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**Cognición social y procesamiento emocional en pacientes con
esquizofrenia**

MEMORIA PARA OPTAR AL GRADO DE DOCTOR

PRESENTADA POR

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COGNICIÓN SOCIAL Y PROCESAMIENTO EMOCIONAL EN PACIENTES CON ESQUIZOFRENIA

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SOCIAL COGNITION AND EMOTIONAL PROCESSING IN PATIENTS WITH SCHIZOPHRENIA

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“Tenía la idea de que al poner nombre a los problemas, éstos se materializan y ya no es posible ignorarlos; en cambio, si se mantienen en el limbo de las palabras no dichas, pueden desaparecer solos, con el transcurso del tiempo”.

Isabel Allende
La casa de los espíritus
Barcelona: Círculo de Lectores, 1995, p. 146

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Formato de la tesis

Este trabajo se acoge a un formato de artículos publicados o aceptados para publicación. Dicho formato queda regulado según el artículo 10.3 de la normativa de desarrollo del Real Decreto 99/2011, de 28 de enero (BOE 10/02/2011), que regula los estudios de doctorado en la Universidad Complutense (acuerdo de Consejo de Gobierno de 6 de noviembre de 2012, publicado en el BOUC 14, de 21/12/2012) permite la presentación de Tesis Doctorales como compendio de publicaciones. El acuerdo de Consejo de Gobierno de 23 de abril de 2015 (BOUC 10, de 29/04/2015) modifica la citada normativa quedando artículo 10.3 tal como sigue:

“Se podrán presentar Tesis Doctorales en “formato publicaciones”. En las publicaciones que compongan la Tesis el doctorando deberá haber participado como autor principal y se habrán editado en revistas de la especialidad recogidas en índices de calidad contrastados o de similar nivel científico en libros. El director y tutor del doctorando certificarán el carácter de la aportación del doctorando en las publicaciones aportadas. La recopilación de publicaciones deberá siempre acompañarse de una introducción, que incluya una revisión del estado actual del tema, los objetivos y/o hipótesis, una discusión integradora y las conclusiones. Cuando se presente una Tesis Doctoral en este formato se deberán aportar los permisos del resto de los autores de las publicaciones incluidas”.

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Grupos de investigación

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Imagen de cubierta

La imagen de cubierta es una adaptación realizada por Marcos Martínez Villares de “El Atlas de las Emociones”, una herramienta interactiva creada por P. Ekman y su hija, E. Ekman en respuesta a una petición del Dalai Lama. Se trata de una forma de visualizar, identificar y explorar las 5 emociones primarias (ira, miedo, asco, tristeza y alegría) así como sus estadios, acciones, desencadenantes y estados de ánimo asociados, con el fin de ayudar a las personas a comprender mejor cómo influyen en nuestra vida.

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RESUMEN

Cognición social y procesamiento emocional en pacientes con esquizofrenia

1. Introducción

La esquizofrenia es un síndrome severo y crónico que presenta un conjunto de síntomas positivos, negativos y cognitivos que pueden llegar a ser muy limitantes. Aunque los antipsicóticos han mostrado ser eficaces en el tratamiento de los síntomas positivos, su eficacia es más limitada en el caso de los síntomas negativos y cognitivos. Precisamente el funcionamiento cognitivo y no la sintomatología positiva ha mostrado ser una variable predictiva de la capacidad funcional de los pacientes diagnosticados con esquizofrenia. De hecho, el funcionamiento social disminuido ha sido propuesto como rasgo distintivo y objetivo de tratamiento en la esquizofrenia. En 2009, el encuentro titulado “*The Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia (CNTRICS)*” puso de relieve que además de los déficit cognitivos “fríos” (independientes del contenido emocional), los pacientes con esquizofrenia sufren a menudo problemas en el procesamiento tanto social como emocional. Uno de los niveles de estudio de la cognición social es el reconocimiento facial de emociones, que ha mostrado tener un importante papel en las interacciones sociales. Según la literatura existente, los pacientes con esquizofrenia muestran limitaciones en su capacidad para interpretar estas señales emocionales. Sin embargo, existe poco consenso acerca de la causa, la naturaleza y las consecuencias de estas limitaciones. Con los estudios presentados en esta tesis esperamos poder aportar resultados de interés para un mayor conocimiento en este ámbito de investigación.

2. Objetivos

El principal objetivo de este trabajo es estudiar el proceso de reconocimiento de expresiones faciales en pacientes con esquizofrenia. Uno de los primeros propósitos fue estudiar si los pacientes muestran un déficit específico en el reconocimiento de expresiones faciales, o por el contrario, estos se deben a dificultades más generales en el procesamiento de estímulos faciales. El siguiente sub-objetivo fue explorar el propio déficit en el reconocimiento de expresiones faciales, estudiando los patrones de

atribución emocional ante caras emocionales y neutras, siendo esta una medida indirecta de la ambigüedad con la que es percibida cada emoción. Otro de los sub-objetivos fue estudiar la evolución del déficit en el reconocimiento afectivo, comparando de manera transversal pacientes en diferentes estadios clínicos de la esquizofrenia. Finalmente, se intentó comprobar si el contexto visual emocional influye en las evaluaciones que los pacientes hacen ante estímulos faciales emocionalmente neutros.

3. Resultados

Resumiendo los principales resultados encontrados en esta tesis, podemos decir que los pacientes con esquizofrenia muestran un bajo rendimiento en tareas de reconocimiento facial de emociones. No ocurre así en el caso de tareas que implican el procesamiento de aspectos no emocionales de las caras, como la identificación del género, donde los pacientes muestran un rendimiento comparable a los controles. Con respecto a las diferencias entre fases del trastorno, en las fases iniciales las dificultades encontradas en las tareas afectivas se ven restringidas a las expresiones de miedo, mientras que en las fases más crónicas, estas dificultades parecen generalizarse a todas las emociones negativas y las caras emocionalmente neutras. Los pacientes en estadios iniciales del trastorno muestran un patrón de respuestas ante caras neutras idéntico al de sus controles, al contrario de lo que ocurre con los pacientes crónicos. Adicionalmente, las tareas especialmente diseñadas para ello mostraron que las emociones negativas, positivas y neutras son percibidas por los pacientes como estímulos más ambiguos (esto es, mostrando potencialmente más de una emoción) comparados con el grupo control. Finalmente, en presencia de información contextual emocional, los pacientes mostraron una tendencia a categorizar las caras emocionalmente neutras como de miedo en mayor medida que los controles. Sin embargo, en presencia de contextos neutros (congruentes en términos de valencia con las caras presentadas), los pacientes no difirieron de los controles en sus evaluaciones de los estímulos faciales.

4. Conclusiones

Con esta tesis se ha tratado de explorar en profundidad algunos aspectos relevantes de la cognición social y en concreto el procesamiento emocional en pacientes diagnosticados de esquizofrenia. Como principal conclusión puede decirse que los pacientes con esquizofrenia no presentan problemas en el procesamiento de aspectos faciales invariables no relacionados con la emoción, como es el caso del género. Esto,

sin embargo, no ocurre en el caso del reconocimiento de aspectos cambiantes de los estímulos faciales, como son los que dan lugar a las expresiones emocionales. Los déficits encontrados en el procesamiento facial de emociones parecen incrementarse en estadios crónicos del trastorno, comparados con los pacientes que se encuentran en las primeras fases. De hecho, los pacientes crónicos perciben además las expresiones faciales emocionales (tanto positivas como negativas) así como las neutras de un modo más ambiguo que la población no clínica. Finalmente, ante información contextual neutra, los pacientes mejoran su reconocimiento de los estímulos faciales neutros, cosa que no ocurre cuando la información contextual es emocional. Es por tanto que los futuros programas de rehabilitación psicosocial deberían plantearse la inclusión de claves contextuales para entrenar y mejorar el reconocimiento de las expresiones faciales de la emoción en pacientes con esquizofrenia.

SUMMARY

Social cognition and emotional processing in patients with schizophrenia

1. Introduction

Schizophrenia is a chronic and severe syndrome manifested through a set of positive, negative and cognitive symptoms that can be very disabling. Although the second-generation antipsychotic drugs are effective in treating positive symptoms, the efficacy against negative and cognitive symptoms is not nearly as good as it should be. Precisely, cognitive functioning, and not positive symptoms, had significant concurrent and predictive relationships with functional outcomes in patients with schizophrenia. In fact, the poor social functioning has been proposed as a hallmark and also treatment target of the disorder. The “Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia (CNTRICS)” meeting (2009) pointed out that in addition to “cold” (emotion-independent) cognitive deficits, people with schizophrenia often present prominent deficits in social and emotional processing. One level of study of social cognition is facial affect recognition, which has shown to play an important role in social interaction. According to literature, patients with schizophrenia experience limitations in their ability to interpret those emotional signals. There is however less consensus about the cause, nature and outcome of these limitations. With the studies

presented in this thesis we would like to fill in some way the existing gaps on this matter.

2. Objectives

The main goal of the present work was to explore facial affect recognition in patients with schizophrenia. The first aim was to assess whether patients with schizophrenia show a specific deficit on facial affect recognition rather than a general face processing impairment. The second objective was to assess the deficit in emotion recognition itself. For this purpose, the patterns of emotion attribution to emotional as well as neutral faces were explored, as an indirect way to determine the ambiguity with which facial expressions were perceived. A further objective focused on the study of the development of the deficit, for that purpose a cross-sectional comparison between patients at early and chronic stages of the disorder on face affect recognition was carried out. Finally, the last goal was to study the influence of visual contextual information on evaluations of patients over emotionally neutral facial stimuli.

3. Results

Summarizing the main results reported in the present thesis, it has been shown that patients perform poorly on tasks involving face affect processing. By contrast, on tasks involving processing of non-emotional facial features (i.e. gender identification) patients performed as accurate as controls. Regarding differences between clinical stages, at early stages the impairments found in affect recognition are restricted to fear expressions, while at chronic stages of the disorder the impairments generalized to all negative basic emotions as well as to emotionally neutral expressions. Furthermore, patients at early stages of the disorder showed a preserved pattern of responses to neutral faces, as opposed to chronic patients. Additionally, specially designed tests indicated that patients perceive negative as well as positive and neutral expressions as more ambiguous (that is, as potentially expressing different emotions) than controls. Finally, in presence of contextual information, patients tended to categorize neutral faces as depicting fear to a higher extent than controls in presence emotional context information. However, in presence of neutral contexts (congruent in terms of valence with faces), patients and controls did not significantly differ in their evaluations of facial stimuli.

4. Conclusions

This thesis pursued the aim to explore in detail the social cognition and, specifically, emotion perception performance in patients with diagnosis of schizophrenia. As a main conclusion, we observed that when task demands were centered on the identification of invariant facial features, such as gender recognition, patients were as accurate as controls. This, however, is not true in the case of recognition of changeable aspects of faces such those that occur during emotional expressions. The impairments found on facial affect recognition seem widespread at chronic stages compared to early stages of the illness. In fact, chronic patients perceived facial expressions of emotions (both positive and negative) as a more ambiguous stimulus than non-clinical population. Finally, when context information was neutral, patients showed an intact recognition of neutral facial stimuli, which was not the case when the context was emotionally laden. Therefore, future psychosocial rehabilitation programs should include contextual information, to train and improve facial expression of emotion recognition in patients with schizophrenia.

CHAPTER 1: THEORETICAL BACKDROP

The importance of nonverbal communication

“Dogs when approaching a strange dog, may find it useful to show by their movements that they are friendly, and do not wish to fight. When two young dogs in play are growling and biting each other's faces and legs, it is obvious that they mutually understand each other's gestures and manners”.

With this sentence, Charles Darwin, (1872, p.65) identified some elements of behavior that could be considered a mean of non-verbal communication in animals. In the case of social animals, the power of intercommunication between the members of the same community,—and with other species, between the opposite sexes, as well as between the young and the old,— is of the highest importance to them. This is generally effected by means of the voice, but it is certain that gestures and expressions are also mutually intelligible (Darwin, 1872). Humans not only use articulate language to communicate with others, they use —as well as animals do- inarticulate cries, gestures, and expressions. One of the most informative signals in humans is the facial expression of emotion. A person's face can tell us many things (such as sex, age, race...), but it can also give the observer clues as to what that person is feeling, be like a window into the person's emotional state or give us an idea of what the person will do next (Ekman, 1997). For typically developing infants, faces have special significance, as they provide nonverbal information important for communication and survival (Darwin, 1872). In fact, face recognition ability is present during the first 6 months of life. Also, a visual preference for faces (Goren, Sarty, & Wu, 1975) and the capacity for very rapid face recognition (Walton & Bower, 1993) has shown to be present at birth.

There has been a large debate about the primary function of facial expressions of emotion (Russell, 2003). Darwin (1872) and others like Ekman (1997) or Izard and Malatesta (1987) suggested that emotional expressions are automatic displays that occur as a function of the emotional experience of the individual. According to these authors, although the expression may impart information to observers, the transmission of information is not their function. Instead, for these authors, the expression is just an

automatic consequence of the individual's experience (Ekman, 1997). On the other hand, some authors like Blair (2003) or Fridlund (1994) described human emotional expressions as serving a crucial communicatory role, allowing the rapid transmission of valence information from one individual to another. Being communication their primitive function or not, it is uncontested that facial expressions help others to understand our mental states and act accordingly. Imagine the following situation: this morning your boss appears at the office showing lowered brow, thinned lips and flared nostrils. If you are able to “read” his face, you will notice that this is not the best day to ask for a pay rise. The ability to understand other's feelings has a critical adaptive value in our social world. Imagine now that your friend shows upwardly slanted eyebrows and a frown. This friend is making you know that he/she is seeking support. Responding appropriately to these everyday situations would help us to establish good relationships and to create/maintain a fruitful social network.

Social cognition and face perception

The inferences about inner states, desires, goals and even stable personality traits on the basis of facial expression and facial appearance (e.g., Frith, 2008; Lieberman, 2011; Oosterhof & Todorov, 2008; Rizzolatti & Craighero, 2004) are a significant part of social cognition, that is, the set of mental mechanisms and processes through which we make sense of the behavior of our conspecifics. Adolphs, (2001, p.231) defined social cognition as “the ability to construct representations of the relation between oneself and others and to use those representations flexibly to guide social behavior”. Smooth and efficient communication in the course of social interaction require correct identification and decoding of changes in facial expressions that provide the observer clues as to what the expresser is feeling and about her/his immediate intentions (Ekman, 1997).

The modern study of emotion and emotional expression can be traced back to Tomkins' theory (1962), which introduced the idea of a small set of “basic” emotions evolved to meet specific adaptive purposes. Izard (1971) and Ekman, (Ekman, Friesen, & Ellsworth, 1972; Ekman & Friesen, 1975; Ekman, 1973, 1989, 1994) amongst others, took on this approach to set out their research into the universal and cross-cultural

aspects of facial expressions. Ekman and colleagues argued that there is unambiguous evidence of universality for the expressions of happiness, anger, disgust, sadness, fear, and surprise (Ekman & Oster, 1979). The weight of evidence supports this (Ekman, 1994; Izard, 1994), although there have been some authors calling it into question (e.g., Crivelli, Russell, Jarillo, & Fernández-Dols, 2016; Pilowsky & Katsikitis, 1994; Russell, 1994). The criticism focuses on the theory of basic emotions itself and consequently, on the existence of the corresponding universal facial signals (Turner & Ortony, 1992). Some authors suggest that, instead of being external manifestations of unitary basic emotions, facial expressions might be decomposed into elements that are each related to a more primitive emotional component (e.g., effort, increased attention or arousal changes). It is obvious that in everyday life, these six basic expressions occur relatively infrequently. Humans are capable of producing thousands of expressions that vary in complexity, intensity and meaning (Lien, Cohn, Kanade, & Li, 1998). However, it sometimes feels necessary to segment reality to undertake an in-depth study of the basic levels that compose it.

Assuming that there is a set of basic emotions which can be expressed through different facial configurations, initially, the question of just how accurately people can tell whether someone is happy, angry, or sad was approached (Bruner & Tagiuri, 1954; Klineberg, 1938; Landis, 1924). Later studies emphasized that despite differences in language and culture, observers agree to a certain extent on their classification of at least some facial expressions (Buck, 1984; Ekman, 1982; Izard, 1971). There have been several transcultural studies regarding the recognition of facial expressions of emotion (Ekman, 1994; Ekman & Friesen, 1971; Izard, 1994; Russell, 1994). However, the idea that some emotions such as Happiness, Sadness or Fear are readily recognized through facial expressions, whatever sociocultural background the facial expressions are evaluated in, has been discussed. For example, there is some evidence for cultural differences in the perception of the strength of emotions (Ekman, Rolls, & Perrett, 1992) and the meaning attributed to some facial expressions such as those of fear across cultures (Crivelli et al., 2016). Empirical research promoted by this discussion has yielded the possibility of the existence of a gradient of accuracy in the recognition of different expressions, which is influenced by many factors. A relevant meta-analysis carried out by Elfenbein and Ambady, (2002) concluded that there is different degree of agreement in the recognition of different facial expressions of emotion, with some

expressions (Happiness and Anger) showing high cross-cultural recognition accuracy and others losing some of their meaning across cultural boundaries.

Stimuli used in facial affect recognition studies have included drawings, cartoons, photographs, slides, and videos. The development of materials for a particular study with no attention paid to psychometric properties has been usual. The Pictures of Facial Affect (Ekman & Friesen, 1976) are a notable exception. Although the Ekman and Friesen (1976) slides remain the most widely used, more modern sets of slides such as the NimStim set (Tottenham et al., 2009) have been developed including enough racial or ethnic diversity and open- and closed-mouth versions of each expression, which can be useful to experimentally control for perceptual differences (e.g., toothiness).

Social cognition and facial affect recognition in patients with schizophrenia

Schizophrenia is a chronic and severe disorder manifested through a set of symptoms that can be very disabling, with important impact on personal, familiar and social functioning and quality of life of the person affected by it (Jobe & Harrow, 2005; Tomotake, 2011). Schizophrenia is formally characterized by three distinct symptom clusters ‘positive’ in the sense of productive symptoms such as delusions or hallucinations, ‘negative’ in the sense of a deficit, -this category includes blunted affect, emotional withdrawal or difficulty in abstract thinking- and ‘cognitive’ that include deficits in basic processes such as memory, attention, working memory, and executive function. The median lifetime prevalence estimates for persons were 4.0 per 1,000 and 7.2 per 1,000 for lifetime morbid risk (McGrath, Saha, Chant, & Welham, 2008) and the life expectancy of patients with schizophrenia is 12-15 years shorter than general population (van Os et al., 2009). In Spain, the health care costs associated with schizophrenia account for 2.7% of total public healthcare expenditure (Oliva-Moreno et al., 2006). Although the new second-generation antipsychotic drugs are effective in treating positive symptoms with a reduced burden of motor side-effects (compared with first generation antipsychotics), the efficacy against negative and cognitive symptoms is not nearly as good as it should be (Leucht et al., 2009). In fact, the negative and

cognitive symptoms tend to be chronic and are associated with long-term effects on social function (Owen, Sawa, & Mortensen, 2016). However, a review of the literature, suggests that specific domains of cognitive functioning, and not positive symptoms, had significant concurrent and predictive relationships with functional outcomes in patients with schizophrenia (Bowie et al., 2008; Bowie, Reichenberg, Patterson, Heaton, & Harvey, 2006; M. J. Green, 1996; Leifker, Bowie, & Harvey, 2009; Malla & Payne, 2005; Milev, Ho, Stephan Arndt, & Andreasen, 2005) and that the relationship of cognitive functioning to social and adaptive functioning remains significant despite differing levels of negative symptom severity (McGurk, Moriarty, & Harvey, 2000). In fact, the poor social functioning has been considered a hallmark of the disorder (Carter et al., 2009). It is very interesting to note that previous to the name of ‘schizophrenia’ introduced by Swiss psychiatrist, Eugene Bleuler (1911), some authors such as Phillippe Pinel (1806), Benedict Augustin Morel (1852) and Emil Kraepelin (1893) referred to it as a type of dementia to emphasize the deteriorating course of the disorder. There is no doubt that for the first authors to describe the disorder, the cognitive deficit attained great importance. In fact, during the last 15-20 years, there has been a resurgence of interest in the cognitive alterations of schizophrenia (van Os et al., 2009).

In 2009, the Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia (CNTRICS) meeting pointed out that in addition to “cold” (emotion-independent) cognitive deficits, people with schizophrenia often present prominent deficits in social and emotional processing (Carter et al., 2009). There is a bunch of literature showing that the recognition and interpretation of facial expressions of emotion, a main component of social cognition, is impaired in schizophrenia (for reviews see Edwards, Jackson, & Pattison, 2002; Kohler, Walker, Martin, Healey, & Moberg, 2010; Mandal, Pandey, & Prasad, 1998). Two approaches can be taken: encoding and decoding. In the encoding studies, patients' ability to express different facial emotions was examined. The decoding studies were conducted to examine patients' ability to understand others' facial expressions of emotions (Harper, Wiens, & Matarazzo, 1978) and they are, as it was mentioned above, the key to understand patients' ability to understand social behavior of their conspecifics.

A meta-analysis carried out by (Kohler et al., 2009) revealed a large deficit in emotion perception in schizophrenia, irrespective of task type, representing a robust finding in schizophrenia that appears to be moderated by certain demographic and

clinical factors. Illness related factors included age of onset, where a later age of onset was related to greater impairment; antipsychotic treatment, being patients using first-generation antipsychotics the most impaired and clinical symptoms (here, results were mixed and based on the instruments employed). In fact, many other authors have reported no significant correlation between emotion recognition and illness duration, symptoms, inpatient/outpatient status, and medication levels (e.g., Addington & Addington, 1998; Bellack, Blanchard, & Mueser, 1996; Salem, Kring, & Kerr, 1996).

The next reasonable step was to address the question of the specificity of the affect recognition deficit itself. While a general deficit in the recognition of emotional expressions has been reported (Kohler et al., 2003) recognition impairments specific to particular expressions have been more frequently found, especially for faces expressing negative emotions such as anger or sadness (e.g., Bediou et al., 2005; Janssens et al., 2012), although deficits in discrimination of emotion in happy faces, where patients had to select either one of the simultaneously offered faces as “more happy”, have also been described (Sachs, Steger-wuchse, Kryspin-exner, Gur, & Katschnig, 2004). Morrison, Bellack and Mueser (1988) pointed out that the inconsistent results regarding whether patients with schizophrenia experience difficulties with negative emotions could be partly due to the differential discriminatory power of the test stimuli. In the same vein, some authors have suggested that impaired recognition of negative expressions by schizophrenia patients might be related to the different discriminability of positive and negative expressions (Johnston, Devir, & Karayanidis, 2006; Johnston, Katsikitis, & Carr, 2001). The existence of different facial expressions for negative emotions would produce a gradation in task difficulty when recognition of positive and negative expressions is compared. Specific negative emotions have shown to be represented by facial configurations with an unique and universally recognized signal value (Ekman et al., 1987). However, Adolphs (2002), pointed out that negative expressions are more difficult to recognize and more easily confusable for general population because their corresponding facial configurations include facial movements that are shared with other expressions. It has been suggested is that facial expressions of negative emotions overlap to a high degree, thus increasing their confusability and leading to reduced accuracy. This characteristic of negative expressions would pose additional problems to schizophrenia patients due to aberrant processing in neural networks involved in perceptual analysis (Johnston, Stojanov, Devir, & Schall, 2005) or to higher noise of

internal representations (Bach, Buxtorf, Grandjean, & Strik, 2009). By contrast, according to Ekman (1992), positive emotions appear to have no a unique signal value, but instead all share the *Duchenne smile* (i.e., raised lip corners accompanied by muscle contraction around the eyes), so it can be assumed that matching emotions with their corresponding facial configuration should be easier in the case of positive compared to negative ones.

The case of neutral faces, that is a plain face expressing neither negative nor positive emotions, deserves particular focus; however, many studies on emotion recognition did not include them. Kohler et al. (2003) found that patients with schizophrenia more commonly attributed emotional valence to non-emotional faces than healthy comparison subjects. The few studies exploring this matter found that patients misidentified neutral cues as emotional, in particular showing a negative bias. A positive error bias in schizophrenia was however supported in a previous study, but this was in the context of discriminating sad from happy emotions (Heimberg, Gur, Erwin, Shtasel, & Gur, 1992). Apart from this study, the little literature addressing this issue usually finds a negative bias, showing patients a tendency to identify neutral faces as depicting disgust (Kohler et al., 2003) and anger in the case of patients with actively paranoid symptomatology compared to those who had not paranoid symptoms at the moment of the evaluation (Pinkham, Bressinger, Kohler, Gur, & Gur, 2011). Even prior to the full-blow of the disorder, individuals at high risk to develop a psychotic disorder showed a tendency to misattribute negative emotions to neutral faces more often than controls (Brown & Cohen, 2010; Eack et al., 2010; van Rijn et al., 2011). Impaired classification of neutral or non-emotional faces in the schizophrenia sample may have implications for understanding symptoms. In fact, clinically stable patients have shown to be more likely to identify neutral facial expressions as emotional, imputing negative valence to such expressions (Kohler et al., 2003). Perhaps even stable patients are more likely to identify neutral facial expressions as emotional, imputing them negative valence. However, further investigation is needed to clarify the role of emotional attribution to neutral stimuli in the experience of psychosis and its fluctuations over the course of the disorder.

How specific is the impairment?

Although many studies have examined the recognition of facial affect by schizophrenia patients and most have found evidence of impairment (Edwards et al., 2002; Mandal et al., 1998; Pinkham, Penn, & Perkins, 2003), this does not mean that facial emotion processing is a core deficit itself in the context of schizophrenia. In fact, patients with schizophrenia perform poorly on almost all cognitive tasks (Chapman & Chapman, 1973). There is an ongoing debate on whether the facial emotion recognition deficit in schizophrenia is specific, in the sense of being disproportionate to that seen in other areas of cognition, and several authors have argued that this has not been demonstrated conclusively (Edwards et al., 2002; Johnston et al., 2001; Kerr & Neale, 1993). For example, Pomarol-Clotet et al. (2010) found that when steps were taken to reduce the effects of general intellectual impairment, there was no deficit in identifying facial emotions in schizophrenia. For that reason, several studies have tried to compare patient's performance on different tasks involving processing of non-emotional features of faces (e.g., face identity and gender). In these studies, similar impairments in emotion recognition and other face-related tasks, such as gender recognition, have been found (Pomarol-Clotet et al., 2010; Salem, Kring, & Kerr, 1996). However, specific impairment in expression recognition with gender recognition preserved has also been reported (Bediou, Krolak-Salmon, & Saoud, 2005). There are also results suggesting that the specificity of the deficit might be related to the chronicity of the clinical condition (Penn et al., 2000). Furthermore, there is no agreement with regards to the abnormal neural mechanisms underlying this deficit. Some explanations have focused upon limbic system abnormalities (Gur et al., 2002; Kohler et al., 2003; Phillips et al., 1999), whereas others have implicated early visual processes relating to the structural encoding of faces (Bediou et al., 2007; Johnston, Stojanov, Devir, & Schall, 2005; Michalopoulou et al., 2008). There is wide agreement that facial emotion processing deficits in schizophrenia represent both a potential window onto abnormalities in brain function associated with the condition and a potential target for cognitive remediation strategies aimed at improving social functioning and quality of life in patients (Johnston et al., 2010).

A dimension not very often controlled when studying facial emotion processing in schizophrenia is the intensity (i.e. the degree to which faces express emotions) of the expressions used as stimuli. The study of the influence of emotional intensity on facial affect recognition in patients with schizophrenia has not been addressed as broadly as emotion recognition in previous publications, and could have contributed to the divergence of findings. The first study to include low- and high-intensity emotional expressions showed that patients with schizophrenia did not benefit from greater emotional intensity to the extent that healthy subjects benefited. This relative lack of benefit was found for all emotions combined and was most pronounced for fear (Kohler et al., 2003). This result was confirmed by another study published a couple of years later (Bediou, Krolak-Salmon, et al., 2005). However, it seems necessary to further explore the recognition of facial affect by patients with schizophrenia in stimuli depicting different expressions of emotions varying in intensity to assess in detail to what extent (if at all) patients are able to recognize them.

Scarce literature exists on the topic of recognition of affect through other cues rather than facial expressions by schizophrenia patients. There are very few studies which have examined both face and voice perception in the same individuals with schizophrenia. Edwards, Jackson, & Pattison (2002) reviewed several studies that explored emotion recognition via facial affect and affective prosody in schizophrenia, all using static pictures and audio-tapes. They found support for recognition deficits in both modalities in chronic schizophrenia, and also a significant positive association between abilities in the two perceptive channels. Likewise a study with first-episode schizophrenia patients supported small but consistent deficits in recognition of fear and sadness across both communication channels (Edwards, Pattison, Jackson, & Wales, 2001). However, the multi-channel investigations have usually shortcomings such as collapsing the analysis across all emotions. Then, the subsequent failure to consider which emotions are more difficult to process by individuals with schizophrenia will need to be overcome in future research.

Is the deficit in face affect recognition different across clinical staging in schizophrenia?

Social cognitive deficits in emotion perception have been proposed as a potential endophenotype for schizophrenia (Eack et al., 2010; Leppänen, Niehaus, Koen, & Toit, 2008). Endophenotypes have emerged as an important concept in the study of complex neuropsychiatric diseases. They represent simpler clues to genetic underpinnings than the disease syndrome itself, promoting the view that psychiatric diagnoses can be decomposed or deconstructed (Gottesman & Gould, 2003). However, to be endophenotypes for psychiatric disorders, cognitive, or neuropsychological outcomes must meet certain criteria. The four primary criteria proposed for an endophenotype are that 1) it is present in probands with the disorder, 2) it is not state-related (that is, it does not occur only during clinical episodes) but instead is present early in the disease course and during periods of remission, 3) it is observed in unaffected family members at a higher rate than in the general population and 4) it is heritable (M. F. Green, Horan, & Lee, 2015). Following this approach, it is important to study face affect recognition at different stages of the disorder, taking it as a first approximation to be able to consider social cognition as an endophenotype for schizophrenia.

Emotion recognition deficits have been proposed as a core feature of schizophrenia, representing “vulnerability-linked impairments, which are augmented during symptom exacerbation” (Penn, Corrigan, Bentall, Racenstein, & Newman, 1997, p.123) rather than an indicator of state factors and/or chronicity (Mueser, Penn, Blanchard, & Bellack, 1997). Following this reasoning, these impairments should be apparent in clinically stabilized first-episode outpatient samples. Studying individuals with ‘first-episode’, ‘early schizophrenia’, or ‘recent-onset’ disorders helps to minimize the influence of variables such as institutionalization, the long-term effects of medication, and general psychosocial deterioration (Kane & Barnes, 1995), and could be a valuable method for homogenizing variability due to the course of the disorder (Keshavan & Schooler, 1992).

Several studies have compared emotion recognition performance in early stage and chronic schizophrenia patients, in an attempt to establish if these deficits are stable or on the contrary, vary over time. However, the comparison of recent onset and chronic

patients is not without its challenges. The very few longitudinal studies on this matter have followed patients during relatively short periods of time (usually a few months, or years) and have found stable impairments in both first- and multi-episode patients in cognition, social functioning and facial affect recognition (Addington, Saeedi, & Addington, 2006; Nuechterlein, Ventura, Subotnik, & Bartzokis, 2014) and even in remitted patients (Ventura et al., 2015). On the other hand, cross-sectional studies comparing patients at different stages of the disorder did not provide a direct test for change in emotion recognition performance, but for evident reasons are usually more abundant. Using this design, several authors have found similar deficits in early and later stages in facial affect recognition indeed (Comparelli et al., 2013; Pinkham et al., 2007; Sachs et al., 2004; Vohs et al., 2014). Only one study found greater impairments in emotion perception in individuals with chronic schizophrenia compared to first episode psychosis (Kucharska-Pietura, David, & Masiak, 2005). However, as it was mentioned above, cross-sectional studies are limited by the fact that they are carried out at one time point and give no indication of the sequence of events at different stages of the disorder. That's why we have to be extremely cautious when carrying out that kind of studies, and make comparisons with appropriated control groups. The first step before conducting cross-sectional studies comparing clinical samples should be to ensure that there are no developmental changes over the time course in non-clinical samples, which is the case of emotion recognition abilities (Sonneville & Verschoor, 2002; Widen & Russell, 2003). Schizophrenia is a mental disorder that usually appears during late adolescence and early adulthood, when although no precise borders can be defined, brain maturational processes are not completed. For that reason, including appropriate comparison controls must be a priority to avoid assuming that results are attributable to the disorder effect rather than to normal development. The studies mentioned above have severe limitations on this regard and their conclusions could be seriously questioned.

Context influence

In view of the foregoing, it is imperative to explore new ways to make patients with schizophrenia improve their facial affect recognition abilities. In everyday social

interaction, faces of our conspecifics do not appear in isolation. Usually, we have broader information such as body gestures (Meeren, van Heijnsbergen, & de Gelder, 2005) and environmental cues (de Gelder et al., 2006). Maybe when a facial expression seems difficult to classify, contextual information could help, or even determine the judged emotion. In fact, situational information was shown to be especially influential when a non-basic emotion is judged (Carroll & Russell, 1996).

Accurate facial emotion perception thus requires attending to both target emotional and situational cues that allow people to put the expression into context, in order to facilitate the generation of an appropriate response. In an attempt to find clues that could help patients to disambiguate facial expressions, context information could be considered as a candidate to determine which label best suites to a facial configuration. Especially when this facial configuration is shared by several emotions, as in the case of fear and surprise (Kim et al., 2004). If so, making patients aware of such information could be included as a target in psychosocial interventions.

Evidence shows that patients with schizophrenia do not fully make use of context information during non-social reasoning (Stratta, Daneluzzo, Bustini, Prosperini, & Rossi, 1999). Some studies have shown that patients did not utilize available contextual information and that reduced context processing in schizophrenia is related to impaired performance on social cognitive tasks (Penn, Ritchie, Francis, Combs, & Martin, 2002). Furthermore, direct examination of the use of social contextual information in schizophrenia has recently demonstrated impaired use of visual context to categorize facial emotion, especially when contextual cues suggested a complex mental state paired with a negative or threat-related expression (e.g., anger, fear, sadness) (Green, Waldron, & Coltheart, 2007). In this study, facial affect processing ability was a significant predictor of the successful social context integration. In this regard, Monkul et al. (2007) examined the impact of social contextual information upon the perception of emotional intensity in schizophrenia using a five-point Likert scale, but they failed to find that context could change patients' evaluations.

There still remains much to be done in this field. Previous studies have employed emotional faces associated with contexts, which may be leading patients to confound information coming from both sources. As it was mentioned above, patients

tend to misattribute emotional meaning to neutral faces. Maybe studying the influence of contextual information on neutral or non-emotional stimuli could provide relevant information about the use of emotional context, having a single source of emotional information, different from a face. This kind of comparison would contribute to understand the extent context information modifies the perception of neutral facial stimuli in patients with schizophrenia and controls.

Clinical implications

There is an initial point which needs to be cleared up: although schizophrenia patients, as a group, have shown specific social cognition deficits against a background of general cognitive dysfunction, there is no doubt that there are also large individual differences. The idea that this diversity is caused by the existence of different subgroups of patients has extensively been debated (e.g. Malaspina et al., 2004; Roy, Merette, & Maziade, 2001; Wolkin et al., 1989). Some authors have tried to abolish the diagnosis by arguing that lumping together patients with sometimes contradictory symptoms under one label is completely useless (van Os, 2016). Although it highlights some important points about labels used by professionals, from our point of view, as well as others' (Hamilton, 2016; Lawrie, 2016; Sommer & Carpenter, 2016) using the term as an integrator category would help clinicians as well as researchers to find those things that this very assorted group of patients shares. The aim of the present work was to explore symptoms considered “core” features of the disorder that unify patients with schizophrenia under this (controverted) label. As mentioned, some experts also share this point of view.

Schizophrenia is one of the most disabling psychiatric disorders, which is usually associated with an important long-term functional impairment. Identifying the risk factors that increase such impairment is of great importance not only for the development of effective drugs but also for efficient and integrated rehabilitation programs. From the development of antipsychotics the main therapeutic target has moved from positive symptom resolution to translate gains to functional outcome and quality of life (Remington, Foussias, & Agid, 2010). The clinical relevance of facial affect recognition deficits is shown by their specific relationship with social competence

and functioning (e.g., Kee, Green, Mintz, & Brekke, 2003). In the case of schizophrenia, although general deficits in face processing have been described, only affect recognition deficits correlated with social functioning (Hooker & Park, 2002). There was also evidence that facial affect recognition did partially mediate the relationship between cognitive and social functioning in schizophrenia patients (Addington et al., 2006). Furthermore it has been shown that social functioning predicted conversion to psychosis, at least among males at clinical high-risk for psychosis (Walder et al., 2013). Pharmacotherapy has demonstrated to have clinical efficacy for controlling positive symptoms but not for negative or cognitive symptoms. A deeper knowledge of processes involving social cognition would facilitate the development of efficient psychotherapeutic approaches, which would result in an improvement of the functionality and quality of life in patients with schizophrenia. But, why having a correct social functioning is important for patients? A correct social functioning would facilitate patients to build a social network which should provide them support and care. Social support has been postulated to serve as a protective factor that facilitates coping and competence, thus modulating the adverse effects of social and environmental stressors (Anthony & Liberman, 1986; Boyd, 1994; O'Connor, 1994). Social support is defined as a personal experience, as opposed to a set of objective circumstances. Certain specific health-sustaining functions of social support can be reduced to: (a) esteem support, or information that one is esteemed, accepted, or affirmed; (b) informational support, sometimes referred to as advice or coping support; (c) affiliative support aimed at facilitating positive affective moods; and (d) instrumental support, or the provision of either tangible or intangible aid (Buchanan, 1995). Furthermore, social interactions have demonstrated to be behavioral determinants of positive emotions (Fredrickson, 2005; Waugh & Fredrickson, 2006), and it goes without saying that positive emotions are desirable in a person's life. Nowadays, the increasing capacity of clinicians to control the positive symptoms of many patients and the emphasis on returning them to the community, has resulted in a growing interest in promoting "quality of life" of patients as the next therapeutic target (Heinrichs, Hanlon, & Carpenter, 1984). Quality of life is the patient's own subjective view of well-being and satisfaction with her/his life (Skantze, Malm, Dencker, May, & Corrigan, 1992). There is also evidence that impaired social functioning impacts quality of life (Penn et al., 1997), therefore, it should be taken into account as a measure of treatment success and considered the ultimate goal of interventions.

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CHAPTER 2: OUTLINE OF THIS THESIS

The main goal of the present work was to study emotion recognition in patients with schizophrenia on different tasks involving face affect processing. Based on the current state of knowledge described in the introductory section, two related sub-goals were proposed. On the one hand, we aimed to study face affect recognition in patients with schizophrenia as a cognitive process. To that end the modulatory aspects that influence patients' ability to determine the emotion expressed by a face, such as response format or the contextual information available were explored. On the other hand, we aimed to study the development of the deficit by comparing face affect recognition at two stages of the clinical course of schizophrenia: the early stages of the disorder and the chronic phase. The studies reported in this thesis are, however, in chronological order of realization.

As it was stated previously, the first goal reported in **chapter 3** was to further explore whether face processing impairments in schizophrenia are circumscribed to recognition of facial expressions of emotion. For this purpose, a comparison between a group of patients with schizophrenia and a group of paired controls in a task involving face processing of non-emotional features such as gender categorization was carried out. The novelty of this study was that a non-emotional task was performed over facial emotional stimuli, in order to make it comparable with facial emotion recognition tasks. Results reported in this chapter (in addition to those reported in subsequent chapters) would allow us to clarify whether patients show a general face processing impairment. Once this differentiation was clear, the next step was to explore their recognition of facial expressions, paying attention to different aspects of the emotion recognition to delimit the scope of the deficit.

Previous literature has shown that face affect recognition impairments are more consistent with regard to negative emotions (e.g., anger, fear or sadness) compared to expressions of happiness. One hypothesis is that the internal representations of emotional expressions are less differentiated and have poorly defined boundaries in patients with schizophrenia than in controls. In an attempt to explore this hypothesis, the experimental task reported in **chapter 4** was conceived to answer this question.

Traditional experiments usually show participants a face, and then they are asked to select the label that better describes the emotion expressed by that face. However, selecting the best word to describe the feeling does not mean that other words would also describe, although to a lesser extent, the emotion expressed by the stimuli. This procedure makes researchers to not record all the information about the way that both patients and controls process facial expressions. It can be argued that while both patients and controls are able to perceive different emotions expressed by a single facial stimulus, controls perceive one of them as “dominant” (Ekman, Friesen, & Ellsworth, 1972), and this is the reason why they tend to “agree” to a greater extent compared to patients with schizophrenia. Patients probably do not perceive one of the emotions as “dominant” (or at least, not with the same strength), and this leads them to show more frequent confusions between different expressions, mainly in the case of negative emotions. For this purpose, in this experiment each face was presented to participants four times. Each time they were asked for “how much anger/fear/sadness/happiness can you see in this face?” Their responses provided valuable information to estimate how ambiguous each emotion was for both patients and controls. The experimental design constituted the main innovation of this study, as it means a better understanding of the processing of different emotions and it has never been used before in schizophrenia patients.

Regarding the sub-goal of studying the possible changes of the deficit associated with the stage, we aimed to test whether or not these specific deficits for face affect recognition are present from the very beginning of the disorder in a manner that would tentatively constitute an endophenotype for schizophrenia. Several studies have tried to explore the presence of face affect recognition deficits at different stages of schizophrenia. Even more, their presence has been investigated prior to the first psychotic episode of the disorder, in individuals at clinical or genetic high risk for psychosis. This particularly important question has not always been properly addressed. When impairments shown by patients with severe mental illness are explored, researchers should remain focused on what is considered “normal” in general population. This is even more important in the case of schizophrenia, a mental disorder that usually manifests an early onset, during late childhood or adolescence. Not paying attention to normal development of mental processes would lead to misunderstand results, finding deficits where there are just ‘processes to develop’. In **chapter 5**,

performance of young patients at the very first stages of schizophrenia was compared with appropriate controls, matched in terms of sex and age (thus considered at the same stage of development) in a facial affect recognition task. Concurrently, chronic patients were compared with a different control group, matched in terms of age and sex as well. The main strength of this study was that this kind of comparison has hardly been employed previously, and it is, however, much more appropriated to avoid drawing potentially biased conclusions. Results found in this study will be more useful for designing remediation strategies to better match illness stage to interventions. Then, and related to the sub-goal of the study emotion recognition as a process, the pattern of responses to neutral faces, which has shown to be one of the most impaired stimuli when comparing schizophrenia patients with controls, was explored. The fact that patients tended to categorize non-emotional faces as emotional has been put forward as a proof of their aberrant attribution of salience to non-emotional (or low-emotional) stimuli. This kind of processing might explain some clinical symptoms of the disorder.

Reached this point, the need for finding strategies to help patients to better recognize emotions expressed by faces has therefore become essential. Traditional research has focused on the perceptual and affective processing of faces, in absence of any other sources of information. However, in daily life, facial expressions are usually perceived within a certain situational context. Some studies have shown that processing of facial expressions is influenced by contextual information. However, evidence has shown that patients with schizophrenia did not utilize available contextual information. Previous studies have employed emotional faces as well as emotional contexts. Perhaps a previous step should have been to explore the influence of context information on neutral or non-emotional faces. This was the main innovation of this study, and was made for two reasons: first, these kinds of stimuli have shown to be especially sensitive in the case of patients with schizophrenia and second, it would keep the emotional information of the context from mixing with emotional information of the facial stimulus. In **chapter 6**, this issue has been tried to be addressed by asking patients to evaluate in terms of emotional label and valence neutral faces. These faces were presented along with positive and negative as well as non-emotional contexts. Then, contexts themselves were also subject to evaluations. The possible influence of emotional valence of contexts on face judgments would allow opening a new line of research focused on stimulus-driven attention to target facial features.

Finally, in **chapter 7** the results of all studies presented in this thesis are summarized, followed by the general conclusions concerning the nature and outcome of social cognition deficits in schizophrenia. Then, as a thesis work is not the end, but rather the beginning of the research career, future lines of research are highlighted, as a goal to keep in mind in the near future.

Method

Each study included in the present thesis has a detailed description of the methods used for each specific experimental design. The purpose of this section is to provide a brief overview of the sample, materials and design that coincide in some of the chapters, of course each one with its own characteristics and particularities.

Participants

All participants that took part in the studies presented in this thesis gave their consent prior to their inclusion. They were informed that the data they had supplied would be handled in a responsible manner and anonymously. All experiments fulfill both the ethical and legal requirements and were approved by the Ethics Committee.

Adult participants described in chapters 3, 4 and 5 were part of the same sample. They were evaluated in two sessions (separated by no more than four days). Different participants composed the sample described in chapter 6. Both samples of chronic schizophrenia outpatients were recruited from the Hospital Universitario 12 de Octubre (Madrid, Spain). The sample of first episode inpatients was recruited from the Hospital Infantil Universitario Niño Jesús (Madrid, Spain). All patients were diagnosed and evaluated by experienced psychiatrists. Each group's performance was compared with a similar number of control participants, matched in age and gender, with no self-reported history of mental disorder and no history of psychosis in first-degree relatives, and recruited from the same socio-cultural environment than patients. All participants that took part in this thesis were evaluated with the same computer equipment.

Materials

The basic material included in this thesis for experiments reported in chapters 3 to 5, was a set of 40 pictures from the NimStim data set (Tottenham et al., 2009),

selected based on a previous unpublished study. Pictures were converted to grey scale and cropped to conceal most of the hair and to remove distracting, noisy aspects that are not informative of emotional expression. In the pilot study, all pictures from the NimStim (once processed) were evaluated by an independent sample of 30 participants (students from the school of psychology) in terms of emotional label and emotional intensity. Then, the final set of stimuli was selected from the entire set, including only those pictures that reached, at least, a minimum recognition agreement of 75% of the participants.

In chapter 6, participants were presented 42 pictures taken from the KDEF (Karolinska Directed Emotional Faces) collection (Lundqvist & Litton, 1998) showing neutral expressions. The final selection was based on their ratings of valence, arousal and trustworthiness. It was sought that faces were affectively neutral, with low arousal values and a medium trustworthiness value. Afterwards, 42 context pictures (14 positive, 14 neutral, and 14 negative) were selected from the EmoMadrid dataset (“EmoMadrid affective picture database”, n.d.). Context pictures were selected attending to their valence and arousal values, trying to select the more positive and negative pictures, with higher arousal values and smaller standard deviation to ensure most of the people agreed in their evaluations.

Task design

Presentation of stimuli and registration of responses were controlled with the E-Prime 2.0 software, using self-generated task designs.

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CHAPTER 3: NON-EMOTIONAL FEATURES OF FACES

3.1. Introduction

The first question to address is to what extent deficits found in patients with schizophrenia are due to a general face processing, or on the contrary, to specific facial affect recognition impairments. Bruce and Young (1986) proposed a cognitive model emphasizing a distinction between processes involved in the recognition of identity (i.e. properties that are invariant across different views and facial expressions) and those involved in the recognition of changeable features such as the expression or speech-related mouth movements. This distinction has been supported by behavioral studies where recognition of identity and expression appear to proceed relatively independently. For example, familiarity facilitates performance on tasks involving processing of face identity, but not on tasks focusing on facial expressions of emotions (Young, McWeeny, Hay, & Ellis, 1986). Thus, a neural systems model that emphasizes a distinction between the representation of invariant (e.g., identity, gender) and changeable (e.g., facial expression, eye direction) aspects of faces has also been proposed. In this model, the representation of invariant aspects would mainly rely on the face-responsive region of the fusiform gyrus, whereas the representation of changeable aspects relies more on the face-responsive region in the superior temporal sulcus (Haxby, Hoffman, & Gobbini, 2000). The representation of identity should be relatively independent of the representation of the changeable aspects of a human face; otherwise, a change in expression or a speech-related movement could be misinterpreted as a change of identity. Following this model, it would be reasonable to think that one kind of representation could be selectively affected, independently from the other.

A “face-specific” deficit in schizophrenia has previously been established. Results suggested that performance of patients on tasks involving processing of non-facial stimuli (that share common elements such as familiarity (e.g., cars) and social relevance (e.g., gait)) was better compared with processing of non-emotional features of face stimuli (e.g., identity or gender) (Darke, Peterman, Park, Sundram, & Carter, 2013). However, the specificity and nature of this deficit remains unclear. There is abundant research pointing to the existence of a deficit in recognition of facial affect (for reviews see Edwards, Jackson, & Pattison, 2002; Kohler, Walker, Martin, Healey,

& Moberg, 2010; Mandal, Pandey, & Prasad, 1998). Some authors have tried to investigate whether this poorest recognition of facial affect in schizophrenia patients is based on a general impairment of face processing (e.g., Johnston, Devir, & Karayanidis, 2010; Johnston, Katsikitis, & Carr, 2001). There has been little research comparing performance of patients in emotional and non-emotional tasks involving face processing and these few studies have reported contradictory results. On the one hand, similar impairments in emotion recognition and other facial tasks, such as face recognition have been found (Pomarol-Clotet et al., 2010; Salem, Kring, & Kerr, 1996). However, specific impairment in expression recognition with preserved gender recognition (Bediou, Krolak-Salmon, Saoud, & Henaff, 2005) and age-discrimination (Schneider et al., 2006) has also been reported. The stimuli used on each study could account for the discrepancies found. Patients have shown more difficulties in recognizing some emotions over others (see Elfenbein & Ambady, 2002 for a meta-analysis), then, the emotional facial expressions presented to patients could be interfering to a different degree with recognition of invariable aspects. For example, the study by Bediou et al. (2005) comparing performance of patients with schizophrenia on gender vs. expression recognition only included expressions of disgust, fear and happiness. The study by Salem et al. (1996) included expressions of the following emotions: happy, sad, angry, afraid, surprised, and ashamed, and the study by Pomarol-Clotet et al. (2010) included the same expressions but the expression of disgust instead of shame. However, the fact that any of these studies included faces with no emotional expression to be compared with those that show movements of eyes and mouth as result of an emotional expression could represent a methodological shortcoming. Only the study by Schneider et al. (2006) included faces expressing different emotions (happiness, sadness, anger, fear) and no emotion (neutral). Despite the fact that results were collapsed across expressions, differential impairment was found in patients with schizophrenia for processing emotional faces. However, comparing age recognition on faces depicting specific expressions and neutral ones was not possible.

The results of a study carried out by Penn et al. (2000), comparing samples of acutely ill and extended-care patients with non-clinical controls, suggested that the specificity of the deficit might be related to the chronicity of the clinical condition. More specifically, in this study, acutely ill patients showed a specific deficit in affect

recognition, but chronic patients demonstrated a more general deficit in face perception. Undoubtedly, additional research will be required to confirm this result.

Studies aiming to compare recognition of emotional and non-emotional aspects of faces in patients with schizophrenia are scarce and found mixed results. There is a lack of studies comparing recognition of non-emotional facial features of faces expressing emotions and neutral faces, which could be a key to explain discrepancies. It could be suggested that the facial expressions interfere with recognition of non-emotional aspects while in the case of the neutral faces the recognition of those aspects could remain preserved. The main goal of this study was to assess whether patients with schizophrenia show impairments in a task involving recognition of invariable aspects of faces compared to healthy controls. In the present study, we included faces showing different emotional expressions as well as neutral faces, being the emotional expression a task-irrelevant feature. The inclusion of both types of facial stimuli and its separated analysis and interpretation has not been employed previously. Our hypothesis is that patients will perform as accurate as controls at least in the recognition of gender of faces expressing fear and happy emotions which were included in the study carried out by Bediou et al. (2005). Conversely, we have no prior results about what to expect in the case of the neutral faces. There is previous research showing impairments in the recognition of facial affect of neutral faces (Kohler et al., 2003) but not on recognition of invariant aspects. The only study that includes neutral expressions (Schneider et al., 2006) found no differences between patients and controls in an age-discrimination task, so it would be reasonable to expect the same result in a task involving other invariant aspects of face processing such as gender. However, as it was mentioned above, they did not differentiate results between emotional/non-emotional faces, so up to our knowledge this is the first study to address this question. Finally, some studies have suggested an interaction of gender of poser with the gender of observer in general population (Erwin et al., 1992; Rahman, Wilson, & Abrahams, 2004) and some others have not (Hugdahl, Iversen, & Johnsen, 1993). For that reason, the gender of the participant was included in the analysis as a possible explanatory variable.

3.2. Method

3.2.1 Participants

Nineteen clinically stable outpatients (13 male, 6 female) whom their treating psychiatrists consecutively referred took part in this study (see Table 3.1). 20-paired controls (11 male, 9 female) with no self-reported history of mental disorder and no history of psychosis in first-degree relatives were selected as comparison group. All patients were diagnosed with schizophrenia according to DSM-IV-TR criteria (American Psychiatric Association, 2000). All patients were on atypical antipsychotic treatment and had been clinically stable (no hospital admissions, no changes in treatment and no significant psychopathological changes) for at least six months before inclusion. Clinical status was evaluated using the Spanish version (Peralta & Cuesta, 1994) of the Positive and Negative Syndrome Scale (PANSS) (Kay, Fiszbein, & Opfer, 1987). The written informed consent was obtained from all participants prior to their inclusion in the study. The Ethics Committee approved the procedure.

	Patients (n=19)	Controls (n=20)	Statistic (<i>p</i>)
	Mean (SD)	Mean (SD)	
Age	43.8 (SD 9.5)	42.3 (SD 12.8)	$t = -.438$ ($p = .664$) Cohen's $d = .133$
Gender (% male)	68%	45%	$\chi^2 = .742$ ($p = .514$) $r = .137$
Years of education	9.57 (SD 4.3)	12.05 (SD 3.9)	$t = -1.87$ ($p = .069$) Cohen's $d = -.604$
Age of onset of the disorder	25.9 (SD 7.4)	-----	-----
PANSS-Positive	12.2 (SD 3.7)	-----	-----
PANSS-Negative	17.4 (SD 8.1)	-----	-----
PANNS-GP	26.7 (SD 9.1)	-----	-----
CPZ*	206.45 (SD 128.63)	-----	-----

Table 3.1. Sample demographics and clinical status of patients.

*Chlorpromazine equivalent dose (mg/day).

3.2.2 Materials

Forty pictures from the NimStim face set (Tottenham et al., 2009) were used as stimuli. The faces corresponded to eight different models (four female, four male) each showing neutral, happy, angry, fearful or sad expressions. Pictures were converted to grey scale, cropped to conceal most of the hair. The stimuli were presented on a 15''

LCD monitor (refresh rate 60Hz). See Figure 3.1 for samples of stimuli used in the present work.



Figure 3.1. Samples of stimuli selected from de NimStim stimulus set depicting happy, sad, fear angry and neutral expressions.

3.2.3 Experimental task

In the gender recognition task participants were asked to indicate the gender of each face, in a two-alternative forced choice (“male” vs. “female”) by pressing with the mouse 2 buttons presented on the screen. For counterbalancing purposes, half of the participants were presented the male button at the bottom right of the screen, and the other half at the bottom left part. See figure 3.1 for examples of stimuli.

3.2.4 Data Analysis

A $2 \times 2 \times 2 \times 5$ repeated measures ANOVA was performed on accuracy data. The variables Group (patients, controls) and Sex of the participant (male, female) were the between group factors. The Gender of the model (male, female) and Emotion (happy, angry, fearful, sad and neutral) were the within-subjects factors. The Greenhouse–Geisser and Bonferroni corrections were applied (significant when $p \leq .05$).

3.3. Results

Analysis of performance in the gender task showed no differences in accuracy between patients and controls $F(1,35) = 1.123, p = .297, \eta^2_p = .031$. Also, main effect of Sex of the participant was not found significant $F(1,35) = 1.315, p = .259, \eta^2_p = .036$.

Neither the Gender of the model nor the Emotion were significant $F(1,35) = 2.409$, $p = .13$, $\eta^2_p = .064$ and $F(4,140) = 1.705$, $p = .152$, $\eta^2_p = .046$ respectively. Finally, none of the interactions was significant ($p_s > .05$). Table 3.2 shows accuracy data for each group and condition.

Stimuli		Control		Patient	
		Female	Male	Female	Male
		Mean Acc (SD)		Mean Acc (SD)	
Female	Angry	1 (0.0)	1 (0.0)	1 (0.0)	0.96 (0.093)
	Fear	1 (0.0)	1 (0.0)	1 (0.0)	1 (0.0)
	Happy	1 (0.0)	1 (0.0)	1 (0.0)	0.98 (0.069)
	Neutral	1 (0.0)	1 (0.0)	1 (0.0)	0.98 (0.069)
	Sad	1 (0.0)	0.97 (0.075)	0.95 (0.1)	0.98 (0.069)
Male	Angry	1 (0.0)	1 (0.0)	1 (0.0)	1 (0.0)
	Fear	1 (0.0)	1 (0.0)	1 (0.0)	1 (0.0)
	Happy	1 (0.0)	1 (0.0)	1 (0.0)	1 (0.0)
	Neutral	1 (0.0)	1 (0.0)	1 (0.0)	1 (0.0)
	Sad	1 (0.0)	0.97 (0.075)	1 (0.0)	1 (0.0)

Table 3.2. Mean accuracy results for the Gender Recognition Task.

3.4. Discussion

Results of a gender identification task comparing performance of patients with schizophrenia and controls are reported in this study. As a novelty, stimuli included emotional and neutral facial expressions, which were a task-irrelevant characteristic, to test the influence of changeable aspects of facial stimuli in the recognition of gender. Results showed that patients were not different from their comparison group in the gender recognition task. Thus, patients were capable of performing a non-emotional face categorization task with similar accuracy to that of the control group. Additionally, there was no effect of emotion on gender recognition, leading us to deduce that emotional expressions do not affect the recognition of invariant facial features such as those that are informative of a person's gender, at least in terms of correct responses. Thus, we can conclude that with exactly the same stimuli than those presented in face affect recognition studies, patients performed with a comparably high degree of accuracy. This result supports findings of Bediou et al. (2005) and Schneider et al. (2006) where gender recognition and age-discrimination respectively were preserved in

schizophrenia patients. It should be taken into account that patients that took part in the study by Schneider et al. (2006) showed more impairment on emotion discrimination even though the non-emotional task was considered harder (based on the low accuracy scores of patients and control subjects). As there are studies with patients with schizophrenia that found impairments in the recognition of the invariant aspects of the faces in terms of identity (Pomarol-Clotet et al., 2010; Salem et al., 1996), it might be suggested a distinction between the representation of identity and other invariant aspects of a face such as age and gender. This differentiation could help explain discrepancies between studies. Nevertheless, clinical variables of the samples or even task design differences could also be a plausible explanation for discrepancies found in literature. Regarding clinical variables, as it was discussed in the introductory section, the differences of patients' chronicity may be influencing outcomes. The study of recognition of invariant vs. changeable facial features at different stages of the disorder needs to be further investigated in the future as it was demonstrated in a previous study that extended-care patients showed a general deficit in face perception compared to acutely ill patients (Penn et al., 2000).

In the present experiment, we found that men and women did not differ in a gender categorization task. They performed equally when recognizing the gender of faces belonging to the same and opposite sex. This behavioral result was previously reported by Sun, Gao and Han (2010). But this is not the case of Cellerino, Borghetti and Sartucci (2004), who found a sex difference in the efficiency of face gender categorization. In their experiment, female participants were more efficient in recognizing female faces. Following this result, they propose that even recognition of male and female faces are different cognitive processes. Results reported in the present study, as well as those reported by other authors (e.g. Hugdahl et al., 1993; Y Sun, Gao, & Han, 2010) do not support this differentiation. Maybe task design or the conditions under which stimuli were presented can explain discrepancies among results. In fact, despite behavioral results, Sun et al. (2010) found that attention to gender modulates both the early encoding of facial structures and late evaluative process of faces to a greater degree in women than in men, however this does not lead to a differential behavioral performance between men and women.

From data reported in this study, it can be concluded that recognition of aspects of facial structure that are invariant across changes in expression and other movements

of the eyes and mouth seems to be relatively preserved in schizophrenia patients. However, although the perception of these characteristics is important for social interaction, there is no doubt that perception of the changeable aspects of faces plays a far greater role during interpersonal communication (Haxby et al., 2000). That's why remediation strategies will still be needed for patients with schizophrenia in the field of facial affect recognition as well as social cognition skills. It is for this reason that exploring the recognition of facial expressions of emotions in depth is the main objective of the following chapters.

The present study has several limitations. First, due to the small sample size, conclusions with respect to a specific versus generalized deficit need to be taken with extreme caution and require replication with a bigger sample. Second, a broad investigation including both emotional and non-emotional facial stimuli and several tasks aiming to explore processing of invariant aspects of faces such as gender, identity and age taken together in a within-subjects design will be necessary to draw relevant conclusions.

In conclusion, patients with schizophrenia showed accurate performance on a gender categorization task irrespective of the expression depicted by facial stimuli including as a novelty emotional and neutral faces analyzed separately. This encouraging result leaves the need to further explore deficits in recognition of facial expressions of emotions. As perception of invariant aspects of faces seems to be relatively preserved in the case of patients with schizophrenia, researchers have now the challenge of further explore under which conditions patients with schizophrenia exhibit facial affect recognition deficits.

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CHAPTER 4: PATTERNS OF EMOTION ATTRIBUTION

Preamble

Chapter 4 corresponds to a published article with the following reference:

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As a way to integrate the article, it is preceded by a brief preamble explaining the importance of this study in the thesis.

After showing in Chapter 3 that face processing impairments of patients with schizophrenia are not generalized to invariant aspects of faces such as gender, the main goal of the present work was to delve into aspects of face affect processing. Literature converges reporting specific impairments in the recognition of facial expressions of negative emotions in the case of patients. However, the nature of this deficit remains unknown. It has been proposed that negative expressions are more difficult to recognize and more easily confusable because their corresponding facial configurations share some features (Adolphs, 2002). This characteristic would pose an additional difficulty for patients, leading to noisy internal representations of negative facial expressions. If this were true, a possible way to test this hypothesis would be to use a format that allowed participants to evaluate each facial stimulus in different emotional labels. The pattern of responses resulting from this study will tell us whether patients perceive different emotions in a facial expression corresponding to a single emotion (or at least, to a greater extent than controls) especially in the case of negative emotions.

Most of the previous studies used a forced-choice word association format to evaluate patient's ability to recognize facial expressions of emotions. However, this procedure is not the most appropriate to test this hypothesis because it doesn't allow participants to make several judgments over the same stimulus (Ekman, Friesen, & Ellsworth, 1972). In the following experiment, as improvement, each expression was

presented four times to give participants the opportunity to evaluate them in terms of different emotions. Resulting data would allow making a more detailed picture of cognitive representation of facial expressions for both patients and controls.

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Patterns of Emotion Attribution are Affected in Patients with Schizophrenia

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Abstract. Deficits in facial affect recognition have been repeatedly reported in schizophrenia patients. The hypothesis that this deficit is caused by poorly differentiated cognitive representation of facial expressions was tested in this study. To this end, performance of patients with schizophrenia and controls was compared in a new emotion-rating task. This novel approach allowed the participants to rate each facial expression at different times in terms of different emotion labels. Results revealed that patients tended to give higher ratings to emotion labels that did not correspond to the portrayed emotion, especially in the case of negative facial expressions ($p < .001$, $\eta^2 = .131$). Although patients and controls gave similar ratings when the emotion label matched with the facial expression, patients gave higher ratings on trials with "incorrect" emotion labels ($p_s < .05$). Comparison of patients and controls in a summary index of expressive ambiguity showed that patients perceived angry, fearful and happy faces as more emotionally ambiguous than did the controls ($p < .001$, $\eta^2 = .135$). These results are consistent with the idea that the cognitive representation of emotional expressions in schizophrenia is characterized by less clear boundaries and a less close correspondence between facial configurations and emotional states.

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Cognitive impairment as a characteristic of schizophrenia is currently well established and documented (Barch & Ceaser, 2012; Kahn & Keefe, 2013; Nielsen, 2011; Sponheim et al., 2010). A specialized cognitive domain that has recently been a focus of attention in connection to schizophrenia is that of social cognition, that is, the set of processes by which we draw inferences about the beliefs and intentions of others (e.g., Green & Horan, 2010; Sergi et al., 2007; Widen & Russell, 2010). Due to its recognized importance in schizophrenia and the evidence suggesting that impairments in social cognitive processes may be a mediator between neurocognitive deficits and functional outcome, social cognition had been included as a

domain in the MATRICS Consensus Cognitive Battery (MCCB; Marder & Fenton, 2004; Nuechterlein et al., 2004; Nuechterlein et al., 2008; Rodríguez-Jiménez et al., 2012). Deficits in a main component of social cognition, the recognition and interpretation of facial expressions of emotion, are well documented in schizophrenia (for reviews see Edwards, Jackson, & Pattison, 2002; Kohler, Walker, Martin, Healey, & Mober, 2010; Mandal, Pandey, & Prasad, 1998). This finding is of potential clinical relevance because there is evidence that impaired emotion recognition of faces is specifically related to social competence and function in this disorder (e.g. Hooker & Park, 2002; Rassovsky, Horan, Lee, Sergi, & Green 2011). Moreover, the study of impaired emotion recognition by schizophrenia patients might provide clues with respect to the relationship between deficits in the social/emotional domain and variations in brain function in schizophrenia. For example, there is evidence from neuroimaging studies suggesting that failure to activate brain regions involved in perceptual and affective processing during emotional valence discrimination might underlie impaired recognition of facial expressions in schizophrenia (Gur et al., 2002; Johnston, Stojanov, Devir & Schall, 2005; Phillips et al., 1999).

Although the deficit in recognition of facial affect by patients with schizophrenia is well established (Amminger et al., 2012; Lee, Gosselin, Wynn, & Green, 2011), some aspects remain unclear. With respect to

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emotional expressions, a key controversial issue is the extent of the deficit (Lee et al., 2013; Pomarol-Clotet et al., 2010). While a general deficit in the identification of facial expressions of emotion has been reported in some studies (e.g., Kohler, Turner, Gur, & Gur, 2004), a more frequent pattern is that of preserved recognition of positive expressions and impaired recognition of negative ones (e.g., Bediou et al., 2005; Combs, Michael, & Penn, 2006; Janssens et al., 2012; Kohler et al., 2003). This finding might be related to the fact that while the smile is the only facial signal universally perceived as expressing approachability and positive affect (e.g., Ekman & Keltner, 1997) negative emotion can be expressed in multiple ways through facial expressions that are less easily discriminated. This relatively poorer discrimination of negative expressions is found in non-clinical samples (e.g. Palermo & Coltheart, 2004) and is more pronounced in patients with schizophrenia (e.g. Bryson, Bell, & Lysaker, 1997; Kohler et al., 2003). An explanation based on the different discriminability of positive and negative expressions has been proposed by Johnston, Katsikitis, and Carr (2001), and Johnston, Devir, and Karayanidis (2006). These authors interpret the deficits shown by patients in terms of a gradation in task difficulty due to the lower discriminability of negative expressions. What these authors propose is that the facial expressions of negative emotions overlap to a high degree, thus increasing their confusability and leading to reduced accuracy. A similar argument has been put forward by Adolphs (2002), who has pointed out that negative expressions are more difficult to recognize and more easily confusable because the corresponding facial configurations include facial movements that are common with other expressions. This characteristic of negative expressions would pose additional problems to patients with schizophrenia due to aberrant processing in neural networks involved in perceptual analysis (Johnston, Stojanov, Devir, & Schall, 2005) or higher noise of internal representations (Bach, Buxtorf, Grandjean, & Strik, 2009).

In the present study we explore the hypothesis that the internal representations of emotional expressions are less differentiated and have poorly defined boundaries in patients with schizophrenia than in controls, leading to more frequent confusions between different expressions in the case of negative emotions. A possible way to explicitly test this prediction would be to allow the participants to rate each expression in terms of different labels. We used a multiple emotion-rating task in which each expression was presented on several trials accompanied each time by a different emotion label. The participant's task was to give a rating of the extent to which that specific expression represented the emotion corresponding to the present label. This procedure allows the collection of multiple responses

for each individual expression based on which the degree of clarity or ambiguity with which it is perceived can be estimated. Our specific prediction was that patients with schizophrenia would show more distributed attribution profiles, with high ratings on emotion labels that do not correspond to the emotion portrayed by the face. This should be especially so in the case of faces expressing negative emotions, showing the higher confusability of these expressions in the patient's sample.

Method

Sample

The present study was carried out with nineteen clinically stable outpatients, who were consecutively referred by their treating psychiatrists, and with twenty controls with no self-reported history of psychiatric illness. All patients had been diagnosed with schizophrenia including 16 with paranoid schizophrenia, one with residual schizophrenia and two patients with schizophreniform disorder according to DSM-IV criteria (APA, 1994), using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I; First, Spitzer, Gibbon, & Williams, 1995). All patients were on atypical antipsychotic treatment and had been clinically stable (no hospital admissions, no changes in treatment and no significant psychopathological changes) for at least six months before inclusion. Clinical status was evaluated using the Spanish version of the Positive and Negative Syndrome Scale (PANSS; Kay, Fishbein, & Olper, 1987; Peralta & Cuesta, 1994) following the five-factor model proposed by Wallwork, Fortgang, Hashimoto, Weinberger, and Dickinson (2012) and confirmed by Rodriguez-Jimenez et al. (2013). See Table 1 for patient and control's demographics. Written informed consent was obtained from all participants prior to their inclusion in the study.

Materials

Forty pictures from the NimStim face set (Tottenham et al., 2009) were used as stimuli. The faces corresponded to eight different models (four female, four male) each showing neutral, happy, angry, fearful or sad expressions. Pictures were converted to grey scale, cropped to conceal most of the hair and equated in contrast energy ($crms = 0.2$). The stimuli were presented on a 15" LCD monitor (refresh rate 60Hz).

Procedure

The task was designed with the aim of allowing the participants to evaluate each expression in terms of different emotions. To this end, each picture was presented four times on randomly distributed trials.

Table 1. Sample demographics and clinical status. The PANSS factors were calculated using the consensus five-factor model of Wallwork et al., 2012.

	Patients (<i>n</i> = 19)	Controls (<i>n</i> = 20)	Statistic (<i>p</i>)
	<i>M</i> (<i>SD</i>)	<i>M</i> (<i>SD</i>)	
Age	43.8 (9.5)	42.3 (12.8)	<i>T</i> = -.438 (<i>p</i> = .664)
Gender (% male)	68%	45%	χ^2 = .742 (<i>p</i> = .514)
Years of education	9.57 (4.3)	12.05 (3.9)	<i>T</i> = -1.87 (<i>p</i> = .069)
Age of onset of the disorder	25.9 (7.4)	-----	-----
PANSS-Positive	7.52 (2.73)	-----	-----
PANSS-Negative	14.26 (7.88)	-----	-----
PANNS-Disorganized	6 (1.88)	-----	-----
PANNS- Depressed	5.79 (2.48)	-----	-----
PANSS- Excited	4.89 (2.35)	-----	-----

On each trial a face appeared centered on the screen and below it an emotion label (“happiness”, “anger”, “sadness” or “fear”) with a continuous 1 to 9 scale (See Figure 1). The participant was instructed to indicate, by clicking on the appropriate section of the scale, how much of each emotion was expressed by the face. This procedure allowed the participants to attribute different emotional meanings to the same face at different times and with similar or different levels. More clearly defined or easily discriminated expressions should receive low ratings on all emotion categories except the correct one. On the other hand, less discriminable expressions should show a more distributed profile, with high ratings on incorrect categories.

Data Analysis

As a first analysis, a Student’s *t*-test was performed to study that patients and controls were not different in age or years of education. A chi-square analysis was performed to investigate differences in gender distribution.

After that, the patterns of emotion attribution to the different expressions by the patient and control groups are presented. These profiles can be understood as representing the extent to which participants discriminated between different expressions. Steeper profiles with maximum rating in the “correct” emotion label (i.e. fear for fearful faces) and very low ratings in the other labels would indicate accurate discrimination.

Two different analyses were performed with the data obtained in the multiple-rating task. Patients and controls were compared in two repeated measures analyses of variance (ANOVA) model with diagnosis as a between group factor (patients, control subjects). First, the attribution profiles of the different facial expressions were submitted to a 2×5×4 mixed ANOVA with participant Group (patient versus control) as the

between-subjects factor and Expression (angry, fearful, happy, neutral and sad) and Emotion Label (anger, fear, happiness and sadness) as the repeated measures factors.

Second, groups were compared in a summary index that provided an estimation of the perceived emotional ambiguity of each expression. A 5 × 2 ANOVA was performed on the ambiguity results, with Emotion Label and Group as factors. Perceived emotional ambiguity was computed into an index for each expression and participant (Fernandez-Cahill, 2012). This ambiguity index (AI) was calculated by averaging the ratings for all emotion labels except the one with the maximum rating (\bar{X}_i), usually the one corresponding to the portrayed emotion and dividing this mean by that maximum rating (X_{max}), as indicated by the following formula:

$$AI = \frac{\bar{X}_i}{X_{max}}$$

Using this formula, higher AI values are obtained when ratings are more evenly distributed across different emotion labels, that is, when a given expression receives relatively high ratings on different emotion labels. Values closer to 1 denote higher expressive ambiguity and those closer to 0 denote lower expressive ambiguity. This index was correlated in the clinical group with the depressed factor of the PANSS, calculated following the model given by Wallwork, Fortgang, Hashimoto, Weinberger, and Dickinson (2012) in order to control mood effects on the performance of the patients, which could explain some of the results.

For all repeated measures ANOVA analyses reported in the present paper, the Greenhouse-Geisser correction was applied when the sphericity assumption was violated. Post-hoc analyses were performed according to Bonferroni (significant when $p \leq .05$). Tests were carried out with the statistical package IBM SPSS Statistics 20.

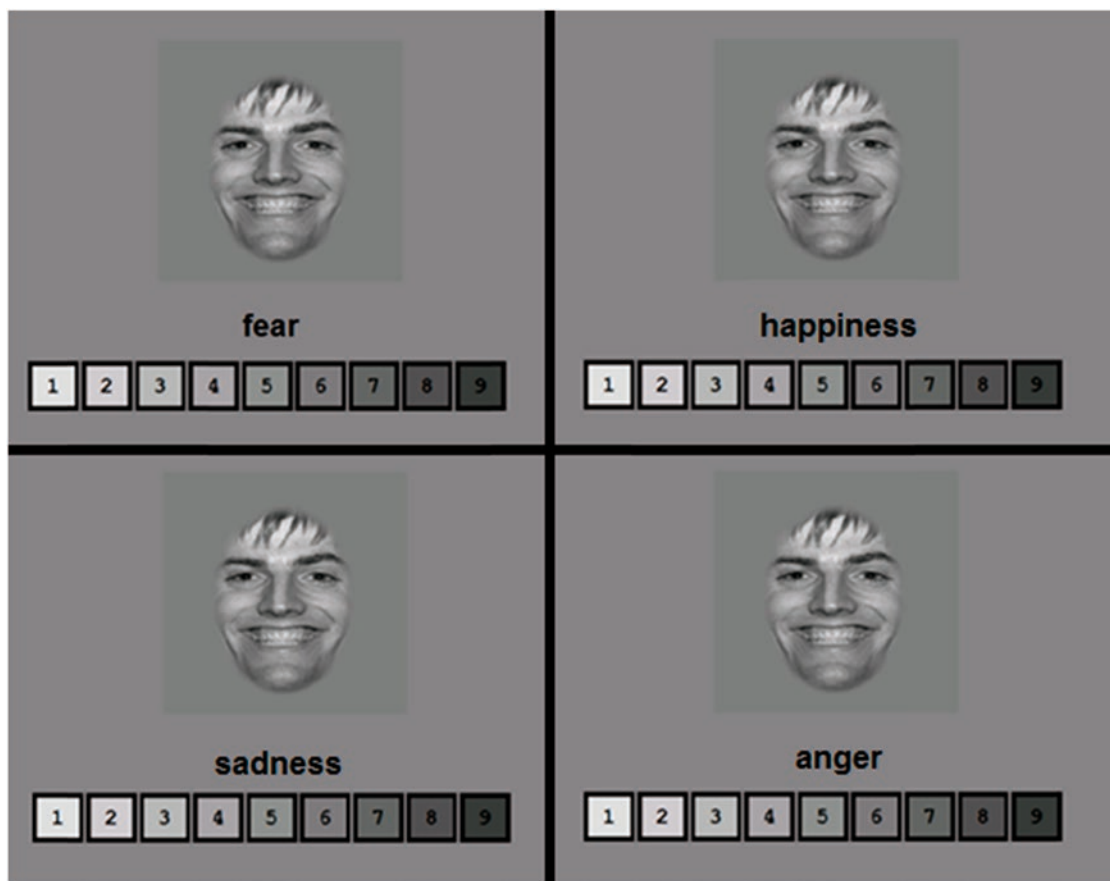


Figure 1. Example of 4 different trials in the Multiple-Emotion Rating Task.

Results

Firstly, no differences between controls and patients were found on socio-demographic characteristics such as age $t = -.438$, ($p = .664$), distribution of gender $\chi^2 = .742$ ($p = .514$) or years of education, $t = -1.87$, ($p = .069$) (See table 1).

Figure 2 presents the patterns of emotion attribution to the different expressions by the patient and control groups.

As a first analysis, ratings of each facial expression on the different Emotion Labels were compared between the patient and control groups. The results of the analysis showed a main effect of Group, $F(1, 37) = 20.59$ $p < .001$, $\eta^2 = .358$, with patients with schizophrenia giving significantly higher ratings ($M = 3.75$, $SEM = .2$) than controls ($M = 2.45$, $SEM = .19$). Significant two-way interactions of Expression \times Group, $F(4, 148) = 2.68$, $p = .034$, $\eta^2 = .068$ and of Emotion Label \times Group were also found, $F(3, 111) = 3.53$ $p = .026$, $\eta^2 = .079$. Finally, the three-way Expression \times Emotion Label \times Group interaction was also significant, $F(12, 444) = 5.575$ $p < .001$, $\eta^2 = .131$. In order to explore this interaction, ratings of each expression on each emotion label were compared between groups in the post-hoc analysis.

These comparisons revealed a common pattern for the three negative expressions (anger, fear and sadness). In this case, patients and controls gave similar ratings on the “correct” emotion label. However, patients gave significantly higher ratings to the three negative expressions than the controls on the “incorrect” labels ($p_s < .05$).

As a second analysis, mean AI values for the patient and control groups are presented in Figure 3. The analysis performed on the AI results, revealed main effects of Group, $F(1, 37) = 9.05$ $p = .005$, $\eta^2 = .197$ with higher AI values for patients ($M = .5$, $SEM = .03$) than controls ($M = .37$, $SEM = .03$). Also a significant Emotion \times Group interaction, $F(4, 148) = 5.75$ $p < .001$, $\eta^2 = .135$ was found. Paired comparisons in post-hoc analysis showed differences between groups, with higher AI values in the patient’s group for the faces showing angry, fearful and happy expressions ($p_s < .05$). No differences were found in the case of sad and neutral faces. Finally, within-group comparisons showed that for controls both sad and neutral faces were perceived as more ambiguous than angry ($p = .016$ and $p < .001$ respectively), fearful ($p = .009$ and $p < .001$ respectively) and happy faces ($p = .001$ and $p < .001$ respectively).

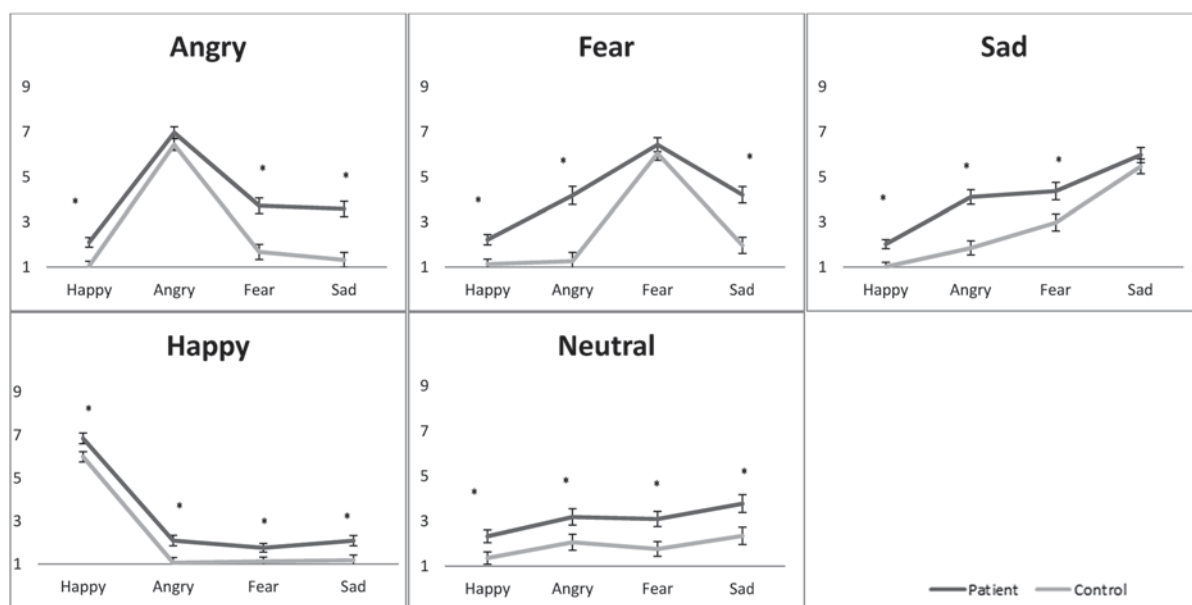


Figure 2. Mean rating attributed for each facial expression.

* $p < .05$.

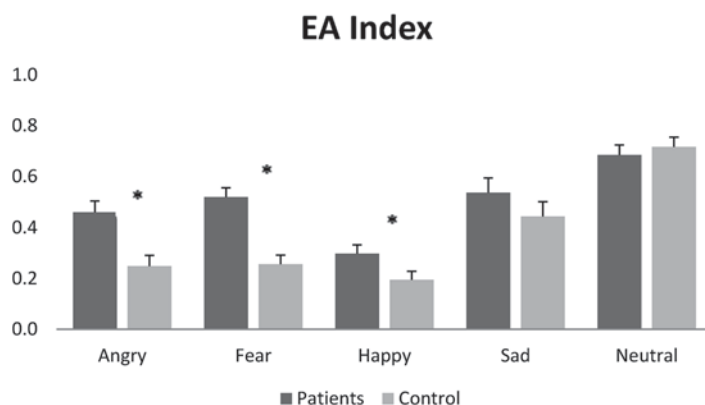


Figure 3. Mean ambiguity index calculated with EA Index for each facial expression. Error bars denote Standard Error Mean.

* $p < .05$.

In the case of patients, happy faces were less ambiguous than angry ($p < .001$), fearful ($p < .001$), sad ($p = .001$) and neutral faces ($p < .001$). At the same time, neutral faces were perceived as more ambiguous than angry ($p = .001$) and fearful faces ($p = .023$).

Finally, there wasn't any correlation between the Ambiguity Index of each emotion and the depressed factor of the PANSS ($p_s > .05$) for the patient's group.

Discussion

The aim of the present study was to evaluate the patterns of emotion attribution to faces showing different expressions in patients with schizophrenia. To this end a new multiple-rating task that allowed the participant to rate each expression on different emotion labels was used.

The results obtained revealed a different pattern of attribution of emotion to faces between patients with schizophrenia and controls. While both patients and controls gave similar ratings on the "correct" emotion label, patients gave significantly higher ratings to the three negative expressions than the controls on the "incorrect" labels. As was predicted, patients showed more distributed patterns of emotion attribution to faces showing negative expressions (Combs et al., 2006; Kohler et al., 2003).

An ambiguity index was computed as a summary measure of the extent to which a given expression was perceived as showing different emotions and thus could be said to be perceived as emotionally ambiguous. According to this measure, patients tended to perceive

angry, fearful and happy expressions as more ambiguous than the controls did. However, no differences between groups were observed in the case of sad and neutral faces. Within-group comparisons also showed differences between patients and controls. Patients perceived all negative expressions as more ambiguous expressions than happy ones. However, in the case of controls sad and neutral faces were perceived as more ambiguous than angry, fearful and happy faces. There were no correlations between this index and the depressed factor of the PANSS, suggesting that differences in the clinical sample's mood were not a main determinant of the results.

A more detailed picture of the patterns of emotion attribution can be obtained by comparing the attribution profiles of the patient and control groups. This comparison showed first that the patients tended to give significant higher ratings than controls on all emotion labels to happy and neutral faces. For example, in the case of happy faces patients gave higher ratings in both correct and incorrect emotion labels. This result might be interpreted as showing a general trend to overestimate the emotional expressiveness of faces. However, the more differentiated pattern that emerged in the case of negative expressions (anger, fear and sadness) does not fit with this interpretation. In this case, patients gave higher ratings on the "incorrect" emotion labels but did not differ from the controls in their ratings on the "correct" label. The patient group was especially more likely to give each negative expression higher ratings on other "incorrect" negative emotions. For example, although both groups of participants gave similar fear ratings to fearful faces, patients also attributed more anger and sadness than did the controls to those same faces. Thus, the patient group was perfectly accurate in their estimate of the extent to which fearful, angry or sad faces expressed the corresponding emotions. Nonetheless, they were more likely to attribute different negative emotions to each single negative expression.

As it was discussed in the introduction (Bach et al., 2009; Johnston et al., 2005), it has been proposed that the cognitive representation of facial expressions of emotion is characterized by a relative lack of clarity and the presence of internal noise. These characteristics would lead to impaired discrimination between different expressions, affecting especially the ability to differentiate the expressions corresponding to negative emotions that have a higher degree of overlap. Consistently with this explanation, the results of the present study confirmed that patients with schizophrenia are less accurate than controls in their emotional attributions to faces showing negative expressions (Bediou et al., 2005; Janssens et al., 2012). The methodology employed, with a multiple rating task and a

continuous response format allowed us to show that this inaccurate performance was not due to an under-attribution of the correct emotion (i.e., the degree of fear attributed to fearful faces) but to an over-attribution of the incorrect ones (i.e., anger attributed to fearful faces). Thus, this result is consistent with the idea that poor recognition of negative expressions is due to a poor differentiation among this category of emotional expressions. On the other hand, the low rating of the faces showing negative expressions on the "happiness" label indicates that patients were perfectly capable of differentiating between negative and positive expressions. These results, of course, are consistent with the repeated finding of a specific deficit in the recognition of negative expressions by patients with schizophrenia (for reviews see Edwards et al., 2002; Mandal et al., 1998). However, most previous studies have used procedures that allow only one single response to each facial expression. The specific pattern of errors that would give a more detailed picture of the deficit is usually not reported. One exception is the study by Kohler et al. (2003), where the analysis of the misattribution patterns showed that patients over-attributed negative emotions to neutral faces. Still in this case the use of a single-response procedure might have underestimated the extent to which the patient and control samples differed in their attribution pattern for other facial expressions. One main advantage of the multiple-rating task is precisely that its more open format allows for such differences to emerge, allowing a more in-depth estimation of emotion recognition deficits in patients with schizophrenia.

The findings of the current study have potential clinical relevance and provide some clues to understanding some difficulties experienced by patients with schizophrenia in social situations. In daily situations mistaking negative expressions could lead patients to misidentify the feelings of others. Some symptoms such as distrust, hostility, poor rapport or apathetic social withdrawal could be partially explained by the inability to discriminate appropriately among negative expressions. Also, these results are consistent with functional neuroimaging studies in which a failure to activate brain regions involved in affective processing could explain impaired recognition of facial expressions (Gur et al., 2002; Johnston et al., 2005).

It should be noted that studies comparing patients with schizophrenia –even more with chronic schizophrenia– with controls present some limitations. Due to the many ways in which patients and controls differ in cognitive and emotional domains it is difficult to attribute to definite causal factors the differences found in the present study. Also, it would be highly reductionist to attribute the differences only to the diagnosis. For example, in the chronic phase of schizophrenia

there are many external variables that can contribute to the deficits showed by patients like general psychopathology, overall distress or long term use of antipsychotics. Although not without problems either, one way to minimize the influence of factors associated to chronicity would be to test the rating task in a first-onset schizophrenia group of patients. Some attempts in this direction have been already made (e.g. Addington et al., 2008, Comparelli et al., 2013 and Pinkham, Penn, Perkins, Graham, & Siegel, 2007). While this is true, it must also be said that studying the performance of chronic patients is interesting in itself because it gives us a picture of how the disorder together with the additional factors associated to chronicity influence their behavior.

We finish by noting other limitations and possible further developments of our study. First it would be suitable to evaluate a bigger sample size in order to increase the generalization of our conclusions. Another limitation was that we did not carry out a structured evaluation of the mental status of the control sample. Ideally, this group without a self-reported history of psychiatric illness should have been assessed with some structural interview in order to appropriately establish the absence of mental disorders. Further developments of this study will concentrate on exploring the specific conditions under which patients with schizophrenia show preserved or impaired attribution of emotion to human faces. Finally, the study of the differences between first-onset and chronic schizophrenia on face recognition and the possible relationship of this domain with functional outcome might open up new lines of cognitive remediation and prevention of social isolation in patients with schizophrenia.

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CHAPTER 5: COMPARISON BETWEEN CLINICAL STAGES OF SCHIZOPHRENIA

Preamble

Chapter 5 corresponds to a published article with the following reference:

Romero-Ferreiro, M. V., Aguado, L., Rodriguez-Torresano, J., Palomo, T., Rodriguez-Jimenez, R., & Pedreira-Massa, J. L. (2016). Facial affect recognition in early and late-stage schizophrenia patients. *Schizophrenia research*, 172(1), 177-183. <http://dx.doi.org/10.1016/j.schres.2016.02.010>

As a way to integrate this article, it is preceded by a brief preamble explaining the importance of this study in the thesis.

The study of cognitive processes in people with mental disorders is a challenging work. Given the cognitive and emotional differences between patients and controls, it is really hard to strictly attribute differences to the effect of the disorder. Studies examining chronic patients can be tainted by illness-related confounds such as long-term medication effects, stigmatization or social isolation they commonly experience. Thus, the impact of these types of studies is to a certain extent, limited. Some studies have tried to overcome these limitations by studying high-risk individuals. However, identifying non-psychotic individuals at increased risk for developing schizophrenia spectrum disorders is not trouble-free. For example, two follow-up studies for 5 and 10 years respectively have revealed that only between 15-24 per cent fully develop psychotic disorders, likewise a recent meta-analysis revealed a consistent transition risk between 18% (after 6 months of follow-up) and 36% (after 3 years) (see Fusar-Poli et al, 2012 for a meta-analysis; Gooding, Tallent, & Matts, 2005; Kwapil, 1998). Thus, although not the best solution, including samples of recent-onset psychotic individuals seems to be the least bad option. These kinds of patients have a diagnosis, but have no long history of disease, and confound factors that may be contributing to the functional outcome are relatively controlled at the very first stages. With the purpose of studying face affect recognition in patients at different stages of

schizophrenia, the following experiment was carried out. Participants were presented facial expressions of emotions (anger, fear, sadness, happiness, and neutral) and they had to select the label that better described the expression. The main strength of this work was that both clinical samples were compared with controls matched in terms of age and sex, to separate contribution of age and diagnosis. This is crucial in a mental disorder that usually manifests during late childhood/adolescence, a crucial moment in the evolutionary development.

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Facial affect recognition in early and late-stage schizophrenia patients



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ABSTRACT

Prior studies have shown deficits in social cognition and emotion perception in first-episode psychosis (FEP) and multi-episode schizophrenia (MES) patients. These studies compared patients at different stages of the illness with only a single control group which differed in age from at least one clinical group. The present study provides new evidence of a differential pattern of deficit in facial affect recognition in FEP and MES patients using a double age-matched control design. Compared to their controls, FEP patients only showed impaired recognition of fearful faces ($p = .007$). In contrast to this, the MES patients showed a more generalized deficit compared to their age-matched controls, with impaired recognition of angry, sad and fearful faces ($p_s < .01$) and an increased misattribution of emotional meaning to neutral faces. PANSS scores of FEP patients on Depressed factor correlated positively with the accuracy to recognize fearful expressions ($r = .473$). For the MES group fear recognition correlated positively with negative PANSS factor ($r = .498$) and recognition of sad and neutral expressions was inversely correlated with disorganized PANSS factor ($r = -.461$ and $r = -.541$, respectively). These results provide evidence that a generalized impairment of affect recognition is observed in advanced-stage patients and is not characteristic of the early stages of schizophrenia. Moreover, the finding that anomalous attribution of emotional meaning to neutral faces is observed only in MES patients suggests that an increased attribution of salience to social stimuli is a characteristic of social cognition in advanced stages of the disorder.

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1. Introduction

A specialized cognitive domain that has recently been emphasized in connection to schizophrenia is that of social cognition, that is, the set of processes by which we draw inferences about the beliefs and intentions of others (e.g., Green and Horan, 2010). Acknowledging its importance in schizophrenia illness and the evidence suggesting that impairments in this domain may be a mediator between neurocognitive deficits and functional outcome (Schmidt et al., 2011), evaluation of social cognition has been included in the MATRICS Consensus Cognitive Battery (MCCB) (Nuechterlein et al., 2008; Rodríguez-Jimenez et al., 2012). Social cognition includes domains such as theory of mind (ToM), attributional style or social perception. A crucial component of social cognitive abilities is facial affect recognition and deficits in the recognition and interpretation of facial expressions of emotion are well documented in schizophrenia (Edwards et al., 2002; Kohler et al., 2010).

The pattern most frequently found is that of preserved recognition of positive expressions (happiness) and impaired recognition of negative ones (anger, fear, sadness and disgust) (e.g., Bediou et al., 2005; Combs et al., 2006; Janssens et al., 2012; Kohler et al., 2003).

Recently the interest in the study of social cognition (Ventura et al., 2015; Bertrand et al., 2007) and emotion perception (Comparelli et al., 2013) in first-episode schizophrenia has increased and there is evidence that impaired performance is present before the full expression of the disorder (Addington et al., 2008; Allott et al., 2014; Amminger et al., 2012; Corcoran et al., 2015; Edwards et al., 2001; see Phillips and Seidman, 2008, for a review and van Donkersgoed et al., 2015 for a meta-analysis). Several studies have compared emotion recognition performance in early stage and chronic schizophrenia patients, in an attempt to establish if these deficits are stable or vary over time. However, the comparison of recent onset and chronic patients is not without its challenges. The few longitudinal studies on this matter have followed patients during relatively short periods of time. For example Addington et al. (2006) followed patients over one year and found that both first- and multi-episode patients were impaired in cognition, social functioning and facial affect recognition and that first-episode subjects showed stable deficits over the first year despite improved

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symptomatology. Similarly, Ventura et al. (2015) followed first episode patients during six months and found stable ToM deficits even in remitted patients.

Cross-sectional studies comparing patients at different stages of the illness have shown deficits in facial affect recognition (Comparelli et al., 2013; Pinkham et al., 2007; Sachs et al., 2004; Vohs et al., 2014), usually reporting similar deficits in early and later stages. For example, Comparelli et al. (2013) found no differences among prodromal, first episode or multi-episode schizophrenia patients when data were corrected for socio-demographic and clinical variables. In the same line, Vohs et al. (2014) found no differences between first episode psychosis and prolonged psychosis groups in different measures of social cognition. Pinkham et al. (2007) and Sachs et al. (2004) also found deficits in emotion recognition tasks and emotion perception for patients of early and chronic schizophrenia. Nevertheless an exception is the study by Kucharska-Pietura et al. (2005) who found greater impairments in emotion perception in individuals with chronic schizophrenia.

The study of differences in emotion recognition abilities between patients at different stages of the illness is of potential clinical relevance because there is evidence that impaired performance is specifically related to social competence and functioning on the first stages (Fett et al., 2013; see Irani et al., 2012 for a meta-analysis). Designing social cognitive remediation strategies in this regard should be in accordance with the deficits. If there were differences in facial emotion recognition at different stages of the illness the intervention should suit the specific deficits of each stage.

Although comparative studies with non-clinical samples have shown that accurate recognition of at least some basic emotions develops relatively early (e.g., Soken and Pick, 1992; Widen and Russell, 2003) the accuracy and speed with which emotional expressions are recognized and the sensitivity to subtle expressive changes continues to develop during adolescence before reaching peak performance in adulthood (e.g., De Sonneville et al., 2002; Thomas et al., 2007). Studies on facial expression recognition in the general population have consistently shown that happy expressions are recognized faster and more accurately than any other basic emotional expression including anger, fear, sadness, disgust, and surprise (Calder et al., 2000; Leppänen and Hietanen, 2003; Nelson and Russell, 2013; see Nummenmaa and Calvo, 2015, for a review). Moreover, there is evidence of age-associated changes in the accuracy with which negative and positive emotional expressions are recognized (Iidaka et al., 2002; Lambrecht et al., 2012). From this point of view, it is clear then, that reported deficits in schizophrenia patients that are not based in comparisons with age-appropriate control groups run the risk of over- or underestimating possible differences with controls. In order to rule out this possibility it is crucial to include control groups that are equated in terms of age, but up to our knowledge there is no prior research on facial affect recognition comparing adult and adolescent patients with the corresponding age-matched controls. This type of comparison would provide a better method to evaluate the separate contribution of age (i.e., cohort) and schizophrenia (i.e., diagnosis) to the deficits in affect recognition reported in previous studies.

The main goal of the present study was to assess performance on facial affect recognition in early- and late-stage patients with schizophrenia, comparing each group with appropriate age-matched controls. Our main interest was in knowing if the patients of the early-stage sample also showed impaired recognition of negative expressions compared to their age-matched controls as is usually found in chronic patients. The general tendency points that deficits in facial affect recognition are similar in first and later stages of the illness, so we should expect to find the same differences between both early stage and late stage schizophrenia patients compared with healthy controls. However, we wanted to confirm if these differences still can be found when FEP and MES patients are compared with an appropriated control group, matched in terms of sex and age. Secondly, as a way to assess the potential contribution of medication dose and severity of

symptomatology, it was analyzed the correlation of these variables and recognition of facial affect. To this purpose, we conducted a cross-sectional study comparing a group of multi-episode schizophrenia patients (MES) and first-episode psychosis patients (FEP) with their corresponding gender and age-matched control groups on a facial affect recognition task.

2. Method

2.1. Participants

The present study was carried out including 19 multi-episode schizophrenia (MES) outpatients, who were consecutively referred by their treating psychiatrists. All MES patients had been diagnosed with schizophrenia according to ICD-10 criteria (WHO, 1992), and had >6 years of evolution of the illness. The MES patients had been clinically stable (no hospital admissions, no changes in treatment and no significant psychopathological changes) for at least 6 months. Exclusion criteria were currently substance abuse (except for caffeine and nicotine), history of brain injury or intellectual disability. The first episode psychosis (FEP) group included 21 patients (<18 years) who were defined as having psychotic symptoms of <1 year and were diagnosed according to ICD-10 (WHO, 1996) for children and adolescents criteria with schizophrenia or schizotypal disorder. They were evaluated at their first contact with mental health services as soon as the psychiatrist considered that the patient was able to collaborate. Data from those patients who met criteria for schizotypal disorder were included in the study only if after a few months the corresponding psychiatrist confirmed that their diagnosis developed into schizophrenia. All patients were on atypical antipsychotic treatment except for one of the MES group. The MES patient group was recruited from the “Hospital Universitario 12 de Octubre” (Madrid, Spain) and the FEP patient group from the “Hospital Infantil Universitario Niño Jesús” (Madrid, Spain). Each group's performance was compared to that of a similar number of control participants matched in age and gender with no self-reported history of psychotic illness and recruited from the same socio-cultural environment than patients. Patients and controls were evaluated with the same computer equipment in a room enabled for this purpose.

The procedure was approved by the Ethics Committee and the informed consent was obtained from all participants (and their parents in the case of minors) prior to their inclusion in the study.

2.2. Materials

2.2.1. Facial affect recognition

Forty pictures from the NimStim set (Tottenham et al., 2009) were used as stimuli. The faces corresponded to nine Caucasian models (five female, four male), each showing happy, angry, fearful, sad or neutral expression. Pictures were converted to gray scale, equated in luminance and cropped to conceal most of the hair to remove distracting, noisy aspects that are not informative of emotional expression (Calvo and Lundqvist, 2008). The stimuli were presented on a 15” LCD monitor (refresh rate: 60 Hz). Pictures were selected based on a previous pilot study with a sample of 30 students from the Complutense University of Madrid. The participants in this pilot study were asked to rate each picture in terms of valence and arousal and to select the label that best described the expression shown by each face. We selected those faces that reached a minimum recognition agreement of 75% as stimuli for the present study. This procedure was previously used in Romero-Ferreiro et al. (2015).

2.2.2. Clinical assessment

Clinical status was evaluated using the Spanish version (Peralta and Cuesta, 1994) of the Positive and Negative Syndrome Scale (PANSS – Kay et al., 1987, see Table 1). The Positive and Negative Syndrome

Table 1
Sample demographics and clinical status.

	FEP (n = 20)	FEP controls (n = 20)	Statistic (p)	MES (n = 19)	MES controls (n = 20)	Statistic (p)
Age	15.6 (SD 1.63) [12–18]	15.20 (SD 1.6) [12–17]	$t = -.78$ ($p = .44$)	43.89 (SD 9.5) [27–59]	42.3 (SD 12.87) [20–67]	$t = .438$ ($p = .664$)
Gender (% male)	65%	65%	$\chi^2 = .00$ ($p = 1.00$)	68%	55%	$\chi^2 = .742$ ($p = .514$)
PANSS-Positive	15.15 (SD 6.24)	–		7.52 (SD 2.73)	–	$t = -4.98$ ($p < .001$)
PANSS-Negative	29.45 (SD 5.63)	–		14.26 (SD 7.88)	–	$t = -6.94$ ($p < .001$)
PANNS-Disorganized	15.5 (SD 3.05)	–		6.00 (SD 1.88)	–	$t = -11.62$ ($p < .001$)
PANNS-Depressed	17.65 (SD 5.57)	–		4.89 (SD 2.35)	–	$t = -9.39$ ($p < .001$)
PANSS-Excited	8.15 (SD 2.48)	–		5.78 (SD 2.48)	–	$t = -2.89$ ($p = .006$)
CPZ ^a	206.45 (SD 128.63)	–		510.66 (SD 390.07)	–	$t = 3.23$ ($p = .004$)

^a Chlorpromazine equivalent dose (mg/day).

Scale (PANSS) published in 1987 by Kay et al. is a well-known semi-structured interview consisting of a 30-item, 7-point severity scale [1 (absence of psychopathology) to 7 (extremely severe)]. It assesses a wide range of symptoms in schizophrenia. The test consists of 'positive', 'negative' and 'general psychopathology' symptom sub-scales. In the present study, following a detailed literature review, it was calculated the NIMH researchers Wallwork et al. (2012) consensus 5-factor model for the PANSS (Positive, Negative, Disorganized, Excited, and Depressed) that has been recently recommended rather than some of the original PANSS sub-scales (Marder et al., 2011). This model was confirmed by our group in a Spanish sample (Rodriguez-Jimenez et al., 2013).

2.3. Experimental tasks

Participants were asked to indicate the emotion shown by each face, choosing among six options: "happiness", "anger", "sadness", "fear", "no emotion" and "other emotion". In order to make the expressions more conspicuous and help recognition, each expressive face immediately followed the corresponding neutral face, each with 1000 ms of duration. Responses were entered by clicking on different boxes showing the emotion names. The scores were calculated based on percentage of correct responses.

2.4. Data analysis

First of all, t-tests were performed to compare demographics between each clinical sample and their corresponding control group as well as clinical status between FEP and MES. A repeated measure analyses of variance (ANOVA) was performed on accuracy data with Diagnosis (patients, controls) and Cohort (adult, adolescent) as between group factors and Emotion as the within-subjects factor. The Greenhouse–Geisser and Bonferroni corrections were applied (significant when $p \leq .05$). Pearson correlation was conducted in order to explore the relation between facial affect recognition performance and symptomatology and medication dosage.

3. Results

The FEP group did not differ from their controls in terms of gender distribution and age ($p > .05$). In the same way, the MES group did not differ from their corresponding controls in these variables ($p > .05$). However, FEP and MES patients were different in symptom severity (PANSS subscales) ($p < .05$), as well as in terms of dose of antipsychotic medication (chlorpromazine equivalent dose) ($p = .004$) (see Table 1).

Main effects of Emotion $F(4,300) = 36.906$, $p < .001$, $\eta^2_p = .33$ and Diagnosis were obtained, $F(1,75) = 21.603$, $p < .001$, $\eta^2_p = .224$. Overall, performance was superior in the controls ($M = 83.56$, $SEM = 1.97$ and $M = 70.5$, $SEM = 2.00$, respectively). The Cohort \times Diagnosis interaction was also significant, $F(1,75) = 6.803$, $p = .011$, $\eta^2_p = .083$. While young and adult controls did not differ ($M = 81.99$, $SEM = 2.79$ vs. $M = 85.12$, $SEM = 2.79$ respectively), the FEP group showed

significantly better general affect recognition ($M = 76.26$, $SEM = 2.79$) than MES group ($M = 64.74$, $SEM = 2.86$).

The Emotion \times Cohort interaction was significant, $F(4,300) = 3.04$, $p = .018$, $\eta^2_p = .039$. Adolescents performed better than adults with angry ($M = 88.66$, $SEM = 2.45$ vs. $M = 81.11$, $SEM = 2.48$) and neutral ($M = 77.65$, $SEM = 4.74$ vs. $M = 62.42$, $SEM = 4.8$) expressions. Finally, the three-way Emotion \times Group \times Cohort interaction, $F(4,300) = 2.77$, $p = .027$, $\eta^2_p = .036$, showed a significant Cohort effect only in the case of the patients (see Table 2). Thus, the specific pattern of emotion recognition performance relative to the corresponding age controls changed from the FEP to the MES sample, with a more severe and generalized impairment of recognition of negative expressions and an increased trend to judge neutral faces as emotionally expressive in MES patients. When groups were compared, MES patients showed poorer recognition than FEP of angry ($M = 85.62$, $SEM = 3.47$ vs. $M = 69.74$, $SEM = 3.56$) and neutral ($M = 79.32$, $SEM = 6.7$ vs. $M = 46.71$, $SEM = 6.87$) expressions. No differences between young and adult controls appeared ($p_s > .05$).

In order to provide a more detailed picture of the results obtained with neutral faces, Fig. 1 presents the corresponding error patterns (i.e. the responses to neutral faces considered 'incorrect' as participants gave a response different from "no emotion"). Different error patterns are shown in chronic patients and in their controls. However, the error patterns of the FEP patients and their controls were virtually identical. Statistical analysis confirmed these impressions. While the error pattern for neutral faces in the younger groups (FEP and controls) was exactly the same, $\chi^2 = .466$, $p = .977$, the two adult groups showed a significantly different distribution of errors, $\chi^2 = 12.604$, $p = .013$.

Finally in an attempt to explore the relationship between performance in our experimental task and severity of symptoms measured with the five-factor model of the PANSS and the mean dose of antipsychotic medication, a Pearson's correlation analysis was performed. We found that FEP patient's scores on the Depressed factor was positively correlated with the accuracy with which they recognized fearful expressions ($r = .473$, $p = .035$). For the MES patients group, recognition of fearful faces was positively correlated with negative symptoms ($r = .498$, $p = .03$) and recognition of sad and neutral expressions was inversely correlated with disorganized symptoms ($r = -.461$, $p = .047$ and $r = -.541$, $p = .017$) respectively. However, dose of antipsychotic medication showed no correlation with accuracy on any facial expression ($p_s > .05$).

4. Discussion

Recognition of facial affect was assessed in first-episode psychosis and chronic schizophrenia patients and compared against sex and age-matched controls. Compared to the corresponding controls, FEP patients showed significant impairment in the recognition of fear but preserved recognition of anger, sadness, happiness and neutral expressions. A more generalized impairment of emotion recognition was observed in the MES patients' sample. These patients showed a general impairment in the recognition of all negative expressions (fear, anger and sadness). Moreover, chronic patients showed a bias

Table 2
Emotion recognition accuracy (percentage correct).

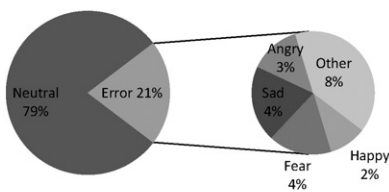
Emotion	FEP (n = 20)		FEP controls (n = 20)		p value	d'	MES (n = 19)		MES controls (n = 20)		p value	d'
	Mean	SD	Mean	SD			Mean	SD	Mean	SD		
Angry	85.62	15.32	91.69	10.5	n.s.	0.09	69.73	23.31	92.5	9.42	<.001	1.32
Fear	57.94	28.07	77.5	14.39	.007		61.84	24.46	82.5	20.83	.005	0.95
Sadness	64.01	25.99	67.32	22.67	n.s.		48.68	31.15	73.75	20.63	.003	0.96
Happiness	94.43	13.37	97.5	6.53	n.s.		96.71	7.02	98.75	3.84	n.s.	
Neutral	79.32	23.77	75.98	32.32	n.s.		46.71	34.06	78.12	28.92	.002	1.03

identifying neutral faces as emotionally expressive. Only happy faces were recognized with similar accuracy by MES patients and controls. Finally, a direct comparison with the FEP group showed a significant drop in identification accuracy of angry and neutral faces in the MES group.

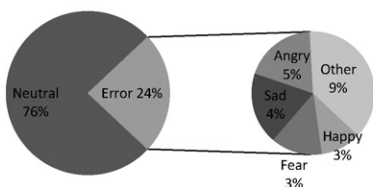
The results reported here are consistent with previous studies showing significant impairments of emotion recognition in schizophrenia patients (e.g., Amminger et al., 2012; Kohler et al., 2004; see Kohler et al., 2009, for a meta-analysis). Evidence on the presence of this deficit early in the development of the disorder (e.g., Addington et al., 2006; Herbener et al., 2005; Pinkham et al., 2007) would suggest that it is a feature of the socio-cognitive phenotype of schizophrenia. However, our results indicate that at early stages, the deficit is restricted to fear expressions and that a more generalized deficit of facial affect recognition appears during later stages. Unfortunately, there is scant evidence on the influence of chronicity on affect recognition in schizophrenia. In the study by Pinkham et al. (2007) early and chronic patients performed worse than controls but did not differ from each other. Similar impairments in first-episode and in chronic patients were also reported by Addington et al. (2006). However, larger and more generalized deficits in chronic patients were reported by Kucharska-Pietura et al. (2005). Similarly, other studies have found that ultra-high risk patients show moderate difficulties compared to the larger effects found in schizophrenia patients (see van Donkersgoed et al., 2015 and Savla et al., 2013 for a meta-analysis of ultra-high risk and schizophrenia patients respectively). In any case, a shortcoming of the studies with early and adult schizophrenia patients is that performance was compared against a single control adult sample. As stated in the introductory section, this comparison entails the risk of misestimating the deficit in the younger sample.

Previous studies with chronic schizophrenia patients have usually found poorer recognition of negative expressions (e.g. Bediou et al., 2005; Bryson et al., 1997; Kohler et al., 2004; Kucharska-Pietura et al., 2005; Walker et al., 1984). Among these, recognition of fear is usually most impaired (e.g., Bryson et al., 1997; Kohler et al., 2003; Edwards et al., 2002). In fact, this pattern is not qualitatively different from that observed in non-clinical samples, where poorer discrimination of negative expressions is usually found (e.g. Biehl et al., 1997; Calvo and Lundqvist, 2008; Palermo and Coltheart, 2004; Tottenham et al., 2009). Moreover, recognition of negative expressions tends to decline with age (see Ruffman et al., 2008, for a meta-analytic study). These developmental and aging-associated trends have been related to the differential development of feature versus configural processing (e.g., Mondloch et al., 2003), variations in visual scanning strategies (Wong et al., 2005) or to age-associated changes in affective bias (e.g., Mather and Carstensen, 2005). It is interesting to note that variations in these domains have been also described in schizophrenia patients (Joshua and Rossell, 2009; Wong et al., 2005; Seok et al., 2006). These similarities suggest that chronicity in schizophrenia might speed up the decline in the ability to recognize facial affect that is associated to normal aging, especially in the case of negative expressions, although this does not necessarily mean that these changes can be explained by a common underlying mechanism. As suggested by some authors, impaired recognition of negative expressions by schizophrenia patients might be related to the different discriminability of positive and negative expressions (Johnston et al., 2001; Johnston et al., 2006). The relatively lower discriminability of negative expressions would produce a gradation in task difficulty when recognition of positive and negative expressions is compared. More specifically, it is proposed that facial

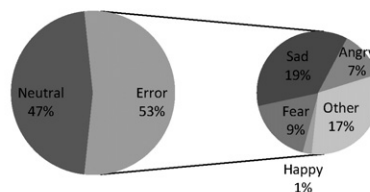
FEP response pattern to neutral faces



FEP control's response pattern to neutral faces



MES response pattern to neutral faces



MES control's response pattern to neutral faces

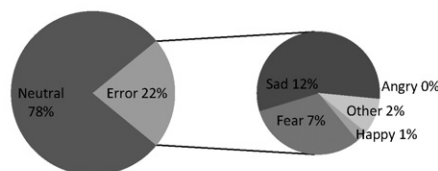


Fig. 1. Response pattern to neutral faces.

expressions of negative emotions overlap to a high degree, thus increasing their confusability and leading to reduced accuracy. A similar argument has been put forward by Adolphs (2002), who has pointed out that negative expressions are more difficult to recognize and more easily confusable because the corresponding facial configurations include facial movements that are shared with other expressions. This characteristic of negative expressions would pose additional problems to schizophrenia patients due to aberrant processing in neural networks involved in perceptual analysis (Johnston et al., 2005) or to higher noise of internal representations (Bach et al., 2009).

The only expression for which we found impaired recognition in the FEP group was fear. In contrast, MES patients showed a generalized impairment in the recognition of negative expressions. This is consistent with the results of the meta-analysis performed by Barkl et al. (2014a) that conclude that early-onset and first-episode psychosis patients show poorer recognition of fear expressions (in addition to disgust and surprise, emotions not included in the present study). In fact, Allott et al. (2014) found that accuracy results identifying neutral and fearful emotions predicted transition to a psychotic disorder in ultra-high risk young patients. Similarly, Barkl et al. (2014b) and Allott et al. (2015) reported that deficits in emotion recognition of early-onset psychosis and first-episode schizophrenia respectively, were circumscribed to fear, anger and disgust expressions. It is interesting to note that Allott et al. (2015) found poorer recognition of fearful expressions not only in early-onset psychosis patients but also in their first-degree relatives. These results suggest that impaired recognition of fearful expressions might be an early cognitive marker in the first stages of psychosis. Again, this might not be entirely different to the results of studies comparing non-clinical samples of different ages. For example, Calder et al. (2003) found less accurate recognition of anger, sadness and fear expressions in the older samples, a trend confirmed in a meta-analytic study (Ruffman et al., 2008).

Regarding our second goal, a positive correlation was found in FEP patients between recognition of fearful expressions and the PANSS depressed factor. A connection between the accuracy to recognize fearful expressions and the severity of psychopathology has been described before. For example, Allott et al. (2014) found that accuracy in identifying neutral and fearful expressions predicted transition to a full-blown psychotic disorder in an ultra-high risk sample. A more general result has been reported by Vohs et al. (2014). In this case, social cognition scores in first episode psychosis patients were inversely associated with negative and disorganized symptoms. However, recognition scores were collapsed across expressions and the relative contribution of specific expressions is unknown. If anything, it can be said that the correlations reported in Vohs et al.'s study are more similar to those found in our MES sample where recognition of sad and neutral expressions was inversely correlated with disorganized symptoms. This discrepancy could be due, at least in part, to the fact that FEP patients of the current study were younger than FEP patients of Vohs et al.'s study. The fact that recognition of fearful faces was positively correlated with negative symptoms for MES patients and with depressed symptoms for FEP patients could be reflecting a bias of these patients showing a better performance on some negative emotions, in this case, for fearful expressions.

A new finding in the present study was that MES patients showed and increased tendency to attribute emotional expressivity to neutral faces compared to both their age-matched controls and the FEP group. Chronic patients were especially likely to select the options “sadness” and “other emotions” to describe what the neutral faces expressed. It is also important to note the difference between the error patterns of the adolescent and adult control samples. Interestingly, the response pattern of MES patients can be considered more similar to the FEP patients controls' than to MES controls' response pattern. Having this in mind it is clear that a comparison of the FEP and MES samples with a single adult control group would have led to the wrong conclusion that both patient samples showed an anomalous pattern of emotion

attribution to neutral faces. Thus, the comparison with age-matched controls provides a more accurate description of the way in which recognition of facial affect at different stages in the evolution of schizophrenia deviates from normative performance. The finding of erroneous emotion attribution to neutral faces by chronic schizophrenia patients seems consistent with the results of neuroimaging studies. For example, Hall et al. (2008) found increased amygdala activation to neutral faces in these patients. In a similar vein, chronic schizophrenia patients have been found to show heightened amygdalar and hippocampal activity (Holt et al., 2005) and increased peripheral arousal (Williams et al., 2004) in the presence of neutral faces. Unfortunately, complementary information on recognition accuracy is lacking because no explicit emotion task was assigned to the participants in these studies. Thus, we don't know the extent to which these anomalous response patterns are causally associated to emotion misattribution to neutral faces. As pointed out by Hall et al. (2008), increased sensitivity to neutral faces might be the consequence of an aberrant attribution of salience to external and internal events. Salience misattribution has been proposed by Kapur (2003) as a mechanism underlying some aspects of psychotic experience, possibly mediated by an imbalance in dopamine neurotransmission. What our results indicate is that anomalous attribution of salience to social stimuli might not be a stable characteristic of social cognition in schizophrenia. Rather, these attributional deficits seem to appear at relatively advanced stages in the development of the disorder.

We finish by noting some limitations of the present study. First, as the higher PANSS scores in the FEP patients suggest, illness severity and clinical status is different between patient groups. This discrepancy is frequently found in studies in which patients in early stages are compared with chronic patients. A second important limitation is that the cross-sectional design of the study does not allow firm conclusions on the evolution of affect recognition abilities in schizophrenia, it is considered as a future goal to keep in mind. Finally, it would be suitable to evaluate a bigger sample size and to include a measurement of general neurocognitive/IQ functioning in order to increase the generalization of our conclusions.

The findings of the present study have important clinical implications because emotion recognition has shown to be associated with social functioning (Irani et al., 2012). Social skills emerge gradually through childhood and adolescence and reflect a dynamic interplay between the individual and his or her environment. Disruptions to social skills can contribute to psychological distress, social isolation, and reduced self-esteem and may impact greatly on quality of life (Beauchamp and Anderson, 2010). So adapting early interventions to the needs of patients at first stages of psychosis might help to prevent them from future problems in their social life. Future research will help us to clarify which interventions are more successful helping young patients to preserve as much emotion recognition abilities as possible.

To sum up, we have provided new evidence of a differential pattern of impairment in the recognition of facial expressions of emotion at different stages of schizophrenia using a double age-matched control design. Compared to FEP patients, MES patients showed a more generalized deficit that spared only recognition of happy expressions. Adult patients showed further an increased tendency to misattribute emotional meaning to neutral faces. The relatively preserved facial affect recognition at first stages of schizophrenia even in acutely ill patients is encouraging from the clinical point of view. Psychosocial interventions like those based on the clinical staging model (Cross et al., 2014) could improve or at least maintain competence in affect recognition in younger patients (Killackey and Yung, 2007; Marshall and Rathbone, 2011). On the other hand, the anomalous pattern of emotion attribution to neutral faces observed in chronic patients suggests a new target for therapeutic intervention with this patient group. Intervention in this domain is of high clinical relevance because affect recognition performance is directly related to social competence and impaired social functioning, having an impact on quality of life (Penn et al., 1997)

and predicting outcome in schizophrenia (Perlick et al., 1992; Sullivan et al., 1990).

In light of these results our main conclusions are (1) that while chronic patients show widespread emotion recognition deficits, patients at early stages of psychosis manifest a deficit restricted to the recognition of fear; (2) MES patients misattribute the emotional meaning of neutral faces and their error pattern for these faces clearly differs from that of their controls; (3) Finally, depressed (for FEP) and negative (for MES) PANSS factor were correlated with better recognition of fearful expressions, while disorganized PANSS factor correlated with worse recognition of sad and neutral expressions only for chronic patients.

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Contributors

VR and LA designed the study.
VR, LA, JRT, TP, RR and JLP managed the literature search and review.
VR, JRT and JLP selected the sample and evaluated patients.
VR, LA, RR and JLP undertook the statistical analysis.
VR, LA, RR and JLP wrote the first draft of the manuscript.
VR, LA, RR and JLP wrote the second draft of the manuscript.
All authors contributed to and have approved the final manuscript.

Conflict of interest

The authors report no biomedical financial interests or potential conflicts of interest.

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CHAPTER 6: CONTEXT INFLUENCE

6.1. Introduction

Facial expressions play a highly relevant role in social communication, allowing us to make inferences about emotions and internal states of our interlocutors. While a large portion of research has focused on the perceptual and affective processing of faces, in absence of any other sources of information, in daily life, facial expressions are usually perceived within a certain situational context. Context has shown to play a modulatory role in information processing, influencing the choice between possible interpretations, by making relevant signals more salient, and by grouping those that go together (Phillips & Silverstein, 2003).

Regarding how contextual information influences processing of stimuli, Baddeley (1982) distinguished between two types of context. The first one is the interactive context, defined by the fact that it affects the meaning, or the interpretation of the target event. For instance, a semantic context which makes it possible to disambiguate the meaning of a homophone is undoubtedly interactive in nature. In contrast, an independent context does not interfere with the interpretation of the target event. An example of independent context comes from a study in which lists of words were studied 'on land' or 'under water' (Godden & Baddeley, 1975). In this case, the environmental context is encoded independently of and in parallel with the target information. It is important to note that the distinction proposed by Baddeley does not match the distinction between verbal and physical contexts, as the above examples might suggest. For example, the ground of a picture can serve as an interactive context for the interpretation of an ambiguous figure. Similarly, the pairing of semantically unrelated context/target words can be an example of independent context.

Some studies have explored the relation between a facial expression and the context in which it appears, mostly under the interactive context approach, and results consistently converge in the influence of contextual information in perception and processing of facial expressions of emotion, substantially modifying their neural processing (see Wieser & Brosch, 2012 for a review).

However, when contextual influence on a target processing has been investigated in schizophrenia, considerable discrepancies in results are noted. It has been shown that schizophrenia patients fail in tasks involving interactive (non-emotional) contexts with semantic target information, especially in the case of patients with thought disorder, which are more affected by this deficit (Bazin, Perruchet, Hardy-Bayle, & Feline, 2000). Indeed, Cohen and Servan-Schreiber (1992) presented a study where context was interactive, as it helped to disambiguate the meaning of the target word. Using a lexical disambiguation task, they found that patients were able to use context over a small temporal range. More specifically, patients made significantly more meaning errors when the context came first compared to when the context came last. They concluded that a disturbance in the internal representation of contextual information in schizophrenia patients could provide a common explanation for deficits found in several attention and language related tasks. Probably, this result is pointing out that the disturbances in the maintenance of contextual information for its use poses an added difficulty for patients. In fact, during cognitive processing, contextual information is actively held in mind in such a form that it can be used to formulate a proper response (Cohen, Barch, Carter, & Servan-Schreiber, 1999). Deficits in working memory (WM) have been identified as a cardinal cognitive symptom of schizophrenia, present in all modalities examined (for meta-analysis, see Lee & Park, 2005). For that reason, when context is presented before the target, WM impairments could lead to wrongly conclude that schizophrenia patients show a failure in context integration when it could be explained –at least in part- in terms of a deficit in WM. A possible solution to strictly explore context influence may be to present face-context compounds (i.e., overlaid faces on the center of a context stimulus) after the context presentation, avoiding a substantial need for WM involvement.

In this regard, some studies have included a measurement of context processing with no emotional content such as the Continuous Performance Test (CPT) as performance on this task depends on the representation and maintenance of context provided by the cue (e.g., Chung, Mathews, & Barch, 2011; Green et al., 2007). Chung et al. (2011) found a correlation between performance on CPT and the ability to use contextual knowledge (visual and verbal) to derive meaning from conversations displayed in videotaped vignettes. Therefore, they suggested that deficits in context

processing may be contributing to both “hot” (emotion-laden) and “cold” (emotion-independent) cognitive processing aspects of cognition in schizophrenia.

On the other hand, an earlier study carried out by Bazin & Perruchet (1996) has shown that patients with schizophrenia and control subjects used contextual information to the same extent and reached the same level of performance in an implicit associative memory test. Thus a tentative conclusion is that context processing in tasks involving no interactive context is preserved. Thus, one may say that the impairment in context processing concerns only tasks involving interactive context in the case of patients with schizophrenia. Nevertheless, almost all previous studies have used semantic context (i.e., words or sentences) with no emotional content whereas it is known that patients present a deficit in the processing of semantic information (e.g., Besche et al., 1997; Mathalon et al., 2002). For that reason the influence of other types of contexts needs to be further explored.

Regarding studies that had used context information to explore emotional processing, very few have actually included affective contexts to this end. One of the few studies including emotional pictures as context found that patients were less influenced by contextual cues than controls, as they evaluated similarly the intensity of the emotion from images of people with and without background (Monkul et al., 2007). In the same line, patients showed impaired utilization of contextual information for specific story-face pairs (Green et al., 2007). In this study, facial affect processing ability was a significant predictor of the successful social context integration. Concerning the target stimulus to be evaluated, previous studies that have used faces have presented them showing emotional expressions. Keeping in mind that schizophrenia patients have shown to be more likely to make an erroneous interpretation when the social information is ambiguous (Corrigan & Nelson, 1998) it is surprising that very few studies have explored whether contextual cues can influence the recognition of ambiguous stimuli, such as subtle facial expressions (i.e. expressions with minimized muscle movements). This manipulation can provide information about how context can bias stimuli processing under ambiguity. To our knowledge, there is only one study with schizophrenia patients including subtly surprised faces (Chung & Barch, 2011). In this study, individuals with schizophrenia showed a preserved influence of context information on facial emotion recognition. Again, those patients with schizophrenia that better performed on tasks involving processing of non-social

context (measured with a version of CPT) showed a stronger influence of context on valence ratings of facial expressions, although only in the negative context condition. As stated previously, this result provides further evidence that in schizophrenia, similar mechanisms may influence the processing of context for both social and non-social information. There is also another study that found intact situational context processing in schizophrenia, suggesting that patients benefit from situational context when interpreting ambiguous facial expressions (Lee et al., 2013). Both patients and controls rated faces as more afraid when they were paired with fear-inducing sentences (note that semantic context is presented in this study) and as more surprised when they were paired with surprise-inducing sentences, thus the degree of modulation was comparable across groups. Authors have proposed that this relatively preserved area of social cognition should be considered as a starting point in the development of social cognition remediation programs.

Given that the way in which patients with schizophrenia make use of contextual information remains controversial and that its influence on identification of neutral faces has not been thoroughly investigated, the main goal of the present work was to study whether emotion recognition was influenced by interactive contextual information to the same extent in patients with schizophrenia than in healthy controls. For this purpose, participants were asked to evaluate neutral faces that were presented along with situational images used as interactive contexts, in terms of valence and emotional label. Neutral faces were selected as targets because we have found them to be especially ambiguous for schizophrenia patients (Kohler et al., 2003; Romero-Ferreiro et al., 2016; Romero-Ferreiro, Aguado, Rodriguez-Torresano, Palomo, & Rodriguez-Jimenez, 2015). On each trial, contextual information remained in the display when participants judged faces to ensure that participants had such information available during the task and, as far as possible, to avoid the involvement of WM.

6.2. Method

6.2.1. Participants

Twenty-three clinically stable inpatients (close to be discharged from the Acute Psychiatric Unit) who were consecutively referred by their treating psychiatrists took part in this study. 22 controls paired in age and sex with no self-reported history of psychotic disorder and no history of psychosis in first-degree relatives were selected as

comparison group. All patients were diagnosed with schizophrenia except one patient diagnosed with schizoaffective disorder according to DSM-IV-TR criteria (American Psychiatric Association, 2000) using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First, Spitzer, Gibbon, & Williams, 1995) and were on atypical antipsychotic treatment. Clinical status was evaluated using the Spanish version (Peralta & Cuesta, 1994) of the Positive and Negative Syndrome Scale (PANSS) (Kay, Fiszbein, & Opfer, 1987) (See Table 6.1 for sociodemographics and clinical status). The written informed consent was obtained from all participants prior to their inclusion in the study. The procedure was approved by the Ethics Committee.

	Patients (n=23)	Controls (n=22)	Statistic (<i>p</i>)
	Mean (SD)	Mean (SD)	
Age	36.35 (10.8)	37.3 (12.4)	$t = .022$ ($p = .983$) Cohen's $d = -.08$
Gender (% male)	69.6%	54.5%	$\chi^2 = 1.079$ ($p = .299$) $r = .154$
Years of education	9.76 (2.2)	13.91 (2.1)	$t = -6.007$ ($p < .001$) Cohen's $d = -1.92$
Years of evolution	7.88 (9.97)	-----	-----
PANSS-Positive	20.65 (6.23)	-----	-----
PANSS-Negative	25.73 (8.39)	-----	-----
PANNS-GP	49.26 (10.07)	-----	-----
CPZ*	521.31 (305.18)	-----	-----

Table 6.1. Sample demographics and clinical status of patients.

*Chlorpromazine equivalent dose (mg/day).

6.2.2. Materials

Stimuli consisted of 42 pictures taken from the KDEF (Karolinska Directed Emotional Faces) collection (Lundqvist & Litton, 1998). The faces corresponded to different models (21 female, 21 male) all of them showing neutral expressions. Pictures were converted to grey scale, cropped to conceal most of the hair. Pictures were selected attending to their valence values from database reported in appendix A of a previous study (Aguado, Román, Fernández-Cahill, Diéguez-Risco, & Romero-Ferreiro, 2011). There, faces were rated in terms of valence, arousal and trustworthiness in a 1 to 9 Likert scale (ranging from 1, meaning not at all for Trustworthiness,

unpleasant for Valence and calming for Arousal, to 9, meaning a lot for Trustworthiness, very pleasant for Valence and very activating for Arousal), only those rated between 4 – 6 of average valence (i.e. “real” neutral faces) were selected ($M = 4.97$, $SD = .54$). The mean value of selected faces was 4.76 ($SD = .76$) for trustworthiness and 4.66 ($SD = .62$) for arousal ratings. 42 context pictures (14 positive, 14 neutral and 14 negative) were selected from the EmoMadrid dataset (“EmoMadrid affective picture database”, n.d.). Context pictures were selected attending to their valence and arousal values, trying to select the more positive and negative pictures, with higher arousal values and smaller standard deviation to ensure that results were as consistent as possible. The mean valence value was -1.62 ($SD = .12$) for negative contexts and 1.26 ($SD = .12$) for positive ones in a -2, very negative, to 2, very positive (0 is the neutral value) scale. No differences in mean arousal values between positive ($M = 1.62$, $SD = .09$) and negative ($M = 1.6$, $SD = .07$) contexts were found $t(26) = .77$, $p = .449$. The arousal scale ranged from -2, very calming, to 2, very arousing; 0 is the neutral value. The neutral contexts had a mean valence of .004 ($SD = .017$) and mean arousal of -.05 ($SD = .24$). The stimuli were presented on a 15” LCD monitor (refresh rate 60Hz).

6.2.3. Experimental task

Experimental procedure can be observed in Figure 6.1. In the first task participants were presented an emotional context during 1 second, then, superimposed to the context, a neutral face was presented. Patients were instructed to consider the contexts as the situation in which the person represented by the face was. Then, they were asked to rate the emotion expressed by the face by choosing among one of six options (sad, angry, fearful, other, happy, and neutral) and the valence in a 1 to 9 Likert scale (ranging from “not at all unpleasant” to “very pleasant”). For counterbalancing purposes, three groups of random faces were made (ensuring that half of them were males and half females) which were associated with each type of context (positive, neutral, negative) the same number of times.

We considered that it was important to test whether that context is perceived by patients in the same way than controls. For that reason, participants were asked to rate the emotional valence of pictures used as contexts (in this case, no explicit judgment of

emotional label was required) in a 1 to 9 Likert scale (ranging from “not at all unpleasant” to “very pleasant”).

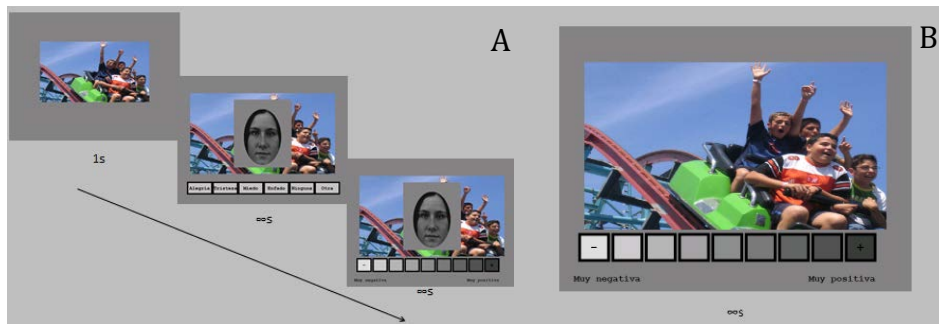


Figure 6.1. A. Example of a trial in the face evaluation task. B. Example of a trial of the context evaluation task.

6.2.4. Data Analysis

First of all, simple comparisons (chi-square for gender distribution and t tests for age and years of education) between patients and controls on sociodemographics were performed.

A 2 x 3 x 6 repeated measures ANOVA was performed on frequencies of label selection in the context influence task. The variable Group (patients, controls) was the between-group factor and the Valence of the context (positive, neutral, negative) and the selected label (Emotion) (sad, angry, fearful, other, happy, and neutral) were the within-subjects factors. For this analysis, data from one schizophrenia subject was removed, as the most of the trials were not responded. These data are based on the mean selection of each label for all subjects taking into account that there were 42 trials.

Finally, two 2 x 3 repeated measures ANOVA were performed on the valence ratings of neutral faces and emotional contexts. The variable Group (patients, controls) was the between group factors and the Valence of the context (positive, neutral, negative) was the within-subjects factor. The Greenhouse–Geisser and Bonferroni corrections were applied (significant when $p \leq .05$).

6.3. Results

As Table 6.1 shows, patients did not differ from controls in terms of age $t = .022$ ($p = .983$) and gender distribution $\chi^2 = 1.079$ ($p = .299$). However, they significantly differed on mean years of education $t = -6.007$ ($p < .001$).

Regarding label selection to categorize neutral faces preceded by contexts, a significant interaction Emotion x Group was found, $F(5,210) = 3.87$, $p = .002$, $\eta^2_p = .084$. Paired comparisons showed that patients selected significantly more frequently the label “fear” ($M = 2.81$, $SEM = .294$) than controls ($M = 1.47$, $SEM = .294$). By contrast, controls selected the label “neutral” more frequently ($M = 4.47$, $SEM = .599$) than patients ($M = 2.57$, $SEM = .599$). Moreover, as it can be seen in Figure 6.2, an Emotion x Group x Valence context was also significant $F(10,420) = 2.42$, $p = .008$, $\eta^2_p = .055$. When the contextual information was emotional (i.e. negative and positive), patients selected significantly more frequently the label “fear” ($M = 4.63$, $SEM = .545$; $M = 2.95$, $SEM = .368$, respectively) than controls ($M = 2.5$, $SEM = .545$; $M = 1.27$, $SEM = .368$, respectively) and controls selected the label “neutral” more frequently ($M = 4.72$, $SEM = .667$; $M = 4.72$, $SEM = .728$, respectively) than patients ($M = 1.95$, $SEM = .354$; $M = 2.54$, $SEM = .728$, respectively). In the case of neutral contexts, patients and controls did not differ in the selection of labels to categorize the faces presented (all $p_s > .05$).

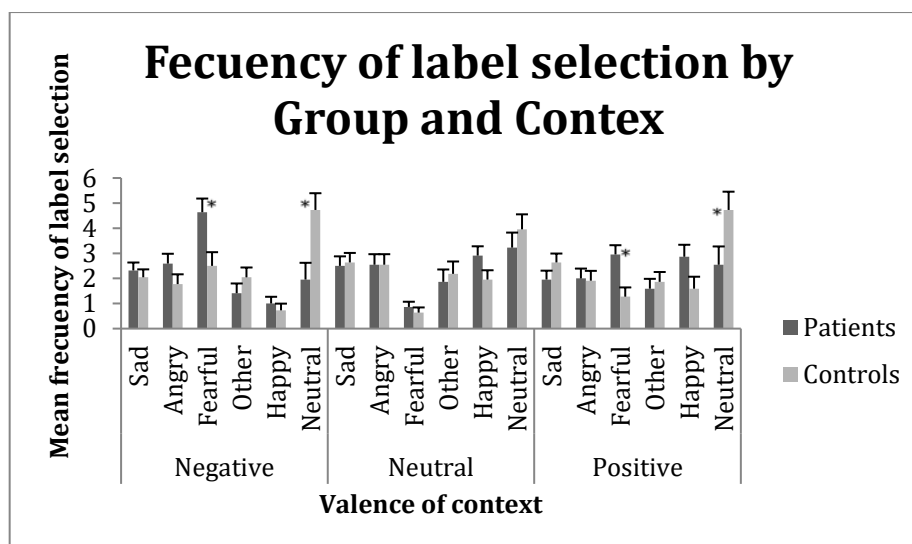


Figure 6.2. Frequency of label selection separated by contextual valence and group. (Error bars denote Standard Error Mean). * $p < .05$.

As expected, the analysis of ratings of faces showed a main effect of valence of context $F(2,86) = 7.362, p < .001, \eta^2_p = .146$. Neutral faces preceded by a negative context were evaluated as more negative ($M = 4.22, SEM = .165$) compared to when they followed positive ($M = 4.67, SEM = .152$) and neutral contexts ($M = 4.77, SEM = .137$). However, this effect was similar for patients and controls given that the main effect of group ($p = .314$) and the interaction Valence of context x Group ($p = .306$) did not reach statistical significance.

Finally, participants evaluated the pictures showed as contexts in the context influence task. Analysis of ratings of contexts showed that patients and controls did not differ in their evaluations as there was no main effect of Group ($p = .682$). However, the Valence of context x Group interaction resulted significant $F(2,86) = 4.082, p = .02, \eta^2_p = .087$. Within-group comparisons showed that ratings for positive, negative and neutral contexts were significantly different ($M = 6.91, SEM = .291; M = 2.24, SEM = .184; M = 5.62, SEM = .205$, respectively for patients; $M = 7.44, SEM = .298; M = 1.97, SEM = .188; M = 5.06, SEM = .209$, respectively for controls). Finally, as expected, positive, negative and neutral contexts significantly differed on their valence ratings for both patients and controls ($M = 7.17, SEM = .208; M = 2.11, SEM = .131; M = 5.34, SEM = .146$, respectively), $F(2,86) = 340.85, p < .001, \eta^2_p = .888$.

6.4. Discussion

In this study, patients and controls were compared in a context-target task, where context added extra visual information (in the form of pictures) to judge the target facial stimulus. The main innovation of this study was that context information was emotional but target faces were emotionally neutral. This prevents emotion of contexts from being mixed with emotions of faces and hence allows determining the exclusive influence of emotional context on facial evaluations. Another improvement of this study was the maintenance of contextual information at the moment of response to minimize the need of resorting to memory. Results reported in the present study can be divided in two main findings. On the one hand, patients did not significantly differ from controls in their evaluations of emotional pictures presented as contexts. This result highlights the fact that when the affective value of stimuli (other than faces) has to be evaluated, responses of patients and controls do not differ. In the same line, patients were not

significantly different from controls when rating the valence of the neutral faces presented along with emotional contexts. Thus, affective ratings were influenced by the context to the same extent in both groups. More specifically, participants rated faces presented along with negative contexts as more negative compared to when they were presented with positive or neutral contexts. This could be considered as a “priming effect”, in which a negative context induced participants to rate faces as slightly more unpleasant than when they were presented along with a positive or neutral context. Therefore, it is plausible to admit that patients process the valence of the contexts and that they transfer it to the facial stimuli in a similar way that controls did. This result goes hand in hand with previous studies that used subtle facial expressions as target stimuli. As it was mentioned previously, the study by Chung & Barch (2011) concluded that individuals with schizophrenia showed an intact influence of context information on facial emotion recognition. In the same line, Lee et al. (2013) found intact situational context processing in schizophrenia, suggesting that patients benefit from situational context when interpreting ambiguous facial expressions.

On the other hand, when participants were asked to evaluate facial stimuli in terms of emotional category, specific differences between patients and controls emerged. In presence of positive and negative contexts, patients tended to categorize neutral faces as depicting fear more frequently than controls. Also, faces were less frequently categorized as emotionally neutral by patients than by controls. These two effects did not occur when the context was neutral. Only when the context was either positive or negative responses of patients and controls were significantly different. Positive and negative pictures selected had similar high arousal values, so it is quite difficult to discern whether this effect was due to the valence, arousal or a combination of both. In fact, it is possible that the selection of positive stimuli might be influencing this finding. The positive pictures were selected aiming to have as high arousal values as possible, for example showing scenes such as roller coasters or high risk sports. Although they are considered positive by most people, it is true that they might also elicit fear or at least qualm feelings in many others. Nevertheless, an effect of context Valence (positive pictures were rated as more pleasant than neutral and negative ones) and no Valence of context x Group interaction effects were found in the present study. This result rules out the possibility of a misinterpretation of positive contexts by patients. In either case, it seems that when context had high emotional content, it

triggered a response bias in patients with schizophrenia. The fact that patients selected more often fear labels and less often neutral labels than controls did fits perfectly with those studies that point out the emotions of fear and neutral expressions as the earliest and most predictive impairment in patients with schizophrenia (Allott et al., 2014; Barkl, Lah, Harris, & Williams, 2014; Romero-Ferreiro et al., 2016) and even in unaffected first-degree relatives (Allott et al., 2015).

Considering results found along this work, a noteworthy result was the fact that when a neutral context is presented, patients with schizophrenia are able to categorize neutral faces as neutral and not as fearful, just as controls. It could be hypothesized that when congruent contextual information is provided to patients, they are able to correctly categorize a neutral face as showing no emotion. In other words, patients have shown to interpret neutral faces as emotional even in absence of context (Romero-Ferreiro et al., 2015), however, when neutral context information accompanies those faces, patients correctly identified them as neutral, at least to the same extent than controls. A plausible explanation could be that while patients are not able to correctly process the affective valence of neutral faces presented alone, the neutral context information helps them to counteract this deficit. In the case of the present study, only neutral contexts actually matched with faces and they have led patients to correctly interpret the neutrality of the faces. However, in the case of positive or negative contexts, patients appear not to get the discrepancies between the face and the contexts and let themselves be influenced by contextual information more than controls. This novel result would open a new line of research, which could lead to create new social intervention programs in which emotional judgments of patients should be based on available contextual information as long as it provides information in the same direction as the face. Also, as a following step, it would be necessary to train patients in the identification of non-emotional stimuli when they are inserted in a complex situational context laden with affective content, as this situation can also occur in real life.

Regarding the practical implications, in everyday life, an individual's face almost always appears within a situational context, which may arise from other people, the physical environment surrounding the face, as well as multichannel information from the sender. Even the perceiver may provide situational context, including his/her own expectations or implicit processing biases such as race bias. Thus, the perception of facial expressions is presumably always influenced by contextual variables (Wieser &

Brosch, 2012). For that reason, it is important to integrate the context when inferring the internal state of our interlocutor. Patients seem to get the valence of the contexts and the hint that it puts into neutral faces correctly. However, emotional contextual information exerts an excessive influence in determining the specific emotion expressed by a neutral face, leading to attribute fear to those facial stimuli. As it was suggested by Lee et al. (2013), patients with schizophrenia may benefit more when psychosocial rehabilitation programs provide richer situational information. Otherwise, although patients would learn how to correctly identify facial expressions it could hardly facilitate social interactions and social learning as they always contain information about the context. One proof of this is that Barrett and Kensinger (2010) found in general population that visual context is routinely encoded when facial expressions are observed. Participants remembered the context more often when asked to label an emotion in a facial expression than when asked to judge the expression's simple affective significance (which could be done on the basis of the structural features of the face alone). Therefore, it is crucial to include contextual cues and instructions of how to integrate them in the understanding of complex social situations during social cognition training programs. In fact, when neutral contexts are presented, it has been demonstrated that they help patients to correctly identify neutral faces. Then, it also feels necessary to include them in those programs to filter when the emotional contexts add excessive emotional content to the situation.

The present study has several limitations. Firstly, contextual influence on neutral faces cannot be extrapolated to emotional faces. For that reason, there is a need for further investigation on this field. Secondly, we cannot rule out the possibility that participants responded the emotion they considered the person "must be feeling" instead of exclusively the emotion expressed by the face, as they were told that faces belonged to persons that were involved in those contexts. Finally, the sample size is an issue in this study. Future research would tell if the results presented in this study are replicable with bigger samples.

It can be concluded that when a categorization in terms of valence is required, patients show a performance comparable to controls. This categorization has been considered as a first step, in which facial stimuli expressing positive and negative emotions are differentiated (Aguado, Dieguez-Risco, Méndez-Bértolo, Pozo, & Hinojosa, 2013; Diéguez-Risco, Aguado, Albert, & Hinojosa, 2015). Then, the second

step is to select within the emotional valence a specific emotion that better describes the stimulus. This is a much more sophisticated part of the emotional processing that constitutes a significant step forward, deeper than the discrimination of affective valence. Taken together, these results suggest that patients show a specific deficit in the processing/representation of emotional categories whereas the basic affective dimensions (i.e. arousal and valence) are preserved in patients with schizophrenia. But this only occurs when contextual information adds emotional value to the situation that does not match the emotion expressed by the face.

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CHAPTER 7: GENERAL DISCUSSION AND CONCLUSIONS

“...se dará tiempo al tiempo, que suele dar dulce salida a muchas amargas dificultades”.

Miguel de Cervantes,
Novelas Ejemplares I (La Gitanilla).
Madrid: Cátedra, 2005, p. 133

Summary

The main goal of the present work was to explore facial affect recognition in patients with schizophrenia, including samples at early and chronic stages of the disorder. There is no doubt that face affect recognition plays an important role in social interaction and that patients with schizophrenia experience limitations in their ability to interpret those emotional signals. There is however less consensus about the cause, nature and outcome of these limitations. With the studies presented in this thesis we hope to have filled in some gaps in this matter. **Chapter 1** provides a general overview of the state of the art. In **chapter 2** the aims of the present work are summarized. The study reported in **chapter 3** investigates the claim that patients show a specific deficit on facial affect recognition rather than general face processing impairments. Then, in **chapter 4** the patterns of emotion attribution to emotional as well as neutral faces are explored. **Chapter 5** focuses on the study of face affect recognition at early and chronic stages of the disorder. In **chapter 6**, the influence of visual contextual information on evaluations of emotionally neutral facial stimuli is assessed. Finally, in **chapter 7**, the results of these studies are summarized and integrated with the most important findings in the literature. Also, the limitations of the studies are mentioned and the future lines of research that follow this thesis are highlighted.

General discussion

Summarizing the main results reported in the present thesis, it was shown that patients perform poorly on tasks involving face affect processing, as opposed to tasks

involving processing of non-emotional facial features (i.e. gender identification). The impairments found in affect recognition at early stages are restricted to fear expressions, while they are generalized to all negative basic emotions as well as to emotionally neutral expressions at chronic stages of the disorder. Additionally, specially designed tests indicated that patients perceive negative as well as positive and neutral expressions as more ambiguous (that is, as potentially expressing different emotions) than controls. Finally, patients tended to categorize neutral faces as showing fear rather than showing “no emotion” to a higher extent than controls did in presence of emotional context information. However, in presence of neutral contexts, patients and controls did not significantly differ in their evaluations of facial stimuli. Results of each of these studies had been extensively discussed with respect to working hypothesis and previous literature. That is why in the general discussion the most important aspects and the convergence of some results will be highlighted.

Is the impairment in face affect recognition due to a general face processing deficit?

The first step was to explore whether facial affect recognition deficits reported in literature were due to a more general face processing impairment. With the aim of comparing patients and controls recognition of non-emotional facial properties, a gender recognition task with emotional expressions was designed. The results showed that patients' performance was comparable to that of controls when faces had to be classified on the basis of gender attributes. Patients were capable to identify the gender of a face as efficiently as controls, even when that face was showing an emotional expression. At first sight, one may think that this result could be due to the fact that, compared to emotion recognition, gender recognition involved only two response alternatives, thus making the task easier. However, studies on emotion recognition employing only two emotions (and thus, two response alternatives) have reported deficits in schizophrenia patients compared to depressive and non-clinical individuals (Heimberg, Gur, Erwin, Shtasel, & Gur, 1992). Consequently, it is unlikely that the response format could explain these results. Although some studies disagree (Pomarol-Clotet et al., 2010; Salem, Kring, & Kerr, 1996), recognition of aspects of facial structure that are invariant

across changes in expression seems to be relatively preserved in patients with schizophrenia. For example, studies about gender recognition and age-discrimination (Bediou, Krolak-Salmon, Saoud, & Henaff, 2005; Schneider et al., 2006 respectively) found (as we did) that patients performed with a high degree of accuracy. However, although the discrimination of these characteristics is important for social life, detecting and interpreting changeable aspects plays a far greater role during interpersonal communication. For this reason, the major part of this work has been dedicated to this issue.

Is the deficit in face affect recognition different across clinical staging in schizophrenia?

The second step was to explore the processing of changeable facial features, which are informative of the emotional state of individuals and its stability over the course of the disorder. Kohler et al. (2009) carried out a meta-analysis including 86 studies and showed a large deficit in emotion perception in patients with chronic schizophrenia compared to controls. However, the presence of illness-related factors that moderate the severity of impairment has been highlighted. In the case of schizophrenia, these factors can be acquired over the evolution of the disease and run the risk of being considered core features rather than external effects. In this regard, outcome assessment based on a staging approach has been suggested to be more appropriated. Defining discrete stages according to progression of disease “creates a prevention-oriented framework for understanding pathogenesis” (McGorry, 2007, p.859; McGorry et al., 2007). Therefore, the best solution would be to study patients at their very first stages of the disorder, as soon as their clinical condition allows for the evaluation. For this purpose, recent onset and chronic patients were compared with non-clinical individuals, belonging to the same age range, and considered at the same stage of development. Results indicated that while chronic patients showed a generalized impairment of emotion recognition, young patients performed similarly to their corresponding controls, except for recognition of fearful faces. Although this study is based on a novel design that takes into account the clinical stage of the disorder and the development of patients, results agree well with previous studies with first-episode

schizophrenia patients, that supported small but consistent deficits in recognition of fear and sadness across facial expression and affective prosody (Edwards, Pattison, Jackson, & Wales, 2001). In fact, fear has shown to be more difficult to identify than any other emotion in the general population, again either through facial expressions (Kirouac & Doré, 1983) or vocal cues (Johnson, Emde, Scherer, & Klinnert, 1986). Also, fear expressions have been found to be most impaired in well-established schizophrenia in both modalities (e.g. Mandal & Rai, 1987). Similarly, Kohler et al. (2003) found that patients showed less benefit from increased intensity for all emotions combined, and the difference was most pronounced for fear. It could thus be suggested that fear recognition is the earliest and most impaired emotion over the course of schizophrenia. Furthermore, a recent review of 48 studies evaluating social cognition in first episode psychosis confirms that impaired recognition of fear and sadness is the most consistent result found in literature (Healey, Bartholomeusz, & Penn, 2016). The main conclusion to be drawn from these results is that face affect recognition in first-episode patients is not as impaired as in chronic patients, and this should be taken into account when designing intervention strategies tailored to the impairment profile characteristic of each stage in the evolution of the disorder.

Ambiguity of emotional expressions

In chapter 4, patients have shown a higher tendency to perceive different emotions in a single facial expression. As stated, this result has been interpreted as due to a noisy representation of face-emotion correspondences. Even though patients gave similar ratings than controls for the “correct” label in the case of negative emotions, they also tended to give higher ratings on other negative labels. This means that while patients are aware of the “dominant” emotion expressed by a given face, they are also more likely than controls to attribute it other negative emotions. This result supports Adolphs' theory (2002), in which negative expressions are considered more easily confusable because their corresponding facial configurations include common expressive features.

An unexpected but very interesting result was that patients tended to give higher ratings on all emotional labels to neutral and happy expressions. This result suggests a

general tendency to attribute emotional content to both emotional and non-emotional expressions. This tendency is not accounted for the valence of stimuli since it is present with negative, positive or neutral stimuli.

Summarizing the results obtained using the Ambiguity Index (AI), angry, fear and happy expressions were perceived as more ambiguous by patients than by controls. Results on angry and fear expressions were expected, as recognition of negative emotions is usually more impaired in the case of patients (Bediou, Franck, et al., 2005). But the fact that happy expressions were perceived as more ambiguous was completely unexpected, even more when happiness was the only emotion identified by chronic patients with similar accuracy than controls. However, deficits in emotion discrimination with happy faces have been described in literature (Sachs, Stegerwuchse, Kryspin-exner, Gur, & Katschnig, 2004) which makes this result at least, plausible, or less unexpected. Once again, this result highlights that emotion recognition and evaluation of related aspects such as emotion attribution are not necessarily controlled by the same cognitive processes. On the other hand, the lack of differences between patients and controls in the case of sad and neutral faces probably finds its explanation in the fact that these two emotions are perceived by controls with a high ambiguity. Therefore, differences between patients and controls decreased. Sad expressions presented the lowest accuracy scores as can be seen in chapter 5, being the most difficult expression to recognize for all participants who took part in the study (patients and controls). This result could be explaining its high ambiguity scores. In the case of neutral faces, a design flaw could be playing a role. As the rating scale has no zero, it was inevitable to attribute at least one point to each emotional label. In this case, a consistent response of the minimum rate in all labels would lead to a resulting maximum ambiguity value (i.e. 1). However, in the light of the higher AI index for neutral faces, it can be therefore assumed that patients and controls did not perceive any expression in particular with stronger intensity than controls on neutral faces. Although it is true that ratings of patients were higher than those given by controls for all labels, especially in the case of fear and sadness.

From the above considerations, it clearly seems that patients perceive faces as highly emotional stimuli. This might play an important role on their own interpretation of the world. Future research should explore this matter and its possible relationship with the delusional themes in actively psychotic patients.

The case of neutral faces

Patients have shown a tendency to over-attribute emotional meaning to neutral faces. In chapter 5 the tendency of patients to categorize neutral faces as emotional was reported. Unlike adult controls, chronic patients (and, to a lesser extent young patients and their controls) tended to attribute sadness, fear and anger to apparently non-emotional faces. Furthermore, while adult controls show a high rate of correct identification of neutral faces, the error pattern showed by chronic patients as well as by young patients and their controls is very similar. In the light of this result, one might conclude that schizophrenia inhibits the expected “normal” development of emotion recognition, or, in this case, the recognition of neutral faces as showing no emotion.

Taking one-step forward, as can be seen in chapter 6, neutral faces were presented along with neutral and emotional contexts with the aim of exploring the influence of contextual information on their evaluations. First, when asked to rate them in terms of valence, patients and controls differed neither in their evaluation of contexts nor in their evaluation of neutral faces. Participants rated neutral faces presented with negative contexts as slightly more unpleasant than when they were presented with positive or neutral contexts. This effect (that is similar to the priming effect) was comparable for both groups, which leads us to think that the valence of the context influences face perception, in the same way for patients and controls. However, when the emotion expressed by the neutral face has to be categorized, differences between patients and controls emerge.

On the other hand, results of emotion categorization showed that neutral faces were mistaken as emotional by patients with schizophrenia when they were evaluated in presence of negative and positive contexts. Specifically, neutral faces were categorized as fearful by patients more often than by controls. Additionally, those faces were categorized as neutral by controls more often than by patients. This result is consistent with results showed in chapter 5 as well as with previous studies in which poor categorization of fear and neutral expressions is the earliest and most predictive impairment in patients with schizophrenia and unaffected first-degree relatives (Allott et al., 2014, 2015; Barkl, Lah, Harris, & Williams, 2014). It could be suggested that this occurs because the degree of difficulty of this task is greater than the valence judgment.

Emotion categorization is -as suggested by other authors (Aguado, Dieguez-Risco, Méndez-Bértolo, Pozo, & Hinojosa, 2013; Diéguez-Risco, Aguado, Albert, & Hinojosa, 2015)- a complex mental operation that follows a previous evaluation based on the dimension of valence. When this first judgment is given, a second and deeper processing mechanism starts to identify the specific emotion category of the stimulus. We hypothesized that this second step is the key point in which patients show specific impairments, at least in the case of emotional stimuli. In the case of neutral faces, patients had shown to have severe difficulties to not imbue them emotional content. Emotional contextual information has shown to bias the response of patients which already occurred when faces were presented in absence of contextual information. It is important to note that when a neutral context was present, patients were capable to identify neutral faces as emotionally neutral, which could be considered a milestone. In some way, the presence of neutral context has resulted in an accurate performance of patients when categorizing neutral faces. It could be proposed that when additional information about the absence of emotionality is available, patients are able to get this information and correctly categorize neutral faces. This novel result could be proposed as a base to develop training programs to improve the ability of patients to categorize neutral stimuli, which is one of the big challenges experts would have to deal with. Of course, new studies that confirm this result should be necessary, but this finding may open a new line of research to develop more effective social interventions for patients with schizophrenia.

Clinical implications

Along the introductory section, the importance of understanding others' mental states has been highlighted. In some way, efficient communication with our conspecifics depends on correct identifications of their facial expressions. Although proper identification of others' feelings does not imply to give an appropriate response to them, it represents a prerequisite for satisfactory social interactions. In the case of patients with schizophrenia, significant deficits have been shown in both face affect recognition and social functioning (Bowie et al., 2008; Bowie, Reichenberg, Patterson,

Heaton, & Harvey, 2006; Green, 1996; Leifker, Bowie, & Harvey, 2009; Malla & Payne, 2005; Milev, Ho, Stephan Arndt, & Andreasen, 2005).

Whether all these results are an effect of the course of the disorder, social isolation, chronic medication or other issues is not completely understood. It has been suggested in a meta-analysis that facial affect recognition deficits cannot be accounted for positive, negative, or overall symptom scores measured by the PANSS (Kohler et al., 2009). However, it is true that a connection between the accuracy to recognize some facial expressions and the severity of psychopathology has been described before. For example, Allott et al. (2014) found that accuracy in identifying neutral and fearful expressions predicted transition to a first episode of psychosis in an ultra-high risk sample. Interestingly, in chapter 5 a positive correlation was found between recognition of fearful expressions and depressive symptoms in first episode patients and negative symptoms in the case of chronic patients. This result could mean that patients who have predominantly depressive and negative symptoms show a negative bias, categorizing facial expressions more frequently as fearful, thus, increasing their accuracy on fear expressions. Additionally, in the case of chronic patients, recognition of sad and neutral expressions was inversely correlated with disorganized symptoms. In this case, results are probably due to the fact that patients with these symptoms are clinically worse and their accuracy has been affected. These are however tentative explanations with little theoretical and empirical ground, and they need to be further explored.

On the other hand, the tendency of patients with schizophrenia to attribute emotional content to non-emotional stimuli, widely discussed in previous chapters, may have implications for understanding some psychotic symptoms, especially positive symptomatology. During an acute psychotic episode people with schizophrenia frequently magnify insignificant occurrences, which can lead them to misinterpret reality. But probably, as it was found by Kohler et al. (2003) and supported by our results, even stable patients are more likely to identify neutral facial expressions as emotional, attributing negative valence to such expressions. Whether this feature is present in remission as well as during acute phases will tell us if it could be considered a stable characteristic of schizophrenia.

Applicability

After an extensive revision of literature and with all of this information at hand, we know that a lot remains to be done regarding the improvement of social cognition abilities in patients with schizophrenia. As discussed in the introductory section, the efficacy of antipsychotic drugs on cognitive symptoms is very limited (Leucht et al., 2009), but a meta-analytic review carried out by Kurtz and Richardson (2011) demonstrated that there were moderate-large effects of social cognitive training procedures on face affect recognition, so we must continue on this course. Currently, there are numerous examples of training programs, from laboratory tasks aiming to increase visual attention to relevant features of emotional faces (Combs et al., 2008; Russell, Green, Simpson, & Coltheart, 2008) to group-based interventions (Penn, Roberts, Combs, & Sterne, 2007). Towards the aim to create/improve remediation strategies, which should be the final goal of research on mental disorders, it should be considered that each facial expression of emotion would probably need specific interventions, depending mainly on the stage of the disorder in which the patient finds him/herself. Psychosocial interventions like those based on the clinical staging model that has the potential to better match illness stage to intervention could improve or at least, maintain competence in affect recognition in younger patients (Marshall & Rathbone, 2011). For example, the model proposed by Cross et al. 2014 allows clinicians to provide more personalized and responsive care, especially to young people with attenuated syndromes (sub-threshold disorders) who have a clear need for mental health care but who may not otherwise receive it. Early interventions have demonstrated to reduce the duration of untreated psychosis, to produce better outcomes in terms of symptomatic and functional domains, and is cheaper than standard models of care (Killackey & Yung, 2007).

Limitations

As any research work, this one is not free from limitations. First of all, (1) we are aware that our sample is relatively small to draw general conclusions. Our future

goal is to replicate results presented in this series of studies with a bigger sample to ensure that our findings are representative of the schizophrenia disorder. Second, (2) results from the cross-sectional study presented in this work should be considered as a first approximation to the study of face affect recognition at different stages of the disorder. Undoubtedly, carrying out a longitudinal study would have been more appropriate. Third, (3) although almost all patients were on atypical antipsychotic medication, the antipsychotic drug and the dosage were not controlled, which could have had some influence on the results reported. Finally, (4) linked with the previous shortcoming, the between-patient variability in terms of age, treatment and illness-duration could have been a source of error variance and may have interfered with results.

Nevertheless, the professionals who have contributed to this interdisciplinary work strongly believe that this series of studies offer valuable contributions to the existing literature. First, experimental control of confounding variables has been a key principle in all the studies presented in this thesis. We have attempted to control the influence of cognitive processes such as working memory, language (need for verbal labeling), or even the evolutionary development of the individuals. Also stimuli were carefully selected based on ratings from a pilot study and processed to delete noisy aspects that were not informative of emotional expression. Controlling these variables would allow drawing more robust conclusions. Second, the study design has been developed to have practical applicability. The aim of this work has been to enable clinicians to incorporate the results found to social interventions.

Future research lines

There still remains much to be done. Despite the many words written and spoken on this topic, we know surprisingly little about social cognition in schizophrenia. For that reason, it's worth thinking about new ways to approach the problem of developing the social skills of patients with severe mental illness.

In a first step, we should continue exploring emotion recognition abilities in labs. I therefore believe that my next step is to continue exploring face affect

recognition in patients with schizophrenia. Given that patients have shown to be (with limited exceptions) as accurate as controls when recognizing facial expressions of happiness, I wonder if they are also able to distinguish an authentic smile (i.e. Duchenne smile) (Duchenne & Cuthbertson, 1990) from a fake smile, in which only the zygomatic major muscle is voluntarily contracted to show politeness. This study will help us to have a better understanding of patients' processing of complex mental states (for example those involving irony) and detecting real intentions of their interlocutor. Secondly, gaze detection and specifically joint attention is becoming a new target in social cognition research. As a shared experience, it is an example of the fluent reciprocity of human nonverbal communication ability, closely related to theory of mind and social cognition. Joint attention has been widely studied in patients with autism but there is no research in the field of schizophrenia. The study of this social skill involving the use of eye contact in conjunction with facial expressions opens a new possibility to develop the understanding of social cognition in schizophrenia and a target in social interventions.

From a general point of view, the final objective of any research work should be responding to human problems, and researchers investigating mental disorders have the responsibility of using their empirical results to promote the progress of remediation strategies, because this is what really gives meaning and value to our work. Lately, there is a growing need for bringing perspectives of basic and applied knowledge together, especially in the field of health sciences. Therefore, my very ultimate goal is to create a new intervention paradigm based on the social cognition needs detected in first episode patients following the footsteps of the Orygen Youth Health program developed by the University of Melbourne (Australia) under the project HORYZONS (Alvarez-Jimenez et al., 2013). This highly novel online intervention fits perfectly with the needs of first episode psychosis patients and should be a worthy goal of which we must not lose sight. Working closely (as before) with professional researchers and clinicians from groups to which I belong (Instituto de Investigación Sanitaria Hospital 12 de Octubre (i+12), CIBERSAM, Grupo de Neurociencia Afectiva y Social (UCM)) will allow me to further develop my activities in the field of translational science.

Conclusions

This thesis pursued the aim to explore in detail the social cognition and, specifically, emotion perception performance in patients with diagnosis of schizophrenia. We hope to have contributed to further clarify the nature and specificity of the impairments usually described in this severe mental disorder. The conclusions derived from the studies that this thesis comprises are as follows:

- ❧ Patients are as accurate as controls when task demands were centered on the identification of invariant facial features, such as gender recognition.
- ❧ On tasks involving facial emotion recognition patients show poor performance compared to control subjects.
- ❧ The impairments found on facial affect recognition might widespread at chronic stages compared to early stages of the illness. Specifically, young patients show a preserved pattern of responses to neutral faces and impaired recognition circumscribed to fearful expressions.
- ❧ Chronic patients were more prone to perceive more than one negative expression in a specific facial configuration (corresponding to a single emotion), not only in the case of negative emotions, but also with positive and neutral expressions. It can be said that patients perceived facial expressions of emotions as a more ambiguous stimuli than non-clinical population.
- ❧ Patients have shown to integrate context properly when face and context are congruent in terms of valence. In presence of neutral contexts, patients did not differ from controls in emotion categorization of neutral faces.
- ❧ Future social cognition training programs should focus on providing patients contextual information, helping them integrate information from different sources.

With this thesis we hope to have provided new data to contribute the understanding of the social cognition deficit in patients with schizophrenia. We should not forget that social cognition is responsible for a high percentage of the variance of the functioning and quality of life of these patients and that better social cognition remediation programs are needed since not all the pharmacological tools are effective

for those symptoms. In this sense, our main goal was to study in depth facial emotion processing in patients with schizophrenia in an attempt to better understand mechanisms underlying this cognitive process but also for providing information that can be useful for clinicians to design intervention strategies.

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