical antipsychotics are safer than typical antipsychotics, but they still have severe side effects. For that reason, clinicians start to increase the number of atypical, or to add a typical to patient's treatment only after confirming that one atypical does not control sufficiently the main symptomatology (Fragou et al., 2012).

There were no sociodemographics data that could explain the low adherence of patients who withdraw and the ones who finished the study; only negative symptoms were different between these two groups. Negative symptoms have been closely related to functionality in the literature (Strauss, Sandt, Catalano, & Allen, 2012). Therefore the sub-sample which withdrew was potentially more capable to proceed with their normal life and having a minor need for a treatment demand and completing follow-ups.

Nearly half of the sample had a schizophrenic spectrum disorder, according to the literature (Thompson et al., 2001). The rate of schizophrenia diagnoses at the end of the longitudinal follow up was lower than in past studies with FEP (Chan et al., 2012; Leeson, Harrison, Ron et al., 2011; Leeson, Sharma, Harrison et al., 2011; Mintz et al., 2004), and at the same time the rate of un-specified psychosis was higher than what literature refers (Mintz et al., 2004; Thompson et al., 2001) suggesting either the need of the clinicians for longer follow-ups

to determine a specific diagnosis or/and the attitude of prudence before displaying a diagnosis (schizophrenia) which is associated to severe bias and stigma in the general population (Durand-Zaleski, Scott, Rouillon, & Leboyer, 2012; Lysaker, Roe, Ringer, Gilmore, & Yanos, 2012). However, most of the patients had a more specific clinical diagnosis at the end of six-month follow-up period.

Although a follow-up of six months has been labeled as insufficient to offer an accurate diagnosis by some researchers (Haahr et al., 2008), Saeedi et al. (2007) observed that only 6% of the total FEP population changed their diagnosis when the follow up period was extended up to one year.

The overall sample presented severe clinical symptomatology at the time of baseline assessment although symptoms improved substantially over the follow-up. This improvement in clinical symptomatology was probably related to the effect of the antipsychotic treatment as the main common intervention that patients received (Fragou et al., 2012). However, negative symptoms did not have as a good response to drugs as positive symptoms did, and they became more relevant and disturbing. Probably because symptoms as the positive, which diminish over time, made outshine the negative symptoms at baseline.

The attributional style scores show that patients presented a tendency to think that the causes of events are internal, stable, global and that are under their control. This pattern is stronger for positive events than negative events. Silverman and Peterson (1993) compared the scores on the ASQ between schizophrenic patients and a healthy control group. Congruent with the results of the present study, their results showed a higher tendency to the pattern mentioned above when positive events are assessed. Other studies in the literature found the same pattern

(Fraguas et al., 2008; Jolley et al., 2006; Martin & Penn, 2002). But, in Silverman and Peterson's study, the healthy group tended to see negative events as external, unstable and unglobal. This tendency among the healthy control group is higher than the one in the patients group, and may reflect a healthy coping style. Traditionally AS has been explored in psychosis literature with the main goal of better understanding paranoid patients, that is, finding possible personality traits which can be treated on therapy. Lately, some researchers have shown an interest to further explore whether AS is related to symptoms in some way. Results so far have been incongruent. One possible reason for this incongruence could be the complexity of the concept and the difficult to measure it. Several authors expressed in their articles the troubles they have had trying to measure AS (Fraguas et al., 2008; Jolley et al., 2006). Also, some patients in our study rejected to collaborate in the completion of this set of data due to the difficulty of the scale employed despite correctly completing all the rest of the protocol. As result, many times patients referred they were not able to answer what the Attributional Style Questionnaire asked them. Fraguas et al. (2008) referred that up to 21.4% of patients rejected to complete the same AS scale. The scales which measure AS require a big effort in abstraction, and abstract thinking is one of the impaired domains among psychotic patients (Levin, 1984; Seidman et al., 2002; Voglmaier, Seidman, Salisbury, & McCarley, 1997). The rate of rejection of the present study (14.6%) was lower than the one of Fraguas et al. (2008); this difference could be also due to the type of samples recruited. Fraguas et al. (2008) included chronic schizophrenic and schizoaffective patients. Bargain of the difficulties that patients have to fill the questionnaire, it could be possible that a new, more ecologic, scale is needed. Also is possible that a concept as complex as attributional style need more complex explanatory models about it relationship with other variables. Aboveall, when a relation with other concept such complex as insight is explored. Therefore, future studies could be focus on possible not direct

relations among AS and insight, and explore possible interactions that AS have over the relationship of insight with other variables.

Concerning the neurocognitive performance of the sample, it reveals the neurocognitive impairment that has been found previously in other studies (Ojeda et al., 2010; Sánchez et al., 2009). The impairment that the illness causes is supported by the disagreement between premorbid IQ and the performance after the FEP.

## 6.2. INSIGHT SCORES AND CHANGES OVER TIME

The present results confirm past literature in which lack of insight was highly present in FEP samples although the level of insight in its different dimensions, increased significantly over the follow up periods. (Mintz et al., 2004; Saravanan et al., 2010). More specifically, the present data suggest that this improvement is much greater during the first two months after onset, helping to better define the moment in which the improvement of these dimensions take place. Previously, authors had located the change of a more global view of insight as occurring un-specifically during the three (Mintz et al., 2004) to six (Saravanan et al., 2010) first months of the illness. According to this, in the present sample the significant improvement of general insight, SUMD total score or PANSS G12 item, continued from two-month to six-month follow-up. Though two of the four dimensions that did not significantly change after the two-month follow up had a p value close to 0.05, but still not significant, and the general insight still improved from two months on. It could be that these data are showing a process of stabilization in which the more specific measures of insight (insight dimensions) get stable at two-month, and the general insight (more sensitive) needs a longer period to stabilize. This idea is supported by the results of a previous study by Mintz et al. (2004), who found that general

insight in patients is stable from month 3 on. More studies exploring the general insight and its dimensions every month during the first 6 months after the onset could clarify and support the present results. The rates of patients with lack of general insight are up to 83.6% at baseline, and it diminishes over time with up to 66.7% at two-month follow-up, and up to 61.7% at six-month follow-up. However, the rates for the insight dimensions are lower than the ones for general insight. These differences could be caused by the fact that the criteria for presenting good insight are stricter in FEP (Amador et al., 1994), and a cumulative effect is obtained in the general score since it is score from the three dimensions scores and finally, the general score is more sensitive. Of note, PANSS G12 rates of lack of illness are similar to the SUMD rates at baseline, but they differ on the following assessments in more than 30 points of percentage. These discrepancies could be reflecting a possible underestimation of insight, and could also explain differences referred in literature depending on the measure included.

Regarding the level of insight associated to each diagnosis group (schizophrenic spectrum disorder and non-schizophrenic spectrum disorder), results showed differences between the two diagnosis groups at baseline and at two-month follow up. Although, insight scores at six-month follow-up reveal a tendency to unification between the two diagnosis groups. According to these results, Wiffen et al. (2011) also found differences in insight between diagnostic groups in a one-year longitudinal study with FEP. When differences are found between groups, as expected, the schizophrenic spectrum disorder is the one who presents higher scores of insight, that is to say, poorer insight. The group of non schizophrenic spectrum disorder includes diagnoses with more affective symptomatology, it could explain the lower rates of insight scores on this diagnosis group, since diagnoses associated with low mood tended to have higher insight scores and vice versa (Collins, Remington, Coulter, & Birkett, 1997; Freudenreich et al., 2004; Lewis, 2004). This idea is supported by the studies in chronic patients that do not find differences in insight between the diagnosis groups (David et al., 1995;

Varga et al., 2007), or the studies with FEP that do find differences (Ayesa-Arriola et al., 2011). As far as the writer of this work knows, there are two more studies which explore this issue on a sample of FEP and take into account the different insight dimensions. Ayesa et al. (2011) made a comparison between the patients with good and poor insight in a sample of 164 FEP, and found that both the group of poor insight about the mental disease and the group of poor insight of the social consequences of having a mental disorder, had significantly more schizophrenic diagnoses (Ayesa-Arriola et al., 2011). However, Segarra et al. (2012) did not find differences in any of the insight dimensions between the group of schizophrenic patients and the group of schizoaffective patients (Segarra et al., 2012). Of note, the last study has a selected FEP sample, and only included schizophrenic, schizoaffective and schizophreniform disorders. The lack of other affective diagnoses could explain at least partially, the divergence of results.

In short, the present study reveals insight improvements over the first two months after the FEP, and from there, insight starts to remain more stable. At the same time, the differences in insight scores between schizophrenic spectrum disorder and non-schizophrenic spectrum disorder groups show that groups have different levels of insight until the sixth month. Therefore, between the two-month assessment and the six-month assessment, differences on insight scores of both groups start to disappear. As a whole, these results suggest that patients with schizophrenic spectrum disorder present a worse insight in the initial phases after the FEP, which -the same as the insight of the non-schizophrenic spectrum disorder group- improves quickly during the first months after the FEP. And finally, both reach similar levels of insight. Summarizing, the present results highlight the possible role of insight as a predictive variable of the diagnosis when the moment of its assessment is taken into account. However, more studies with longer follow-ups are needed to clarify whether the tendency observed in this study is maintained over time. Several clinical conclusions are discussed in the appendix III.



### 6.3. CROSS-SECTIONAL ETIOLOGICAL MODELS OF INSIGHT AT TWO-MONTH FOLLOW-UP.

An etiological general model is suggested by the results of this study, and surprisingly, unlike other studies, traditional clinical symptoms or neurocognitive measures resulted not to be included in the model. Variables more often included into the informed models included positive symptoms, negative or depressive symptoms and neurocognitive measures, mainly frontal function or executive function (Segarra et al., 2012). Contrary, the present study included only two variables arisen as the major explanatory of insight and its dimensions; mania scores and cognitive reserve explain from 32% to 42% variance of insight, despite the inclusion of clinical symptoms and neurocognitive performance. This model started to arise as such when cross-sectional analyses were performed, but it became stronger when longitudinal insight was analyzed. This change is probably influenced by the insight own change; when a six-month insight is used, the model becomes stronger and more defined and it is the moment in which it is possible to consider insight as stable. Among the insight's dimensions from the SUMD, the only dimension that differs on its explanatory model is the insight of the effects of medication (item 2 SUMD), this model comprises only neurocognitive scores, even though the two-month cross-sectional regression also revealed a model which contained cognitive reserve and mania.

The present model obtained was composed by cognitive reserve and mania, suggesting that a higher presence of manic symptoms and a lower level of cognitive reserve explain the severity of the lack of insight. The cognitive reserve hypothesis proposes that those with higher premorbid intellectual function are more able to cope with the impact of neural insult either because of higher brain structural reserve or because of better functional capacity to use compensatory forms of neural processing. Barnett et al. (2006) have proposed that in

schizophrenia, better cognitive reserve may result in fewer psychotic and neurocognitive symptoms either because of superior reasoning skills or because of the ability to inhibit the abnormal neural processing that mediates psychotic symptoms. Therefore, our results could support the Barnett et al. (2006) hypothesis, or at least, the idea that cognitive reserve plays a protective role in psychosis. The way in which these two variables, insight and cognitive reserve, are related to each other could be due to patients with lower rates of cognitive reserve would have fewer resources to compensate the neurocognitive impairment of illness, and consequently higher neurocognitive impairment. Moreover since metacognition has been related to the neurocognitive capacity (Nicolo et al., 2012), neurocognitive impairment could limit the patient's metacognitive capacity of elaborate complex mental representations of themselves and others, and use the mechanism which would allows patients to cope with stressors. An impoverished metacognition has been linked with poor insight (Lysaker et al., 2011).

As far it has been possible to know, this is the first study that uses a cognitive reserve measure with FEP samples, instead of a premorbid IQ measure, to explore the etiology of insight. On the present study, even though the reliability of the measure did not reach the gold standard, the results obtained in its relation and interaction with other variables in this study are strong and sound, and support the inclusion of cognitive reserve in future studies. One of the pending tasks for future studies would be exploring improved measures of cognitive reserve in this population before replicating any data.

Conversely, the un-expected variable included in the models was the mania measure. Only one previous study has explored manic symptoms in relation with insight in FEP (Ayesa et al., 2011). And these authors obtained three models for the 3 insight dimensions explored,

which were composed by clinical variables (positive and negative symptoms) and also mania symptoms, stressing for the first time in literature the role of mania symptoms in relation to the level of insight. Congruent with the present study, Ayesa et al. (2011) found that better insight was related to lower mania symptoms. Although manic symptoms are also frequent in psychosis (Yen et al., 2003), most of the literature has focused on the relationship between insight and depression. The present is a somehow unexpected finding also because mania is more central to bipolar disorders, and as mentioned, the published literature did not explore the potential role of mania in insight in patients with psychosis. However, impaired insight is also frequently observed in patients with bipolar disorder, particularly during pure manic episodes (Cassidy et al., 2010). A big rate of bipolar disorders in the sample could have disguised the results, but the present study only included 16.6% of bipolar disorders. A methodological issue that may be also relevant to this discussion is the fact that the YMRS (the mania scale) include a specific item to rate insight (this item measures whether patients admit change, illness or need of treatment). It is possible that scores on this item made the scale to have a strong correlation with the other insight measures. However, this rationality contrasts with another similar fact: the positive and disorganization PANSS dimensions include the G12 item about awareness of illness. Despite so, none of the clinical dimensions were entered into the explanatory models of insight that were obtained in this study.

Insight about the neurocognitive impairment has shown in this study an independent nature as the explanatory model obtained for this dimension of insight was completely different to the ones obtained for clinical insight. To begin with, insight about cognitive impairment did not follow the differential pattern observed between the diagnostics groups, although the change over time is similar to clinical insight. In this study, insight about the neurocognitive impairment has been related to age, one of the neurocognitive variable (resistance to

interference or concentration) and negative symptoms. Although the statistical support of this data is not as strong as for the other dimensions of insight, the pattern of relationship between insight about neurocognitive impairment and negative symptoms has been previously reported in the literature (Bayard et al., 2009; Lecardeur, Briand, Prouteau et al., 2009).

However, some studies have informed of a poor relationship between insight of neurocognition and neurocognitive performance as measured by objective tools (Moritz et al., 2004) Future studies will be needed to further clarify the relation of insight about neurocognitive impairment and other clinical or neurocognitive variables.

One interesting conclusion from these results is that integrative models seem be a better way to reach a sounder comprehension of insight, unlike some of the partial conclusions derived from correlational and regression analysis studies. To the best of our knowledge, this is the first time that the same model consistently explains all the insight dimensions. Although this is one of the few studies which included a larger amount of variables to be explored, still the total percentage of variance explained was limited to the 32 - 43%, and therefore, other factors are still involved in the explanation of insight in psychosis. In one of the most comprehensive studies published about insight, Ritsner et al. (2007) included a very large range of variables (sociodemographic, clinical, temperament and coping style variables) to also analyse explanatory models of the insight dimensions. Similarly to the present study, authors found that the models obtained explained only up to the 30% of insight dimension's variance. But the sample used by Ritsner et al. (2007) was composed by chronic patients, so similar studies with PEP which also include cognitive reserve and affective symptoms are needed to clarify the role of each variable. Moreover, contrary to Ritsner et al. (2007), the present study found that insight about the treatment effect is the dimension more related to neurocognitive variables and insight

of illness and the consequences of the illness were strongly related to cognitive reserve. This suggests that insight about the treatment effect and about the neurocognitive impairment are partially caused by neurocognition.

It is important to notice that none of the considered, as frontal function measures represented in this study mainly by the WCST had a relevant role on the final results. And therefore this data do not support the frontal function hypothesis as the main cause of the lack of insight in the illness. The conceptual defensive model in the literature has neither been supported by our results, specifically by the role of the attributional style variables in the models obtained. After considering the effect of the main variables, attributional style did not contribute to explain any variance in the study.

#### 6.4. ROLE OF INSIGHT PREDICTING FUNCTIONALITY

Despite the defined role of mania and cognitive reserve in explaining insight, when the focus of the analysis moved to explore future functional outcome, insight and mania symptoms no longer played a role in the study. However, cognitive reserve remained showing a key role in the analysis, and negative symptoms arise as predictor of outcome. This model imply that patients with a larger cognitive reserve and less severe negative symptoms after the FEP will potentially present a better functional outcome at least until the sixth month. These are not surprising finding since the literature has repeatedly associated both, negative symptoms (Peña et al., 2012) and cognitive reserve (Barnett et al., 2006) to functional outcome in pathology. These results also could clarify the findings obtained by Leeson, Sharma, Harrison et al. (2011), who reported that among patients with higher premorbid IQ abilities, some of them presented a better outcome than the other ones. They discussed about the possible role of cognitive reserve

on this difference, and the present result support that idea (Leeson, Sharma, Harris et al., 2011). Therefore could be that cognitive reserve has a higher role explanatory and predictive of functional outcome than premorbid IQ.

Our results offer a closer picture of the complexity of the interactions explaining final outcome in psychosis. Once the correlations between all the measures of insight and functional outcome were deeply explored through mediational analyses, the role of insight became specified as a significant mediator of a more complex relationship between negative symptoms and cognitive reserve with functionality. These results are sustained by all the dimensions of insight except again, insight of the neurocognitive impairment.

These mediational models reveal that traditional lineal approximation to the exploration of the relationship between insight and other variables in psychosis may be insufficient. The future research in this literature should benefit of incorporating more recent statistical tools which help to explore the complex interactions which were the objective of this study. For example, a structural equation modeling equations could be ideal to check a model in which cognitive reserve, negative symptoms, insight and functionality were all integrated together to define additional interactions among all of them. However, for such a study a significantly larger sample of patients should also be recruited.

## 6.5. STUDY LIMITATIONS

This study includes several limitations that should be address and limited the generalization of the findings:

1) The sample size which is proper to do general analysis, becomes insufficient when facing for example a structural equations modeling approach as just mentioned in the previous section. Independent meditational models were explored because the size of the sample was not enough to carry on a structural equation modeling including both negative symptoms and cognitive reserve as predictors of functionality being mediated by the different insight dimensions. Studies exploring this hypothesis could clarify more accurately the role of insight in predicting functionality.

2) Due to the fact that several diagnoses had a very short prevalence on the sample, it was not possible to specifically compare them with the other ones, so clinical diagnoses were grouped in two general groups (schizophrenic spectrum disorders and non-schizophrenic spectrum disorders).

3) Since the interest was to explore insight during the first months after the onset the study had a 6 months follow-up. The reasons for choosing this longitudinal framework have already been explained. However, once analyzed the prevalent role of time/course in some of the variables in the illness, six months result limited when aiming to explore some additional changes in later phases of psychosis.

5) The cognitive reserve measure used. Although this study followed the literature recommendations to create the cognitive reserve variable, the Cronbach's alpha value obtained could be improved. To carry out deeper studies about the concept of cognitive reserve on FEP, how to measure it should precede the investigation. Cognitive reserve is an emergent concept which has arisen recently in the mental illness literature and a lack of validated scales for this population is the main limitation to explore it objectively at the present. The measures which

traditionally score cognitive reserve are design for elderly adults, and they use to explore lifetime data about occupation (for example, length of the longest job, perceived prestige and/or salary are common indices) or leisure activities (for example, intellectual, social and physical activities). The use of these measures in PEP is limited by the youth of this kind of population, since, for example, most of them are still students. Other authors from a different field of literature (dementia) have recently suggested to also including measures of brain (tissue) reserve as part of the concept of cognitive reserve (Nithianantharajah & Hannan, 2009). Such an approach would require including neuroimaging procedures but could be a focus of interest in psychosis as it has become in some neurological conditions already (Sumowski, Chiaravalloti, Wylie, & Deluca, 2009).

4) The inclusion criteria of this study were very restricted in terms of months of evolution of the illness since onset, which delimited the duration of untreated psychosis of the sample (maximum 12 months). Nevertheless, a possible influence of DUP cannot be rejected and future studies must include it.



## **7. CONCLUSIONS**

A parallel exploration of insight over the first months after the FEP, altogether with its different dimensions, reveals that insight dimensions stabilize before insight in general. Besides, insight and the clinical variables do not follow the same evolutionary pattern across time; insight starts stabilizing before clinical variables do. Up to 43% of insight variance is explained by cognitive reserve and negative symptoms, which to date have not been relevant variables in the study of insight, arise as the main explanatory variables of insight. And finally, insight has not a direct relation with functional outcome, but a mediator role arise between the predictors (cognitive reserve and depression) and functional outcome.

- 1) General insight and its dimensions improve over time. While insight dimensions are stable two-month on, global insight improves at least until six months.
- 2) Insight about neurocognitive impairment is an independent dimension of the traditional insight with its own etiological model.
- 3) Patients with schizophrenic spectrum disorder have higher insight scores, but at two months these scores start to be similar than the ones of the group with non-schizophrenic spectrum disorder.
- 4) The explanatory models of insight included mania and cognitive reserve as main variables.
- 5) The predictive model of functionality included depression and cognitive reserve. Insight is a mediator between these two variables and functional outcome.

## **8. CONCLUSIONES**

El estudio del insight a lo largo de los primeros meses tras un PEP y teniendo en cuenta las diferentes dimensiones de insight revela, que éstas se estabilizan antes que el insight general. Y que además, el insight y las variables clínicas no siguen el mismo patrón evolutivo a lo largo del tiempo, siendo el insight quien empieza a estabilizarse antes que las variables clínicas. Las variables reserva cognitiva y síntomas maníacos, hasta ahora no centrales en el estudio del insight, surgen como las principales variables explicatorias de insight y sus dimensiones. Finalmente, la relación hallada entre insight y funcionalidad no es directa, sino que insight actúa de mediador entre funcionalidad y sus predictores.

- 1) Tanto el insight general como las dimensiones del insight mejoran a lo largo del tiempo. Mientras que las dimensiones de insight son estables a partir de los dos meses, el insight general continúa mejorando al menos hasta los 6 meses.
- 2) El insight sobre los déficits cognitivos es una dimensión independiente the insight tradicional, y posee su propio modelo etiológico.
- 3) Los pacientes con psicosis del espectro esquizofrénico tienen un peor insight, pero a los seis meses de seguimiento los niveles de insight empiezan a ser similares a los del grupo de pacientes con psicosis del espectro no esquizofrénico.
- 4) Las principales variables que explican insight son reserva cognitiva y síntomas maníacos.

5) La reserva cognitiva y los síntomas negativos surgen como las variables que predicen funcionalidad. El role del insight se define como mediador entre estos predictores y funcionalidad.

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APPENDIX 1

(Cuadernillo De Recogida de Datos)

## **CUADERNO DE RECOGIDA DE DATOS**

**CONCIENCIA DE ENFERMEDAD EN  
PRIMEROS EPISODIOS PSICÓTICOS**

**MODELOS EXPLICATIVOS Y VALOR  
PREDICTIVO EN LA RESPUESTA  
TERAPÉUTICA**

**GOBIERNO VASCO: ESTUDIO MULTICÉNTRICO**

## *Esquema del Estudio*

	BASAL	MES 2	MES 6
<b>DATOS SOCIODEMOGRÁFICOS</b>			
Datos sociodemográficas	x		
<b>VARIABLES CLÍNICAS</b>			
Diagnóstico psiquiátrico	x		x
Evaluación síntomas clínicos	x	x	x
Grado conciencia de enfermedad	x	x	x
Evaluación del Estilo Atributivo		x	
Medidas de funcionamiento	x	x	x
Tratamiento psicofarmacológico administrado	x	x	x
Variables relacionadas con el tratamiento (cumplimiento, actitud)		x	x
<b>VARIABLES NEUROPSICOLÓGICAS</b>			
Evaluación neuropsicológica		x	

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**CRITERIOS DE SELECCIÓN**

**DATOS SOCIODEMOGRÁFICOS**

**DATOS DE LA ENFERMEDAD**

INICIO DE LA ENFERMEDAD

DIAGNÓSTICO

OTRAS ENFERMEDADES

TRATAMIENTO FARMACOLÓGICO

**EVALUACIONES PSIQUIÁTRICAS**

ENTREVISTA DIAGNÓSTICA SEMI-ESTRUCTURADA SCID-I: PSICOSIS

ESCALA DE SÍNDROME POSITIVO Y NEGATIVO DE LA ESQUIZOFRENIA (PANSS)

ESCALA MONTGOMERY-ASBERG PARA LA DEPRESIÓN (MADRS)

ESCALA DE YOUNG PARA LA EVALUACIÓN DE LA MANÍA (YMRS)

ESCALA SUMD (ABREVIADA)

ESCALA GEOPTE

ESCALA DE EVALUACIÓN DE LA ACTIVIDAD GLOBAL (GAF)

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**DATOS CLÍNICOS DEL SEGUIMIENTO**

**TRATAMIENTO FARMACOLÓGICO**

TRATAMIENTO ADMINISTRADO

CUMPLIMIENTO Y ACTITUD

ESCALAS AUTO-APLICADAS; MORINSKI-GREEN Y DAI DE AWAD

**EVALUACIONES PSIQUIÁTRICAS**

ENTREVISTA DIAGNÓSTICA SEMI-ESTRUCTURADA SCID-I: PSICOSIS

ESCALA DE SÍNDROME POSITIVO Y NEGATIVO DE LA ESQUIZOFRENIA (PANSS)

ESCALA MONTGOMERY-ASBERG PARA LA DEPRESIÓN (MADRS)

ESCALA DE YOUNG PARA LA EVALUACIÓN DE LA MANÍA (YMRS)

ESCALA SUMD (ABREVIADA)

ESCALA GEOPTE

**EVALUACIÓN NEUROPSICOLÓGICA**

**ESTILO ATRIBUTIVO**

ESCALA DE EVALUACIÓN DE LA ACTIVIDAD GLOBAL (GAF)

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***VISITA MES 6******37***

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**DATOS CLÍNICOS DEL SEGUIMIENTO****TRATAMIENTO FARMACOLÓGICO****TRATAMIENTO ADMINISTRADO****CUMPLIMIENTO Y ACTITUD**

ESCALAS AUTO-APLICADAS; MORINSKI-GREEN Y DAI DE AWAD

**EVALUACIONES PSIQUIÁTRICAS****ENTREVISTA DIAGNÓSTICA SEMI-ESTRUCTURADA SCID-I: PSICOSIS****ESCALA DE SÍNDROME POSITIVO Y NEGATIVO DE LA ESQUIZOFRENIA (PANSS)****ESCALA MONTGOMERY-ASBERG PARA LA DEPRESIÓN (MADRS)****ESCALA DE YOUNG PARA LA EVALUACIÓN DE LA MANÍA (YMRS)****ESCALA SUMD (ABREVIADA)****ESCALA GEOPTÉ****ESCALA DE EVALUACIÓN DE LA ACTIVIDAD GLOBAL (GAF)**

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***HOJA DE FINALIZACIÓN******47***

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## **CONSENTIMIENTO INFORMADO GENERAL**

**Título de la investigación:** Conciencia de enfermedad en primeros episodios psicóticos. Modelos explicativos y valor predictivo en la respuesta terapéutica. IP. Dr. Miguel Gutiérrez.

Investigador: Dr. \_\_\_\_\_  
Lugar de realización: Dpto. de Psiquiatría. Hospital \_\_\_\_\_

**PROPÓSITO DEL ESTUDIO:** Las personas diagnosticadas de sufrir un primer episodio psicótico, tienen diferentes formas de interpretar lo que los profesionales denominamos enfermedad mental, o sus síntomas. No es extraño que la opinión del paciente y de su médico difiera a la hora de interpretar los fenómenos que experimenta el paciente, y que el paciente no lo considere una enfermedad mental, mientras que su médico sí lo haga. Esta diferencia de criterio entre profesional y paciente ha generado bastante discusión entre los profesionales de la salud mental, y se cree que puede estar condicionada por varios aspectos, como: a) los síntomas de la enfermedad, b) el funcionamiento intelectual del paciente, y/o c) el grado de control que el paciente interpreta que tiene sobre los acontecimientos que le rodean o le suceden.

El presente estudio pretende determinar por un lado el grado de desacuerdo entre el criterio de un profesional de la salud mental y el del paciente, y en qué medida, las tres posibles causas de este desacuerdo antes señaladas, explican el mismo. Así mismo, se pretende determinar como la percepción e interpretación del paciente sobre lo que ocurre puede estar relacionado con el cumplimiento del tratamiento pautado por su psiquiatra. Con todo ello, el objetivo final es alcanzar un mayor conocimiento sobre los mecanismos que llevan a percibir al paciente su enfermedad de una determinada manera (en ocasiones diferente a la de su médico), y cómo dicha percepción puede influir sobre el curso y pronóstico de la enfermedad.

Mediante este documento lo que solicitamos es su colaboración en esta investigación, y para ello debemos realizar una serie de pruebas, que en ningún momento suponen riesgo para su salud.

**EXPLICACIÓN DEL ESTUDIO:** A los pacientes que cumplan criterios para entrar en el estudio y deseen participar en el mismo, se les realizará una evaluación que tiene las siguientes partes: 1) Entrevista clínica. Permite determinar al médico qué síntomas están presentes y en qué medida y valorar la interpretación del paciente de lo que los profesionales denominan enfermedad mental; 2) Administración de tests que permiten medir el funcionamiento intelectual relacionado con procesos de atención y abstracción; 3) Los pacientes completarán unos cuestionarios relacionados con su percepción de control sobre los acontecimientos del entorno y sobre su opinión acerca de la medicación. El total de la evaluación puede llevar alrededor de dos horas (media hora más o menos) y se podrá realizar en varias sesiones y días de acuerdo con el deseo y disponibilidad del paciente. Una vez concluida esta primera valoración, se

realizará un seguimiento a los 2 meses, 6 meses y un año. Durante dichas visitas, se repetirán las entrevistas clínicas para valorar el curso de la enfermedad y se realizará una extracción sanguínea, que permitirá determinar el grado en que el paciente está tomando la medicación.

**RIESGOS/BENEFICIOS:** No se esperan beneficios adicionales a los propios del tratamiento habitual, salvo que el clínico, y el paciente si así lo desea, pueden conocer con mayor exactitud el estado cognitivo-intelectual del paciente. La participación en el presente estudio no conlleva ningún riesgo para el paciente.

**CONFIDENCIALIDAD:** Ni los nombres, ni cualquier otro dato que pueda llevar a la identificación de los pacientes que participen en el estudio serán publicados en ninguno de los trabajos que se deriven de esta investigación (Ley Orgánica 15/1999, de 13 de diciembre de protección de datos de carácter personal). Los resultados de este estudio únicamente serán utilizados para el mejor conocimiento del trastorno que usted padece.

**COSTE/COMPENSACIÓN:** No existe ningún coste por participar en este estudio. Todas las entrevistas y pruebas que se realicen durante el estudio no supondrán coste alguno para el paciente. El paciente no recibirá compensación económica por participar en el estudio.

**ALTERNATIVAS DE PARTICIPACIÓN:** Su participación en este estudio es completamente voluntaria.

**DERECHO AL ABANDONO DEL ESTUDIO:** El paciente tiene derecho a abandonar el estudio en cualquier momento sin que ello suponga perjuicio alguno en el tratamiento o cuidados recibidos por parte de su clínico habitual.

\_\_\_\_\_  
Nombre del paciente

\_\_\_\_\_ He leído y comprendido este consentimiento informado

\_\_\_\_\_ La información de este consentimiento informado me ha sido explicada.

\_\_\_\_\_  
Firma del investigador  
legal

\_\_\_\_\_  
Firma del paciente, tutor o representante  
legal

En \_\_\_\_\_, a \_\_\_\_\_ de \_\_\_\_\_ de 200\_\_

NOTA: Se harán tres copias del consentimiento informado: una será para el investigador principal, otra para la historia clínica del paciente y la última para el paciente o sus familiares.



## Visita Basal – Día 0

Fecha: \_\_\_/\_\_\_/\_\_\_

### CRITERIOS DE SELECCIÓN

#### CRITERIOS DE INCLUSIÓN

	SI	NO
Edad comprendida entre los 18 y los 45 años.	<input type="radio"/>	<input type="radio"/>
Presencia de al menos un síntoma psicótico positivo (delirios y/o alucinaciones) en el momento del reclutamiento, con una evolución inferior a un año	<input type="radio"/>	<input type="radio"/>
Consentimiento informado para el estudio por escrito del paciente, tutor o representante legal.	<input type="radio"/>	<input type="radio"/>
<i>Si ha señalado alguna de estas opciones el paciente debe EXCLUIRSE del estudio</i>	_____ ↑	

#### CRITERIOS DE EXCLUSIÓN

	SI	NO
Comorbilidad con otros trastornos del Eje I, incluido el consumo de tóxicos (excepto el consumo esporádico). Se excluirán aquellos pacientes que den positivo a la prueba de tóxicos en orina realizada de forma rutinaria, excepto en los casos en que la clínica psicótica persista tras 15 días de abstinencia.	<input type="radio"/>	<input type="radio"/>
Presencia de enfermedades orgánicas del sistema nervioso central (SNC), antecedentes de traumatismos craneoencefálicos con pérdida de conciencia, retraso mental.	<input type="radio"/>	<input type="radio"/>
Trastornos generalizados del desarrollo.	<input type="radio"/>	<input type="radio"/>
Embarazo y lactancia.	<input type="radio"/>	<input type="radio"/>
<i>Si ha señalado alguna de estas opciones el paciente debe EXCLUIRSE del estudio</i>	_____ ↑	

## ***DATOS SOCIODEMOGRÁFICOS***

### **DATOS DE IDENTIFICACIÓN** *(no enviar a la Base de Datos)*

---

Nombre y apellidos del paciente: \_\_\_\_\_

Psiquiatra de estudio: \_\_\_\_\_

Psiquiatra Clínico: \_\_\_\_\_

Lugar de tratamiento habitual: \_\_\_\_\_

Dirección: \_\_\_\_\_

Población: \_\_\_\_\_ Código Postal: \_\_\_\_\_

Provincia: \_\_\_\_\_

Teléfono: \_\_\_\_\_ - \_\_\_\_\_

**DATOS SOCIODEMOGRÁFICOS**

---

EDAD: \_\_\_\_\_ años FECHA DE NACIMIENTO: \_\_\_/\_\_\_/\_\_\_

SEXO: ① Mujer; ② Varón

RAZA: ① Caucasiano

② Negro africano

③ Negro caribeño

④ Hispano

⑤ Otros, especificar: \_\_\_\_\_

ESTADO CIVIL: ① Soltero

② Casado

③ Separado/Divorciado

④ Viudo

⑤ Otros, especificar → \_\_\_\_\_

TIPO DE CONVIVENCIA: ① Solo/a

② Con Pareja

③ Con esposo/a

④ Con hijos

⑤ Familia de origen ( padre, madre, ambos)

⑥ Asistida

⑦ Otros, especificar → \_\_\_\_\_

NIVEL EDUCACIONAL: ① Superiores completos

② Secundarios (ESO o equivalente) completos

③ Primarios (Primario o equivalente) completos

④ Primarios incompletos

⑤ Sin estudios / analfabeto-a

Nº de años estudiados: \_\_\_\_\_ años

SITUACIÓN PROFESIONAL ACTUAL : ① Ama de casa/nunca ha tenido profesión

② Trabajador activo

③ Paro con subsidio

④ Paro sin subsidio

⑤ Incapacidad transitoria

⑥ Incapacidad total/gran invalidez

⑦ Pensionista jubilado

⑧ Otros \_\_\_\_\_



**CONSUMO DE DROGAS:**

	Consumo actual (último mes)		Diagnóstico de abuso o dependencia según DSM-IV		Consumo actual según análisis toxicológico		
	Sí	No	Sí	No	Sí	No	NE*
Tabaco							
Alcohol							
Cannabioides							
Anfetamina							
Opioides							
Cocaína							
Otros: _____							

*Fecha del último análisis:* \_\_ / \_\_ / \_\_

Si fumador, consumo diario: \_\_\_\_\_ cigarros/día

**Datos antropométricos:**      Peso: \_\_\_\_\_ kg      Talla: \_\_\_\_\_ cm

**TRATAMIENTO ADMINISTRADO**

*Fecha instauración tratamiento antipsicótico:* \_\_ / \_\_ / \_\_

**MEDICACIÓN ANTIPSICÓTICA ADMINISTRADA A PARTIR DE VISITA BASAL:**

Medicación	Dosis (mg/día)
_____	_____
_____	_____
_____	_____

**OTRA MEDICACIÓN ADMINISTRADA A PARTIR DE VISITA BASAL:**

Medicación	Dosis (mg/día)
_____	_____
_____	_____
_____	_____

**TRATAMIENTO PSICOFARMACOLÓGICO PREVIO:**

¿Había recibido el paciente algún tratamiento psicofarmacológico previo?

o No

o Sí, especificar:

Psicofármaco	Dosis media (mg/día)	Duración (semanas)
_____	_____	_____
_____	_____	_____
_____	_____	_____

## EVALUACIONES PSIQUIÁTRICAS

### ESCALA DE SÍNDROME POSITIVO Y NEGATIVO DE LA ESQUIZOFRENIA (PANSS)

**INSTRUCCIONES:** Marque con un círculo la evaluación apropiada para cada ítem de la entrevista clínica que se especifica a continuación. Consulte el manual de evaluación anexo para las definiciones de los ítems, la descripción de los puntos concretos y el procedimiento para la puntuación.

*1= ausente; 2= mínimo; 3= leve; 4=moderado; 5= moderadamente grave; 6= grave; 7= extremo.*

**1) SUBESCALA POSITIVA**

P1	Delirios .....	1	2	3	4	5	6	7
P2	Desorganización conceptual .....	1	2	3	4	5	6	7
P3	Comportamiento alucinatorio .....	1	2	3	4	5	6	7
P4	Excitación .....	1	2	3	4	5	6	7
P5	Grandiosidad.....	1	2	3	4	5	6	7
P6	Susplicacia .....	1	2	3	4	5	6	7
P7	Hostilidad.....	1	2	3	4	5	6	7

SUBTOTAL

**2) SUBESCALA NEGATIVA**

N1	Embotamiento afectivo .....	1	2	3	4	5	6	7
N2	Retraimiento emocional .....	1	2	3	4	5	6	7
N3	Contacto pobre .....	1	2	3	4	5	6	7
N4	Retraimiento social .....	1	2	3	4	5	6	7
N5	Dificultad en el pensamiento abstracto.....	1	2	3	4	5	6	7
N6	Espontaneidad y fluidez de conversación .....	1	2	3	4	5	6	7
N7	Pensamiento estereotipado.....	1	2	3	4	5	6	7

SUBTOTAL

**3) SUBESCALA DE PSICOPATOLOGIA GENERAL**

G1	Preocupaciones somáticas .....	1	2	3	4	5	6	7
G2	Ansiedad .....	1	2	3	4	5	6	7
G3	Sentimientos de culpa.....	1	2	3	4	5	6	7
G4	Tensión .....	1	2	3	4	5	6	7
G5	Manierismos y posturas .....	1	2	3	4	5	6	7
G6	Depresión.....	1	2	3	4	5	6	7
G7	Retardo motor .....	1	2	3	4	5	6	7
G8	Falta de colaboración.....	1	2	3	4	5	6	7
G9	Contenidos inusuales del pensamiento .....	1	2	3	4	5	6	7
G10	Desorientación .....	1	2	3	4	5	6	7
G11	Atención deficiente.....	1	2	3	4	5	6	7
G12	Ausencia de juicio e "insight" .....	1	2	3	4	5	6	7
G13	Trastornos de la volición .....	1	2	3	4	5	6	7
G14	Control deficiente de impulsos .....	1	2	3	4	5	6	7
G15	Preocupación .....	1	2	3	4	5	6	7

G16 Evitación social activa ..... 1 2 3 4 5 6 7

SUBTOTAL

**PUNTUACION TOTAL** (suma de los 3 subtotales)**ESCALA MONTGOMERY-ASBERG PARA LA DEPRESIÓN (MADRS)****1. Tristeza aparente**

El paciente expresa abatimiento, tristeza y desesperación a través de la voz, el gesto y la expresión mímica.

Evalúese en función de la gravedad e incapacidad para ser animado.

0. No tristeza
- 1.
2. Parece desanimado, pero se anima fácilmente
- 3.
4. Parece triste e infeliz la mayor parte del tiempo
- 5.
6. Parece desgraciado todo el tiempo. Extremadamente abatido

**2. Tristeza expresada**

El enfermo aporta datos verbales sobre su humor deprimido, independientemente de que lo exprese por su apariencia o no. Incluye ánimo bajo, abatimiento, desesperanza, sentimiento de desamparo.

Evalúese de acuerdo con la intensidad, duración e influenciabilidad del humor por las circunstancias:

0. Tristeza ocasional en consonancia con las circunstancias ambientales
- 1.
2. Tristeza que cede (se anima) sin dificultad
- 3.
4. Sentimientos de tristeza o abatimiento profundo, pero el humor es todavía ligeramente influenciable por las circunstancias externas
- 5.
6. Continua e invariable tristeza, abatimiento, sentimiento de desgracia

**3. Tensión interior**

El paciente expresa sentimientos de malestar indefinido, nerviosismo, confusión interna, tensión mental que se vuelve pánico, temor o angustia.

Evalúese de acuerdo con la intensidad, frecuencia o duración de la tranquilidad perdida:

0. Placidez aparente. Sólo manifiesta tensión interna
- 1.
2. Ocasionales sentimientos de nerviosismo y malestar indefinido
- 3.
4. Continuos sentimientos de tensión interna o sentimientos de pánico que aparecen intermitentemente y que el paciente puede dominar, pero con dificultad
- 5.
6. Angustia o temor no mitigado. Pánico abrumador

**4. Sueño reducido**

El paciente expresa una reducción en la duración o en la profundidad de su sueño en comparación a cómo duerme cuando se encuentra bien.

0. Sueño como los normales

- 1.
2. Leve dificultad para dormir o sueño ligeramente reducido: sueño ligero
- 3.
4. Sueño reducido o interrumpido al menos durante 2 horas
- 5.
6. Menos de 2 o 3 horas de sueño

**5. Disminución del apetito**

El paciente expresa una reducción del apetito respecto al que tiene cuando se encuentra bien.

Evalúese la pérdida del deseo de alimento o la necesidad de forzarse uno mismo a comer.

0. Apetito normal o aumentado
- 1.
2. Apetito ligeramente disminuido
- 3.
4. No apetito. Los alimentos saben mal
- 5.
6. Necesidad de persuasión para comer

**6. Dificultades de concentración**

El paciente expresa dificultades para mantener su propio pensamiento o para concentrarse.

Evalúese de acuerdo con la intensidad, frecuencia y grado de la incapacidad producida.

0. Ninguna dificultad de concentración
- 1.
2. Dificultades ocasionales para mantener los propios pensamientos
- 3.
4. Dificultades en la concentración y el mantenimiento del pensamiento que reduce la capacidad para mantener una conversación o leer
- 5.
6. Incapacidad para leer o conversar sin gran dificultad

**7. Laxitud.Abulia**

El paciente expresa o presenta dificultad para iniciar y ejecutar las actividades diarias.

0. Apenas hay dificultades para iniciar las tareas.No hay inactividad
- 1.
2. Dificultad para iniciar actividades
- 3.
4. Dificultades para comenzar sus actividades rutinarias, que exigen un esfuerzo para ser llevadas a cabo
- 5.
6. Completa laxitud, incapacidad para hacer nada sin ayuda

**8. Incapacidad para sentir**

El paciente expresa un reducido interés por lo que le rodea o las actividades que normalmente producían placer. Reducción de la capacidad para reaccionar adecuadamente a circunstancias o personas.

0. Interés normal por las cosas y la gente
- 1.
2. Reducción de la capacidad para disfrutar de los intereses habituales
- 3.
4. Pérdida de interés en lo que le rodea, incluso con los amigos o conocidos
- 5.
6. Manifiesta la experiencia subjetiva de estar emocionalmente paralizado, anesthesiado, con incapacidad para sentir placer o desagrado, y con una falta absoluta y/o dolorosa pérdida de sentimientos hacia parientes y amigos

**9. Pensamientos pesimistas**



--

El paciente expresa pensamiento de culpa, autorreproche, remordimiento, inferioridad, ideas de ruina, ideas de pecado.

0. No hay pensamientos pesimistas
- 1.
2. Ideas fluctuantes de fallos, autorreproches o autodepreciaciones
- 3.
4. Persistentes autoacusaciones o ideas definidas, pero todavía razonables de culpabilidad o pecado. Pesimismo
- 5.
6. Ideas irrefutables de ruina, remordimiento o pecado irremediable. Autoacusaciones absurdas e irreducibles

**10. Ideación suicida**

El paciente expresa la idea de que la vida no merece vivirse, de que una muerte natural sería bienvenida, o manifiesta ideas o planes suicidas.

0. Se alegra de vivir. Toma la vida como viene
- 1.
2. Cansado de vivir. Ideas suicidas fugaces
- 3.
4. Manifiesta deseos de muerte, ideas suicidas frecuentes. El suicidio es considerado como una solución, pero no se han elaborado planes o hecho intención
- 5.
6. Planes explícitos de suicidio cuando exista una oportunidad. Activa preparación para el suicidio

<b><i>PUNTUACIÓN TOTAL</i></b>		
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**ESCALA DE YOUNG PARA LA EVALUACIÓN DE LA MANÍA (YMRS)**

**1. Euforia**

- Ausente
- Dudosa o leve
- Hipertimia subjetiva clara, optimista, seguro; alegre; aún adecuado
- Hipertimia; humor ya inadecuado
- Euforia, risa inapropiada; canta

**2. Aumento de la actividad motora, energía**

- Ausente
- Aumentada subjetivamente
- Animado; aumento de la gesticulación
- Energía excesiva; hiperactivo a veces; inquieto (aún se puede contener)
- Excitación motora; hiperactividad continua (no se puede contener)

**3. Interés sexual**

- Normal, no aumentado
- Aumento ligero o posible
- Incremento definido al preguntarle
- Interés sexual espontáneo; habla de temas sexuales; hipersexualidad expresada sin preguntarle
- Actos sexuales (hacia otros pacientes, trabajadores del centro o entrevistador)

**4. Sueño**

- Refiere sueño conservado
- Sueño reducido en menos de 1 hora
- Sueño reducido en más de 1 hora
- Refiere disminución en la necesidad de sueño
- Niega necesidad de dormir

**5. Irritabilidad**

- Ausente
- Subjetivamente aumentada
- Irritable episódicamente durante la entrevista; episodios recientes de estar molesto o enfadado en la planta
- Irritable frecuentemente durante la entrevista; cortante, brusco todo el tiempo
- Hostil, falta de cooperación; entrevista imposible

**6. Discurso (ritmo y cantidad)**

- No aumento
- Se siente hablador
- Aumento del ritmo y la cantidad a veces, verborreico a veces
- Verborrea. Aumento importante del ritmo y la cantidad; difícil de interrumpir
- Verborrea ininterrumpible, discurso continuo

**7. Trastorno del lenguaje y del pensamiento**

- Ausente
- Circunstancial; ligeramente distraible; pensamientos rápidos
- Distraible; pierde el hilo conductor; cambia de tema con frecuencia; pensamientos rápidos
- Fuga de ideas; tangencialidad; dificultad para seguirle; hace rimas, ecolalia
- Incoherencia; comunicación imposible

**8. Contenido del pensamiento**

- Normal
- Planes cuestionables, nuevos intereses
- Proyecto(s) especial(es); hiperreligioso
- Ideas de grandeza o paranoides; ideas de referencia
- Delirios; alucinaciones

**9. Conducta alterada-agresiva**

- Ausente, coopera
- Sarcástico, ruidoso a veces, alerta, vigilante
- Demandante; amenazas en planta
- Amenaza al entrevistador; grita; entrevista difícil
- Agresivo; destructivo; entrevista imposible

**10. Vestido**

- Vestido y aseo apropiado
- Mínimamente descuidado
- Poco cuidado personal; moderadamente desaliñado en el vestir; exceso de ropa
- Descuido en el vestir; semivestido; maquillaje estridente
- Totalmente desaliñado; decorado; maquillaje extraño

**11. Insight. Conciencia de si mismo**

- Presente; admite la enfermedad; está de acuerdo con la necesidad de tratamiento
- Duda de la enfermedad aunque la admite poco posible
- Admite cambio en la conducta, aunque niega la enfermedad
- Niega todo cambio de conducta

**PUNTUACIÓN TOTAL**

Debe responder todas las preguntas de esta escala incluso cuando en el paciente todos los síntomas de manía estén ausentes

<b>ESCALA SUMD (ABREVIADA)</b>
--------------------------------

1. Conciencia de poseer un desorden mental
  0. Ítem no relevante
  1. Conciencia
  - 2.
  3. Conciencia intermedia
  - 4.
  5. No hay conciencia
2. Conciencia sobre los efectos de la medicación
  0. Ítem no relevante
  1. Conciencia
  - 2.
  3. Conciencia intermedia
  - 4.
  5. No hay conciencia
3. Conciencia de las consecuencias de su desorden mental
  0. Ítem no relevante
  1. Conciencia
  - 2.
  3. Conciencia intermedia
  - 4.
  5. No hay conciencia
4. Conciencia de poseer alucinaciones (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
5. Conciencia de poseer delirios (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
6. Conciencia de poseer trastornos del pensamiento (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
7. Conciencia de poseer embotamiento afectivo (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
8. Conciencia de poseer anhedonia (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
9. Conciencia de poseer asociabilidad (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_

**PUNTUACIONES**

Suma total ítems conciencia (4-9)	Número total de ítems relevantes	Puntuación
_____	/ _____	= _____

Suma total ítems	Número total de	Puntuación
------------------	-----------------	------------

Atribución (4-9)

ítems relevantes

\_\_\_\_\_ / \_\_\_\_\_ = \_\_\_\_\_

**ESCALA DE COGNICIÓN SOCIAL PARA LA PSICOSIS (GEOPTE)**

INSTRUCCIONES: Marque con un círculo la evaluación apropiada para cada ítem de la entrevista clínica que se especifica a continuación.

*1=no; 2=un poco; 3=regular; 4=bastante; 5=mucho*

1	¿Tiene dificultad para prestar atención?	1	2	3	4	5
2	¿Tiene dificultad para seguir una conversación en la que participan varias personas?	1	2	3	4	5
3	¿Le cuesta aprender cosas nuevas?	1	2	3	4	5
4	¿Se le olvidan los encargos, tareas o recados?	1	2	3	4	5
5	¿Cuándo tienen que hablar con alguien le faltan las pasabras?	1	2	3	4	5
6	¿Le cuesta entender de qué va una película?	1	2	3	4	5
7	¿Le cuesta encontrar el sentido de una conversación?	1	2	3	4	5
8	¿Tiene dificultad para reconocer las emociones de los otros?	1	2	3	4	5
9	Cuando está en un grupo, ¿le suelen decir que interpreta mal las actitudes, miradas o gestos de los demás?	1	2	3	4	5
10	¿Se siente muy sensible a las miradas, palabras o gestos de los otros?	1	2	3	4	5
11	Si está solo en casa y surge algún problema (p.ej., se estropea un electrodoméstico), ¿le resulta difícil encontrar la solución??	1	2	3	4	5
12	¿Le cuesta mantener la higiene personal (estar limpio y aseado)?	1	2	3	4	5
13	¿Le cuesta hacer planes para el fin de semana?	1	2	3	4	5
14	¿Tiene dificultades para hacer amistades?	1	2	3	4	5
15	¿Está insatisfecho en general con su vida sexual?	1	2	3	4	5



**ESCALA DE EVALUACIÓN DE ACTIVIDAD GLOBAL (GAF)**

Hay que considerar la actividad psicológica, social y laboral a lo largo de un hipotético *continuum* de salud-enfermedad. No hay que incluir alteraciones de la actividad debidas a limitaciones físicas (o ambientales). Utilice los niveles intermedios cuando resulte apropiado.

- 100 | *Actividad satisfactoria en una amplia gama de actividades, nunca parece superado por los problemas de su vida, es valorado por los demás a causa de sus abundantes cualidades positivas. Sin síntomas.*  
91
- 90 | *Síntomas ausentes o mínimos (p. ej., ligera ansiedad antes de un examen), buena actividad en todas las áreas, interesado e implicado en una amplia gama de actividades, socialmente eficaz, generalmente satisfecho de su vida, sin más preocupaciones o problemas que los cotidianos (p. ej., una discusión ocasional con miembros de la familia).*  
81
- 80 | *Si existen síntomas, son transitorios y constituyen reacciones esperables ante agentes estresantes psicosociales (p. ej., dificultades para concentrarse tras una discusión familiar); sólo existe una ligera alteración de la actividad social, laboral o escolar (p. ej., descenso temporal del rendimiento escolar).*  
71
- 70 | *Algunos síntomas leves (p. ej., humor depresivo e insomnio ligero) o alguna dificultad en la actividad social, laboral o escolar (p. ej., hacer novillos ocasionalmente o robar algo en casa), pero en general funciona bastante bien, tiene algunas relaciones interpersonales significativas.*  
61
- 60 | *Síntomas moderados (p. ej., afecto aplanado y lenguaje circunstancial, crisis de angustia ocasionales) o dificultades moderadas en la actividad social, laboral o escolar (p. ej., pocos amigos, conflictos con compañeros de trabajo o de escuela).*  
51
- 50 | *Síntomas graves (p. ej., ideación suicida, rituales obsesivos graves, robos en tiendas) o cualquier alteración grave en la actividad social, laboral o escolar (p. ej., sin amigos, incapaz de mantenerse en un empleo).*  
41
- 40 | *Una alteración de la verificación de la realidad o de la comunicación (p. ej., el lenguaje es a veces ilógico, oscuro o irrelevante) o alteración importante en varias áreas como el trabajo escolar, las relaciones familiares, el juicio, el pensamiento o el estado de ánimo (p. ej., un hombre depresivo evita a sus amigos, abandona la familia y es incapaz de trabajar; un niño golpea frecuentemente a niños más pequeños, es desafiante en casa y deja de acudir a la escuela).*  
31
- 30 | *La conducta está considerablemente influida por ideas delirantes o existe una alteración grave de la comunicación o el juicio (p. ej., a veces es incoherente, actúa de manera claramente inapropiada, preocupación suicida) o incapacidad para funcionar en casi todas las áreas (p. ej., permanece en la cama todo el día; sin trabajo, vivienda o amigos).*  
21
- 20 | *Algún peligro de causar lesiones a otros o a sí mismo (p. ej., intentos de suicidio sin una expectativa manifiesta de muerte; frecuentemente violento; excitación maníaca) u ocasionalmente deja de mantener la higiene personal mínima (p. ej., con manchas de excrementos) o alteración importante de la comunicación (p. ej., muy incoherente o mudo).*  
11
- 10 | *Peligro persistente de lesionar gravemente a otros o a sí mismo (p. ej., violencia recurrente) o incapacidad persistente para mantener la higiene personal mínima o acto suicida grave con expectativa manifiesta de muerte.*  
1
- 0 | *Información inadecuada.*

**PUNTUACIÓN TOTAL**

## Visita Mes 2

Fecha: \_\_\_/\_\_\_/\_\_\_

### ¿CONTINÚA EL PACIENTE EN EL ESTUDIO?

o Sí o No, fecha de abandono: \_\_\_/\_\_\_/\_\_\_ (RECUERDE rellenar hoja de finalización)

Datos antropométricos: Peso: \_\_\_\_\_ kg Talla: \_\_\_\_\_ cm

### DATOS CLÍNICOS DEL SEGUIMIENTO

#### ¿Ha sido hospitalizado o dado de alta el paciente desde la visita anterior?

o No o Sí, especificar ⇨

① Hospitalizado	② Alta
Fecha ingreso ___/___/___ ___/___/___	Fecha alta ___/___/___ ___/___/___

#### ¿Ha asistido con regularidad a las citas clínicas prescritas por su clínico?

- ① <25% de las veces                      ③ entre el 50% y 75% de las veces  
 ② entre el 25% y 50% de las veces      ④ entre el 75% y 100% de las veces

### ENFERMEDADES MÉDICAS CONCOMITANTES:

#### ¿Ha padecido el paciente alguna otra enfermedad concomitante desde la visita anterior?

o No o Sí, especificar enfermedad ⇨ \_\_\_\_\_

### TRATAMIENTO ADMINISTRADO

#### MEDICACIÓN ANTIPSICÓTICA:

Medicación	Dosis (mg/día)
_____	_____
_____	_____

Valore el cumplimiento del tratamiento; “el paciente está tomando la medicación.....

- |                                   |                                    |
|-----------------------------------|------------------------------------|
| ① <25% de las veces               | ③ entre el 50% y 75% de las veces  |
| ② entre el 25% y 50% de las veces | ④ entre el 75% y 100% de las veces |

¿Se cambia alguno de los otros tratamientos que el paciente tenía pautados desde la anterior visita?

Sin cambios en el tratamiento

Retirada o inicio de algún tratamiento ⇒ especificar tratamiento que se cambia, tipo de cambio y motivo:⇒

⇒ Tratamiento que se cambia	Tipo cambio			Motivo del cambio		
	Inicio	Retirada	Ajuste de dosis	Respuesta insuficiente o falta de eficacia	Reacciones adversas	Otros
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

**ESCALA AUTO-APLICADA MORINSKI-GREEN**

*Lea detenidamente cada una de las frases siguientes y decida si para usted son verdaderas o falsas. Las frases se refieren únicamente a la medicación psiquiátrica que toma actualmente.*

*Si una frase es verdadera o en su mayor parte verdadera, marque la casilla correspondiente a «verdadera» con una X. Si una frase es falsa o en su mayor parte falsa, marque la casilla correspondiente a «falsa». Si desea cambiar alguna respuesta, tache la respuesta errónea y marque con un círculo la respuesta correcta.*

	VERDADERO	FALSO
1. Alguna vez he olvidado tomar la medicación.....	①	②
2. Tomo la medicación a la hora indicada .....	①	②
3. Cuando me encuentro bien, dejo de tomar la medicación .....	①	②
4. Si alguna vez me encuentro mal, dejo de tomarla .....	①	②

**ESCALA AUTO-APLICADA DAI DE AWAD**

	VERDADERO	FALSO
1. Para mí lo bueno de la medicación supera lo malo .....	①	②
2. Me siento raro/a, "como un zombie" con la medicación .....	①	②
3. Tomo medicación por decisión mía.....	①	②
4. La medicación hace que me sienta más relajado/a .....	①	②
5. La medicación hace que me sienta cansado/a y lento/a.....	①	②



- |   |   |   |
|---|---|---|
| 6. Tomo medicación sólo cuando estoy enfermo/a.....                                   | ① | ② |
| 7. Me siento más normal con la medicación.....  | ① | ② |
| 8. Es antinatural para mi mente y mi cuerpo estar controlado/a por medicaciones ..... | ① | ② |
| 9. Mis pensamientos son más claros con la medicación .....                            | ① | ② |
| 10. Por estar con medicación puedo prevenir caer enfermo.....                         | ① | ② |

## **EVALUACIONES PSIQUIÁTRICAS**

### **ESCALA DE SÍNDROME POSITIVO Y NEGATIVO DE LA ESQUIZOFRENIA (PANSS)**

**INSTRUCCIONES:** Marque con un círculo la evaluación apropiada para cada ítem de la entrevista clínica que se especifica a continuación. Consulte el manual de evaluación anexo para las definiciones de los ítems, la descripción de los puntos concretos y el procedimiento para la puntuación.

*1= ausente; 2= mínimo; 3= leve; 4=moderado; 5= moderadamente grave; 6= grave; 7= extremo.*

**1) SUBESCALA POSITIVA**

P1	Delirios .....	1	2	3	4	5	6	7
P2	Desorganización conceptual .....	1	2	3	4	5	6	7
P3	Comportamiento alucinatorio .....	1	2	3	4	5	6	7
P4	Excitación .....	1	2	3	4	5	6	7
P5	Grandiosidad.....	1	2	3	4	5	6	7
P6	Susplicacia .....	1	2	3	4	5	6	7
P7	Hostilidad.....	1	2	3	4	5	6	7

SUBTOTAL

**2) SUBESCALA NEGATIVA**

N1	Embotamiento afectivo .....	1	2	3	4	5	6	7
N2	Retraimiento emocional.....	1	2	3	4	5	6	7
N3	Contacto pobre.....	1	2	3	4	5	6	7
N4	Retraimiento social .....	1	2	3	4	5	6	7
N5	Dificultad en el pensamiento abstracto.....	1	2	3	4	5	6	7
N6	Espontaneidad y fluidez de conversación .....	1	2	3	4	5	6	7
N7	Pensamiento estereotipado.....	1	2	3	4	5	6	7

SUBTOTAL

**3) SUBESCALA DE PSICOPATOLOGIA GENERAL**

G1	Preocupaciones somáticas .....	1	2	3	4	5	6	7
G2	Ansiedad .....	1	2	3	4	5	6	7
G3	Sentimientos de culpa.....	1	2	3	4	5	6	7
G4	Tensión .....	1	2	3	4	5	6	7
G5	Manierismos y posturas .....	1	2	3	4	5	6	7
G6	Depresión.....	1	2	3	4	5	6	7
G7	Retardo motor .....	1	2	3	4	5	6	7
G8	Falta de colaboración.....	1	2	3	4	5	6	7
G9	Contenidos inusuales del pensamiento .....	1	2	3	4	5	6	7

**Visita Mes 2**

Nº de paciente

G10	Desorientación .....	1	2	3	4	5	6	7
G11	Atención deficiente.....	1	2	3	4	5	6	7
G12	Ausencia de juicio e "insight".....	1	2	3	4	5	6	7
G13	Trastornos de la volición .....	1	2	3	4	5	6	7
G14	Control deficiente de impulsos .....	1	2	3	4	5	6	7
G15	Preocupación .....	1	2	3	4	5	6	7
G16	Evitación social activa .....	1	2	3	4	5	6	7

SUBTOTAL

**PUNTUACION TOTAL** (*suma de los 3 subtotales*)

**ESCALA MONTGOMERY-ASBERG PARA LA DEPRESIÓN (MADRS)****1. Tristeza aparente**

El paciente expresa abatimiento, tristeza y desesperación a través de la voz, el gesto y la expresión mímica.

Evalúese en función de la gravedad e incapacidad para ser animado.

0. No tristeza
- 1.
2. Parece desanimado, pero se anima fácilmente
- 3.
4. Parece triste e infeliz la mayor parte del tiempo
- 5.
6. Parece desgraciado todo el tiempo. Extremadamente abatido

**2. Tristeza expresada**

El enfermo aporta datos verbales sobre su humor deprimido, independientemente de que lo exprese por su apariencia o no. Incluye ánimo bajo, abatimiento, desesperanza, sentimiento de desamparo.

Evalúese de acuerdo con la intensidad, duración e influenciabilidad del humor por las circunstancias:

0. Tristeza ocasional en consonancia con las circunstancias ambientales
- 1.
2. Tristeza que cede (se anima) sin dificultad
- 3.
4. Sentimientos de tristeza o abatimiento profundo, pero el humor es todavía ligeramente influenciable por las circunstancias externas
- 5.
6. Continua e invariable tristeza, abatimiento, sentimiento de desgracia

**3. Tensión interior**

El paciente expresa sentimientos de malestar indefinido, nerviosismo, confusión interna, tensión mental que se vuelve pánico, temor o angustia.

Evalúese de acuerdo con la intensidad, frecuencia o duración de la tranquilidad perdida:

0. Placidez aparente. Sólo manifiesta tensión interna
- 1.
2. Ocasionales sentimientos de nerviosismo y malestar indefinido
- 3.
4. Continuos sentimientos de tensión interna o sentimientos de pánico que aparecen intermitentemente y que el paciente puede dominar, pero con dificultad
- 5.
6. Angustia o temor no mitigado. Pánico abrumador

**4. Sueño reducido**

El paciente expresa una reducción en la duración o en la profundidad de su sueño en comparación a cómo duerme cuando se encuentra bien.

0. Sueño como los normales
- 1.
2. Leve dificultad para dormir o sueño ligeramente reducido: sueño ligero
- 3.
4. Sueño reducido o interrumpido al menos durante 2 horas
- 5.
6. Menos de 2 o 3 horas de sueño

--

**5. Disminución del apetito**

El paciente expresa una reducción del apetito respecto al que tiene cuando se encuentra bien. Evalúese la pérdida del deseo de alimento o la necesidad de forzarse uno mismo a comer.

0. Apetito normal o aumentado
- 1.
2. Apetito ligeramente disminuido
- 3.
4. No apetito. Los alimentos saben mal
- 5.
6. Necesidad de persuasión para comer

**6. Dificultades de concentración**

El paciente expresa dificultades para mantener su propio pensamiento o para concentrarse. Evalúese de acuerdo con la intensidad, frecuencia y grado de la incapacidad producida.

0. Ninguna dificultad de concentración
- 1.
2. Dificultades ocasionales para mantener los propios pensamientos
- 3.
4. Dificultades en la concentración y el mantenimiento del pensamiento que reduce la capacidad para mantener una conversación o leer
- 5.
6. Incapacidad para leer o conversar sin gran dificultad

**7. Laxitud.Abulia**

El paciente expresa o presenta dificultad para iniciar y ejecutar las actividades diarias.

0. Apenas hay dificultades para iniciar las tareas.No hay inactividad
- 1.
2. Dificultad para iniciar actividades
- 3.
4. Dificultades para comenzar sus actividades rutinarias, que exigen un esfuerzo para ser llevadas a cabo
- 5.
6. Completa laxitud, incapacidad para hacer nada sin ayuda

**8. Incapacidad para sentir**

El paciente expresa un reducido interés por lo que le rodea o las actividades que normalmente producían placer. Reducción de la capacidad para reaccionar adecuadamente a circunstancias o personas.

0. Interés normal por las cosas y la gente
- 1.
2. Reducción de la capacidad para disfrutar de los intereses habituales
- 3.
4. Pérdida de interés en lo que le rodea, incluso con los amigos o conocidos
- 5.
6. Manifiesta la experiencia subjetiva de estar emocionalmente paralizado, anestesiado, con incapacidad para sentir placer o desagrado, y con una falta absoluta y/o dolorosa pérdida de sentimientos hacia parientes y amigos

**9. Pensamientos pesimistas**

El paciente expresa pensamiento de culpa, autorreproche, remordimiento, inferioridad, ideas de ruina, ideas de pecado.

0. No hay pensamientos pesimistas
- 1.
2. Ideas fluctuantes de fallos, autorreproches o autodepreciaciones
- 3.
4. Persistentes autoacusaciones o ideas definidas, pero todavía razonables de culpabilidad o pecado. Pesimismo

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- 5.
6. Ideas irrefutables de ruina, remordimiento o pecado irremediable.  
Autoacusaciones absurdas e irreducibles

**10. Ideación suicida**

El paciente expresa la idea de que la vida no merece vivirse, de que una muerte natural sería bienvenida, o manifiesta ideas o planes suicidas.

0. Se alegra de vivir. Toma la vida como viene
- 1.
2. Cansado de vivir. Ideas suicidas fugaces
- 3.
4. Manifiesta deseos de muerte, ideas suicidas frecuentes. El suicidio es considerado como una solución, pero no se han elaborado planes o hecho intención
- 5.
6. Planes explícitos de suicidio cuando exista una oportunidad. Activa preparación para el suicidio

<b><i>PUNTUACIÓN TOTAL</i></b>		
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**ESCALA DE YOUNG PARA LA EVALUACIÓN DE LA MANÍA (YMRS)**

**1. Euforia**

- Ausente
- Dudosa o leve
- Hipertimia subjetiva clara, optimista, seguro; alegre; aún adecuado
- Hipertimia; humor ya inadecuado
- Euforia, risa inapropiada; canta

**2. Aumento de la actividad motora, energía**

- Ausente
- Aumentada subjetivamente
- Animado; aumento de la gesticulación
- Energía excesiva; hiperactivo a veces; inquieto (aún se puede contener)
- Excitación motora; hiperactividad continua (no se puede contener)

**3. Interés sexual**

- Normal, no aumentado
- Aumento ligero o posible
- Incremento definido al preguntarle
- Interés sexual espontáneo; habla de temas sexuales; hipersexualidad expresada sin preguntarle
- Actos sexuales (hacia otros pacientes, trabajadores del centro o entrevistador)

**4. Sueño**

- Refiere sueño conservado
- Sueño reducido en menos de 1 hora
- Sueño reducido en más de 1 hora
- Refiere disminución en la necesidad de sueño
- Niega necesidad de dormir

**5. Irritabilidad**

- Ausente
- Subjetivamente aumentada
- Irritable episódicamente durante la entrevista; episodios recientes de estar molesto o enfadado en la planta
- Irritable frecuentemente durante la entrevista; cortante, brusco todo el tiempo
- Hostil, falta de cooperación; entrevista imposible

**6. Discurso (ritmo y cantidad)**

- No aumento
- Se siente hablador
- Aumento del ritmo y la cantidad a veces, verborreico a veces
- Verborrea. Aumento importante del ritmo y la cantidad; difícil de interrumpir
- Verborrea ininterrumpible, discurso continuo

**7. Trastorno del lenguaje y del pensamiento**

- Ausente
- Circunstancial; ligeramente distraible; pensamientos rápidos
- Distraible; pierde el hilo conductor; cambia de tema con frecuencia; pensamientos rápidos
- Fuga de ideas; tangencialidad; dificultad para seguirle; hace rimas, ecolalia
- Incoherencia; comunicación imposible

**8. Contenido del pensamiento**

- Normal
- Planes cuestionables, nuevos intereses
- Proyecto(s) especial(es); hiperreligioso
- Ideas de grandeza o paranoides; ideas de referencia
- Delirios; alucinaciones

**9. Conducta alterada-agresiva**

- Ausente, coopera
- Sarcástico, ruidoso a veces, alerta, vigilante
- Demandante; amenazas en planta
- Amenaza al entrevistador; grita; entrevista difícil
- Agresivo; destructivo; entrevista imposible

**10. Vestido**

- Vestido y aseo apropiado
- Mínimamente descuidado
- Poco cuidado personal; moderadamente desaliñado en el vestir; exceso de ropa
- Descuido en el vestir; semivestido; maquillaje estridente
- Totalmente desaliñado; decorado; maquillaje extraño

**11. Insight. Conciencia de sí mismo**

- Presente; admite la enfermedad; está de acuerdo con la necesidad de tratamiento
- Duda de la enfermedad aunque la admite poco posible
- Admite cambio en la conducta, aunque niega la enfermedad
- Niega todo cambio de conducta

**PUNTUACIÓN TOTAL**

Debe responder todas las preguntas de esta escala incluso cuando en el paciente todos los síntomas de manía estén ausentes

**ESCALA SUMD (ABREVIADA)**

- 1. Conciencia de poseer un desorden mental
  - 0. Ítem no relevante
  - 1. Conciencia
  - 2.
  - 3. Conciencia intermedia
  - 4.
  - 5. No hay conciencia
- 2. Conciencia sobre los efectos de la medicación
  - 0. Ítem no relevante
  - 1. Conciencia
  - 2.
  - 3. Conciencia intermedia
  - 4.
  - 5. No hay conciencia
- 3. Conciencia de las consecuencias de su desorden mental
  - 0. Ítem no relevante
  - 1. Conciencia
  - 2.
  - 3. Conciencia intermedia
  - 4.
  - 5. No hay conciencia
- 4. Conciencia de poseer alucinaciones (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
- 5. Conciencia de poseer delirios (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
- 6. Conciencia de poseer trastornos del pensamiento (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
- 7. Conciencia de poseer embotamiento afectivo (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
- 8. Conciencia de poseer anhedonia (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
- 9. Conciencia de poseer asociabilidad (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_

**PUNTUACIONES**

Suma total ítems conciencia (4-9)		Número total de ítems relevantes		Puntuación
_____	/	_____	=	_____

Suma total ítems Atribución (4-9)		Número total de ítems relevantes		Puntuación
_____	/	_____	=	_____

**ESCALA DE COGNICIÓN SOCIAL PARA LA PSICOSIS (GEOPTE)**

INSTRUCCIONES: Marque con un círculo la evaluación apropiada para cada ítem de la entrevista clínica que se especifica a continuación.

*1=no; 2=un poco; 3=regular; 4=bastante; 5=mucho*

1	¿Tiene dificultad para prestar atención?	1	2	3	4	5
2	¿Tiene dificultad para seguir una conversación en la que participan varias personas?	1	2	3	4	5
3	¿Le cuesta aprender cosas nuevas?	1	2	3	4	5
4	¿Se le olvidan los encargos, tareas o recados?	1	2	3	4	5
5	¿Cuándo tienen que hablar con alguien le faltan las pasabras?	1	2	3	4	5
6	¿Le cuesta entender de qué va una película?	1	2	3	4	5
7	¿Le cuesta encontrar el sentido de una conversación?	1	2	3	4	5
8	¿Tiene dificultad para reconocer las emociones de los otros?	1	2	3	4	5
9	Cuando está en un grupo, ¿le suelen decir que interpreta mal las actitudes, miradas o gestos de los demás?	1	2	3	4	5
10	¿Se siente muy sensible a las miradas, palabras o gestos de los otros?	1	2	3	4	5
11	Si está solo en casa y surge algún problema (p.ej., se estropea un electrodoméstico), ¿le resulta difícil encontrar la solución??	1	2	3	4	5
12	¿Le cuesta mantener la higiene personal (estar limpio y aseado)?	1	2	3	4	5
13	¿Le cuesta hacer planes para el fin de semana?	1	2	3	4	5
14	¿Tiene dificultades para hacer amistades?	1	2	3	4	5
15	¿Está insatisfecho en general con su vida sexual?	1	2	3	4	5



**ESCALA DE EVALUACIÓN DE ACTIVIDAD GLOBAL (GAF)**

Hay que considerar la actividad psicológica, social y laboral a lo largo de un hipotético *continuum* de salud-enfermedad. No hay que incluir alteraciones de la actividad debidas a limitaciones físicas (o ambientales). Utilice los niveles intermedios cuando resulte apropiado.

- 100 | *Actividad satisfactoria en una amplia gama de actividades, nunca parece superado por los problemas de su vida, es valorado por*  
 91 | *los demás a causa de sus abundantes cualidades positivas. Sin síntomas.*
- 90 | *Síntomas ausentes o mínimos (p. ej., ligera ansiedad antes de un examen), buena actividad en todas las áreas, interesado e*  
 81 | *implicado en una amplia gama de actividades, socialmente eficaz, generalmente satisfecho de su vida, sin más preocupaciones o*  
 81 | *problemas que los cotidianos (p. ej., una discusión ocasional con miembros de la familia).*
- 80 | *Si existen síntomas, son transitorios y constituyen reacciones esperables ante agentes estresantes psicosociales (p. ej.,*  
 71 | *dificultades para concentrarse tras una discusión familiar); sólo existe una ligera alteración de la actividad social, laboral o*  
 71 | *escolar (p. ej., descenso temporal del rendimiento escolar).*
- 70 | *Algunos síntomas leves (p. ej., humor depresivo e insomnio ligero) o alguna dificultad en la actividad social, laboral o escolar (p.*  
 61 | *ej., hacer novillos ocasionalmente o robar algo en casa), pero en general funciona bastante bien, tiene algunas relaciones*  
 61 | *interpersonales significativas.*
- 60 | *Síntomas moderados (p. ej., afecto aplanado y lenguaje circunstancial, crisis de angustia ocasionales) o dificultades moderadas*  
 51 | *en la actividad social, laboral o escolar (p. ej., pocos amigos, conflictos con compañeros de trabajo o de escuela).*
- 50 | *Síntomas graves (p. ej., ideación suicida, rituales obsesivos graves, robos en tiendas) o cualquier alteración grave en la actividad*  
 41 | *social, laboral o escolar (p. ej., sin amigos, incapaz de mantenerse en un empleo).*
- 40 | *Una alteración de la verificación de la realidad o de la comunicación (p. ej., el lenguaje es a veces ilógico, oscuro o irrelevante)*  
 31 | *o alteración importante en varias áreas como el trabajo escolar, las relaciones familiares, el juicio, el pensamiento o el estado de*  
 31 | *ánimo (p. ej., un hombre depresivo evita a sus amigos, abandona la familia y es incapaz de trabajar; un niño golpea*  
 31 | *frecuentemente a niños más pequeños, es desafiante en casa y deja de acudir a la escuela).*
- 30 | *La conducta está considerablemente influida por ideas delirantes o existe una alteración grave de la comunicación o el juicio (p.*  
 21 | *ej., a veces es incoherente, actúa de manera claramente inapropiada, preocupación suicida) o incapacidad para funcionar en*  
 21 | *casi todas las áreas (p. ej., permanece en la cama todo el día; sin trabajo, vivienda o amigos).*
- 20 | *Algún peligro de causar lesiones a otros o a sí mismo (p. ej., intentos de suicidio sin una expectativa manifiesta de muerte;*  
 11 | *frecuentemente violento; excitación maníaca) u ocasionalmente deja de mantener la higiene personal mínima (p. ej., con*  
 11 | *manchas de excrementos) o alteración importante de la comunicación (p. ej., muy incoherente o mudo).*
- 10 | *Peligro persistente de lesionar gravemente a otros o a sí mismo (p. ej., violencia recurrente) o incapacidad persistente para*  
 1 | *mantener la higiene personal mínima o acto suicida grave con expectativa manifiesta de muerte.*
- 0 | *Información inadecuada.*

**PUNTUACIÓN TOTAL**

## MEDIDAS NEUROPSICOLÓGICAS

### ESTIMACIÓN DEL COCIENTE INTELECTUAL

CI Estimado: \_\_\_\_\_

WAIS-III

PD

PE

Vocabulario

\_\_\_\_\_

\_\_\_\_\_

### TEST DE TRAZADO (Trail Making Test) (TMT)

Parte A: \_\_\_\_\_ segundos    Nº Errores: \_\_\_\_

Parte B: \_\_\_\_\_ segundos    Nº Errores: \_\_\_\_\_

### TEST DE STROOP

	<i>Puntuación Directa</i>	<i>Puntuación T</i>
Palabras		
Colores		
Palabras-Colores		
Interferencia		

### WISCONSIN CARD SORTING TEST (WCST)

DIMENSIONES	Puntuación Directa	Puntuación Típica	Puntuación T	Puntuación Centil
Nº de intentos aplicados				
Respuestas correctas				
Nº total de errores				

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Porcentaje de errores				
Respuestas perseverativas				
Porcentaje respuestas perseverativas				
Errores perseverativos				
Porcentaje errores perseverativos				
Errores no perseverativos				
Porcentaje errores no perseverativos				
Respuestas de nivel conceptual				
Porcentaje de respuestas nivel conceptual				

	<b>Puntuación Directa</b>	<b>Puntuación Centil</b>
Número de Categorías completas		
Intentos para completar la 1ª categoría		
Fallos para mantener la actitud		
Aprender a Aprender		

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## ESTILO ATRIBUTIVO

**INSTRUCCIONES:** A continuación se describen una serie de situaciones. Su tarea consiste en imaginar que cada una de estas situaciones le ha ocurrido a usted y contestar una serie de preguntas relacionadas con el **principal factor que usted cree está causando cada una de las situaciones**

**SITUACIÓN 1: Se encuentra Vd. con un amigo y éste le hace cumplidos acerca de su aspecto.** ¿Cuál es la causa principal de que le ocurra esta situación?.....

1.2. a 1.5

La causa de esta situación es totalmente debida a otros motivos	1	2	3	4	5	6	7	La causa de esta situación es totalmente debida a mi mismo
En momentos futuros, esta causa nunca volverá a estar presente	1	2	3	4	5	6	7	En momentos futuros, esta causa siempre estará presente
Esta causa, influye sólo en esta situación	1	2	3	4	5	6	7	Esta causa, influye en otras áreas de mi vida
Esta causa, no es nada controlable por mi	1	2	3	4	5	6	7	Esta causa, es totalmente controlable por mi

1.6. ¿Cómo es de importante para Vd. el hecho de que le ocurra esta situación?

Nada importante	1	2	3	4	5	6	7	Extremadamente importante
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**SITUACIÓN 2: Ha estado Vd. buscando trabajo durante una temporada sin encontrarlo.**

2.1. ¿Cuál es la causa principal de que le ocurra esta situación?.....

2.2. a 2.5

La causa de esta situación es totalmente debida a otros motivos	1	2	3	4	5	6	7	La causa de esta situación es totalmente debida a mi mismo
En momentos futuros, esta causa nunca volverá a estar presente	1	2	3	4	5	6	7	En momentos futuros, esta causa siempre estará presente
Esta causa, influye sólo en esta situación	1	2	3	4	5	6	7	Esta causa, influye en otras áreas de mi vida
Esta causa, no es nada controlable por mi	1	2	3	4	5	6	7	Esta causa, es totalmente controlable por mi

2.6. ¿Cómo es de importante para Vd. el hecho de que le ocurra esta situación?

Nada importante	1	2	3	4	5	6	7	Extremadamente importante
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**SITUACIÓN 3: Vd. llega a ser muy rico.**

3.1. ¿Cuál es la causa principal de que le ocurra esta situación?.....

3.2. a 3.5

La causa de esta situación es totalmente debida a otros motivos	1	2	3	4	5	6	7	La causa de esta situación es totalmente debida a mi mismo
En momentos futuros, esta causa nunca volverá a estar presente	1	2	3	4	5	6	7	En momentos futuros, esta causa siempre estará presente
Esta causa, influye sólo en esta situación	1	2	3	4	5	6	7	Esta causa, influye en otras áreas de mi vida
Esta causa, no es nada controlable por mi	1	2	3	4	5	6	7	Esta causa, es totalmente controlable por mi

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3.6. ¿Cómo es de importante para Vd. el hecho de que le ocurra esta situación?

Nada importante	1	2	3	4	5	6	7	Extremadamente importante
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**SITUACIÓN 4: Un amigo le viene con un problema y Vd. no intenta ayudarle.**

4.1. ¿Cuál es la causa principal de que le ocurra esta situación?.....

4.2. a 4.5

La causa de esta situación es totalmente debida a otros motivos	1	2	3	4	5	6	7	La causa de esta situación es totalmente debida a mi mismo
En momentos futuros, esta causa nunca volverá a estar presente	1	2	3	4	5	6	7	En momentos futuros, esta causa siempre estará presente
Esta causa, influye sólo en esta situación	1	2	3	4	5	6	7	Esta causa, influye en otras áreas de mi vida
Esta causa, no es nada controlable Por mi	1	2	3	4	5	6	7	Esta causa, es totalmente controlable por mi

4.6. ¿Cómo es de importante para Vd. el hecho de que le ocurra esta situación?

Nada importante	1	2	3	4	5	6	7	Extremadamente importante
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**SITUACIÓN 5: Dé Vd. una importante charla y el auditorio reacciona negativamente.**

5.1. ¿Cuál es la causa principal de que le ocurra esta situación?.....

5.2. a 5.5

La causa de esta situación es totalmente debida a otros motivos	1	2	3	4	5	6	7	La causa de esta situación es totalmente debida a mi mismo
En momentos futuros, esta causa nunca volverá a estar presente	1	2	3	4	5	6	7	En momentos futuros, esta causa siempre estará presente
Esta causa, influye sólo en esta situación	1	2	3	4	5	6	7	Esta causa, influye en otras áreas de mi vida
Esta causa, no es nada controlable por mi	1	2	3	4	5	6	7	Esta causa, es totalmente controlable por mi

5.6. ¿Cómo es de importante para Vd. el hecho de que le ocurra esta situación?

Nada importante	1	2	3	4	5	6	7	Extremadamente importante
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**SITUACIÓN 6: Realiza Vd. un proyecto que recibe muchas felicitaciones.**

6.1. ¿Cuál es la causa principal de que le ocurra esta situación?.....

6.2. a 6.5

La causa de esta situación es totalmente debida a otros motivos	1	2	3	4	5	6	7	La causa de esta situación es totalmente debida a mi mismo
En momentos futuros, esta causa nunca volverá a estar presente	1	2	3	4	5	6	7	En momentos futuros, esta causa siempre estará presente
Esta causa, influye sólo en esta situación	1	2	3	4	5	6	7	Esta causa, influye en otras áreas de mi vida
Esta causa, no es nada controlable por mi	1	2	3	4	5	6	7	Esta causa, es totalmente controlable por mi

6.6. ¿Cómo es de importante para Vd. el hecho de que le ocurra esta situación?

Nada importante	1	2	3	4	5	6	7	Extremadamente importante
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**SITUACIÓN 7: Se encuentra a un amigo que actúa hostilmente hacia Vd.**

7.1. ¿Cuál es la causa principal de que le ocurra esta situación?.....

7.2. a 7.5

La causa de esta situación es totalmente debida a otros motivos	1	2	3	4	5	6	7	La causa de esta situación es totalmente debida a mi mismo
En momentos futuros, esta causa nunca volverá a estar presente	1	2	3	4	5	6	7	En momentos futuros, esta causa siempre estará presente
Esta causa, influye sólo en esta situación	1	2	3	4	5	6	7	Esta causa, influye en otras áreas de mi vida
Esta causa, no es nada controlable por mi	1	2	3	4	5	6	7	Esta causa, es totalmente controlable por mi

7.6. ¿Cómo es de importante para Vd. el hecho de que le ocurra esta situación?

Nada importante	1	2	3	4	5	6	7	Extremadamente importante
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**SITUACIÓN 8: No puede llevar a cabo todo el trabajo que se espera de Vd.**

8.1. ¿Cuál es la causa principal de que le ocurra esta situación?.....

8.2. a 8.5

La causa de esta situación es totalmente debida a otros motivos	1	2	3	4	5	6	7	La causa de esta situación es totalmente debida a mi mismo
En momentos futuros, esta causa nunca volverá a estar presente	1	2	3	4	5	6	7	En momentos futuros, esta causa siempre estará presente
Esta causa, influye sólo en esta situación	1	2	3	4	5	6	7	Esta causa, influye en otras áreas de mi vida
Esta causa, no es nada controlable por mi	1	2	3	4	5	6	7	Esta causa, es totalmente controlable por mi

8.6. ¿Cómo es de importante para Vd. el hecho de que le ocurra esta situación?

Nada importante	1	2	3	4	5	6	7	Extremadamente importante
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**SITUACIÓN 9: Su pareja ha estado tratándole con más cariño.**

9.1. ¿Cuál es la causa principal de que le ocurra esta situación?.....

9.2. a 9.5

La causa de esta situación es totalmente debida a otros motivos	1	2	3	4	5	6	7	La causa de esta situación es totalmente debida a mi mismo
En momentos futuros, esta causa nunca volverá a estar presente	1	2	3	4	5	6	7	En momentos futuros, esta causa siempre estará presente
Esta causa, influye sólo en esta situación	1	2	3	4	5	6	7	Esta causa, influye en otras áreas de mi vida
Esta causa, no es nada controlable por mi	1	2	3	4	5	6	7	Esta causa, es totalmente controlable por mi

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9.6. ¿Cómo es de importante para Vd. el hecho de que le ocurra esta situación?

Nada importante	1	2	3	4	5	6	7	Extremadamente importante
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**SITUACIÓN 10: Solicita Vd. un puesto que le interesa mucho (por ejemplo: un trabajo importante, el acceso a una universidad, etc.) y lo consigue.**

10.1. ¿Cuál es la causa principal de que le ocurra esta situación?.....

10.2. a 10.5

La causa de esta situación es totalmente debida a otros motivos	1	2	3	4	5	6	7	La causa de esta situación es totalmente debida a mi mismo
En momentos futuros, esta causa nunca volverá a estar presente	1	2	3	4	5	6	7	En momentos futuros, esta causa siempre estará presente
Esta causa, influye sólo en esta situación	1	2	3	4	5	6	7	Esta causa, influye en otras áreas de mi vida
Esta causa, no es nada controlable por mi	1	2	3	4	5	6	7	Esta causa, es totalmente controlable por mi

10.6. ¿Cómo es de importante para Vd. el hecho de que le ocurra esta situación?

Nada importante	1	2	3	4	5	6	7	Extremadamente importante
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**SITUACIÓN 11: Vá Vd. a una cita amorosa y le sale mal.**

11.1. ¿Cuál es la causa principal de que le ocurra esta situación?.....

11.2. a 11.5

La causa de esta situación es totalmente debida a otros motivos	1	2	3	4	5	6	7	La causa de esta situación es totalmente debida a mi mismo
En momentos futuros, esta causa nunca volverá a estar presente	1	2	3	4	5	6	7	En momentos futuros, esta causa siempre estará presente
Esta causa, influye sólo en esta situación	1	2	3	4	5	6	7	Esta causa, influye en otras áreas de mi vida
Esta causa, no es nada controlable por mi	1	2	3	4	5	6	7	Esta causa, es totalmente controlable por mi

11.6. ¿Cómo es de importante para Vd. el hecho de que le ocurra esta situación?

Nada importante	1	2	3	4	5	6	7	Extremadamente importante
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**SITUACIÓN 12: Obtiene Vd. un ascenso.**

12.1. ¿Cuál es la causa principal de que le ocurra esta situación?.....

12.2. a 12.5

La causa de esta situación es totalmente debida a otros motivos	1	2	3	4	5	6	7	La causa de esta situación es totalmente debida a mi mismo
En momentos futuros, esta causa nunca volverá a estar presente	1	2	3	4	5	6	7	En momentos futuros, esta causa siempre estará presente
Esta causa, influye sólo en esta situación	1	2	3	4	5	6	7	Esta causa, influye en otras áreas de mi vida



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Esta causa, no es nada controlable por mi	1	2	3	4	5	6	7	Esta causa, es totalmente controlable por mi
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12.6. ¿Cómo es de importante para Vd. el hecho de que le ocurra esta situación?

Nada importante	1	2	3	4	5	6	7	Extremadamente importante
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Las 6 situaciones positivas son: 1, 3, 6, 9, 10 y 12  
 Las 6 negativas son: 2, 4, 5, 7, 8 y 11

- **Internalidad- positiva:** media de las puntuaciones dadas a los ítems nº 2 de cada una de las 6 situaciones positivas \_\_\_\_\_
  
- **Estabilidad positiva:** media de las puntuaciones dadas a los ítems nº 3 de cada una de las 6 situaciones positivas \_\_\_\_\_
  
- **Globalidad positiva:** media de las puntuaciones dadas a los ítems nº 4 de cada una de las 6 situaciones positivas \_\_\_\_\_
  
- **Estilo compuesto positivo:** media de las tres puntuaciones anteriores \_\_\_\_\_
  
  
- **Internalidad negativa:** media de las puntuaciones dadas a los ítems nº 2 de cada una de las 6 situaciones negativas \_\_\_\_\_
  
- **Estabilidad negativa:** media de las puntuaciones dadas a los ítems nº 3 de cada una de las 6 situaciones negativas \_\_\_\_\_
  
- **Globalidad negativa:** media de las puntuaciones dadas a los ítems nº 4 de cada una de las 6 situaciones negativas \_\_\_\_\_
  
- **Estilo compuesto negativo:** media de las tres puntuaciones anteriores \_\_\_\_\_
  
  
- **Controlabilidad positiva:** media de las puntuaciones dadas a los ítems nº 5 de cada una de las 6 situaciones positivas \_\_\_\_\_
  
- **Controlabilidad negativa:** media de las puntuaciones dadas a los ítems nº 5 de cada una de las 6 situaciones negativas \_\_\_\_\_



## Visita Mes 6

Fecha: \_\_\_/\_\_\_/\_\_\_

**¿CONTINÚA EL PACIENTE EN EL ESTUDIO?**

Sí     No, fecha de abandono: \_\_\_/\_\_\_/\_\_\_ (RECUERDE rellenar hoja de finalización)

**Datos antropométricos:**    Peso: \_\_\_\_\_ kg    Talla: \_\_\_\_\_ cm

### DATOS CLÍNICOS DEL SEGUIMIENTO

**¿Ha sido hospitalizado o dado de alta el paciente desde la visita anterior?**

No     Sí, especificar ⇨

① Hospitalizado	② Alta
<i>Fecha ingreso</i>	<i>Fecha alta</i>
___/___/___	___/___/___
___/___/___	___/___/___

**¿Ha asistido con regularidad a las citas clínicas prescritas por su clínico?**

- |                                   |                                    |
|-----------------------------------|------------------------------------|
| ① <25% de las veces               | ③ entre el 50% y 75% de las veces  |
| ② entre el 25% y 50% de las veces | ④ entre el 75% y 100% de las veces |

### TRATAMIENTO ADMINISTRADO

**MEDICACIÓN ANTIPSICÓTICA:**

Medicación	Dosis (mg/día)

**Valore el cumplimiento del tratamiento; “el paciente está tomando la medicación.....”**

- |                                   |                                    |
|-----------------------------------|------------------------------------|
| ① <25% de las veces               | ③ entre el 50% y 75% de las veces  |
| ② entre el 25% y 50% de las veces | ④ entre el 75% y 100% de las veces |

**¿Se cambia alguno de los otros tratamientos que el paciente tenía pautados desde la anterior visita?**

Sin cambios en el tratamiento

Retirada o inicio de algún tratamiento ⇨ especificar tratamiento que se cambia, tipo de cambio y motivo:⇨

⇨ Tratamiento que se cambia	Tipo cambio			Motivo del cambio		
	Inicio	Retirada	Ajuste de dosis	Respuesta insuficiente o falta de eficacia	Reacciones adversas	Otros
	0	0	0	0	0	0
	0	0	0	0	0	0

\_\_\_\_\_ 0 0 0 0 0 0

**DIAGNÓSTICO SEGÚN DSM-IV:**

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

**ESCALA AUTO-APLICADA MORINSKI-GREEN**

*Lea detenidamente cada una de las frases siguientes y decida si para usted son verdaderas o falsas. Las frases se refieren únicamente a la medicación psiquiátrica que toma actualmente.*

*Si una frase es verdadera o en su mayor parte verdadera, marque la casilla correspondiente a «verdadera» con una X. Si una frase es falsa o en su mayor parte falsa, marque la casilla correspondiente a «falsa». Si desea cambiar alguna respuesta, tache la respuesta errónea y marque con un círculo la respuesta correcta.*

	VERDADERO	FALSO
1. Alguna vez he olvidado tomar la medicación.....	①	②
2. Tomo la medicación a la hora indicada .....	①	②
3. Cuando me encuentro bien, dejo de tomar la medicación .....	①	②
4. Si alguna vez me encuentro mal, dejo de tomarla .....	①	②

**ESCALA AUTO-APLICADA DAI-AWAD**

	VERDADERO	FALSO
1. Para mi lo bueno de la medicación supera lo malo .....	①	②
2. Me siento raro/a, "como un zombie" con la medicación .....	①	②
3. Tomo medicación por decisión mía.....	①	②
4. La medicación hace que me sienta más relajado/a .....	①	②
5. La medicación hace que me sienta cansado/a y lento/a.....	①	②
6. Tomo medicación sólo cuando estoy enfermo/a.....	①	②
7. Me siento más normal con la medicación.....	①	②
8. Es antinatural para mi mente y mi cuerpo estar controlado/a por medicaciones .....	①	②
9. Mis pensamientos son más claros con la medicación.....	①	②
10. Por estar con medicación puedo prevenir caer enfermo.....	①	②

## EVALUACIONES PSIQUIÁTRICAS

### ESCALA DE SÍNDROME POSITIVO Y NEGATIVO DE LA ESQUIZOFRENIA (PANSS)

**INSTRUCCIONES:** Marque con un círculo la evaluación apropiada para cada ítem de la entrevista clínica que se especifica a continuación. Consulte el manual de evaluación anexo para las definiciones de los ítems, la descripción de los puntos concretos y el procedimiento para la puntuación.

*1= ausente; 2= mínimo; 3= leve; 4=moderado; 5= moderadamente grave; 6= grave; 7= extremo.*

**1) SUBESCALA POSITIVA**

P1	Delirios .....	1	2	3	4	5	6	7
P2	Desorganización conceptual .....	1	2	3	4	5	6	7
P3	Comportamiento alucinatorio .....	1	2	3	4	5	6	7
P4	Excitación .....	1	2	3	4	5	6	7
P5	Grandiosidad.....	1	2	3	4	5	6	7
P6	Susplicacia .....	1	2	3	4	5	6	7
P7	Hostilidad.....	1	2	3	4	5	6	7

SUBTOTAL

**2) SUBESCALA NEGATIVA**

N1	Embotamiento afectivo .....	1	2	3	4	5	6	7
N2	Retraimiento emocional.....	1	2	3	4	5	6	7
N3	Contacto pobre.....	1	2	3	4	5	6	7
N4	Retraimiento social .....	1	2	3	4	5	6	7
N5	Dificultad en el pensamiento abstracto.....	1	2	3	4	5	6	7
N6	Espontaneidad y fluidez de conversación .....	1	2	3	4	5	6	7
N7	Pensamiento estereotipado.....	1	2	3	4	5	6	7

SUBTOTAL

**3) SUBESCALA DE PSICOPATOLOGIA GENERAL**

G1	Preocupaciones somáticas .....	1	2	3	4	5	6	7
G2	Ansiedad .....	1	2	3	4	5	6	7
G3	Sentimientos de culpa.....	1	2	3	4	5	6	7
G4	Tensión .....	1	2	3	4	5	6	7
G5	Manierismos y posturas .....	1	2	3	4	5	6	7
G6	Depresión.....	1	2	3	4	5	6	7
G7	Retardo motor .....	1	2	3	4	5	6	7
G8	Falta de colaboración.....	1	2	3	4	5	6	7
G9	Contenidos inusuales del pensamiento .....	1	2	3	4	5	6	7
G10	Desorientación .....	1	2	3	4	5	6	7
G11	Atención deficiente.....	1	2	3	4	5	6	7
G12	Ausencia de juicio e "insight" .....	1	2	3	4	5	6	7
G13	Trastornos de la volición .....	1	2	3	4	5	6	7
G14	Control deficiente de impulsos .....	1	2	3	4	5	6	7
G15	Preocupación .....	1	2	3	4	5	6	7
G16	Evitación social activa .....	1	2	3	4	5	6	7

SUBTOTAL

**PUNTUACION TOTAL** (suma de los 3 subtotales)

**ESCALA MONTGOMERY-ASBERG PARA LA DEPRESIÓN (MADRS)****1. Tristeza aparente**

El paciente expresa abatimiento, tristeza y desesperación a través de la voz, el gesto y la expresión mímica.

Evalúese en función de la gravedad e incapacidad para ser animado.

0. No tristeza
- 1.
2. Parece desanimado, pero se anima fácilmente
- 3.
4. Parece triste e infeliz la mayor parte del tiempo
- 5.
6. Parece desgraciado todo el tiempo. Extremadamente abatido

**2. Tristeza expresada**

El enfermo aporta datos verbales sobre su humor deprimido, independientemente de que lo exprese por su apariencia o no. Incluye ánimo bajo, abatimiento, desesperanza, sentimiento de desamparo.

Evalúese de acuerdo con la intensidad, duración e influenciabilidad del humor por las circunstancias:

0. Tristeza ocasional en consonancia con las circunstancias ambientales
- 1.
2. Tristeza que cede (se anima) sin dificultad
- 3.
4. Sentimientos de tristeza o abatimiento profundo, pero el humor es todavía ligeramente influenciable por las circunstancias externas
- 5.
6. Continua e invariable tristeza, abatimiento, sentimiento de desgracia

**3. Tensión interior**

El paciente expresa sentimientos de malestar indefinido, nerviosismo, confusión interna, tensión mental que se vuelve pánico, temor o angustia.

Evalúese de acuerdo con la intensidad, frecuencia o duración de la tranquilidad perdida:

0. Placidez aparente. Sólo manifiesta tensión interna
- 1.
2. Ocasionales sentimientos de nerviosismo y malestar indefinido
- 3.
4. Continuos sentimientos de tensión interna o sentimientos de pánico que aparecen intermitentemente y que el paciente puede dominar, pero con dificultad
- 5.
6. Angustia o temor no mitigado. Pánico abrumador

**4. Sueño reducido**

El paciente expresa una reducción en la duración o en la profundidad de su sueño en comparación a cómo duerme cuando se encuentra bien.

0. Sueño como los normales
- 1.
2. Leve dificultad para dormir o sueño ligeramente reducido: sueño ligero
- 3.
4. Sueño reducido o interrumpido al menos durante 2 horas
- 5.
6. Menos de 2 o 3 horas de sueño

**5. Disminución del apetito**

El paciente expresa una reducción del apetito respecto al que tiene cuando se encuentra bien. Evalúese la pérdida del deseo de alimento o la necesidad de forzarse uno mismo a comer.

0. Apetito normal o aumentado
- 1.
2. Apetito ligeramente disminuido
- 3.
4. No apetito. Los alimentos saben mal
- 5.
6. Necesidad de persuasión para comer

**6. Dificultades de concentración**

El paciente expresa dificultades para mantener su propio pensamiento o para concentrarse. Evalúese de acuerdo con la intensidad, frecuencia y grado de la incapacidad producida.

0. Ninguna dificultad de concentración
- 1.
2. Dificultades ocasionales para mantener los propios pensamientos
- 3.
4. Dificultades en la concentración y el mantenimiento del pensamiento que reduce la capacidad para mantener una conversación o leer
- 5.
6. Incapacidad para leer o conversar sin gran dificultad

**7. Laxitud.Abulia**

El paciente expresa o presenta dificultad para iniciar y ejecutar las actividades diarias.

0. Apenas hay dificultades para iniciar las tareas.No hay inactividad
- 1.
2. Dificultad para iniciar actividades
- 3.
4. Dificultades para comenzar sus actividades rutinarias, que exigen un esfuerzo para ser llevadas a cabo
- 5.
6. Completa laxitud, incapacidad para hacer nada sin ayuda

**8. Incapacidad para sentir**

El paciente expresa un reducido interés por lo que le rodea o las actividades que normalmente producían placer. Reducción de la capacidad para reaccionar adecuadamente a circunstancias o personas.

0. Interés normal por las cosas y la gente
- 1.
2. Reducción de la capacidad para disfrutar de los intereses habituales
- 3.
4. Pérdida de interés en lo que le rodea, incluso con los amigos o conocidos
- 5.
6. Manifiesta la experiencia subjetiva de estar emocionalmente paralizado, anesthesiado, con incapacidad para sentir placer o desagrado, y con una falta absoluta y/o dolorosa pérdida de sentimientos hacia parientes y amigos

**9. Pensamientos pesimistas**

El paciente expresa pensamiento de culpa, autorreproche, remordimiento, inferioridad, ideas de ruina, ideas de pecado.

0. No hay pensamientos pesimistas
- 1.
2. Ideas fluctuantes de fallos, autorreproches o autodepreciaciones
- 3.
4. Persistentes autoacusaciones o ideas definidas, pero todavía razonables de culpabilidad o pecado. Pesimismo

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- 5.
6. Ideas irrefutables de ruina, remordimiento o pecado irremediable.  
Autoacusaciones absurdas e irreducibles

**10. Ideación suicida**

El paciente expresa la idea de que la vida no merece vivirse, de que una muerte natural sería bienvenida, o manifiesta ideas o planes suicidas.

0. Se alegra de vivir. Toma la vida como viene
- 1.
2. Cansado de vivir. Ideas suicidas fugaces
- 3.
4. Manifiesta deseos de muerte, ideas suicidas frecuentes. El suicidio es considerado como una solución, pero no se han elaborado planes o hecho intención
- 5.
6. Planes explícitos de suicidio cuando exista una oportunidad. Activa preparación para el suicidio

<b><i>PUNTUACIÓN TOTAL</i></b>		
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**ESCALA DE YOUNG PARA LA EVALUACIÓN DE LA MANÍA (YMRS)**

**1. Euforia**

- Ausente
- Dudosa o leve
- Hipertimia subjetiva clara, optimista, seguro; alegre; aún adecuado
- Hipertimia; humor ya inadecuado
- Euforia, risa inapropiada; canta

**2. Aumento de la actividad motora, energía**

- Ausente
- Aumentada subjetivamente
- Animado; aumento de la gesticulación
- Energía excesiva; hiperactivo a veces; inquieto (aún se puede contener)
- Excitación motora; hiperactividad continua (no se puede contener)

**3. Interés sexual**

- Normal, no aumentado
- Aumento ligero o posible
- Incremento definido al preguntarle
- Interés sexual espontáneo; habla de temas sexuales; hipersexualidad expresada sin preguntarle
- Actos sexuales (hacia otros pacientes, trabajadores del centro o entrevistador)

**4. Sueño**

- Refiere sueño conservado
- Sueño reducido en menos de 1 hora
- Sueño reducido en más de 1 hora
- Refiere disminución en la necesidad de sueño
- Niega necesidad de dormir

**5. Irritabilidad**

- Ausente
- Subjetivamente aumentada
- Irritable episódicamente durante la entrevista; episodios recientes de estar molesto o enfadado en la planta
- Irritable frecuentemente durante la entrevista; cortante, brusco todo el tiempo
- Hostil, falta de cooperación; entrevista imposible

**6. Discurso (ritmo y cantidad)**

- No aumento
- Se siente hablador
- Aumento del ritmo y la cantidad a veces, verborreico a veces
- Verborrea. Aumento importante del ritmo y la cantidad; difícil de interrumpir
- Verborrea ininterrumpible, discurso continuo

**7. Trastorno del lenguaje y del pensamiento**

- Ausente
- Circunstancial; ligeramente distraible; pensamientos rápidos
- Distraible; pierde el hilo conductor; cambia de tema con frecuencia; pensamientos rápidos
- Fuga de ideas; tangencialidad; dificultad para seguirle; hace rimas, ecolalia
- Incoherencia; comunicación imposible

**8. Contenido del pensamiento**

- Normal
- Planes cuestionables, nuevos intereses
- Proyecto(s) especial(es); hiperreligioso
- Ideas de grandeza o paranoides; ideas de referencia
- Delirios; alucinaciones

**9. Conducta alterada-agresiva**

- Ausente, coopera
- Sarcástico, ruidoso a veces, alerta, vigilante
- Demandante; amenazas en planta
- Amenaza al entrevistador; grita; entrevista difícil
- Agresivo; destructivo; entrevista imposible

**10. Vestido**

- Vestido y aseo apropiado
- Mínimamente descuidado
- Poco cuidado personal; moderadamente desaliñado en el vestir; exceso de ropa
- Descuido en el vestir; semivestido; maquillaje estridente
- Totalmente desaliñado; decorado; maquillaje extraño

**11. Insight. Conciencia de sí mismo**

- Presente; admite la enfermedad; está de acuerdo con la necesidad de tratamiento
- Duda de la enfermedad aunque la admite poco posible
- Admite cambio en la conducta, aunque niega la enfermedad
- Niega todo cambio de conducta

**PUNTUACIÓN TOTAL**

Debe responder todas las preguntas de esta escala incluso cuando en el paciente todos los síntomas de manía estén ausentes

**ESCALA SUMD (ABREVIADA)**

1. Conciencia de poseer un desorden mental
  0. Ítem no relevante
  1. Conciencia
  - 2.
  3. Conciencia intermedia
  - 4.
  5. No hay conciencia
2. Conciencia sobre los efectos de la medicación
  0. Ítem no relevante
  1. Conciencia
  - 2.
  3. Conciencia intermedia
  - 4.
  5. No hay conciencia
3. Conciencia de las consecuencias de su desorden mental
  0. Ítem no relevante
  1. Conciencia
  - 2.
  3. Conciencia intermedia
  - 4.
  5. No hay conciencia
4. Conciencia de poseer alucinaciones (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
5. Conciencia de poseer delirios (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
6. Conciencia de poseer trastornos del pensamiento (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
7. Conciencia de poseer embotamiento afectivo (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
8. Conciencia de poseer anhedonia (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_
9. Conciencia de poseer asociabilidad (0-5): \_\_\_\_\_  
Atribución (0-5): \_\_\_\_\_

**PUNTUACIONES**

Suma total ítems conciencia (4-9)	/	Número total de ítems relevantes	=	Puntuación
_____		_____		_____

Suma total ítems Atribución (4-9)	/	Número total de ítems relevantes	=	Puntuación
_____		_____		_____

**ESCALA DE COGNICIÓN SOCIAL PARA LA PSICOSIS (GEOPTE)**

INSTRUCCIONES: Marque con un círculo la evaluación apropiada para cada ítem de la entrevista clínica que se especifica a continuación.

*1=no; 2=un poco; 3=regular; 4=bastante; 5=mucho*

1	¿Tiene dificultad para prestar atención?	1	2	3	4	5
2	¿Tiene dificultad para seguir una conversación en la que participan varias personas?	1	2	3	4	5
3	¿Le cuesta aprender cosas nuevas?	1	2	3	4	5
4	¿Se le olvidan los encargos, tareas o recados?	1	2	3	4	5
5	¿Cuándo tienen que hablar con alguien le faltan las pasabras?	1	2	3	4	5
6	¿Le cuesta entender de qué va una película?	1	2	3	4	5
7	¿Le cuesta encontrar el sentido de una conversación?	1	2	3	4	5
8	¿Tiene dificultad para reconocer las emociones de los otros?	1	2	3	4	5
9	Cuando está en un grupo, ¿le suelen decir que interpreta mal las actitudes, miradas o gestos de los demás?	1	2	3	4	5
10	¿Se siente muy sensible a las miradas, palabras o gestos de los otros?	1	2	3	4	5
11	Si está solo en casa y surge algún problema (p.ej., se estropea un electrodoméstico), ¿le resulta difícil encontrar la solución??	1	2	3	4	5
12	¿Le cuesta mantener la higiene personal (estar limpio y aseado)?	1	2	3	4	5
13	¿Le cuesta hacer planes para el fin de semana?	1	2	3	4	5
14	¿Tiene dificultades para hacer amistades?	1	2	3	4	5
15	¿Está insatisfecho en general con su vida sexual?	1	2	3	4	5

**ESCALA DE EVALUACIÓN DE ACTIVIDAD GLOBAL (GAF)**

Hay que considerar la actividad psicológica, social y laboral a lo largo de un hipotético *continuum* de salud-enfermedad. No hay que incluir alteraciones de la actividad debidas a limitaciones físicas (o ambientales). Utilice los niveles intermedios cuando resulte apropiado.

- 100 | *Actividad satisfactoria en una amplia gama de actividades, nunca parece superado por los problemas de su vida, es valorado por los demás a causa de sus abundantes cualidades positivas. Sin síntomas.*
- 91
- 90 | *Síntomas ausentes o mínimos (p. ej., ligera ansiedad antes de un examen), buena actividad en todas las áreas, interesado e implicado en una amplia gama de actividades, socialmente eficaz, generalmente satisfecho de su vida, sin más preocupaciones o problemas que los cotidianos (p. ej., una discusión ocasional con miembros de la familia).*
- 81
- 80 | *Si existen síntomas, son transitorios y constituyen reacciones esperables ante agentes estresantes psicosociales (p. ej., dificultades para concentrarse tras una discusión familiar); sólo existe una ligera alteración de la actividad social, laboral o escolar (p. ej., descenso temporal del rendimiento escolar).*
- 71
- 70 | *Algunos síntomas leves (p. ej., humor depresivo e insomnio ligero) o alguna dificultad en la actividad social, laboral o escolar (p. ej., hacer novillos ocasionalmente o robar algo en casa), pero en general funciona bastante bien, tiene algunas relaciones interpersonales significativas.*
- 61
- 60 | *Síntomas moderados (p. ej., afecto aplanado y lenguaje circunstancial, crisis de angustia ocasionales) o dificultades moderadas en la actividad social, laboral o escolar (p. ej., pocos amigos, conflictos con compañeros de trabajo o de escuela).*
- 51
- 50 | *Síntomas graves (p. ej., ideación suicida, rituales obsesivos graves, robos en tiendas) o cualquier alteración grave en la actividad social, laboral o escolar (p. ej., sin amigos, incapaz de mantenerse en un empleo).*
- 41
- 40 | *Una alteración de la verificación de la realidad o de la comunicación (p. ej., el lenguaje es a veces ilógico, oscuro o irrelevante) o alteración importante en varias áreas como el trabajo escolar, las relaciones familiares, el juicio, el pensamiento o el estado de ánimo (p. ej., un hombre depresivo evita a sus amigos, abandona la familia y es incapaz de trabajar; un niño golpea frecuentemente a niños más pequeños, es desafiante en casa y deja de acudir a la escuela).*
- 31
- 30 | *La conducta está considerablemente influida por ideas delirantes o existe una alteración grave de la comunicación o el juicio (p. ej., a veces es incoherente, actúa de manera claramente inapropiada, preocupación suicida) o incapacidad para funcionar en casi todas las áreas (p. ej., permanece en la cama todo el día; sin trabajo, vivienda o amigos).*
- 21
- 20 | *Algún peligro de causar lesiones a otros o a sí mismo (p. ej., intentos de suicidio sin una expectativa manifiesta de muerte; frecuentemente violento; excitación maníaca) u ocasionalmente deja de mantener la higiene personal mínima (p. ej., con manchas de excrementos) o alteración importante de la comunicación (p. ej., muy incoherente o mudo).*
- 11
- 10 | *Peligro persistente de lesionar gravemente a otros o a sí mismo (p. ej., violencia recurrente) o incapacidad persistente para mantener la higiene personal mínima o acto suicida grave con expectativa manifiesta de muerte.*
- 1
- 0 | *Información inadecuada.*

**PUNTUACIÓN TOTAL**

## *Hoja de Finalización*

Fecha: \_\_\_/\_\_\_/\_\_\_

**¿Ha finalizado el estudio?**

\_\_\_\_\_ Finalizó el estudio (todas las visitas completas y valorables)

\_\_\_\_\_ Interrupción anticipada

Última visita valorable: \_\_\_/\_\_\_/\_\_\_

**Motivo:**

← Pérdida de seguimiento; causa \_\_\_\_\_

↑ Remisión de los síntomas

→ Falta de colaboración del paciente

↓ Mala cumplimentación persistente

≥ Fallecimiento (especificar causa): \_\_\_\_\_

× Otros (especificar): \_\_\_\_\_

### ***OPINIÓN GLOBAL***

**Comparado con el estado inicial del paciente ¿cómo se encuentra en estos momentos?**

← Mucho mejor

↑ Bastante mejor

→ Ligeramente mejor

↓ Igual

° Ligeramente peor

± Bastante peor

" Mucho peor

### ***OBSERVACIONES***

## APPENDIX II

### THE ATTRIBUTIONAL STYLE IN FEP IS STABLE AFTER OVER TIME AFTER THE BREAKDOWN

**Introduction:** Attributional Style is a stable personality feature. A First Episode Psychosis is the onset of a chronic illness which implies a significant decrease on the cognitive capacity and an increase of negative and depressive symptoms. As far as we know there are no studies that analyze the possible change in personality features as the attributional style. Indeed, social cognition has received special attention in the last decade in the study of psychosis. However, the specific role of attributional style has been scarcely investigated compared to the rest of social cognitive dimensions (emotional processing, social perception and theory of mind). Therefore, little is known about attributional style dimensions and their longitudinal change over time.

**Method:** A study was held with 17 patients with First-Episode Psychosis at two months and 12 months follow-up after the breakdown. Assessments were carried out at two months and one year follow-up. Positive and Negative Syndromes Scale was used to measure symptomatology and attributional style was evaluated using the Attributional Style Questionnaire Spanish Version (ASQ-E).

**Results:** Eight male and nine female composed the sample, which had an average age of 25, 18 years old ( $SD = 5.5$ ), and an average years of education of 10.12 ( $SD = 2.4$ ). Mean and Standard Deviation of clinical and attributional style measures at each period are showed in table A1. Because the size of the sample was lower than 30 Wilcoxon signed rank test were performed to analyze change over time, results are showed in table 1.

Table A1. Descriptive data for PANSS and Attributional Scale Questionnaire scores over time and Wilcoxon signed rank test of time differences.

		2months	12 months	Test <sup>sig</sup>
		IC (95%)	Mean(SD)	
<b>PANSS</b>				
<b>Positive</b>		14.57 (5.45)	11.64 (8.20)	$U = -2.42^*$
<b>Negative</b>		20.40 (7.69)	15.60 (10.06)	$U = -2.13^*$
<b>Disorganization</b>		23,36 (8.94)	17.36 (5.69)	$U = -2.77^{**}$
<b>Excitement</b>		14.14 (3.01)	13.86 (9.20)	$U = -1.65^{0.09}$
<b>Emotional distress</b>		18.87 (5.16)	13.93 (5.12)	$U = -2.31^*$
<b>ASQ</b>				
<b>Internality</b>	Positive	5.15 (0.83)	4.96 (1.19)	$U = -0,63^{0.53}$
	Negative	4.29 (1.13)	3.85 (1.11)	$U = -1,26^{0.21}$
<b>Specificity</b>	Positive	5.10 (0.88)	4.96 (0.86)	$U = -0,46^{0.65}$
	Negative	4.41 (1.01)	4.20 (1.03)	$U = -1,03^{0.30}$
<b>Globality</b>	Positive	4.85 (0.92)	5.17 (1.07)	$U = -0,73^{0.46}$
	Negative	4.02 (1.16)	4.13 (0.78)	$U = -0,18^{0.86}$
<b>Control</b>	Positive	5.04 (1.21)	4.75 (1.15)	$U = -0,21^{0.83}$
	Negative	4.43 (1.47)	3.76 (1.39)	$U = -0,96^{0.34}$
<b>SSB-I</b>		-0.75 (1.17)	-0.76 (1.54)	$U = -1.02^{0.31}$
<b>SSB-C</b>		-0.64 (1.13)	-0.99 (1.39)	$U = -0.65^{0.52}$

CI: Confidence Interval; SD: Standard Deviation; \*  $p < 0.001$ , \*\*  $p < 0.01$  \*  $p < 0.001$ . SSB-I = Self-Serving Bias for internality; SSB-C = Self-Serving Bias for controllability.

All one-year follow-up scores but excitement of PANSS showed a significant change compared to the same scores at two-month follow-up. However, All the ASQ scores did not show a significant change during the same period of time.

**Conclusions:** The attributional style of a FEP is stable over time, in spite of the changes in the illness symptoms. These results are a sign of attributional style being a stable trait, being not important the moment of assessment. Since this is a pilot study, these results must be replicated in bigger samples and with longer periods of follow-up to be able to stay attributional style as a stable trait in psychosis.

## APPENDIX III

### CLINICAL APPROACH

As an added contribution to the present work, several relevant clinical conclusions can be drawn from the results in this study:

- 1) First, the moment in which the clinician measures of patient's insight should be taken into account when diagnosis or functionality is to be anticipated. After the onset of the illness, two-month insight dimensions could be more accurate to anticipate a second diagnosis after a FEP. Patients with higher levels of lack of insight have a higher risk of being diagnosed with a schizophrenic spectrum disorder. This rule can also be followed until 6 months, after that moment, poor insight could be associated with both, schizophrenia and non schizophrenia spectrum disorder. Therefore, to predict the diagnosis group it's recommended using two-month insight levels. The better prediction of the clinical evolution allow the clinician adjust in a proper way the treatment.
- 2) Maniac symptoms have been shadowed by negative symptoms when we talk about FEP. In this study we highlight the possibility of new therapeutic aims focused in treating and controlling manic symptoms as an alternative, so as to improve patients' insight.
- 3) A bigger cognitive reserve would allow patients to count on more resources when facing the illness. Promoting activities that increase people's cognitive reserve would involve a decrease/drop/fall in the impact of pathologies involving the central nervous system produce in people. For that purpose, sensitizing and promoting campaigns for "intellectual health" should be done.



4) The measurement of insight is another clinical relevant aspect. Depending on the scale used and on the time is taken, insight levels might vary. This might imply that the scale used in this basal moment might not be important. But from two months onwards, insight levels can vary from one scale to another; therefore, conclusions should be made based on the used scale. The same conclusions shouldn't be drawn from scores obtained in G12 than in SUMD. G12 item is an insight measure which underestimates patients' insight. On the other hand, the general measure obtained from the SUMD scale is an overestimation of the lack of insight, since criteria for a good insight are more demanding.

5) The ASQ attributional style questionnaire might not be an adequate scale to measure the attributional style construct in psychotic patients due to the scale's difficulty for being completed. A more etiological scale may need to be created, with more simple items in order to evaluate attributional style in psychotic patients.