# Electroencephalographic Event-Related Potentials during social interactions in people with symptoms of Major Depression and Social Anxiety

Lic. Eliana Nicolaisen Sobesky

Dissertation for the Degree of Master in Cognitive Science

Universidad de la República

Uruguay

2019

Advisor: Dra. Victoria Gradin

Co-advisor: Dr. Álvaro Cabana

Laboratory: Center for Basic Research in Psychology
Facultad de Psicología
Universidad de la República

Thesis committee: Dr. Ángel Caputi
Dr. Juan Carlos Valle Lisboa
Dr. Pablo Torterolo

UNIVERSIDAD DE LA REPÚBLICA URUGUAY

CIBPsi CENTRO DE INVESTIGACIÓN BÁSICA EN PSICOLOGÍA

maestría ciencias cognitivas

# Abstract

Social interactions are severely impaired in major depression and social anxiety. Social interactions associated with fairness have been studied using the Ultimatum Game (UG). In the UG, the *responder* receives an offer from a *proposer* about how to divide a sum of money. If the responder accepts the offer, both accumulate the money. If the responder rejects the offer, both accumulates nothing. The UG is comprised by fair (the responder is offered between 40-50% of the total amount of the offer), medium (the responder is offered between 27-33%) and unfair offers (the responder is offered between 18-23%). Previous studies have reported that at least two event-related potentials (ERPs) are modulated by fairness during the UG: the *Medial Frontal Negativity* (MFN) and the *Late Positive Potential/P300* (LPP/P300). To our knowledge, there are no studies analysing ERPs in the UG in major depression and/or social anxiety.

We aimed to study the MFN, the LPP/P300, the behavior and the emotions experienced during the UG in healthy volunteers (Control group, $n = 72$) and volunteers with symptoms of major depression and/or social anxiety (MD/SA group, $n = 63$).

As expected, we found that the rejection of offers increased as the unfairness increased. Also, the medium offers were associated with longer reaction times than unfair offers, and in turn unfair offers were associated with longer reaction times than fair offers. In addition, participants reported less positive emotions and more negative emotions as the unfairness increased. Interestingly, in comparison with the Control group, the MD/SA group reported feeling more sadness in all offers, and specially in medium and unfair offers.

The MFN was associated with more negative mean amplitudes in medium and unfair offers than in fair offers. This component would be modulated by the negative emotional/motivational impact caused by unfairness. Another plausible interpretation is that the volunteers would expect fair offers during the task, and

that the unexpected medium and unfair offers would be associated with error predictions that would evoke the MFN. Interestingly, our results showed a borderline main effect of group in the MFN, suggesting that this component was associated with more negative mean amplitudes in the MD/SA group in comparison with the Control group, across all offers. This effect would be associated with enhanced negative emotions experienced during all levels of fairness during the UG in the MD/SA group, in comparison to controls.

In addition, the LPP/P300 was associated with more positive mean amplitudes in fair offers in comparison with unfair offers, and with more positive mean amplitudes in unfair offers in comparison with medium offers. This result would indicate that fair offers would be associated with more arousal than unfair and medium offers, and that in turn unfair offers would be associated with more arousal than medium offers. An alternative interpretation is that the LPP/P300 would be modulated by the conflict associated with the decision-making of each level of fairness. In this line, the LPP/P300 would be more positive in fair, less conflictive offers in comparison with unfair and medium offers. In turn, this component would be more positive in unfair offers in comparison with medium offers, given that the medium offers are the most conflicting.

Of note, the LPP/P300 was associated with more negative mean amplitudes in the MD/SA group in comparison with the Control group across all offers. This result could be related to less arousal and/or motivation in the MD/SA group in comparison with the Control group. Alternatively, this effect could be related to less attentional resources available to allocate to the task in the MD/SA group in comparison with controls. The lack of attentional resources in the MD/SA group could be due to the activation of other cognitive processes, such as rumination, which would compete for the cognitive resources available. Another interpretation is that this effect could be related to higher levels of conflict experienced during all offers by the MD/SA group.

We aim to contribute to the understanding of social functioning and the neural basis associated with these processes in major depression and social anxiety.

# Resumen

Las interacciones sociales se encuentran severamente afectadas en la depresión mayor y en la ansiedad social. Ciertos procesos relacionados a interacciones sociales justas e injustas se han estudiado utilizando el Ultimatum Game (UG). Durante el UG, el *responder* recibe ofertas de un *proposer* acerca de cómo dividir una cantidad de dinero. Si el responder acepta la oferta, ambos acumulan el dinero. Si el responder rechaza la oferta, ninguno acumulan nada. Durante el UG hay ofertas justas (al responder le ofrecen entre el 40-50% del total), medias (le ofrecen 27-33%) e injustas (le ofrecen 18-23%). Se ha reportado que al menos dos potenciales relacionados a eventos (ERPs, por la sigla en inglés para *Event-Related Potentials*) son modulados por la justicia durante el UG: el *Medial Frontal Negativity* (MFN) y el *Late Positive Potential/P300* (LPP/P300). A nuestro conocimiento, no hay estudios que analicen ERPs durante el UG en depresión mayor y/o ansiedad social.

Este proyecto tuvo como objetivo estudiar el MFN, el LPP/P300, el comportamiento y las emociones experimentadas durante el UG en personas sin historia de trastornos mentales (grupo Control, $n = 72$) y personas con síntomas de depresión mayor y/o ansiedad social (grupo MD/SA, $n = 63$).

Como era esperado, la tasa de rechazo aumentó a medida que aumentaba la injusticia. Además, los tiempos de reacción fueron mayores en las ofertas medias en comparación a las injustas, y mayores en las ofertas injustas en comparación a las justas. Asimismo, los participantes reportaron más emociones negativas y menos emociones positivas a medida que aumentaba la injusticia. Cabe señalar que el grupo MD/SA reportó mayores niveles de tristeza en todas las ofertas, y especialmente en las ofertas medias e injustas.

Además, el MFN se asoció a una amplitud media más negativa en las ofertas medias e injustas en comparación a las justas, lo que reflejaría el impacto emocional/motivacional negativo causado por la injusticia. Otra explicación

posible es que los voluntarios esperarían recibir ofertas justas durante el UG, y que las ofertas medias e injustas inesperadas se asociarían a un error de predicción que modularía el MFN. Cabe destacar que se encontró una tendencia en el efecto principal de grupo en el MFN, sugiriendo que, en todas las ofertas, el MFN estaría asociado a una amplitud media más negativa en el grupo MD/SA en comparación al grupo Control. Este efecto estaría relacionado con emociones negativas acentuadas durante todas las ofertas en el grupo MD/SA en comparación al grupo Control.

Asimismo, el LPP/P300 se asoció a una amplitud media más positiva durante ofertas justas en comparación a injustas, y con una amplitud media más positiva durante ofertas injustas en comparación a medias. Este resultado indicaría que las ofertas justas se asociarían con mayores niveles de arousal en comparación a las ofertas injustas y medias, y que las ofertas injustas se asociarían a mayores niveles de arousal que las ofertas medias. Una explicación alternativa es que el LPP/P300 sería modulado por el nivel de conflicto en la toma de decisiones. En este sentido, el LPP/P300 aparecería más positivo en las ofertas justas, que son las menos conflictivas, en comparación a ofertas injustas y medias. A su vez, el LPP/P300 se asociaría a amplitudes medias más negativas en las ofertas medias, dado que son las más conflictivas, en comparación a justas e injustas.

Cabe resaltar que el LPP/P300 se asoció con una amplitud media más negativa en el grupo MD/SA que en el grupo Control en todas las ofertas. Este resultado podría estar asociado a menores niveles de arousal y/o motivación en el grupo MD/SA en comparación al grupo Control. Alernativamente, este efecto podría estar asociado a menores recursos atencionales disponibles para asignar a la tarea en el grupo MD/SA en comparación al grupo Control. Esto podría deberse a la actividad de otros procesos cognitivos que consumirían recursos cognitivos, como por ejemplo, rumia. Otra interpretación es que este efecto podría deberse a mayores niveles de conflicto experimentado en todas las ofertas en el grupo MD/SA.

Esperamos contribuir al entendimiento del funcionamiento social y de las bases neurales asociadas a estos procesos en la depresión mayor y la ansiedad social.

# Agradecimientos

A la Maestría en Ciencias Cognitivas y a la Sub-Comisión Académica en Ciencias Cognitivas, por la excelente formación académica.

A la Comisión Sectorial de Investigación Científica, al fondo Santiago Achúgar Díaz y al Programa de Desarrollo de las Ciencias Básicas, por financiar este proyecto.

A Victoria Gradin, por orientarme durante este proyecto y por estar siempre a disposición. Por liderar este equipo de investigación y por compartir sus conocimientos y su pasión por la investigación. Por guiarme durante mi desarrollo como investigadora.

A Álvaro Cabana, por orientarme durante este trabajo. Por los aportes al diseño del estudio, y por la guía sustancial en el procesamiento de datos, en la estadística y en la programación. Por guiarme durante mi desarrollo como investigadora.

A Ángel Caputi, Pablo Torterolo y Juan Valle-Lisboa, por evaluar este trabajo y por sus críticas para mejorarlo.

A Dominique Kessel, por transmitir sus conocimientos sobre electroencefalografía, por su orientación durante el procesamiento de datos y por sus contribuciones a la interpretación de resultados. Por sus aportes siempre enriquecedores.

A Valentina Paz, por compartir estos años de investigación y por ser una excelente compañera de trabajo. Por participar en el diseño del estudio, en la adquisición de datos y en la interpretación de resultados. Por realizar entrevistas de evaluación psicológica durante este proyecto. Por transmitirme sus conocimientos de psicología y por las discusiones siempre enriquecedoras.

A Germán Cipriani, Valentina Paz y Alejo Acuña, por tomarse el tiempo para aportar comentarios que mejoraron este trabajo.

A Alfonso Pérez, por enseñarme a programar, por contribuir al diseño del estudio y por sus aportes durante este proyecto.

A Gabriela Fernández-Theoduloz, por transmitirme sus conocimientos sobre psicología y por contribuir en la realización de entrevistas durante este proyecto.

A Ángel Caputi, por recibirme en su laboratorio y enseñarme sobre neurociencias y electroencefalografía. Por estar siempre disponible y por las discusiones siempre enriquecedoras.

A Francisco Cervantes, por sus aportes a la interpretación y discusión de los resultados.

A Eduardo Martínez-Montes, por sus contribuciones.

A Laura Uriarte, Sebastián Morales, Alejo Acuña y Santiago Garat, por sus aportes.

A Camila Zugarramurdi y Emilia Fló, por guiarme en el aprendizaje de la técnica de electroencefalografía.

Al CIBPsi, por proporcionar un lugar de trabajo interdisciplinario y enriquecedor.

A los voluntarios que participaron en este estudio.

A Rosana Sobesky y Daniel Nicolaisen, por su apoyo incondicional, porque gracias a ellos pude recorrer esta etapa.

A mi familia, por estar siempre presente.

A Cecilia de los Santos, por su amistad, por ayudarme a transitar esta etapa y a crecer.

A mis amigos, por la excelente compañía.

# Contents

# List of Abbreviations

**ACC** Anterior Cingulate Cortex

**BDI-II** Beck Depression Inventory-II

**DLPFC** Dorsolateral Prefrontal Cortex
**DSM** Diagnostic and Statistical Manual of Mental Disorders

**EEG** Electroencephalography
**ERP** Event-Related Potential

**fMRI** functional Magnetic Resonance Imaging

**LPP** Late Positive Potential
**LPP/P300** Late Positive Potential/P300
**LSAS** Liebowitz Social Anxiety Scale

**MD** Major Depression
**MD/SA** Major Depression/Social Anxiety
**MFN** Medial Frontal Negativity
**MINI-Plus** Mini International Neuropsychiatric Interview
**mPFC** medial Prefrontal Cortex

**RDoC** Research Domain Criteria
**RewP** Reward Positivity

**SA** Social Anxiety

**UG** Ultimatum Game

**vmPFC** ventromedial Prefrontal Cortex

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# 1 Introduction

Social interactions are relevant for health and well-being. Importantly, social interactions are severely impaired in mental disorders. Mental disorders are prevalent and cause significant impairments to the quality of life. The impairments in social interactions in mental disorders cause suffering to the patients and cause difficulties in the recovery from the disorders. The treatments and diagnosis for mental disorders have important limitations, in part because of the lack of understanding of the neural basis associated to social interactions. This highlights the importance of advancing the knowledge about the social interactions and the neural basis associated to these processes in mental disorders.

Major depression is characterized by anhedonia and sadness. The lifetime prevalence of this disorder is about 17%, affecting more than 300 million people in the world. Social anxiety is characterized by an intense and irrational fear to social interactions. The lifetime prevalence of social anxiety is about 8.4-15%. Social interactions in these disorders appear more negative and deteriorated, and less satisfying.

The neural basis associated to mental disorders have been studied using techniques such as electroencephalography or functional Magnetic Resonance Imaging. However, little is known about the neural basis associated to social interactions in mental disorders. To our knowledge, there are no previous studies analysing the neural basis associated to fairness in major depression and social anxiety.

The Ultimatum Game is a task to study fairness widely used in the fields of behavioral economics and neuroeconomics. Some studies have used electroencephalography to study event-related potentials during fair and unfair social interactions in the Ultimatum Game. These studies reported that the Medial Frontal Negativity and the Late Positive Potential/P300 are modulated by fairness.

We aimed to study event-related potentials during the Ultimatum Game in healthy volunteers and in volunteers with major depression and/or social anxiety. We expected that people with symptoms of major depression and social anxiety would report experiencing more negative emotions during the task. In addition, we expected to find modulations of the MFN and the LPP/P300 in volunteers with these symptoms in comparison to healthy volunteers during the task. We hope to contribute to the understanding of the neural basis associated to social interactions in major depression and social anxiety.

## 1.1 Social interactions

Social interactions are relevant for daily life (Müller-Pinzler et al., 2016) and are considered a basic need for health and well-being (Baumeister and Leary, 1995; Dunkel Schetter, 2017; Pietromonaco and Collins, 2017). Social interactions influence the physiology (Dunkel Schetter, 2017), cognition, behavior and emotions of a person (Baumeister and Leary, 1995; Dunkel Schetter, 2017; Müller-Pinzler et al., 2016). For instance, positive social interactions are related to positive emotions (Baumeister and Leary, 1995; Brown et al., 2007), better overall health and personal growth, better coping with stress and recovery from a negative event, sounder social support and affection (Pietromonaco and Collins, 2017). In turn, negative social interactions are associated with negative emotions (Baumeister and Leary, 1995; Brown et al., 2007), high levels of stress (Pietromonaco and Collins, 2017) and poor health (Baumeister and Leary, 1995). In fact, negative social interactions are considered a risk factor for several diseases (Pietromonaco and Collins, 2017). Importantly, social interactions are highly impaired in mental disorders (Baumeister and Leary, 1995; Dunkel Schetter, 2017).

Despite social interactions being important in daily life and well-being, little is known about the mechanisms through which social interactions affect health (Pietromonaco and Collins, 2017). In addition, the neural basis associated with social interactions remain poorly understood (Chen et al., 2019b; Luo, 2018). One of the reasons for this is that recreating social interactions in the laboratory in an ecological, quantitative and controlled manner is challenging (King-Casas and Chiu, 2012). Advancing the understanding of social interactions (Destoop et al., 2012; Müller-Pinzler et al., 2016; Robson et al., 2019) and the neural basis associated with these processes (Cusi et al., 2012; Müller-Pinzler et al., 2016; Robson et al., 2019) would help to better understand mental disorders. Moreover, it would help to develop more effective diagnostic tools and treatments for these disorders (Cusi et al., 2012).

### 1.1.1 The study of social interactions

From a cognitive approach, social interactions have been mostly studied using tasks of facial emotion recognition or Theory of Mind (Adolphs, 2003; Cusi et al., 2012). In facial emotion recognition tasks, the volunteer is presented with pictures of faces and has to infer which emotion each image is expressing (Cusi et al., 2012). Theory of Mind tasks usually use stories, videos, vignettes, etc., that present a social situation and the volunteer has to infer the mental states (such as desires, intentions or beliefs) of the characters included in it. Despite the fact that these tasks have been essential in the understanding of social interactions, they have some limitations. The most salient constraint is that these tasks do not imply a social interchange between the volunteer and other people (Wang et al., 2015).

In contrast, the fields of behavioral economics and neuroeconomics use tasks that recreate interchanges between agents in a quantitative and controlled manner (King-Casas and Chiu, 2012; Rilling et al., 2008; Sanfey, 2007; Vavra et al., 2017). These tasks have been used to study complex social concepts in health and in mental disorders (Gradin et al., 2015, 2016; King-Casas et al., 2008; Rilling et al., 2008; Wang et al., 2015).

### 1.1.2 Behavioral economics and neuroeconomics in the study of social interactions

Behavioral economics is a field that uses tasks from game theory to study the behavior of people during social interactions, especially decision-making processes (Chen et al., 2019b; Robson et al., 2019; Sanfey, 2007). Neuroeconomics combines knowledge from psychology, neuroscience and economy (Vavra et al., 2017) to study the neural basis of social interactions using behavioral economics tasks in combination with neuroimaging or neurophysiology techniques (Chen et al., 2019b; Luo, 2018; Vavra et al., 2017). Studies in these fields have provided evidence of the behavior and neural basis associated with a variety of complex social situations, such as cooperation

(Gradin et al., 2016; King-Casas et al., 2008; McClure et al., 2007), social hierarchies (Zink et al., 2008) or fairness (Sanfey et al., 2003). One of the most used tasks in the field to study fairness is the Ultimatum Game (Sanfey et al., 2003).

### 1.1.3 The Ultimatum Game

The Ultimatum Game (UG) is a widely used task in behavioral economics and neuroeconomics to recreate fair and unfair social interactions (Güth et al., 1982; Sanfey, 2007) (for an example depicting the task, see Fig. 2). In the UG there are two roles: the *proposer* and the *responder* (Camerer and Fehr, 2004; Sanfey, 2007; Sanfey et al., 2003). The proposer receives an amount of money and has to propose how to divide it between himself/herself and the responder. The responder receives the offer and has to decide whether to accept or reject it. If the responder accepts the offer, the money is divided as the proposer proposed and then both accumulate the corresponding monetary amount. If the responder rejects the offer, neither the proposer nor the responder accumulate money from that offer. The UG is usually designed to present the responder with offers of different levels of fairness. For example, in the study of Crockett et al. (2008) there were fair offers (in which the responder is offered between 40-50% of the total amount of the offer), medium offers (the responder is offered between 27-33%) and unfair offers (the responder is offered between 18-23%).

From an economic perspective, the aim of each player should be to maximize his/her own monetary gains. Therefore, the proposer should offer the minimum amount to the responder (Sanfey, 2007; Sanfey et al., 2003) and the responder should accept all non-zero offers, because it is always better to accumulate something (regardless of how little it is) instead of accumulate nothing (Sanfey, 2007; Sanfey et al., 2003). However, it has been widely documented that the proposers usually propose fair offers (Camerer and Fehr, 2004; Sanfey, 2007; Sanfey et al., 2003) and that the responders tend to reject more offers as unfairness increases (Alexopoulos et al., 2013; Chen et al., 2019a; Destoop et al., 2012; Fabre et al., 2015; Falco et al., 2019; Fernandes et al., 2019; Gradin et al., 2015; Kaltwasser et al., 2016; Luo et al., 2014; Ma et al., 2017; Park et al., 2019; Paz et al., 2017; Peterburs et al., 2017; Polezzi et al., 2008; Qu et al., 2013; Radke et al., 2013; Riepl et al., 2016; Sanfey et al., 2003; Scheele et al., 2013; Van Der Veen and Sahibdin, 2011; Wang et al., 2017, 2014; Wu et al., 2013, 2011; Zhong et al., 2019). In agreement with that, some studies showed that the responder rejected about 50% of the offers in which the proposer offers less than 20% (Fehr and Schmidt, 1999). The behavior of the proposer could be explained in two ways: as an altruistic behavior or as a strategy to avoid rejection of their offers in order to obtain money (Camerer and Fehr, 2004). The rejection of unfair offers by the responders would be explained because of a strong negative emotional reaction produced by unfairness (Sanfey et al., 2003), because of unfairness aversion (Sanfey, 2007) or because of altruistic punishment (Camerer and Fehr, 2004). Altruistic punishment means that the responder prefers to keep nothing and to punish the unfair behavior of the proposer (Camerer and Fehr, 2004). Interestingly, the rejection of unfair offers is shown even in one-shot UGs, where the responder receives one offer from each proposer (Sanfey et al., 2003). Therefore, the altruistic punishment can not affect the subsequent offers that the responder would receive from each proposer, and in consequence would not work as a strategy to maximize own gains in the long term. These results show that people do not behave in a rational way and that social interactions could generate emotions that affect behavior.

The decision-making during the UG has also been studied analysing reaction times. The reaction times during the UG have been reported as longer for medium offers in comparison with unfair (Fabre et al., 2015; Ma et al., 2017; Paz et al., 2017; Polezzi et al., 2008; Wang et al., 2017) and fair offers (Fabre et al., 2015; Ma et al., 2017; Paz et al., 2017; Polezzi et al., 2008; Wang et al., 2017; Zhong et al., 2019), and in turn longer for unfair in comparison with fair offers (Campanha et al., 2011; Chen et al., 2019a; Fabre et al., 2015; Gradin et al., 2015; Ma et al., 2015, 2017; Wang et al., 2017). The slower reaction times during medium offers have been associated with the difficulty in decision-making in these offers (Ma et al., 2017). During fair offers both the motivation to accumulate money and the motivation to sustain a positive social interaction lead to the acceptance of these offers. The longer reaction times during unfair offers would be related to the conflict between the motivation to accumulate money (accept the offer) and the motivation to punish the unfair behavior (reject the offer). During medium offers the decision-making is even more conflicting, because these offers are neither completely fair nor completely unfair, which leads to even longer reaction times (Fabre et al., 2015; Ma et al., 2017).

#### Summary

Social interactions are important for daily life and well-being and are highly impaired in mental disorders. Despite social interactions being important, how they affect health and the neural basis associated with these processes remains poorly understood. One of the reasons for that is because it is challenging to recreate social situations in a quantitative, controlled and ecological valid environment. However, the behavior and the neural basis associated with social interactions have been studied in the fields of behavioral economics and neuroeconomics. These fields provide a way to study complex social situations in a quantitative and controlled manner using tasks of game theory. One of the most used tasks in these fields to study fairness is the UG.

## 1.2 Mental disorders

Mental disorders are complex illnesses (Clark et al., 2017) with high prevalence (Steel et al., 2014; Whiteford et al., 2013). Mental disorders cause severe impairments in health and quality of life (Cieza et al., 2015; Muñoz et al., 2007). In addition to the burden caused in health, mental disorders result in important economic costs (Trautmann et al., 2016).

Importantly, mental disorders are associated with significant impairments in social interactions (Cieza et al., 2015; Kupferberg et al., 2016; Meyer-Lindenberg and Tost, 2012; Plana et al., 2014; Porcelli et al., 2019). Given the importance of social interactions in health and well-being, these impairments cause difficulties in the recovery of the patient (Meyer-Lindenberg and Tost, 2012). For instance, the perceived social dysfunction is predictive of still having a depressive or anxiety disorder two years later (Saris et al., 2017). Moreover, the impairments in social functioning can remain residual after remission (Saris et al., 2017).

### Treatment of mental disorders

It is worth noting that the diagnosis and treatment of mental disorders face a lot of difficulties nowadays. The treatments for mental disorders available today are only partially effective (Jorm et al., 2017). The diagnosis of mental disorders is based in manuals such as the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) or the *International Classification of Diseases* (ICD). Despite the fact that these manuals have been essential in the treatment of mental disorders, they are based in a categorical classification of mental disorders that has several limitations (Clark et al., 2017), such as the accuracy (Sanislow et al., 2014; Schatzberg, 2019).

For instance, it is not clear if the symptoms included in the manuals are the only relevant ones (Schatzberg, 2019). Another reason is that mental disorders are not separate entities, but rather share symptomatology (Clark et al., 2017) and usually appear in comorbidity (Clark et al., 2017; Sanislow et al., 2014). In addition, mental disorders are highly heterogeneous, causing that patients who receive the same diagnosis could share only few symptoms or even not share any symptom (Sanislow et al., 2014). For example, in the case of borderline personality disorder, there are 256 different combinations of symptoms that are considered a valid diagnosis (Sanislow et al., 2014).

Furthermore, today there are no objective measures developed for the diagnosis and follow-up of mental disorders (Clark et al., 2017). Rather, the treatment of mental disorders relies on the evaluation of behavioral and emotional symptoms reported by the patient and observed by the evaluator (Clark et al., 2017; Schatzberg, 2019). Also, the cause of mental disorders is not clear and is considered to be based upon multiple genetic and environmental factors which interact over time (Clark et al., 2017). The difficulties to make an accurate diagnosis in mental disorders affect the selection of an adequate treatment for each patient.

### Research in mental disorders

The difficulties in the diagnosis not only affect treatment but also research in mental disorders. Conforming experimental groups with volunteers with homogeneous symptoms is very difficult and in addition has several limitations. For instance, it excludes cases who could provide valuable information about the disorder (Sanislow et al., 2014). These problems have generated difficulties in the identification of biomarkers that could allow the differentiation between mental disorders (Sanislow et al., 2014).

For that reason, in the last few years there have been efforts to study mental disorders from a transdiagnostic approach (Cieza et al., 2015; Saris et al., 2017). One example of this is the Research Domain Criteria (RDoC), created by the National Institute of Mental Health of the United States of America in 2009 (Clark et al., 2017; Sanislow et al., 2014). RDoC is an alternative frame to guide research in mental disorders, putting the focus on the overlapping multidimensionality of mental disorders (Clark et al., 2017; Sanislow et al., 2014).

### Research Domain Criteria

RDoC is a framework that encourages a transdiagnostic research in mental disorders (Kupferberg et al., 2016). The aim of RDoC is to identify dimensions which are relevant for the functioning of individuals that could guide research in mental disorders, and that in the future could be used for the classification of them (Clark et al., 2017). This approach proposes the study of mental disorders focusing on symptoms or risk factors rather than in the existing categorical classifications. Moreover, it aims to integrate knowledge from molecular biology, cellular biology, pharmacology, behavior and neuroscience (Sanislow et al., 2014). This approach is also focused in the identification of biomarkers relevant for mental disorders (Sanislow et al., 2014).

The detection of biomarkers would be an important advancement in the field of mental disorders. Biomarkers have been proposed as a potential tool for the development of objective methods for the diagnosis and follow-up of mental disorders (Sanislow et al., 2014; Wang et al., 2015). In addition, advancements in knowledge about how people with mental disorders feel, think and behave during social interactions (Cieza et al., 2015; Destoop et al., 2012; Plana et al., 2014; Wang et al., 2015, 2014) and the neural basis associated with these processes is important to better understand these disorders (Meyer-Lindenberg and Tost, 2012; Saris et al., 2017; Wang et al., 2015).

### 1.2.1 Major Depression

Major Depression (MD) is a highly disabling mental disorder (Kalin, 2019; Muñoz et al., 2007; Salagre et al., 2017) characterized by symptoms of anhedonia and sadness (American Psychiatric Association, 2013). MD is a highly heterogeneous disorder (Schatzberg, 2019), presenting symptoms such as fatigue, sleep and eating impairments, guilt, hopelessness and difficulties with concentration and decision-making (American Psychiatric Association, 2013). Importantly, MD is associated with suicide (American Psychiatric Association, 2013; Pulcu and Elliott, 2015; Saveanu and Nemeroff, 2012), with approximately 15% of the patients with MD committing a suicide attempt (Miret et al., 2013).

MD is a highly prevalent mental disorder, with a lifetime prevalence of about 17% (Schatzberg, 2019; World Health Organization, 2017), affecting more than 300 million people in the world (Salagre et al., 2017). The prevalence is two times higher in women than in men (World Health Organization, 2017). This disorder usually appears in adolescence or early adulthood (Weissman et al., 2019) and can be recurrent (Fava and Kendler, 2000; Weissman et al., 2019) or chronic (Fava and Kendler, 2000). In addition to the burden in health, MD also causes big economic costs (Disner et al., 2011; Kalin, 2019; Miret et al., 2013).

MD strongly affects the quality of life and causes suffering to the patients (Kalin, 2019; Whiteford et al., 2013), leading to severe impairments in more than 50% of them (Kessler et al., 2003). In fact, MD is considered one of the world's leading causes of DALYs (*Disability-Adjusted Life Years*, the amount of years of life lost because of disability or premature death caused by the disease) (Whiteford et al., 2013; World Health Organization, 2017). Everyday functioning appears severely affected in MD, impacting family, study (Fava and Kendler, 2000), work (Fava and Kendler, 2000; Muñoz et al., 2007), and finances. MD is also associated with various cognitive impairments that span attention (Salagre et al., 2017), memory, executive functions (Salagre et al., 2017; Weightman et al., 2019) and verbal fluency (Weightman et al., 2019) (for a review, see Iosifescu (2012)). These cognitive impairments often become residual after the remission of the core symptoms (Salagre et al., 2017).

Another characteristic of this disorder is an enhanced negative bias (Disner et al., 2011). People with MD have an enhanced attentional negative bias towards negative information and they remember more negative information (Disner et al., 2011; Kircanski et al., 2012). Moreover, they have more difficulties to inhibit the processing of negative information and to remove negative information from the working memory (Everaert et al., 2012; Kircanski et al., 2012). They also tend to interpret neutral emotional information as negative (Everaert et al., 2012). This enhanced negative bias affects the emotions and heightens the core symptoms of MD (Disner et al., 2011; Kircanski et al., 2012), impairing the remission of the patient (Everaert et al., 2012; Kircanski et al., 2012).

The treatment for MD has a lot of challenges. For instance, the diagnosis of MD is associated with a low level of reliability (Schatzberg, 2019). Moreover, treatments for MD are only partially effective (Fava and Kendler, 2000; Kalin, 2019; Saveanu and Nemeroff, 2012) with about 50% of the cases not responding to the initial treatment (Fava and Kendler, 2000; NICE, 2010), remission rates of 30-40% (Salagre et al., 2017) and with about 10% of the cases becoming chronic (NICE, 2010). Furthermore, the available treatments usually provoke side-effects or have a slow onset of action (Kalin, 2019). Moreover, the outcomes of treatments are variable, and therefore are very difficult to predict in the case of each patient (Kalin, 2019). In addition, MD usually appears with symptoms of anxiety (Schatzberg, 2019). The reports indicate that about 20-30% of patients with MD have comorbid social anxiety (Koyuncu et al., 2019). The difficulties in the diagnosis and treatment of MD are due in part to the lack of understanding of the neural basis of this disorder (Boku et al., 2018).

#### 1.2.1.1 Social interactions in Major Depression

Social interactions are severely affected in MD (Fava and Kendler, 2000; Hirschfeld et al., 2000; Kupferberg et al., 2016; Miret et al., 2013; Muñoz et al., 2007; Pulcu and Elliott, 2015; Saris et al., 2017; Weightman et al., 2019). People with MD have more negative, stressful, conflictive and deteriorated social interactions than healthy people (Hirschfeld et al., 2000; Papakostas et al., 2004; Zlotnick et al., 2000). In comparison with healthy controls, people with MD experience more loneliness (Saris et al., 2017) and have poorer social lives, smaller social networks (Hirschfeld et al., 2000; Weightman et al., 2019), poorer social problem-solving abilities and difficulties communicating with others (Weightman et al., 2019). Moreover, people with MD experience increased sensitivity to emotional social cues (Weightman et al., 2019) and to rejection (Kupferberg et al., 2016), in comparison with controls. It has also been reported that people with MD experience fear of negative evaluation (Koyuncu et al., 2019) and of being humiliated (Gilbert, 2000). In line with that, MD subjects report less satisfying social interactions (Hirschfeld et al., 2000; King-Casas and

Chiu, 2012; Pulcu and Elliott, 2015), less desire to interact with other people (Kupferberg et al., 2016; Weightman et al., 2019) and avoidance of social interactions (American Psychiatric Association, 2013; Fernández-Theoduloz et al., 2019; Koyuncu et al., 2019; Kupferberg et al., 2016; Weightman et al., 2019). Moreover, MD subjects also present impairments in Theory of Mind, with people with MD having difficulties to recognize emotions (Kupferberg et al., 2016; Weightman et al., 2019) and to mentalize (Kupferberg et al., 2016).

The impairments in social interactions in MD are one of the main causes of suffering in these patients (Kessler et al., 2003). In fact, people with MD report more perceived social disability in comparison with healthy volunteers (Saris et al., 2017). Importantly, these impairments are still present after the remission of the core symptoms of MD (Salagre et al., 2017). The improvement of social skills in MD has been proposed as a core factor for the recovery from this disorder (Kupferberg et al., 2016).

Although the evidence mentioned before, it is worth noting that the knowledge about how people with MD experience and behave during social situations remains poorly understood (Kupferberg et al., 2016; Wang et al., 2015; Weightman et al., 2019). Because of that, the detection of potential biomarkers associated with social interactions in MD would be an important advancement in the knowledge about this disorder (Schatzberg, 2019; Wang et al., 2015). For instance, it could lead to the development of more efficient tools for the diagnosis and follow-up of the disorder and to more efficient and personalized treatments (Kalin, 2019; Kupferberg et al., 2016; Weightman et al., 2019).

### 1.2.2 Social Anxiety

Social Anxiety (SA) is characterized by an intense and irrational fear to social situations (such as talking or eating in front of others) (Koyuncu et al., 2019; Müller-Pinzler et al., 2016; Spence and Rapee, 2016), and especially to negative evaluations made by other people (Müller-Pinzler et al., 2016; Spence and Rapee, 2016). People with SA fear offending others or being humiliated, embarrassed (Stein and Stein, 2008) or rejected (Koyuncu et al., 2019). When they interact with others, they experience intense anxiety and physical symptoms such as increased heart and/or breath rate, sweating, trembling, blushing or confusion (Spence and Rapee, 2016). These symptoms make it even more difficult for people with SA to interact with others (Spence and Rapee, 2016). In consequence, they avoid social interactions and tend to isolate (Müller-Pinzler et al., 2016; Spence and Rapee, 2016). Moreover, SA is associated with decreased positive affect, increased negative affect and sadness (Brown et al., 2007).

The prevalence of SA is high (Nagata et al., 2015), with a lifetime prevalence of about 8.4-15% (Koyuncu et al., 2019; Nagata et al., 2015). It is the most common within the anxiety disorders (Goldin et al., 2009). The prevalence is higher in women than in men (Nagata et al., 2015). This disorder usually appears in childhood or in early adolescence (Nagata et al., 2015; Spence and Rapee, 2016) and can become chronic (Nagata et al., 2015; Spence and Rapee, 2016).

Importantly, SA is an incapacitating mental disorder (Muñoz et al., 2007) which affects the quality of life of those affected by it (Nagata et al., 2015; Spence and Rapee, 2016) and cause suffering (Nagata et al., 2015). This disorder also have an impact on work, study, family, finances and social bonds (Koyuncu et al., 2019; Nagata et al., 2015) and is associated with important economic costs (Patel et al., 2002).

In addition, SA is a complex mental disorder with multiple factors associated with its causes (Spence and Rapee, 2016). Moreover, SA is usually comorbid with other mental disorders such as MD (Koyuncu et al., 2019; Nagata et al., 2015; Spence and Rapee, 2016). Also, although some treatments such as cognitive behavioral therapies have resulted efficient in the treatment of SA, the treatment of this disorder has difficulties (Canton et al., 2012). For instance, many people with SA are not accurately diagnosed or treated (Stein and Stein, 2008) and only about 30% of the people with SA receive treatment (Nagata et al., 2015).

#### 1.2.2.1 Social interactions in Social Anxiety

SA highly impairs social interactions (Muñoz et al., 2007; Saris et al., 2017). People with SA experience increased self-consciousness, discomfort and high desires to be alone when they are interacting with others (Brown et al., 2007). People with SA tend to isolate (Teo et al., 2013) and report reduced perceived social support (Torgrud et al., 2004). Some studies have shown that SA is associated with more rumination regarding social interactions and with more negative interpretations of social situations (Spence and Rapee, 2016). In line with that, SA is characterized by a negative cognitive bias associated with their expectations regarding social interactions (Cao et al., 2015; Spence and Rapee, 2016). For instance, people with social anxiety tend to believe that other people have negative opinions about themselves (Cao et al., 2015). In addition, they have lower expectancies about being accepted and about the possibility of being involved in positive social interactions (Cao et al., 2015). In consequence, people with SA overestimate the negative consequences of social interactions and feel that their social skills are not good enough (Hofmann, 2007). Moreover, this disorder is characterized by high sensitivity to criticism and low self-esteem (American Psychiatric Association, 2013).

Because of all the symptoms that people with SA experience in association with social interactions, they tend to avoid to interact with others (Stein and Stein, 2008). Importantly, social factors are considered a risk factor for SA (Teo et al., 2013; Torgrud et al., 2004). However, it is worth noting that although the existence of these evidence, the knowledge about social interactions and the neural basis associated with these processes in SA remains limited (Plana et al., 2014).

### 1.2.3 Behavioral studies using the Ultimatum Game in Major Depression and Social Anxiety

Some studies have analysed decision-making processes in MD during the UG. These studies reported inconsistent results (for reviews see Kupferberg et al. (2016) and Robson et al. (2019)) with some of them showing an increase in the rejection rates of unfair offers in people with MD compared with controls (Scheele et al., 2013; Wang et al., 2014) and others reporting a decrease (Harlé et al., 2010) or no differences (Destoop et al., 2012; Gradin et al., 2015; Pulcu et al., 2015). Other studies reported that people with MD rejected more often all type of offers in comparison with healthy volunteers (Radke et al., 2013; Wang et al., 2014). Moreover, some studies showed that induction of sadness (which is a core emotion of MD) in healthy volunteers, led to an increase in the rejection rates of all type of offers (Harlé et al., 2012) and of unfair offers (Harlé and Sanfey, 2007), in comparison with a neutral emotional induction. The increased rejection rates of unfair offers in MD and in sadness induction has been interpreted in relation to an increased sensitivity towards negative events (Harlé and Sanfey, 2007), with an increased negative emotional reaction evoked by unfairness (Scheele et al., 2013; Wang et al., 2014), with an enhanced negative bias (Harlé and Sanfey, 2007; Scheele et al., 2013) and with reduced social approach behavior (Scheele et al., 2013). The decreased rejection rates of unfair offers in MD has been related to the enhanced negative bias present in MD. In line with that, people with MD would have more negative expectations regarding social interactions in comparison with healthy volunteers, and then unfair offers would be associated with lower expectancy violations in people with MD (Harlé et al., 2010). Another interpretation is that the negative emotions experienced by people with MD would activate emotional regulation processes, which would favour the acceptance of unfair offers (Harlé et al., 2010).

The inconsistency of these results has been related to differences in the methodological implementations of the UG (Pulcu et al., 2015; Wang et al., 2015) and with the differences in the clinical characteristics of the volunteers between the studies (Kupferberg et al., 2016; Luo et al., 2014; Park et al., 2019; Pulcu et al., 2015; Robson et al., 2019; Wang et al., 2015). It has been suggested that, in comparison with healthy volunteers, participants with clinical symptoms of MD show increased rejection rates of unfair offers (Radke et al., 2013; Scheele et al., 2013; Wang et al., 2014) and that participants with subclinical symptoms of MD show decreased rejection rates of unfair offers (Harlé et al., 2010).

As far as we know, there are no reports regarding decision-making during the UG in SA. However, some studies have analysed the effect of symptoms of anxiety on the rejection rates during the UG. In comparison with healthy volunteers, two studies reported no change in the rejection rates in volunteers with symptoms of anxiety (Luo et al., 2014; Park et al., 2019) and one study reported reduced rejection of unfair offers in volunteers with generalized anxiety disorder and panic disorder (Grecucci et al., 2013). The authors suggest that these results would be explained by enhanced worry, lower assertiveness and difficulties to confront others in anxious volunteers (Grecucci et al., 2013). The inconsistency of the results could be due to differences in the severity of the anxiety symptoms between the volunteers included in these studies (Luo et al., 2014; Park et al., 2019) or to differences in the methodological implementations.

As far as we know, there are no studies reporting differences in the reaction times during the UG between healthy volunteers and people with symptoms of MD (Scheele et al., 2013; Wang et al., 2014) and the studies analysing symptoms of anxiety did not report these data (Grecucci et al., 2013; Luo et al., 2014; Park et al., 2019).

**Summary**

MD and SA are prevalent mental disorders that cause severe impairments in quality of life and suffering to the patients. Importantly, MD and SA cause severe difficulties in the social functioning to the patients. However, the way in which people with MD or SA feel, think and behave during social situations remains poorly understood. Given the importance of social interactions in health and the relevance of these processes in both mental disorders, a better understanding of how people with MD and SA experience and behave during social interactions would contribute to the treatment of these disorders.

## 1.3 The study of the neural basis of social interactions

### 1.3.1 Functional Magnetic Resonance Imaging

The neural basis associated with social interactions have been studied using techniques such as functional Magnetic Resonance Imaging (fMRI). Previous research showed brain regions associated with Theory of Mind. For instance, the temporoparietal junction has been reported during processes involving inference, identification and representation of immediate action goals or desires of others (Van Overwalle, 2009). Previous research also showed that the medial prefrontal cortex (mPFC) is related to processes such as intentionality judgements and inferences of traits of others and of oneself (such as inferring the cooperativeness or competitiveness of other people) (Van Overwalle, 2009). Also, the ventromedial prefrontal cortex (vmPFC) has been reported during trait inferences of the self or of close others, such as relatives or friends (Van Overwalle, 2009). In addition, activation in the temporoparietal junction and the mPFC have been related to favourable social situations, such as downward social comparisons (Bault et al., 2011).

Previous research showed increased activity in reward-related brain regions during positive social situations. For instance, the striatum has been reported as more active during downward social comparisons (Bault et al., 2011; Fliessbach et al., 2007; Lindner et al., 2013). Cooperation (Gradin et al., 2016) and fairness (Feng et al., 2015; Gradin et al., 2015) have also been linked to activity of the reward system (the following section will provide additional information regarding fairness). Decision-making and error prediction processes during social interactions also activated these regions (Rilling et al., 2008).

Brain regions associated with cognitive conflict, such as the anterior cingulate cortex (ACC) and with the processing of aversive stimuli, such as the insula, have been reported during negative social situations. For instance, both regions have been reported during social threat (Luo, 2018) and while the participants see someone else experiencing pain (Luo, 2018). In line with that, the insula has been related to risky or aversive social situations, such as inequity (Gradin et al., 2015; Sanfey et al., 2003), not-reciprocated cooperation (Rilling et al., 2008) or upward social comparisons (Fliessbach et al., 2007; Lindner et al., 2013). In addition, the dorsolateral prefrontal cortex (DLPFC), which is related to cognitive control (Lindner et al., 2013), has been associated with costly punishment (Luo, 2018) and with downward social situations (Bault et al., 2011; Lindner et al., 2013).

### Functional Magnetic Resonance Imaging during the Ultimatum Game

Several studies have analysed neural activations during the UG using fMRI (for a review see Wang et al., 2015). These studies reported that fair offers are associated with activation of the striatum (Gradin et al., 2015; Harlé et al., 2012) and of the vmPFC (Feng et al., 2015; Gradin et al., 2015), which is consistent with reward-related processes associated with fairness.

Furthermore, unfair offers have been associated with higher activation of the anterior insula (Feng et al., 2015; Gabay et al., 2014; Gradin et al., 2015; Sanfey et al., 2003). The authors suggested that greater activation of the anterior insula during unfair offers would be associated with negative emotions elicited by unfairness (Sanfey et al., 2003) and with the motivation to punish the unfair behavior of the proposer (Feng et al., 2015). In fact, stronger activation of the anterior insula across all offers has been associated with increased rejection rates in all offers (Harlé et al., 2012). Similarly, the activation of the insula during unfair offers has been associated with the rejection rates of these offers (Sanfey et al., 2003). Another interpretation for the activation of the insula during unfair offers is related to violations of expectations. Given that the anterior insula shows similar activation during disadvantageously unequal and advantageously unequal offers, it has been related to the detection of violations of social norms (Gabay et al., 2014).

Unfair offers were also associated with higher activation in the the DLPFC (Feng et al., 2015; Sanfey et al., 2003). Moreover, both the DLPFC and the anterior insula showed greater activation when an unfair offer was rejected (Luo, 2018). When an unfair offer was accepted, the reports point to a greater activation in the DLPFC (Luo, 2018). However, a meta-analysis done by Gabay et al. (2014) failed to find activation of the DLPFC in response to unfairness, probably given to inconsistencies between the specific regions of the DLPFC activated in the different studies. The DLPFC is associated with executive control and goal maintenance. The authors have suggested that during the UG, activation in the DLPFC would be related to costly and normative decision-making processes associated to the unfair offers (Gabay et al., 2014).

Finally, the ACC, which is associated with cognitive conflict, has been reported with higher activation during unfair offers (Feng et al., 2015; Gabay et al., 2014; Gradin et al., 2015; Sanfey et al., 2003). However, Harlé et al. (2012) reported higher activation of the ACC during fair offers in comparison with unfair offers. The authors have discussed that activation of the DLPFC and the ACC (Feng et al., 2015; Gabay et al., 2014) during unfair offers would be related to the conflict between the motivation to increase the monetary earnings and the motivation to punish unfairness (Sanfey et al., 2003).

### Functional Magnetic Resonance Imaging during the Ultimatum Game in major depression and social anxiety

It has been reported that volunteers with symptoms of MD showed a decreased activation in the striatum in association with fair offers in comparison with healthy volunteers (Gradin et al., 2015). Moreover, this deactivation correlated to anhedonia in the volunteers with symptoms of MD (Gradin et al., 2015). Similarly, during sadness induction, in comparison with a neutral emotional induction, volunteers failed to activate the striatum in response to fair offers in contrast to unfair offers (Harlé et al., 2012). This result has been related to a difficulty to process social rewarding events during social interactions when someone is under sadness induction (Harlé et al., 2012) or has MD (Gradin et al., 2015).

In addition, during an induction of sadness in comparison with a neutral induction, unfair offers were associated with an increase in the activation of the insula, the striatum, the ACC, the DLPFC and the vmPFC (Harlé et al., 2012). The authors interpreted that the activation of the insula during unfair offers in the sadness induction was associated with the processing of aversive events and with the integration of a negative emotional state with the decision-making processes (Harlé et al., 2012). Moreover, stronger activation of the insula across all offers was associated with higher reported sadness (Harlé et al., 2012). The increased activation of the ACC during unfair offers in sadness induction in comparison with neutral induction was related to an increased conflict monitoring and with increased social expectancy violations (Harlé et al., 2012).

### 1.3.2 Electroencephalography and Event-Related Potentials

Electroencephalography (EEG) is a neurophysiological technique which consists of a set of electrodes that are placed in the scalp (Luck, 2014). These electrodes record electrical changes produced by the brain (Hajcak et al., 2010), especially by the cerebral cortex (Luck, 2014). EEG captures activity produced by the summation of postsynaptic potentials in the pyramidal neurons of the cerebral cortex (Luck, 2014).

EEG has a very good temporal resolution in comparison with other techniques used in neuroimaging and neurophysiology, like fMRI (Glazer et al., 2018; Luck, 2014). EEG has a temporal resolution on the level of milliseconds while fMRI has a temporal resolution on the level of seconds (Glazer et al., 2018; Luck, 2014). Because of its good temporal resolution, EEG is suitable for the study and separation of early and fast cognitive processes (Glazer et al., 2018; Hajcak et al., 2010; Kappenman and Luck, 2016; Luck, 2014; San Martín, 2012). In addition, EEG captures a direct measure of neural activity, unlike other techniques like fMRI or PET, that capture physiological changes produced in response to the neural activity (Hajcak et al., 2010; Luck, 2014). In relation to that, the voltage fluctuations captured by EEG reflect neural activity occurring at that time, without delay (Hajcak et al., 2010; Kappenman and Luck, 2016). Other advantages of EEG is that it is safe, non-invasive (Glazer et al., 2018; Kappenman and Luck, 2016; Luck, 2014), less expensive than other techniques (Kappenman and Luck, 2016; Luck, 2014) and easily tolerated by infants, adults or people with mental disorders (Kappenman and Luck, 2016). Given all that, EEG is a very good technique for the identification of biomarkers (Leiser et al., 2011).

One of the disadvantages of EEG is its low spatial resolution (Glazer et al., 2018; Kappenman and Luck, 2016; Luck, 2014). This is because the electric activity is spread through the skull and scalp (Kappenman and Luck, 2016). Therefore, the electrical activity recorded at a single electrode reflects neural activity generated in multiple brain regions (Kappenman and Luck, 2016).

EEG allows the study of Event-Related Potentials (ERPs). The ERPs consist on a series of positive and negative voltage fluctuations that are time-locked to a specific event (Kappenman and Luck, 2016; Luck, 2014). That event can be for instance the presentation of a stimuli or the execution of a response (Hajcak et al., 2010; Kappenman and Luck, 2016). The ERPs are obtained by identifying the occurrence of events in a continuous EEG recording, selecting the signal in a specific time window surrounding these events (epochs), aligning all epochs in time, and finally performing an average. The averaging produces the cancellation of activity which is not in phase with the stimuli, while the activity that is in phase with the stimuli is preserved (Hajcak et al., 2010). This activity corresponds to the ERP. Some of the ERP components that have been associated with social interactions are the Medial Frontal Negativity, the Late Positive Potential and the P300.

#### 1.3.2.1 The Medial Frontal Negativity

The Medial Frontal Negativity (MFN) is a frontocentral component with a latency of about 200-350 ms after stimulus presentation which has a more negative amplitude following negative versus positive outcomes (Gehring and Willoughby, 2002; Sambrook and Goslin, 2015; San Martín, 2012). In fact, the MFN is considered to be a family of components that includes the Error Related Negativity (ERN, also known as feedback Error Related Negativity (fERN)) and the Feedback Related Negativity (FRN, also known as Feedback Negativity (FN)) (Glazer et al., 2018; Nieuwenhuis et al., 2004). Although these components have some differences, some authors have proposed that they reflect the activity of the same neural system (Holroyd and Coles, 2002). As mentioned below, these components have also been related to another component, the Reward Positivity (RewP, also known as feedback correct-related positivity (fCRP)). In this work we will refer to all these components as MFN.

The MFN has a more negative amplitude following monetary losses than monetary gains (Foti and Hajcak, 2009; Gehring and Willoughby, 2002; Glazer et al., 2018; Holroyd et al., 2006; Hu et al., 2017; Nieuwenhuis et al., 2004) and following incorrect responses in comparison with correct responses (Barker et al., 2015; Gehring et al., 1993; Holmes and Pizzagalli, 2008; Huang and Yu, 2018; Judah et al., 2016; Long et al., 2012; Nieuwenhuis et al., 2004). Moreover, the MFN effect (the difference in the MFN amplitude between positive and negative outcomes) was greater following a loss event than a gain event (Gehring and Willoughby, 2002). It has been suggested that the MFN would be associated with an early, fast and coarse evaluation of an event (Hu et al., 2017) and that it would be particularly sensitive to losses (Gehring and Willoughby, 2002).

There are two interpretations about the significance of the MFN. One of the interpretations is that the MFN would be modulated by the motivational/emotional impact of an event (Boksem and De Cremer, 2010; Gehring and Willoughby, 2002) and with the assessment of losses (Gehring and Willoughby, 2002).

The other interpretation of the MFN is related to reinforcement learning theory and considers that the MFN indicates when an outcome is worse than expected (Boksem and De Cremer, 2010; Glazer et al., 2018; Holroyd et al., 2006; Huang and Yu, 2018; Long et al., 2012; Sambrook and Goslin, 2015; San Martín, 2012; Walsh and Anderson, 2012). In light of this theory, evaluations of events are carried out by contrasting the expectations about a future event and its real outcome along a good-vs-bad dimension (Holroyd et al., 2006; Nieuwenhuis et al., 2004; San Martín, 2012). When an outcome is different than its prediction, then an error signal is conveyed which would indicate that the outcome is better or worse than expected (Glazer et al., 2018; Holroyd et al., 2006). This signal would guide an adjustment in the expectations and in the behavior (Glazer et al., 2018; San Martín, 2012) and would be conveyed by the dopaminergic system (San Martín, 2012) to areas such as the ACC (Walsh and Anderson, 2012). This error signal would be measured in the scalp as the MFN, with a more negative amplitude of the MFN during unexpected in comparison with expected outcomes (San Martín, 2012; Walsh and Anderson, 2012). In fact, studies analysing the potential neural source of the MFN have pointed to the ACC (Gehring and Willoughby, 2002; Glazer et al., 2018; Holmes and Pizzagalli, 2008; San Martín, 2012; Walsh and Anderson, 2012). Some authors have suggested that a more negative MFN would be related to a decrease in dopaminergic firing that would disinhibit neurons in the ACC (Walsh and Anderson, 2012). In turn, a more positive MFN would be related to an increase in dopaminergic activity that would inhibit neurons in the ACC (Walsh and Anderson, 2012). This is consistent with the functional role of the ACC on behavioral (Gehring and Willoughby, 2002; San Martín, 2012) and affective control and with its sensitivity to punishments or reward reductions (Gehring and Willoughby, 2002). Moreover, the ACC is considered to integrate reward information from prediction errors and from motivational inputs with the selection of actions (Walsh and Anderson, 2012). Furthermore, activity in the ACC is related to decision-making, social evaluation (Osinsky et al., 2013) and affective processing of physical and social pain (Boksem and De Cremer, 2010).

Nevertheless, some studies have suggested that the MFN would be responsive to positive events, rather than to negative events (Holroyd et al., 2008; Proudfit, 2015). It has been suggested that unexpected positive outcomes would elicit a RewP (Holroyd et al., 2008), which would be related to reward processing of positive events (Proudfit, 2015), to reinforcement learning theory (Glazer et al., 2018; Proudfit, 2015) and to affective processing and motivational states (Glazer et al., 2018).

### The Medial Frontal Negativity in the Ultimatum Game

There exists a considerable body of literature analysing the MFN to occur during the UG. The MFN has been reported as more negative in unfair (Alexopoulos et al., 2013, 2012; Boksem and De Cremer, 2010; Chen et al., 2019a; Fabre et al., 2015; Fernandes et al., 2019; He and Zhang, 2017; Kaltwasser et al., 2016; Ma et al., 2015, 2017; Osinsky et al., 2013; Peterburs et al., 2017; Polezzi et al., 2008; Qu et al., 2013; Riepl et al., 2016; Wang et al., 2017; Zhong et al., 2019) and medium offers (Fabre et al., 2015; Polezzi et al., 2008; Riepl et al., 2016; Wang et al., 2017; Zhong et al., 2019) in comparison with fair offers. Other studies that used a different statistical method also reported a similar effect (Hewig et al., 2011; Mussel et al., 2014). However, Hu et al. (2014) did not find a main effect of fairness in the MFN.

In the UG, the MFN has been interpreted as a bad-vs-good evaluation, with medium and unfair offers being evaluated as bad social situations and fair offers being evaluated as good social situations (Alexopoulos et al., 2012; Boksem and De Cremer, 2010; Fabre et al., 2015; Kaltwasser et al., 2016; Osinsky et al., 2013; Polezzi et al., 2008; Riepl et al., 2016). In this context, the MFN has also been related to the emotional/affective evaluation of outcomes (Alexopoulos et al., 2012; Boksem and De Cremer, 2010), and with processes such as empathy and social pain (Boksem and De Cremer, 2010).

A number of authors have also recognized that the MFN in the UG would respond to error predictions, indicating when an outcome is better or worse than expected (Alexopoulos et al., 2013, 2012; Boksem and De Cremer, 2010; Chen et al., 2019a; Fernandes et al., 2019; Ma et al., 2017; Wu et al., 2011; Zhong et al., 2019). These authors suggested that volunteers must expect fair offers during the UG, and that unexpected unfair offers elicit a MFN (Alexopoulos et al., 2012; Boksem and De Cremer, 2010; Chen et al., 2019a; Wu et al., 2011; Zhong et al., 2019). In the same line, the MFN has also been related to a loss in utility experienced with the inequality of offers (Alexopoulos et al., 2012).

In addition, Zhong et al. (2019) reported that the MFN was more negative in medium compared with unfair offers. They interpreted this result as related to high conflict experienced in medium offers, which would elicit a more negative MFN (Zhong et al., 2019). In a similar vein, Fabre et al. (2015) also related the MFN with the detection of conflicting situations and with conflict monitoring.

It is important to point out that in most of the aforementioned studies, the UG was designed without balancing material utility between levels of fairness (Boksem and De Cremer, 2010; Campanha et al., 2011; Chen et al., 2019a; Fabre et al., 2015; Falco et al., 2019; Hewig et al., 2011; Kaltwasser et al., 2016; Luo et al., 2014; Ma et al., 2015, 2017; Mussel et al., 2014; Osinsky et al., 2013; Polezzi et al., 2008; Qu et al., 2013; Riepl et al., 2016; Wang et al., 2017; Wu et al., 2011; Zhong et al., 2019). This means that the volunteers were offered more money in fair offers than in medium offers, and more money in medium offers than in unfair offers. Taking this into consideration, the modulation of the MFN in these studies could be attributed to monetary gains instead of fairness. To our knowledge, only few studies have used offers balanced by material utility (Van Der Veen and Sahibdin, 2011).

## The Medial Frontal Negativity in Major Depression and Social Anxiety

Some studies have related the MFN to symptoms of MD or SA, finding indications of abnormal feedback sensitivity in people with these symptoms. During gambling tasks, the MFN was more negative across all the conditions in volunteers with symptoms of MD (Tucker et al., 2003) or with symptoms of SA (Judah et al., 2016) in comparison with healthy volunteers. In a similar vein, other studies using gambling tasks showed that the MFN effect was greater in people with symptoms of MD in comparison with healthy volunteers (Mueller et al., 2015). Some studies also reported a more negative MFN after incorrect responses in people with symptoms of MD in comparison with healthy volunteers (Chiu and Deldin, 2007; Holmes and Pizzagalli, 2008). These findings were related to an increased sensitivity to psychological pain and with an enhanced negative bias in MD (Tucker et al., 2003). The results were also related to dysfunctional (Cao et al., 2015; Holmes and Pizzagalli, 2008) or exaggerated (Chiu and Deldin, 2007; Judah et al., 2016; Mueller et al., 2015) processing of unfavourable outcomes in MD and SA. This would indicate that people with MD would experience errors as larger or as more significant than healthy volunteers (Chiu and Deldin, 2007). In addition, this exaggerated processing of the error would require more cognitive resources, competing for these resources with other cognitive processes during the task (Chiu and Deldin, 2007).

Another studies using gambling tasks showed a reduced MFN during positive situations (Liu et al., 2014) or a reduced MFN effect in MD (Foti and Hajcak, 2009) in comparison with healthy volunteers. The authors argued that this blunted response to positive outcomes in MD would be related to anhedonia (Foti and Hajcak, 2009; Liu et al., 2014), reduced positive affect, reduced approach behavior and enhanced negative bias in MD (Foti and Hajcak, 2009).

Moreover, some studies have analysed the MFN during social tasks in MD or SA. When doing a task while being observed by a co-player, in comparison with an isolated condition, the MFN effect was especially greater in volunteers with symptoms of SA, in comparison with controls (Barker et al., 2015). The authors interpret this result in relation to an enhanced reactivity to social situations in SA (Barker et al., 2015). In agreement with that, the MFN effect was greater in people with SA than in control volunteers during a task involving social rejection and acceptance (Cao et al., 2015). These authors also reported that the MFN effect correlated negatively with social acceptance expectancy in real life, indicating that lower expectancies regarding social acceptance would be associated with greater MFN effect (Cao et al., 2015).

Interestingly, some studies analysed the MFN during the UG in relation to symptoms of anxiety and in relation to state and trait, positive and negative affects. One study reported that under mood induction of anger, in comparison with mood induction of happiness or fear, volunteers with high negative affect showed a more negative MFN than volunteers with low negative affect (Riepl et al., 2016). Similarly, the MFN was more negative for unfair offers than fair offers in volunteers with high anxiety symptoms, while this difference was not found in volunteers with low anxiety symptoms (Luo et al., 2014). The authors related this findings to the association between negative affects and high distress and tendency to ruminate, which would modulate the MFN.

### Summary

The MFN is a frontocentral component with a latency of about 200-350 ms after stimuli presentation which has a more negative amplitude in negative outcomes in comparison with positive outcomes. This component has been related with the emotional/motivational evaluation of the stimuli and with reinforcement learning, with more negative amplitudes in negative or unexpected outcomes. Some authors have also linked this component with rewarding processes. Interestingly, during the UG this component appears with a more negative amplitude in medium and unfair offers in comparison with fair offers. This has been related with the emotional/motivational impact of unfairness and with error predictions generated by the unexpected unfair offers. In addition, this component has been reported as being modulated by symptoms of MD or SA, suggesting abnormal processing of outcomes in these disorders. Indeed, the MFN has been proposed as a potential biomarker for mental disorders such as SA (Cao et al., 2015). As far as we know, there are no reports about the MFN during the UG in people with symptoms of MD or SA.

#### 1.3.2.2 The Late Positive Potential/P300

The Late Positive Potential (LPP) and the P300 are two parietal components with positive polarity. The LPP has a latency of about 300-700 ms and is modulated by the valence and by the motivational relevance of the stimuli (Ibañez et al., 2012). The P300 is a family of components comprising the P3a and the P3b. It has a latency of about 300-600 ms and is related to selective attention, automatic attentional modulation, motivation, and working memory (Ibañez et al., 2012). It has been reported as more positive during task-relevant, more arousing (San Martín, 2012) and unexpected outcomes (Glazer et al., 2018; Hajcak et al., 2005). Although these two components are considered different in some fields of the literature, some authors have proposed that both components would reflect the same processes (Polich, 2007), given that both have similar latency and scalp distribution, and respond similarly to specific stimuli. In fact, these similarities complicate the identification of the two components (Hajcak et al., 2010). In relation to that, studies of the UG have shown a late positivity which some authors have named LPP and others P300. Given that the identity of this positive component in the context of the UG is not clear, and that even some authors consider that both components reflect the same processes, in this work we will refer to them as LPP/P300.

One of the interpretations of the LPP/P300 is related to motivated attentional processes. The LPP/P300 has been interpreted in relation to the allocation of motivated attentional resources to salient stimuli (Glazer et al., 2018; Hajcak et al., 2010; Hu et al., 2017; Wu et al., 2011) and with high level motivational/affective evaluations (Glazer et al., 2018; Wu et al., 2011), with more positive amplitudes occurring for subjectively more valuable, intense or motivational stimuli (Hajcak et al., 2010; Hu et al., 2017). For instance, in oddball tasks the LPP/P300 has been reported as more positive with infrequent target stimuli than with frequent standard stimuli (Hajcak et al., 2010; Polich, 2007). It has also been reported as more positive for more rewarding stimuli (Glazer et al., 2018), such as correct responses in comparison with errors (Huang and Yu, 2018), or monetary gains in comparison with both losses (Hu et al., 2017; San Martín, 2012) and outcomes indicating no earnings (Hajcak et al., 2005). However, other studies reported an inverse result, with the LPP/P300 as more positive during monetary losses than gains (Foti and Hajcak, 2009). Furthermore, the LPP/P300 has been reported as more positive for emotional (pleasant and unpleasant) pictures, facial emotional expressions and words, in comparison with non-emotional ones (Hajcak et al., 2010).

Another interpretation of the LPP/P300 is related to memory processes. For instance, in a task that involved memorizing words, the amplitude of the LPP/P300 was larger for stimuli that were recalled later than for stimuli that were not recalled (Polich, 2007). In this context, the LPP/P300 is considered to reflect the categorization of stimuli (Glazer et al., 2018) and the encoding and storage of that information in working memory (Glazer et al., 2018; Hajcak et al., 2010).

In addition, there is evidence showing that cognitive load modulates this component. Some of these results are reported in studies using dual-tasks. During dual-tasks, the subject simultaneously performs a primary and a secondary task, with the aim to modulate cognitive load by varying the difficulty of one of the tasks. Using dual-tasks, the LPP/P300 was found to have less positive amplitude as the difficulty of the primary task increased (Polich, 2007). In line with this, reductions in the LPP/P300 amplitude as the age increases have been associated with limited availability of cognitive resources (Hajcak et al., 2010).

### The Late Positive Potential/P300 in the Ultimatum Game

Some studies have analysed the LPP/P300 during the UG, reporting that the LPP/P300 is associated with a more positive amplitude in fair offers in comparison with unfair offers (Hu et al., 2014; Ma et al., 2015, 2017; Qu et al., 2013; Riepl et al., 2016; Wang et al., 2017) and medium offers (Fabre et al., 2015; Hewig et al., 2011; Hu et al., 2014; Riepl et al., 2016; Wang et al., 2017), and with a more positive amplitude in unfair than medium offers (Fabre et al., 2015; Hewig et al., 2011; Hu et al., 2014). Nonetheless, Luo et al. (2014) reported a more positive LPP/P300 in unfair than fair offers and some authors did not find modulations by fairness in the LPP/P300 (Chen et al., 2019a; Peterburs et al., 2017; Zhong et al., 2019).

Some authors argued that different offers would be associated with motivational/affective significance or arousal, and in turn would receive different allocation of attentional resources (Hu et al., 2014; Ma et al., 2015, 2017). In this framework, fair offers would be more valuable and would be associated with higher motivational/affective significance than unfair offers (Ma et al., 2015, 2017; Qu et al., 2013; Riepl et al., 2016) and medium offers (Hu et al., 2014; Riepl et al., 2016). In turn, unfair offers would be associated with higher motivational/affective significance and with higher arousal than medium offers (Hu et al., 2014).

Other authors have related the effect of fairness in the LPP/P300 with dual-system decision-making processes. There have been efforts to link decision-making during the UG with theories of dual-system processes (Sanfey and Chang, 2008). Dual-system-processes rely on the activation of a *system 1* which is associated with faster and automatic processes and a *system 2* which is associated with slower, more deliberative and cognitively costly processes. Some authors have related the LPP/P300 with this theory interpreting that the more negative LPP/P300 during medium offers would be associated with a change from a fast, automatic decision-making processes (system 1) to a slower, more deliberative decision-making processes (system 2) (Fabre et al., 2015).

### The Late Positive Potential/P300 in Major Depression and Social Anxiety

The LPP/P300 has been related to symptoms of MD and SA. During an auditory-oddball paradigm, volunteers with SA symptoms (Sachs et al., 2004) and with MD symptoms (Gangadhar et al., 1993; Nan et al., 2018) had lower amplitudes of the LPP/P300 in all the conditions of the task, in comparison with healthy volunteers. In line with that, using a gambling task, a study reported reduced LPP/P300 associated with symptoms of MD and anxiety during both monetary gains and losses (Foti and Hajcak, 2009). In addition, volunteers with symptoms of MD (Foti et al., 2010) and with symptoms of SA (Mühlberger et al., 2009) failed to show differences in the LPP/P300 between emotional and neutral facial expressions, in comparison with controls. This results would indicate limited cognitive resources allocated to the task and enhanced self-focused attention in SA (Sachs et al., 2004). In addition, these results would indicate impairments in the evaluation of emotional and neutral facial expressions in SA and in MD. Nonetheless, other studies using similar tasks did not find an influence of MD (Hsu et al., 2015; Kaiser et al., 2003) or of SA (Voegler et al., 2018) in the LPP/P300.

Interestingly Riepl et al. (2016) studied the effect of negative affects in the modulation of the LPP/P300 during the UG, reporting that the LPP/P300 was associated with a less positive amplitude in volunteers with high negative affects than in those with low negative affects. As mentioned earlier, negative affects are associated with MD and with SA. The authors explained this finding with less motivation and less pleasure in volunteers with high negative affects in comparison with volunteers with low negative affects (Riepl et al., 2016).

### Summary

The LPP/P300 is a parietal component with a latency of about 300-700 ms after stimuli presentation. It has been reported with more positive amplitudes in association with more arousing stimuli and with the allocation of more attentional resources to the stimuli. In addition, this component has been linked with cognitive load and with the difficulty of the tasks, with less positive amplitudes in association with higher cognitive load or with more difficult tasks. During the UG this component has been reported with more positive amplitudes in association with fair offers in comparison with unfair offers, and in turn with more positive amplitudes in association with unfair in comparison with medium offers. This suggest that fair offers are associated with higher motivation or arousal than unfair offers, and in turn unfair offers with higher motivation or arousal than medium offers. In addition, during gambling and oddball tasks, this component has been reported with less positive amplitudes in volunteers with symptoms of MD or SA in comparison with healthy volunteers. This would indicate less cognitive resources available to allocate to the task in MD and SA in comparison with controls.

# 2 Research problem

Major depression and social anxiety are disabling mental disorders. Social interactions appear highly impaired in these disorders. The neural basis of major depression and social anxiety remain unclear. The UG is a useful task to study fair and unfair social interactions in a controlled and quantitative manner and can be used in combination with neuroimaging or neurophysiological techniques.

To our knowledge, there are no studies reporting the influence of major depression and social anxiety in the ERPs associated with fair and unfair social situations during the UG. With the aim to contribute to the understanding of the early neural activation associated with social interactions in major depression and social anxiety, we used EEG to analyse ERPs during the UG in people with symptoms of these disorders in comparison with healthy controls.

## 2.1 Objectives

### General Objectives

- To study decision-making, reaction times, emotional response and early neural activations associated with fair and unfair social interactions during the UG in volunteers with symptoms of major depression and/or social anxiety (MD/SA group) in comparison with healthy volunteers (Control group).

### Specific Objectives

- To study the rejection rates and reaction times to fair, medium and unfair offers in the UG in participants with symptoms of major depression and/or social anxiety in comparison with healthy participants.
- To study the emotions reported after encountering fair, medium and unfair offers during the UG in participants with symptoms of major depression and/or social anxiety in comparison with healthy participants.
- To study the mean amplitudes of the MFN and the LPP/P300 associated with fair, medium and unfair offers during the UG in participants with symptoms of major depression and/or social anxiety in comparison with healthy participants.

## 2.2 Hypothesis

### 2.2.1 Behavior

#### 2.2.1.1 Decision making

Based on the previous findings reporting rejection rates during the UG:

- We expected that the participants in general would reject more offers as unfairness increases.
- Given that the rejection rates of offers in the UG in people with depressive (Destoop et al., 2012; Gradin et al., 2015; Harlé et al., 2010; Pulcu et al., 2015; Radke et al., 2013; Scheele et al., 2013; Wang et al., 2014) or anxiety (Grecucci et al., 2013; Luo et al., 2014; Park et al., 2019) symptoms has been inconsistent, and that there are not previous reports in social anxiety, we did not have a clear hypothesis regarding the rejection of offers in the MD/SA group.

#### 2.2.1.2 Reaction times

Based on the previous findings reporting reaction times during the UG:

- We expected that the participants in general would show longer reaction times in medium offers than in unfair and fair offers, and in turn longer reaction times in unfair offers than in fair offers.
- Given that the few studies that reported reaction times in people with symptoms of MD during the UG did not find an effect of MD in the reaction times (Scheele et al., 2013; Wang et al., 2014), and given the lack of reports in anxiety or SA, we did not have a clear hypothesis regarding the reaction times in the MD/SA group.

### 2.2.2 Emotional reports

Based on the previous findings reporting emotional reaction during the UG in healthy volunteers (Gradin et al., 2015; Hewig et al., 2011; Paz et al., 2017; Wu et al., 2013) and volunteers with symptoms of MD or anxiety (Gradin et al., 2015; Pulcu et al., 2015; Wu et al., 2013):

- We expected that participants in general would report more negative emotions (anger, sadness, betrayal and devaluation) and less positive emotions (happiness) as unfairness increases.
- Given that people with major depression and/or social anxiety experience a strengthened negative bias and more intense negative emotions during social interactions in comparison with healthy people, we expected that the MD/SA group would report more negative emotions in unfair offers than the Control group.
- Taking into account that anhedonia is a symptom present in major depression and social anxiety, we expected that the MD/SA group would report less positive emotions towards fair offers than the Control group.

### 2.2.3 Medial Frontal Negativity

Previous studies analysing the MFN during the UG in healthy volunteers reported more negative amplitudes associated with unfair (Alexopoulos et al., 2013, 2012; Boksem and De Cremer, 2010; Chen et al., 2019a; Fabre et al., 2015; Fernandes et al., 2019; He and Zhang, 2017; Kaltwasser et al., 2016; Ma et al., 2015, 2017; Osinsky et al., 2013; Peterburs et al., 2017; Polezzi et al., 2008; Qu et al., 2013; Riepl et al., 2016; Wang et al., 2017; Zhong et al., 2019) and medium offers (Fabre et al., 2015; Polezzi et al., 2008; Riepl et al., 2016; Wang et al., 2017; Zhong et al., 2019) in comparison with fair offers. This effect has been associated with the negative emotions elicited by unfairness and with prediction errors, with more negative amplitudes for stimuli associated with higher negative emotions and with prediction errors. In addition, the MFN has also been interpreted as being modulated by rewards (RewP), with a more positive amplitude for more rewarding stimuli (Holroyd et al., 2008; Proudfit, 2015).

Regarding MD and SA, the MFN has been reported as more negative across all the conditions during gambling tasks in volunteers with symptoms of MD (Tucker et al., 2003) or of SA (Judah et al., 2016) in comparison with healthy volunteers. Some studies also reported a more negative MFN after negative situations in people with symptoms of MD in comparison with healthy volunteers (Chiu and Deldin, 2007; Holmes and Pizzagalli, 2008). Interestingly, during the UG volunteers with high negative affect showed a more negative MFN than volunteers with low negative affect (Riepl et al., 2016). Similarly, the MFN was more negative for unfair offers than fair offers in volunteers with high anxiety symptoms, while this difference was not found in volunteers with low anxiety symptoms (Luo et al., 2014). These findings were related to an increased sensitivity to psychological pain and with an enhanced negative bias in MD and SA (Cao et al., 2015; Tucker et al., 2003).

Moreover, other studies reported a reduced MFN during positive situations (Liu et al., 2014) or a reduced MFN effect in MD (Foti and Hajcak, 2009) in comparison with healthy volunteers. This effect has been related to anhedonia (Foti and Hajcak, 2009; Liu et al., 2014), reduced positive affect, reduced approach behavior and enhanced negative bias in MD (Foti and Hajcak, 2009).

Based on the previous findings:

- Across all subjects, we expected to find a more negative mean amplitude of the MFN in medium and unfair offers in comparison with fair offers.
- Given that people with major depression and social anxiety experience more intense negative emotions during social interactions (Brown et al., 2007; Hirschfeld et al., 2000; Papakostas et al., 2004; Zlotnick et al., 2000) and a strengthened negative bias (Cao et al., 2015; Disner et al., 2011; Spence and Rapee, 2016), we expected that in medium and unfair offers the MD/SA group would be associated with a more negative mean amplitude in the MFN than the Control group.

- Taking into consideration that people with major depression and social anxiety experience positive social interactions as less rewarding, enjoyable and satisfying than healthy people (Brown et al., 2007; Hirschfeld et al., 2000; King-Casas and Chiu, 2012; Kupferberg et al., 2016; Pulcu and Elliott, 2015; Weightman et al., 2019), we expected that in fair offers the MD/SA group would exhibit a less positive mean amplitude in the MFN than the Control group.

### 2.2.4 Late Positive Potential/P300

The LPP/P300 has been associated with the amount of attentional resources allocated to the stimuli and with the arousal of the stimuli. Particularly in the UG, this component has been reported with a more positive amplitude in fair offers in comparison with unfair offers (Hu et al., 2014; Ma et al., 2015, 2017; Qu et al., 2013; Riepl et al., 2016; Wang et al., 2017) and medium offers (Fabre et al., 2015; Hewig et al., 2011; Hu et al., 2014; Riepl et al., 2016; Wang et al., 2017), and with a more positive amplitude in unfair than medium offers (Fabre et al., 2015; Hewig et al., 2011; Hu et al., 2014). The authors have interpreted that the equal distributions in fair offers would be associated with higher arousal and motivational significance (Ma et al., 2015, 2017; Qu et al., 2013; Riepl et al., 2016), in comparison with unfair or unequal distributions. Moreover, Hu et al. (2014) have interpreted that both fair and unfair offers would be associated with higher arousal and motivational significance than medium offers.

In addition, during all the conditions of gambling and oddball tasks, this component has been reported with less positive amplitudes in volunteers with symptoms of MD (Foti and Hajcak, 2009; Gangadhar et al., 1993; Nan et al., 2018) or SA (Sachs et al., 2004) in comparison with healthy volunteers.

Interestingly, Riepl et al. (2016) reported less positive amplitudes of the LPP/P300 in association with high negative affects than in low negative affects. The authors argued that this finding would be related to less motivation in volunteers with high negative affects in comparison with those with low negative affects (Riepl et al., 2016).

Based on this evidence:

- Across all subjects, we expected that the mean amplitude of the LPP/P300 would be more positive in fair than unfair offers. Moreover, we expected that unfair offers would be associated with a more positive mean amplitude of the LPP/P300 than medium offers.
- Given that people with symptoms of MD (American Psychiatric Association, 2013) or SA (Brown et al., 2007) experience high negative affects and anhedonia, we expected that the MD/SA group would exhibit less positive mean amplitudes in the LPP/P300, specially in fair offers, which have previously been interpreted as rewarding and motivationally salient (Hu et al., 2014; Ma et al., 2015; Riepl et al., 2016).

# 3 Methods

## 3.1 Participants

This project was carried out according to the Declaration of Helsinki (World Medical Association, 2014) and was approved by the Comité de Ética of the Facultad de Psicología of the Universidad de la República, in accordance with the current regulations regarding research with humans (Decree CM/515). The participation in the study was voluntary and written informed consents were obtained from all the participants.

We recruited two groups of volunteers: a *Control group* ($n = 72$) including volunteers without history of mental disorders and a *MD/SA group* ($n = 63$) including volunteers with symptoms of major depression and/or social anxiety. The two groups were matched on the basis of sex, age, coursed years of education, completed years of education, area of study, skilful hand and nicotine consumption (Table 1). The inclusion criteria for the study were:

- For all participants:
  - being 18-35 years old
  - being students in a university
  - being native speakers of Spanish
  - having normal or corrected to normal vision
  - not having visual or motor impairments that would hinder the performance during the task
  - absence of personal history of neurological disorders
  - not being pregnant
  - not current bereavement
- For the Control group:
  - scoring <16 in the BDI-II and scoring <55 in the LSAS (both administered in the psychological interview and in the experimental session)

  - absence of personal history of mental disorders
  - never having taken psychiatric medication
- For the MD/SA group
  - at least one of the following:
    * scoring $\geq$16 in the BDI-II (administered in the psychological interview and in the experimental session) and meeting the diagnostic criteria for major depressive episode according to the MINI-Plus
    * scoring $\geq$55 in the LSAS (administered in the psychological interview and in the experimental session) and meeting the diagnostic criteria for social anxiety disorder according to the MINI-Plus
  - not having taken psychiatric medication in the last three weeks

We decided to conform a single MD/SA group given that, as mentioned earlier, both disorders share same features related to impairments in social interactions. In both disorders, social interactions are experienced as more negative and with less satisfaction than in healthy controls. Moreover, both disorders share a series of symptoms and characteristics that affect social interactions, such as low self-esteem, strengthened negative bias, rumination, anxiety symptoms and social avoidance. The results presented in this thesis were similar in volunteers with symptoms of major depression and in volunteers with symptoms of social anxiety, as shown in the Appendix.

In order to avoid confound variables usually found in clinical groups, such as consumption of psychiatric medication, ongoing psychological treatment or cognitive difficulties due to severity of the illness, we focused in the recruitment of a sub-clinical sample. The recruitment of students is widely used because it facilitates the inclusion of volunteers with sub-clinical symptoms and has been implemented in previous studies of our group (Fernández-Theoduloz et al., 2019; Gradin et al., 2015, 2016).

## 3.2 Study announcement

We announced this study using a website page[1] developed for this project which was distributed via e-mail and social media associated with the Universidad de la República. The website was hosted in a server of the Facultad de Psicología of the Universidad de la República, guaranteeing data protection and confidentiality.

This website exhibited a brief explanation of the project and the inclusion criteria. It also had a list of some of the characteristic symptoms of major depression and social anxiety. An online informed consent was included. If the person accepted to participate in the study (agreed in the informed consent), the form continued to the following pages, but if the person did not the form finalized. In the case that the person accepted to participate in the study, the website continued to a form including personal information questions, the *Beck Depression Inventory-II* (BDI-II) (Beck et al., 1961; Sanz et al., 2005) and the *Liebowitz Social Anxiety Scale* (LSAS) (Bobes et al., 1999; Liebowitz, 1987). The volunteers also stated if they felt identified or not with the symptoms listed.

The website page was completed by 593 people (Fig. 1). We contacted all the volunteers by phone and invited the participants who fulfill the following criteria to a psychological interview:

- volunteers who did not identify themselves with any of the symptoms listed and scored <16 in the BDI-II and scored <55 in the LSAS and never took psychiatric medication.
- volunteers who either
  - identified themselves with the depressive symptoms listed and scored $\geq$16 in the BDI-II and did not take psychiatric medication in the last 3 weeks,
  - or identified themselves with the social anxiety symptoms listed and scored $\geq$55 in the LSAS and did not take psychiatric medication in the last 3 weeks

[1] http://www.estudios.cibpsi.psico.edu.uy/node/10

- or identified themselves with the depressive and social anxiety symptoms listed and scored ≥16 in BDI-II and scored ≥55 in LSAS and did not took psychiatric medication in the las 3 weeks.

Those people who were not invited to the psychological interview were contacted by phone and we explained them the reason why they were not invited. We suggested to all volunteers that scored ≥16 in the BDI-II or ≥55 in the LSAS to consult to a health professional.

## 3.3 Psychological interview

The psychological interviews were carried out in the Centro de Investigación Básica en Psicología (CIBPsi) of the Facultad de Psicología at the Universidad de la República. At the start of the interview the researcher explained the project to the volunteer and gave him/her an information sheet. The information sheet had been sent previously to the volunteer via e-mail. The volunteer had the opportunity to make any question regarding the project. Then, the volunteer signed a paper-based informed consent. Only in the case that the volunteer had identified himself/herself with clinical symptoms, an open interview was included. In the open interview the researcher inquired about the presence of symptoms of mental disorders in different stages of life. The next step was based in the *Mini International Neuropsychiatric Interview* (MINI-Plus, version 5.0.0 in Spanish) (Ferrando et al., 1998; Lecrubier et al., 1997), which is a structured interview that checks for the presence or history of symptoms of some mental disorders according to the DSM-IV (including major depressive episode and social anxiety disorder). In addition, the volunteers filled in again the BDI-II and LSAS and the scorings were checked again for inclusion criteria.

If the participant met the inclusion criteria, then the following psychological questionnaires were administered:

- *Anticipatory and consummatory interpersonal pleasure scale* (ACIPS) (Gooding et al., 2016; Gooding and Pflum, 2014)

- *Social avoidance and distress* (SAD) (Watson and Friend, 1969; Zubeidat et al., 2007)
- *Fear of negative evaluation* (FNE) (Watson and Friend, 1969; Zubeidat et al., 2007)
- *Rosenberg self-esteem scale* (RSES) (Rojas-Barahona et al., 2009; Rosenberg, 1965)
- *Iowa-Netherlands comparison orientation scale* (INCOM) (Buunk et al., 2005; Gibbons and Buunk, 1999)

Moreover, the *Inventory of interpersonal problems* (IIP) (Horowitz et al., 1988; Salazar et al., 2010) was sent via e-mail and the participants completed it online before the experimental session. All the psychological questionnaires were administered in their Spanish version.

If the volunteer did not meet the inclusion criteria, the researcher explained why he/she could not continue participating in the study and gave him/her a reward for their collaboration. The rewards were non-monetary (a cinema ticket or a pendrive) and were the same reward than those who came to the experimental session received.

All the volunteers who assisted to the psychological interview and had symptoms of mental disorders were advised to consult to a health professional. Those who were interested were derived to the "Policlínica Psicológica-Servicio de Consulta y atención psicológica" in the Hospital de Clínicas.

To the psychological interviews assisted 166 volunteers (Fig. 1). Of them, 31 did not meet the inclusion criteria. One hundred and thirty five participants were invited to the experimental session and conformed the final sample (Table 1). Of them, 72 were assigned to the Control group (67 women) and 63 to the MD/SA group (57 women). The 63 participants assigned to the MD/SA group included 22 with symptoms of major depression, 30 with symptoms of social anxiety, and 11 with symptoms of both disorders.

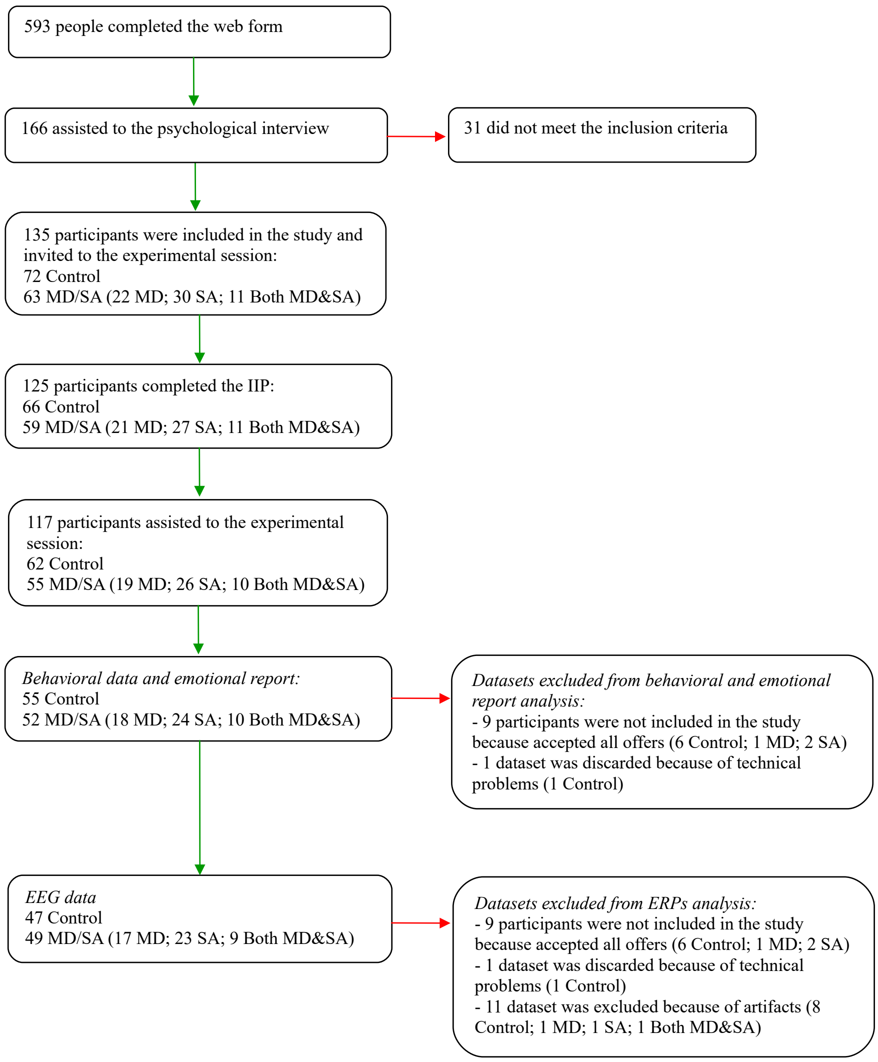


**Figure 1:** Details of participants recruitment

## 3.4 Experimental session

The experimental sessions were carried out in the Laboratorio de Psicofisiología of the Centro de Investigación Básica en Psicología. The experimental sessions consisted in completing psychological questionnaires, playing the UG while EEG recording was done and providing emotional reports regarding the UG.

During the experimental sessions, the following psychological questionnaires were

**Table 1:** Details of the participants.

| | Control | MD/SA | p-value |
|---|---|---|---|
| n | 72 | 63 | |
| Sex (F/M) | 67/5 | 57/6 | 0.58 NS |
| Age | 22.5 ±3.8 | 23.5 ±4.4 | 0.17 NS |
| Coursed years of education | 15.8 ±2.8 | 15.9 ±2.9 | 0.89 NS |
| Completed years of education | 14.2 ±2.6 | 13.5 ±2.2 | 0.07 NS |
| Nicotine consumption (N/Y) | 62/10 | 53/10 | 0.75 NS |
| Skillful hand (L/R) | 12/60 | 7/56 | 0.35 NS |
| Area of study (health/social-arts/natural-technologies) | 45/12/15 | 39/14/10 | 0.61 NS |

Table 1: p-values correspond to independent-samples T tests.

administered in their Spanish version:

- BDI-II
- LSAS
- *Snaith-Hamilton pleasure scale* (SHAPS) (Fresán and Berlanga, 2013; Snaith et al., 1995)
- *State-trait anxiety inventory* (STAI) (Guillén-Riquelme and Buela-Casal, 2011; Spielberger, 1970)
- *Positive and negative affect schedule* (PANAS) (Dufey and Fernandez, 2012; Watson et al., 1988)

The scorings of the BDI-II and of the LSAS were again checked for inclusion criteria.

### 3.4.1 Ultimatum Game

The UG was explained to the participant using a paper-based diagram similar to the one depicted in the Fig. 2. The researcher told the participant that *"in this task there are two roles: the proposer and the responder. You are going to play* *as responder. In each trial of the task you will see a silhouette representing the proposer. We gave to this proposer an amount of money, and the proposer had to make an offer about how to divide it between himself/herself and you. You will see the offer and you have to decide if you want to accept or reject it. If you accept the offer, the money will be divided as proposed and both will receive your part of the offer. If you reject the offer, you and the proposer will receive zero in this trial".*

A cover story was used to enhance the social aspect of the task. The participant was told that in a previous stage of the project we invited a series of volunteers who played as proposers and made offers for the participants. The researcher showed to the participant a series of pictures and said that they were some of the volunteers who made the offers. During the task the participant could not associate any offer with the pictures. Instead, the same gender-neutral silhouette was used to represent all the proposers in all of the trials in order to avoid that the participants would experience possible biases in their responses based in features of the pictures. We obtained signed informed consents from the volunteers who provided a picture to use in this experiment. The participant was told that at the end of the session he/she was going to receive a non-monetary reward according to the amount of money that he/she accumulated during the task. Also, after all the experimental sessions were carried out, each proposer would receive a non-monetary reward according to the amount of money that he/she accumulated during the experimental sessions. To further strengthen the social aspect of the task, the participant was also offered the option to make offers for future participants, this way having the possibility to gain an extra reward. The researcher emphasized that, if the participant agreed, later he/she could send a picture of himself/herself y e-mail to add to the folder of pictures. The data of these offers are not analysed in this report. After the explanation of the task the participant practised it in the computer.

To minimize the effects of the use of the cover story, at the beginning of the session the researcher said that *"not all of the details of the project can be explained at this moment because it would be a lot of information, but at the end of the session there would be a moment to explain all the aspects of the* *experiment in depth and you can make any question that you want regarding the project"*. At the end of the session the participant was debriefed. The researcher told the participant that in fact the offers were made by the research team and that the offers that he/she made in the role of proposer would not be added to the task for future sessions. The need to use cover stories in studies of social interactions was also explained. The researcher asked if the use of the cover story caused annoyance and everyone reported not feeling it. Studies of social interactions usually use cover stories to enhance the social aspects of the task (Fernández-Theoduloz et al., 2019; Gradin et al., 2015, 2016; Müller-Pinzler et al., 2016; Paz et al., 2017; Sanfey et al., 2003). The participants usually do not report to feel discomfort regarding the use of cover stories. Finally, the participant received a non-monetary reward for his/her collaboration (a cinema ticket or a pendrive).

The UG was coded in PsychoPy2 (version v1.80.01). The UG consisted in 168 offers classified in three levels of fairness: 56 fair offers (the participant was offered 40-50% of the total amount of the offer), 56 medium offers (the participant was offered 27-33%) and 56 unfair offers (the participant was offered 18-23%) (Fig. 2). The offers were designed in accordance to the study of Crockett et al. (2008). The levels of fairness were balanced regarding material utility, so the amount of money offered to the participant was the same in each level of fairness (Table 2). This procedure avoids a confounding regarding monetary gains between the levels of fairness.

The task had four blocks separated by pauses where the participant was allowed to rest some minutes. The levels of fairness were balanced within the blocks and presented in a randomized order. The responses were given by pressing the "Z" and "M" keys of the keyboard with each hand. The assignment of each key to acceptance or rejection was counterbalanced within each level of fairness and block. If the participant did not respond to an offer in 2500 ms after the appearance of the buttons, the task continued to the next trial. The complete task lasted about 30 minutes.

During this experimental session the participants also did another task about social comparisons. The data of this task was analysed by MSc Valentina Paz and is reported elsewhere (Paz, 2018). The order of both tasks was counterbalanced between the participants.

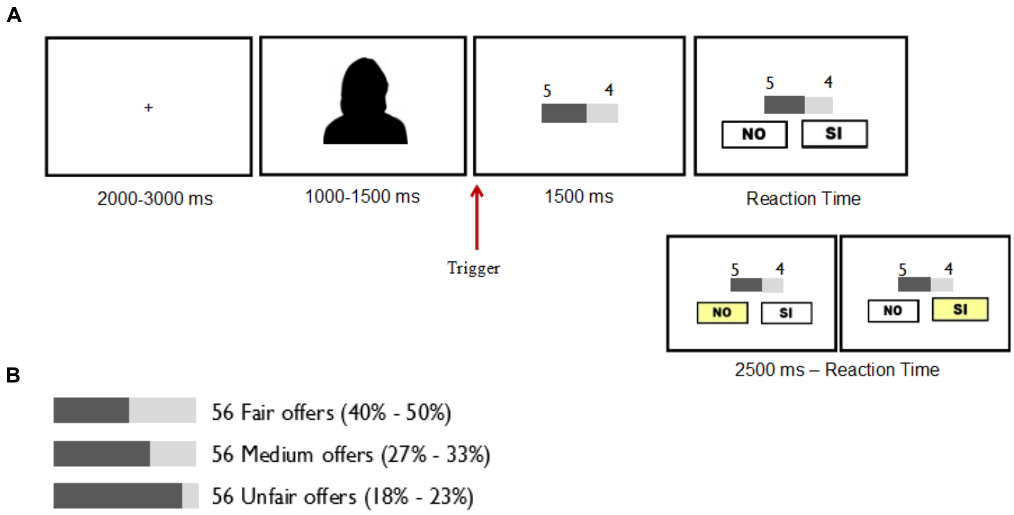


**Figure 2:** Ultimatum Game. A) On each trial the participant was presented with a silhouette representing the proposer of this offer. Subsequently, the participant was presented with the offer made by this proposer. After 1500 ms of the start of the offer screen, the buttons appeared and the participant was allowed to respond by pressing the "YES" (in Spanish, "SI") or "NO" button. Once the participant pressed the button it turned yellow. Event-Related Potentials are measured locked to the presentation of the offer (trigger). B) The UG consisted in 168 offers classified in three levels of fairness: 56 fair offers (the participant was offered 40-50% of the total amount of the offer), 56 medium offers (the participant was offered 27-33%) and 56 unfair offers (the participant was offered 18-23%).

### 3.4.2 Emotional reports regarding the Ultimatum Game

After the task, the participant was presented with 12 offers that he/she saw during the task (4 offers of each level of fairness, balanced by material utility) (Table 2). The participant rated on nine-point Likert scales the level of happiness (in Spanish, *felicidad*), sadness (*tristeza*), anger (*enojo*), betrayal (*traición*) and devaluation (*desvalorización*) that he/she felt while seeing each of these offers during the UG.

**Table 2:** Offers evaluated in the emotional report.

| | Fair | Medium | Unfair |
|---|---|---|---|
| The responder is offered 8 | 8/8 | 16/8 | 32/8 |
| The responder is offered 7 | 7/7 | 14/7 | 28/7 |
| The responder is offered 4 | 4/4 | 8/4 | 16/4 |
| The responder is offered 2 | 2/2 | 4/2 | 8/2 |

Table 2: Offers evaluated in the emotional report. The number at the left side is what the proposer wants to keep, the number at the right side is what the proposer offers to the responder. The offers were balanced by material utility.

### 3.4.3 EEG data acquisition

The EEG signal was recorded using a Biosemi ActiveTwo system (Biosemi, B.V., Amsterdam, Netherlands). A continuous recording was made using 64 Ag/AgCl active channels placed in the scalp and mounted using an elastic cap in accordance to the 10/20 international system (Jasper, 1958). Electrooculographic data was recorded in the outer canthi and above and below of the left eye. Two additional channels were placed at both mastoids. The activity recorded was referenced online to the Common Mode Sense (CMS) and grounded to a passive electrode (Driven Right Leg, DRL) creating a feedback loop that drives the average potential of the participant to the AD-box reference potential. Data were digitalized with a sampling rate of 256 Hz with a fifth-order low-pass sinc filter with a -3 dB cutoff at 52 Hz. Events were marked in the EEG signal at the beginning of each offer screen (offer-locked) and when the participant pressed the button (response-locked). The response-locked data is not analysed in this report. To avoid anticipatory activity respect to the presentation of the offer (Luck, 2014), the screen presented previous to each offer (proposer silhouette) had an irregular duration (jitter between 1000-1500 ms). To improve the quality of the data the participants were asked to remain relaxed, to maintain the gaze in the centre of the screen and to move as little as possible during the recording.

## 3.5 EEG data cleaning

Data was preprocessed offline in Matrix Laboratory (MATLAB) using the FieldTrip toolbox (Oostenveld et al., 2011). Data were re-referenced to the average of the two mastoids. Continuous data was filtered using a band-pass Butterworth filter at 0.1 - 30 Hz with two-pass direction. An Independent Component Analysis (Jung et al., 2000) was performed in order to visually identify and then eliminate components with a topography according to lateral ocular movements or eyeblinks. Epochs were defined between -200 ms before the onset of the offer to 900 ms after the onset of the offer. A baseline correction was performed using the average of the voltage in the 200 ms preceding the offer. Time series averaged over conditions for each channel were visually inspected in order to detect noisy channels, which were then corrected by interpolation using the distance-weighted average of neighbour channels located at a distance of at least 5.5 cm to the noisy channel. Individual epochs were visually inspected in order to detect and eliminate noisy trials. As before, time series were inspected to identify and interpolate remaining noisy channels. Interpolation was performed in 21 subjects with a maximum of 8 channels in each subject. Subjects with less than 25 clean trials in each condition were excluded from the analysis in order to maintain an adequate signal to noise ratio.

## 3.6 Statistical data analyses

The statistical data analysis were performed using RStudio and SPSS (Statistical Package for the Social Sciences).

### Psychological questionnaires

We performed independent-samples *t* tests in order to compare the Control and MD/SA groups in the scores obtained in the psychological questionnaires regarding:

- depressive symptoms (BDI-II applied in the experimental session)
- anhedonia (SHAPS)
- social avoidance and distress (SAD)
- fear of negative evaluation (FNE)
- social anxiety symptoms (LSAS applied in the experimental session)
- state and trait anxiety (STAI)
- social comparison orientation (INCOM)
- positive and negative affects (PANAS)
- self-esteem (RSES)
- anticipatory and consummatory interpersonal pleasure (ACIPS)
- interpersonal problems (IIP)

The Welch-Satterthwaite correction was applied when homogeneity of variances could not be assumed. Effect sizes were computed as Cohen's $\delta$. As the psychological questionnaires were administered in different stages (psychological interview, experimental session, etc.) the sample size varies for each questionnaire (details in Table 3 and in Table 4).

### Behavioral data and emotional reports

We analysed the rejection rates, reaction times and emotional reports for 107 participants (55 Control, 52 MD/SA). Data of 9 participants could not be analysed because they accepted all offers and data from 1 additional participant because of technical problems during data acquisition. We performed two-way repeated-measures ANOVAs using fairness (fair, medium, unfair) as within subjects factor, group (Control, MD/SA) as between subjects factor, and the fairness*group interaction on the rejection rates, reaction times and scores of each emotion reported (happiness, anger, sadness, betrayal and devaluation). Greenhouse-Geisser correction was used for non-sphericity. Post-hoc comparisons were performed to determine the significance of pairwise contrasts using the Bonferroni correction procedure. In order to break down interaction terms, simple effects analyses were conducted (comparisons of the effects of one independent variable between the levels of the other). We report size effects as partial eta-squared (${\eta^2}_p$).

### ERPs detection

Of the 117 EEG datasets acquired, we could not analyse 9 because the participants accepted all offers, data from 1 additional participant because of technical problems during data acquisition and data from 11 additional participants because of artifacts in the signal. EEG data of 96 participants was analysed (47 Control, 49 MD/SA -including 17 volunteers with symptoms of major depression, 23 with symptoms of social anxiety and 9 with symptoms of both disorders-) (Fig. 1). As recommended in Kappenman and Luck (2016), visualization of grand-grand averages (time series data averaged over conditions and subjects or average of grand-averages) at channels were the ERPs of interest were reported before (FCz and Cz for the MFN; Pz for the LPP/P300) (Boksem and De Cremer, 2010; Van Der Veen and Sahibdin, 2011) was performed to identify their time windows. The MFN was identified in the time window of

250-350 ms and the LPP/P300 in the time window between 475-700 ms after offer onset. For the MFN, we selected the channels previously reported in the study of this component (F1, Fz, F2, FC1, FCz, FC2). For the LPP/P300 we selected the channels were voltage was maximal in the time window of 475-700 ms (P1, Pz, P2, PO3, POz, PO4, P3, P4). The topographies of the MFN (Kaltwasser et al., 2016; Peterburs et al., 2017) and of the LPP/P300 (Fabre et al., 2015; Riepl et al., 2016) found in our study is similar to previously reported. Each ERP was computed as the mean amplitude in the time window of interest and over the channels of interest.

### ERPs analyses using Mixed Linear Models

The classical approach to study ERPs involves averaging the EEG signal corresponding to the presentation of stimuli of the same category (for example, averaging in each subject the signal associated with the presentation of all fair offers). This approach has the advantage of cancelling noise present in the EEG signal (activity not specific to the presentation of the offers). However, this approach does not allow the study of modulations of ERPs along the duration of the task, which could shed light on the processes that these ERPs reflect (San Martín, 2012). Taking this into consideration, some studies have used Linear Models to analyse ERPs (Brush et al., 2018; Volpert-Esmond et al., 2018). This method allows the definition of models that include trial number as regressor, and then the signal analysed does not need to be averaged over trials.

We implemented Mixed Lineal Models (MLMs) to analyse ERPs. We designed two models for each ERP component (MFN and LPP/P300). The Model 1 included the mean voltage as response variable, the subject as random effect, and the fairness, the group, the trial and all their interactions (fairness*group, fairness*trial, group*trial and fairness*group*trial) as fixed effects. The Model 2 included the mean voltage as response variable, the subject as random effect, and the fairness, the group, the trial and the fairness*group interaction as fixed effects. For each ERP component we tested if Model 1 or Model 2 had the best fitting according to the Akaike Information Criterion (AIC). In the case of MFN, the Model 1 ($AIC = 89091$) was selected over Model 2 ($AIC = 89092$). For the LPP/P300, the Model 2 ($AIC = 90426$) was selected over Model 1 ($AIC = 90429$).

### ERPs analyses using Principal Component Analysis

A widespread practice in the literature to study ERPs involves the identification and selection of time windows and spatial regions of interest by visual inspection. This method is susceptible to the introduction of subjective bias and to inter-judge discrepancies in ERP definition. In order to check if ERP data analysed with the MLMs were subjected to this kind of bias, we also performed a data-driven analysis to study ERPs. This analysis involves a two-step covariance-matrix-based Principal Component Analysis (PCA) and is useful to discriminate overlapped ERP components and to define time windows and spatial regions mathematically.

The first step of the analysis is a temporal PCA (tPCA) which computes the covariance between ERP time points. The time points that pertain to the same component tend to have high covariance and the time points that do not tend to have low covariance. The result is a set of temporal factors (TF) made up of highly covarying time points, which ideally correspond to different ERP components. Extracted temporal factors are quantified in factor loadings and factor scores, which are linearly related to amplitudes. We determined the number of TF to be extracted using a scree test. The extracted factors were submitted to promax rotation in order to maximize the interpretability of the resulting components, at the expense of their orthogonality. By visual inspection we selected those temporal components that had a similar latency to ERPs of interest (MFN and LPP/P300) and submitted it to the second step of analysis.

In the second step, we submitted the rotated factors corresponding to the components of interest to a spatial PCA (sPCA). The sPCA differentiates between spatial factors (SF) (spatial regions) pertaining to each one of the temporal components studied. The scalp points that pertain to a SF tend to have high covariance and the scalp points that pertain to different SFs tend to have low covariance. Each of the SFs ideally reflect different behaviors of the TF (or ERP component) in scalp areas. For each TF, we determined the number of SFs to be extracted using a scree test. The SFs extracted were also submitted to promax rotation. The factor scores of the SFs that had similar topography to ERPs of interest were selected and submitted to two-way repeated-measures ANOVAs using fairness (fair, medium, unfair) as within subjects factor, group (Control, MD/SA) as between subjects factor, and the fairness*group interaction. The Greenhouse-Geisser correction was applied in cases where the hypothesis of equality of variances was not met. Effect sizes were computed as partial eta-square (${\eta^2}_p$).

# 4 Results

## 4.1 Psychological questionnaires

The results of the *t* tests showed differences between the Control and the MD/SA group regarding psychological variables.

The MD/SA group, in comparison with the Control group, scored higher on depressive symptoms (BDI-II applied in the experimental session, $t_{56.98} = -14.25, p < 0.000, \delta = -2.64$), social anxiety symptoms (LSAS applied in the experimental session, in the total score $t_{68.83} = -17.96, p < 0.000, \delta = -3.34$; and in the subscales of fear/anxiety ($t_{74.11} = -16.0, p < 0.000, \delta = -2.97$) and avoidance ($t_{66.57} = -17.64, p < 0.000, \delta = -3.28$)), social avoidance and distress (SAD, $t_{82.97} = -24.5, p < 0.000, \delta = -4.24$), fear of negative evaluation (FNE, $t_{132} = -17.46, p < 0.000, \delta = -3.02$), trait anxiety (STAI subscale trait, $t_{105.75} = -21.11, p < 0.000, \delta = -3.67$), state anxiety (STAI subscale state, $t_{71.03} = -11.58, p < 0.000, \delta = -2.14$), social comparison orientation (INCOM, $t_{131} = -5.24, p < 0.000, \delta = -0.91$), anhedonia (SHAPS, $t_{55.65} = -6.29, p < 0.000, \delta = -1.16$) and negative affects (PANAS negative , $t_{71.32} = -11.37, p < 0.000, \delta = -2.12$) (Fig. 3 and Table 3).

The MD/SA group, in comparison with the Control group, scored lower on anticipatory and consummatory interpersonal pleasure (ACIPS, $t_{89.11} = 9.74, p < 0.000, \delta = 1.69$), self-esteem (RSES, $t_{101.35} = 15.73, p < 0.000, \delta = 2.74$) and positive affects (PANAS positive, $t_{114} = 15.76, p < 0.000, \delta = 2.93$) (Fig. 3 and Table 3).

Moreover, the MD/SA group scored higher than the Control group in the total score of interpersonal problems ($t_{115.17} = -13.44, p < 0.000, \delta = -2.41$), and also in the subscales of domineering/controlling ($t_{123} = -3.17, p = 0.002, \delta = -0.57$), vindictive/self-centered

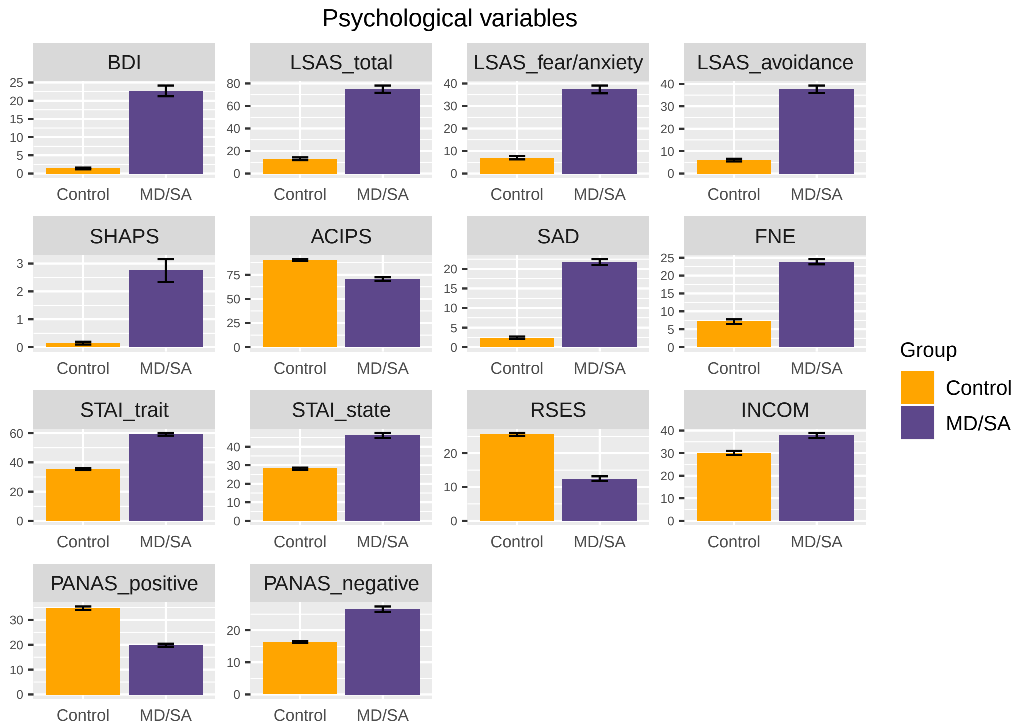


**Figure 3:** Scoring of psychological questionnaires. BDI-II: "Beck Depression Inventory-II" / LSAS: "Liebowitz Social Anxiety Scale" / SHAPS: "Snaith-Hamilton pleasure scale" / STAI: "State-trait anxiety inventory" / PANAS: "Positive and negative affect schedule" / ACIPS: "Anticipatory and consummatory interpersonal pleasure scale" / SAD: "Social avoidance and distress" / FNE: "Fear of negative evaluation" / RSES: "Rosenberg self-esteem scale" / INCOM: "Iowa-Netherlands comparison orientation scale". Error bars depict one standard error. For more information see Table 3.

($t_{109.26} = -4.95, p < 0.000, \delta = -0.89$), cold/distant ($t_{91.21} = -10.95, p < 0.000, \delta = -1.96$), socially inhibited ($t_{87.85} = -13.01, p < 0.000, \delta = -2.33$), non-assertive ($t_{123} = -12.99, p < 0.000, \delta = -2.33$), overly accommodating ($t_{123} = -7.64, p < 0.000, \delta = 1.37$), self-sacrificing ($t_{123} = -6.76, p < 0.000, \delta = -1.21$) and intrusive/needy ($t_{123} = -3.25, p = 0.001, \delta = -0.58$) (Fig. 4 and Table 4).

It was observed that both participants who met diagnostic criteria for major depression and participants who met diagnostic criteria for social anxiety

**Table 3:** Scoring of psychological questionnaires.

| Questionnaire | Group | n | Mean | Std. Deviation |
|---|---|---|---|---|
| BDI-II | Control | 62 | 1.39 | 1.93 |
| | MD/SA | 55 | 22.69 | 10.94 |
| LSAS-total | Control | 62 | 13.06 | 9.82 |
| | MD/SA | 54 | 74.94 | 23.60 |
| LSAS-fear/anxiety | Control | 62 | 7.06 | 6.13 |
| | MD/SA | 54 | 37.37 | 12.69 |
| LSAS-avoidance | Control | 62 | 6.00 | 4.76 |
| | MD/SA | 54 | 37.57 | 12.38 |
| ACIPS | Control | 72 | 90.21 | 7.50 |
| | MD/SA | 62 | 70.55 | 14.28 |
| SAD | Control | 72 | 2.40 | 2.64 |
| | MD/SA | 62 | 21.76 | 5.72 |
| FNE | Control | 72 | 7.13 | 5.42 |
| | MD/SA | 62 | 23.85 | 5.66 |
| RSES | Control | 72 | 25.58 | 3.70 |
| | MD/SA | 61 | 12.44 | 5.56 |
| INCOM | Control | 72 | 30.13 | 7.65 |
| | MD/SA | 61 | 37.80 | 9.24 |
| SHAPS | Control | 62 | 0.15 | 0.40 |
| | MD/SA | 55 | 2.75 | 3.04 |
| STAI_trait | Control | 72 | 35.31 | 5.27 |
| | MD/SA | 61 | 59.30 | 7.43 |
| STAI_state | Control | 62 | 28.13 | 4.52 |
| | MD/SA | 55 | 46.04 | 10.65 |
| PANAS_positive | Control | 62 | 34.66 | 5.55 |
| | MD/SA | 54 | 19.81 | 4.43 |
| PANAS_negative | Control | 62 | 16.32 | 2.74 |
| | MD/SA | 54 | 26.56 | 6.10 |

Table 3: BDI-II: "Beck Depression Inventory-II" / LSAS: "Liebowitz Social Anxiety Scale" / SHAPS: "Snaith-Hamilton pleasure scale" / STAI: "State-trait anxiety inventory" / PANAS: "Positive and negative affect schedule" / ACIPS: "Anticipatory and consummatory interpersonal pleasure scale" / SAD: "Social avoidance and distress" / FNE: "Fear of negative evaluation" / RSES: "Rosenberg self-esteem scale" / INCOM: "Iowa-Netherlands comparison orientation scale". For more information see Fig. 3.

contributed to the differences of the MD/SA in comparison with the Control group regarding psychological variables (Fig. A1 and Table A1) and interpersonal problems (Fig. A2 and Table A2).

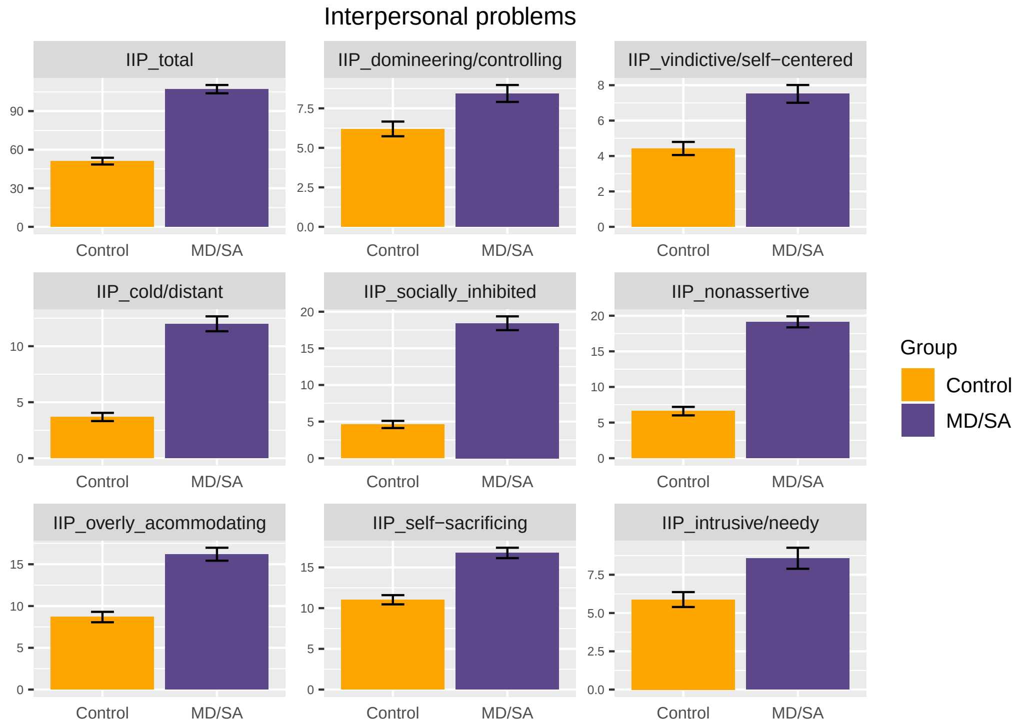


**Figure 4:** Scoring of inventory of interpersonal problems. Error bars depict one standard error. For more information see Table 4.

## 4.2 Behavioral results

### 4.2.1 Decision making

We found a main effect of fairness in the rejection rates of offers ($F_{2,206} = 522.51, p < 0.000, {\eta^2}_p = 0.84$) (Fig. 5 A and Table 5). Post-hoc tests indicated that unfair offers were rejected more often than medium offers, and that in turn medium offers were rejected more often than fair offers ($p < 0.0001$). The main effect of group ($F_{3,103} = 0.66, p = 0.58, {\eta^2}_p = 0.02$) and the group*fairness interaction ($F_{6,206} = 1.15, p = 0.34, {\eta^2}_p = 0.03$) were not significant.

**Table 4:** Scoring of inventory of interpersonal problems.

| Questionnaire | Group | n | Mean | Std. Deviation |
|---|---|---|---|---|
| IIP-total | Control | 66 | 51.11 | 21.35 |
| | MD/SA | 59 | 107.07 | 24.81 |
| domineering/controlling | Control | 66 | 6.20 | 3.78 |
| | MD/SA | 59 | 8.44 | 4.12 |
| vindictive/self-centered | Control | 66 | 4.42 | 3.00 |
| | MD/SA | 59 | 7.51 | 3.86 |
| cold/distant | Control | 66 | 3.68 | 2.98 |
| | MD/SA | 59 | 12.00 | 5.11 |
| socially inhibited | Control | 66 | 4.61 | 3.98 |
| | MD/SA | 59 | 18.42 | 7.24 |
| nonassertive | Control | 66 | 6.61 | 4.84 |
| | MD/SA | 59 | 19.14 | 5.93 |
| overly acommodating | Control | 66 | 8.68 | 5.05 |
| | MD/SA | 59 | 16.20 | 5.95 |
| self-sacrificing | Control | 66 | 11.03 | 4.59 |
| | MD/SA | 59 | 16.78 | 4.91 |
| intrusive/needy | Control | 66 | 5.88 | 3.96 |
| | MD/SA | 59 | 8.58 | 5.28 |

Table 4: For more information see Fig. 4.

### 4.2.2 Reaction times

We found a main effect of fairness in the reaction times to the decision ($F_{2,206} = 52.14, p < 0.000, {\eta^2}_p = 0.34$) (Fig. 5 B and Table 5). Post-hoc tests indicated that fair offers were associated with faster reaction times than unfair offers ($p = 0.0016$), and that in turn unfair offers were associated with faster reaction times than medium offers ($p < 0.0001$). The main effect of group ($F_{3,103} = 1.93, p = 0.13, {\eta^2}_p = 0.05$) and the group*fairness interaction

($F_{6,206} = 0.56, p = 0.76, \eta^2{}_p = 0.02$) were not significant.

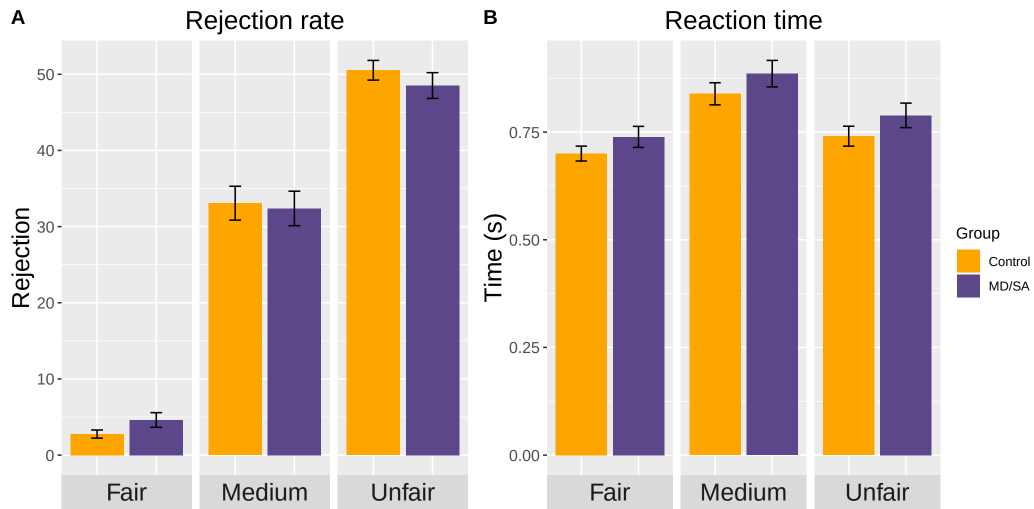


**Figure 5:** Rejection rates and reaction times to offers. Error bars depict one standard error. For more information see Table 5.

**Table 5:** Rejection rates and reaction times to offers.

| Measure | Group | n | Fair | | Medium | | Unfair | |
|---|---|---|---|---|---|---|---|---|
| | | | Mean | Std. Deviation | Mean | Std. Deviation | Mean | Std. Deviation |
| Rejection rate | Control | 55 | 2.76 | 3.96 | 33.07 | 16.51 | 50.53 | 9.58 |
| | MD/SA | 52 | 4.62 | 6.93 | 32.38 | 16.32 | 48.52 | 12.20 |
| Reaction times | Control | 55 | 0.70 | 0.13 | 0.84 | 0.19 | 0.74 | 0.17 |
| | MD/SA | 52 | 0.74 | 0.18 | 0.89 | 0.22 | 0.79 | 0.21 |

Table 5: For more information see Fig. 5.

## 4.3 Emotional reports

We found a main effect of fairness in the reported emotions of happiness ($F_{2,228} = 327.86, p < 0.0000, \eta^2{}_p = 0.74$), sadness ($F_{2,228} = 49.78, p < 0.0000, \eta^2{}_p = 0.30$), anger ($F_{2,228} = 143.36, p < 0.0000, \eta^2{}_p = 0.56$), betrayal ($F_{2,228} = 88.09, p < 0.0000, \eta^2{}_p = 0.44$) and devaluation

($F_{2,228} = 177.40, p < 0.0000, \eta^2{}_p = 0.61$) (Fig. 6 and Table 6). Post-hoc tests indicated that participants reported more anger, sadness, betrayal and devaluation and less happiness ($p < 0.001$) as unfairness increased.

Interestingly, we found a main effect of group in the reported sadness ($F_{1,114} = 7.35, p = 0.0077, \eta^2{}_p = 0.06$), indicating that the MD/SA group reported more sadness than the Control group in all offers. In addition, the fairness*group interaction was significant for the reported emotion of sadness ($F_{2,228} = 5.63, p = 0.0041, \eta^2{}_p = 0.05$). Post-hoc tests indicated that the MD/SA group reported more sadness than the Control group especially in medium ($p = 0.0055$) and unfair ($p = 0.0005$) offers.

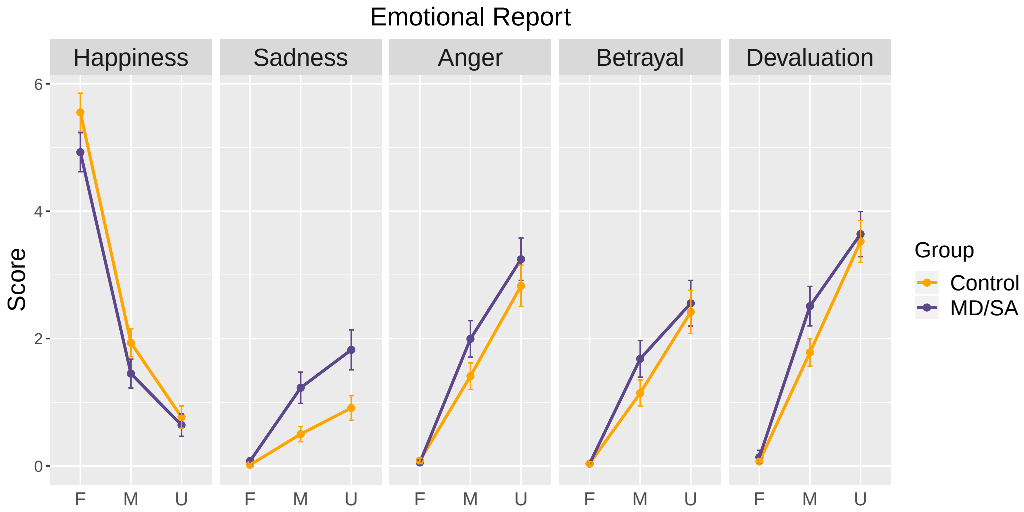


**Figure 6:** Reported emotions during the Ultimatum Game. F: "Fair offers" / M: "Medium offers" / U: "Unfair offers". Error bars depict one standard error. For more information see Table 6.

## 4.4 Event-Related Potentials

### 4.4.1 Medial Frontal Negativity

We found a main effect of fairness in the time window corresponding to the MFN ($\chi^2(2, N = 96) = 11.65, p = 0.0029$) (Fig. 7 A). Post-hoc tests showed that the

**Table 6:** Reported emotions during the Ultimatum Game.

| Emotion | Group | n | Fair | | Medium | | Unfair | |
|---|---|---|---|---|---|---|---|---|
| | | | Mean | Std. Deviation | Mean | Std. Deviation | Mean | Std. Deviation |
| Happiness | Control | 61 | 5.55 | 2.34 | 1.93 | 1.72 | 0.77 | 1.37 |
| | MD/SA | 55 | 4.93 | 2.27 | 1.45 | 1.68 | 0.64 | 1.31 |
| Anger | Control | 61 | 0.08 | 0.36 | 1.41 | 1.63 | 2.83 | 2.53 |
| | MD/SA | 55 | 0.05 | 0.28 | 2.00 | 2.13 | 3.25 | 2.47 |
| Sadness | Control | 61 | 0.02 | 0.13 | 0.50 | 0.93 | 0.91 | 1.52 |
| | MD/SA | 55 | 0.08 | 0.34 | 1.23 | 1.82 | 1.82 | 2.32 |
| Betrayal | Control | 61 | 0.04 | 0.21 | 1.14 | 1.60 | 2.42 | 2.65 |
| | MD/SA | 55 | 0.04 | 0.21 | 1.68 | 2.13 | 2.55 | 2.66 |
| Devaluation | Control | 61 | 0.07 | 0.34 | 1.78 | 1.69 | 3.52 | 2.57 |
| | MD/SA | 55 | 0.14 | 0.81 | 2.51 | 2.30 | 3.64 | 2.63 |

Table 6: For more information see Fig. 6.

mean amplitude of the MFN was more negative in medium ($p < 0.001$) and unfair offers ($p < 0.001$) compared with fair offers. We also found a borderline main effect of group ($\chi^2(1, N = 96) = 3.66, p = 0.0556$) suggesting that the MD/SA group was associated with a more negative mean amplitude in the MFN than the Control group. The fairness*group interaction was also significant ($\chi^2(2, N = 96) = 9.78, p = 0.0075$). Post-hoc tests comparing the levels of fairness within each group showed that in the MD/SA group the MFN was associated with a more negative mean amplitude in medium ($p = 0.0409$) and unfair ($p = 0.0035$) offers in comparison with fair offers, while in the Control group there was a trend in the comparison of medium ($p = 0.0654$) and unfair ($p = 0.0806$) offers with fair offers (Fig. 7 C). Neither the main effect of trial nor the trial*fairness and the group*trial interactions were significant ($p < 0.065$).

In addition, we found a significant fairness*group*trial interaction ($\chi^2(2, N = 96) = 9.76, p = 0.0075$) (Fig. 7 E). Follow-up simple slopes analysis indicated that in the Control group the mean amplitude of the MFN associated with fair offers increased over the trials ($t_{11380} = 2.95, p = 0.0032, b = 0.0013$) whereas all other slopes were not significantly different from zero ($p > 0.0648$). We also found that in the Control group the slope associated with fair offers was significantly different from the slope associated with unfair offers ($t_{11380} = 2.55, p = 0.0109, b = 0.0017$). In addition, our results indicated that the slopes for fair offers were different between the Control and the MD/SA groups ($t_{11380} = 2.62, p = 0.0087, b = 0.0017$). All other comparisons were non significant ($p > 0.069$).

Moreover, we analysed the difference between the intercepts (MFN mean amplitude extrapolated to trial 0) between groups for each level of fairness. The results showed a trend in the comparison of the intercepts associated with unfair offers between the groups ($t_{543.7} = 1.91, b = 0.172, p = 0.0562$), suggesting that the MD/SA group was associated with a more negative mean amplitude for the MFN in trial 0 than the Control group. The comparison of the intercepts of medium and fair offers between the groups were non significant ($p > 0.15$).

**Table 7:** Event-Related Potentials.

| ERP | Group | n | Fair | | Medium | | Unfair | |
|---|---|---|---|---|---|---|---|---|
| | | | Mean | Std. Deviation | Mean | Std. Deviation | Mean | Std. Deviation |
| MFN | Control | 47 | 5.53 | 3.73 | 4.79 | 4.27 | 4.79 | 3.77 |
| | MD/SA | 49 | 5.43 | 3.57 | 4.33 | 3.40 | 4.08 | 3.68 |
| LPP/P300 | Control | 47 | 10.42 | 4.09 | 7.36 | 3.34 | 8.49 | 3.80 |
| | MD/SA | 49 | 9.13 | 4.25 | 5.91 | 3.80 | 6.84 | 4.18 |

Table 7: For more details see Fig. 7 and Fig. 8.

### 4.4.2 Late Positive Potential/P300

Our results showed a significant main effect of trial ($\chi^2(1, N = 96) = 23.55, p < 0.0000$), which indicated that the mean amplitude of the LPP/P300 became more negative as the the task advanced ($t_{11400} = -4.85, b = -0.0009$) (Fig. 8 C). We also found a main effect of fairness on the mean amplitude of the LPP/P300 ($\chi^2(2, N = 96) = 60.45, p < 0.0000$) (Fig. 8 A). Post-hoc tests indicated that the mean amplitude of the LPP/P300 was more positive for fair offers than for unfair offers ($p < 0.00014$), and more positive for unfair offers than for medium offers ($p = 0.0001$). In addition, we

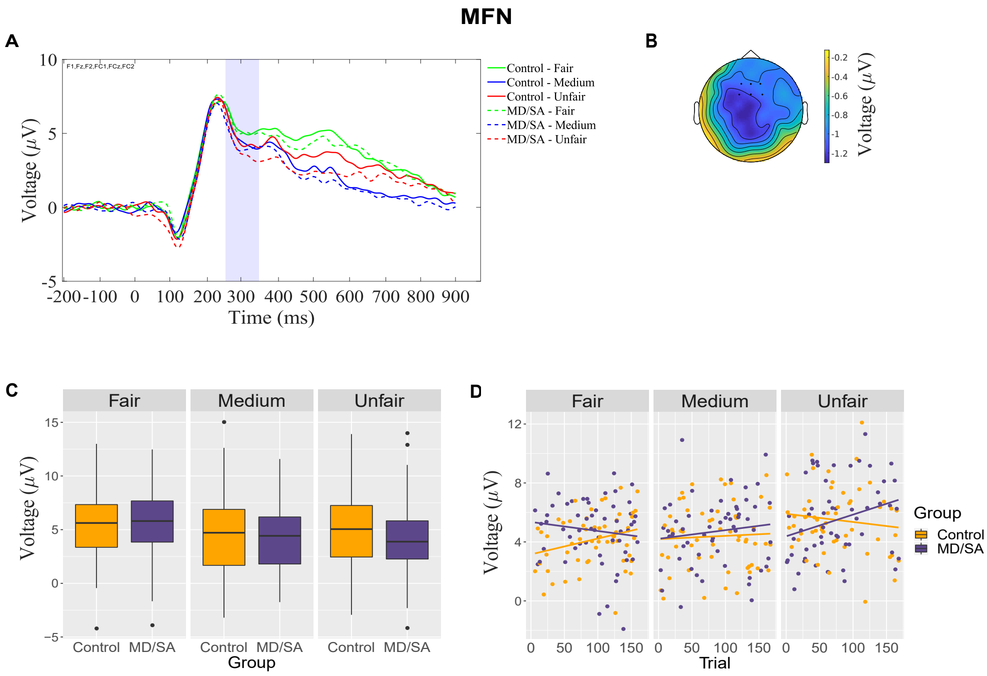


**Figure 7:** Medial Frontal Negativity. A) Grand-average waveform corresponding to the MFN. Each time-series correspond to the average over the channels of interest (F1,Fz,F2,FC1,FCz,FC2). The shadowed region indicates the time window studied (250-350 ms). The origin of the horizontal axis corresponds to the offer presentation. B) Topography corresponding to the difference between fair-unfair in the time window of the MFN. C) Mean amplitude of the MFN over the time window and electrodes of interest. D) Mean amplitude of the MFN along the task. For more details see Table 7.

found a significant main effect of group ($\chi^2(1, N = 96) = 4.28, p = 0.0385$) indicating that the MD/SA group was associated with a less positive mean amplitude of the LPP/P300 than the Control group. The fairness*group interaction was not significant ($p = 0.85$).

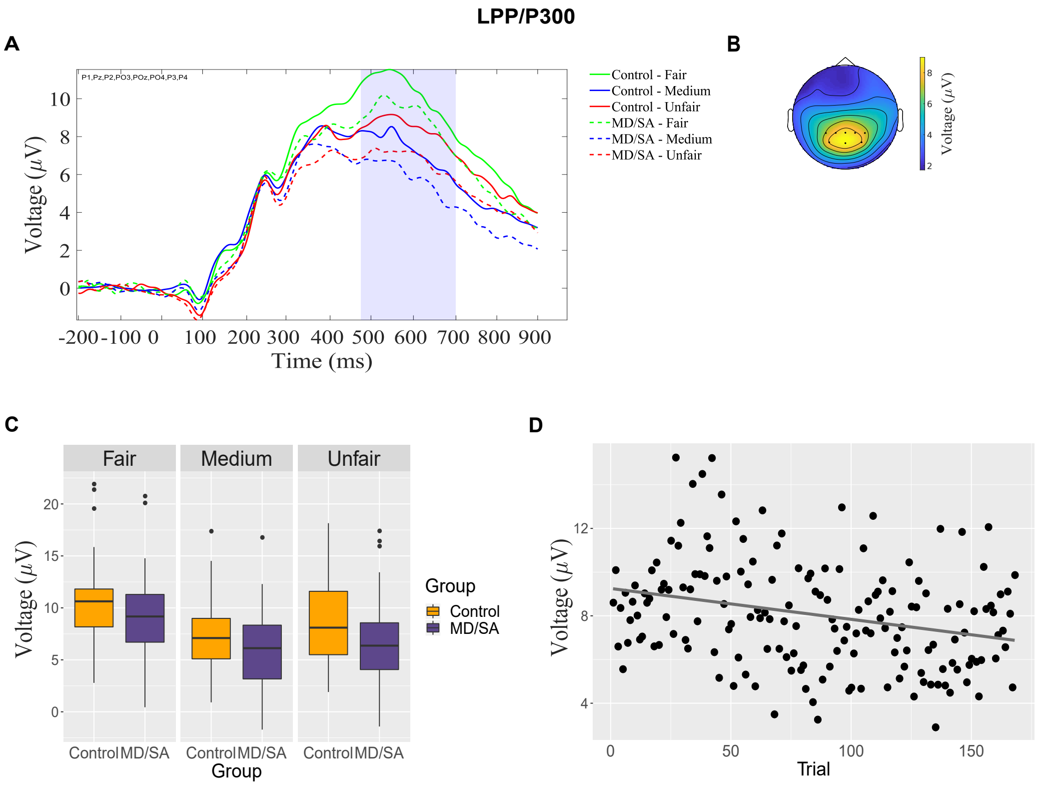


**Figure 8:** Late Positive Potential/P300. A) Grand-average waveform corresponding to the LPP/P300. Each time-series correspond to the average over the channels of interest (P1,Pz,P2,PO3,POz,PO4,P3,P4). The shadowed region indicates the time window studied (475-700 ms). The origin of the horizontal axis corresponds to the offer presentation. B) Topography corresponding to the average over fair, medium and unfair offers in the time window of the LPP/P300. C) Mean amplitude of the LPP/P300 over the time window and electrodes of interest. D) Mean amplitude of the LPP/P300 along the task. Each data point corresponds to the average over subjects and over fairness levels for each trial number. For more details see Table 7.

### 4.4.3 Temporo-spatial decomposition using Principal Component Analysis

Based on the results of the scree test for the tPCA, we extracted 10 TFs (Fig. 9 A). Those TFs that had a similar latency than ERPs of interest were selected to perform the sPCA (TF2 was associated with the MFN and TF1 was associated with the LPP/P300). The scree tests for each one of the mentioned TFs suggested the extraction of 3 SFs in each case. From the SFs extracted from the TF2 scores, the TF2SF1 showed a frontocentral topography (similar to the MFN) (Fig. 9 B) and was selected for further analysis. From the SFs extracted from the TF1 scores, the TF1SF2 showed a parietal topography (similar to the LPP/P300) (Fig. 9 B) and was selected for further analysis. Details of these components are shown in Figure 9 and in Table 8.

The ANOVA over the factor loadings of the TF2SF1 showed a significant main effect of fairness ($F_{2,188} = 7.51, p = 0.0007, {\eta^2}_p = 0.07$). Post-hoc analysis showed that fair offers were associated with different scores than medium ($p = 0.002$) and unfair ($p = 0.005$) offers. The main effect of group and the fairness*group interaction were non significant ($p > 0.49$).

The ANOVA over the factor loadings of the TF1SF2 showed a significant main effect of fairness ($F_{2,188} = 46.4, p < 0.0000, {\eta^2}_p = 0.33$) which indicated that the scores associated with fair offers were significantly different than the scores associated with unfair offers ($p < 0.0001$) and medium offers ($p < 0.0001$), and that the scores associated with unfair offers were significantly different from the scores associated with medium offers ($p = 0.027$). We also found a significant main effect of group ($F_{1,94} = 4.01, p = 0.048, {\eta^2}_p = 0.04$) which indicated that the MD/SA and Control groups were associated with different scores in this component. The fairness*group interaction was non significant ($p = 0.88$).

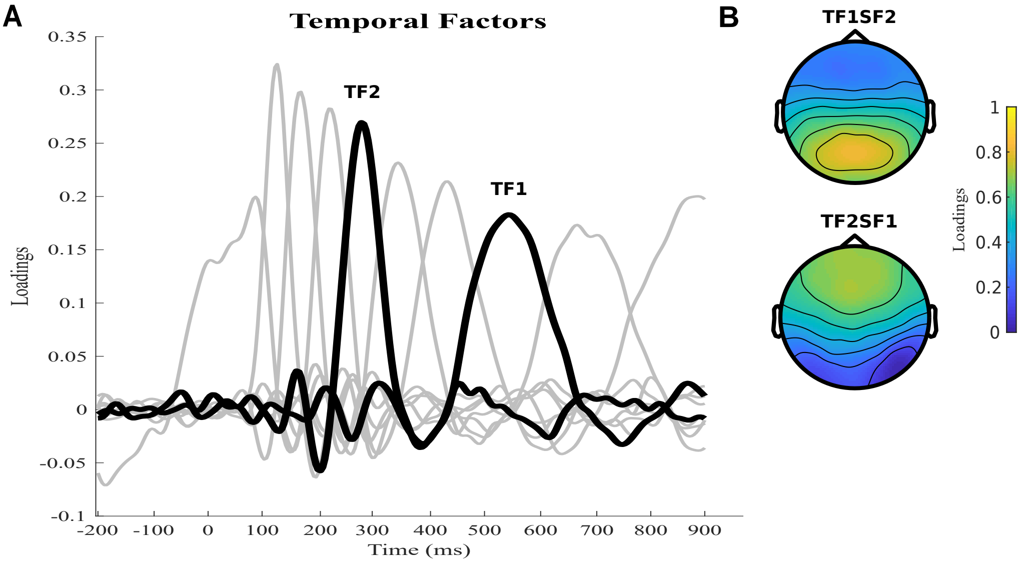


**Figure 9:** PCA decomposition. For more details see Table 8.

**Table 8:** PCA decomposition.

| | Group | n | Fair | | Medium | | Unfair | |
|---|---|---|---|---|---|---|---|---|
| | | | Mean | Std. Deviation | Mean | Std. Deviation | Mean | Std. Deviation |
| TF1SF2 | Control | 47 | 67.45 | 117.76 | -15.65 | 90.90 | 9.31 | 102.31 |
| | MD/SA | 49 | 31.86 | 120.81 | -54.96 | 104.82 | -35.52 | 122.21 |
| TF2SF1 | Control | 47 | 13.17 | 85.78 | -0.21 | 93.33 | -0.77 | 82.23 |
| | MD/SA | 49 | 13.11 | 79.86 | -13.26 | 81.26 | -11.55 | 89.12 |

Table 8: For more details see Fig. 9

# 5 Discussion

This study aimed to analyse the decision-making, reaction times, emotional reaction and neural activation associated with fair and unfair social situations in major depression and social anxiety. With this objective, we invited volunteers with symptoms of major depression and/or social anxiety and healthy volunteers to play the UG during EEG recording. We analysed the rejection rates and reaction times of offers during the UG, the emotions that the volunteers reported after the task and event-related potentials associated with the presentation of offers during the UG.

## 5.1 Behavioral findings

### 5.1.1 Decision making

Our results showed the expected effect of fairness in the rejection rates, with unfair offers being rejected more often than medium offers, and in turn medium offers being rejected more often than fair offers. It has been very well documented that participants reject more offers as unfairness increases (Alexopoulos et al., 2013; Chen et al., 2019a; Destoop et al., 2012; Fabre et al., 2015; Falco et al., 2019; Fehr and Schmidt, 1999; Fernandes et al., 2019; Gradin et al., 2015; Harlé et al., 2012; Kaltwasser et al., 2016; Luo et al., 2014; Ma et al., 2017; Park et al., 2019; Paz et al., 2017; Peterburs et al., 2017; Polezzi et al., 2008; Qu et al., 2013; Radke et al., 2013; Riepl et al., 2016; Sanfey et al., 2003; Scheele et al., 2013; Van Der Veen and Sahibdin, 2011; Wang et al., 2017, 2014; Wu et al., 2013, 2011; Zhong et al., 2019). Our results revealed that the participants in our study perceived the three levels of fairness differently and that they were prone to decline monetary gains in order to punish unfair behavior.

Our results did not show a main effect of group or a group*fairness interaction in the rejection rates of offers. This is in line with previous reports that did not find an effect of symptoms of MD (Destoop et al., 2012; Gradin et al., 2015; Pulcu et al., 2015) or of anxiety (Luo et al., 2014; Park et al., 2019) in the rejection rates during the UG. However, other studies have reported an increased rejection rates of unfair offers in volunteers with symptoms of MD (Scheele et al., 2013) or a reduced rejection rates of unfair offers in volunteers with symptoms of MD (Harlé et al., 2010) or of anxiety (Grecucci et al., 2013), in comparison with healthy volunteers. In accordance with that, other studies reported increased rejection rates across all offers in people with symptoms of MD in comparison with controls (Radke et al., 2013; Wang et al., 2014). Moreover, it was reported that induction of sadness, which is a core emotion in MD, leads to an increase in the rejection rates of all offers (Harlé et al., 2012) and of unfair offers (Harlé and Sanfey, 2007), in comparison with a neutral emotional induction. Some authors argued that the inconsistency of these results would be due to differences in the severity of the symptoms of the volunteers included in the different studies (Kupferberg et al., 2016; Luo et al., 2014; Park et al., 2019; Pulcu et al., 2015; Robson et al., 2019; Wang et al., 2015) or due to differences in the methodological implementations of the UG between the studies (Pulcu et al., 2015; Wang et al., 2015).

The previous results were interpreted linking the increased rejection rates of unfair offers in MD and in sadness induction with increased sensitivity towards negative events (Harlé and Sanfey, 2007), with increased negative emotional reaction evoked by unfairness (Scheele et al., 2013; Wang et al., 2014), with enhanced negative bias (Harlé and Sanfey, 2007; Scheele et al., 2013) and with reduced social approach behavior (Scheele et al., 2013). Moreover, the authors that reported decreased rejection rates of unfair offers in MD argued that this would be related to the enhanced negative bias present in MD, which would lead to negative expectations during social interactions in comparison with healthy volunteers. In line with that, unfair offers would be more expected in people with MD than in healthy volunteers (Harlé et al., 2010). Another interpretation is related to an increased emotional regulation processes in MD, which would favour the acceptance of unfair offers (Harlé et al., 2010). Moreover, results in anxiety have been related to enhanced worry, lower assertiveness and difficulties to confront people in generalized anxiety (Grecucci et al., 2013). To our knowledge, there are no previous reports analysing the behavior of responders in the UG including volunteers with symptoms of SA.

### 5.1.2 Reaction times

Our results showed that medium offers are associated with longer reaction times than unfair and fair offers, and that in turn unfair offers are associated with longer reaction times than fair offers. Our results are in line with previous studies reporting longer reaction times for medium offers in comparison with unfair (Fabre et al., 2015; Ma et al., 2017; Paz et al., 2017; Polezzi et al., 2008; Wang et al., 2017) and fair offers (Fabre et al., 2015; Ma et al., 2017; Paz et al., 2017; Polezzi et al., 2008; Wang et al., 2017; Zhong et al., 2019), and longer reaction times for unfair in comparison with fair offers (Campanha et al., 2011; Chen et al., 2019a; Fabre et al., 2015; Gradin et al., 2015; Ma et al., 2015, 2017; Wang et al., 2017). However, few studies reported longer reaction times for fair in comparison with unfair offers (He and Zhang, 2017; Van Der Veen and Sahibdin, 2011). These results make sense given that fair offers are not associated with great conflict in the decision-making. In fair offers, both the motivation to accumulate money and the motivation to sustain a positive social interaction lead to the acceptance of these offers. However, unfair offers are harder to respond to, because these offers present a conflict between the motivation to accumulate money (accepting the offer) and the motivation to punish the unfair behavior of the proposer (rejecting the offer). This leads to longer reaction times in unfair offers than in fair offers. Medium offers are harder to respond to, because they are neither completely fair nor completely unfair and then the response to these offers is less obvious, which leads to an increased conflict in the decision-making that is reflected in longer reaction times (Fabre et al., 2015). Our results did not show a main effect of group or a group*fairness interaction in the reaction times.

## 5.2 Emotional reports

Our results showed the expected emotional response during the UG, with participants reporting less positive emotions (happiness) and more negative emotions (anger, sadness, betrayal and devaluation) as unfairness increases. This result is in line with previous studies (Gradin et al., 2015; Hewig et al., 2011; Paz et al., 2017; Wu et al., 2013) and provides evidence that the volunteers in our study experienced the three levels of fairness differently.

In addition, our results indicated that, in comparison with the Control group, the MD/SA group reported feeling more sadness in all offers in the UG, and especially in medium and unfair offers. This result is in agreement with other studies that have shown an increased report of negative emotions in MD during the UG. For instance, a study reported that people with MD reported feeling more guilt while receiving unfair offers in comparison with healthy volunteers (Pulcu et al., 2015). Another study found more negative emotional reports associated with unfair offers in volunteers with high trait anxiety in comparison with low trait anxiety (Wu et al., 2013). Also, given that low self-esteem is a risk factor for MD and SA, and that our sample was comprised mainly with women, this result is in line with a previous report of our group that indicated that women with low self-esteem reported more anger towards unfair offers in comparison with women with high self-esteem (Paz et al., 2017).

In contrast, Grecucci et al. (2013) reported that volunteers with generalized anxiety disorder reported less anger associated with unfair offers in comparison with healthy volunteers. This result would be associated with lower levels of assertiveness in generalized anxiety in comparison with controls (Grecucci et al., 2013). Moreover, the study of Gradin et al. (2015) found that people with symptoms of MD reported feeling less happiness during fair offers in comparison with controls. Our study did not find these results.

These results point towards stronger negative emotions during social interactions in people with MD and SA in comparison with healthy volunteers, and specially during negative social situations, such as unfair situations. These results have also been related to an increased negative cognitive bias in MD which affects how these people experience social situations (Wang et al., 2015). This increased negative cognitive bias would make that people with MD focus more on the negative aspects of social situations, such as unfairness (Wang et al., 2015).

More studies are needed to better characterize how people with symptoms of MD, SA and generalized anxiety experience social interactions. Moreover, clarifying which psychological constructs are associated with specific emotions experienced during social interactions would contribute to better understand these mental disorders.

## 5.3 Event-Related Potentials

We studied two ERP components associated with the presentation of fair, medium and unfair offers during the UG: the MFN and the LPP/P300. The emergence of these components was expected given that both have been reported during social interactions and, especially, during the UG. The MFN has been related to the emotional impact of the stimuli, to rewarding processes and to reinforcement learning. The LPP/P300 has been related to attention. We found that fairness modulated these two components. In addition, we found a borderline effect of group in the MFN and a significant effect of group in the LPP/P300.

### 5.3.1 The Medial Frontal Negativity is modulated by fairness

As expected based on previous reports, our results indicated a more negative mean amplitude of the MFN in medium and unfair offers in comparison with fair offers. It has been reported that the MFN is more negative in medium (Fabre et al., 2015; Polezzi et al., 2008; Riepl et al., 2016; Wang et al., 2017; Zhong et al., 2019) and unfair offers (Alexopoulos et al., 2013, 2012; Boksem and De Cremer, 2010; Chen et al., 2019a; Fabre et al., 2015; Fernandes et al., 2019; He and Zhang, 2017;

Kaltwasser et al., 2016; Ma et al., 2015, 2017; Osinsky et al., 2013; Peterburs et al., 2017; Polezzi et al., 2008; Qu et al., 2013; Riepl et al., 2016; Wang et al., 2017; Wu et al., 2011; Zhong et al., 2019) in comparison with fair offers. The studies of Hewig et al. (2011) and Mussel et al. (2014) also reported a similar effect using different statistical methods.

The MFN has been related to the emotional/affective evaluation of the outcomes and with a good-vs-bad appraisal of the stimuli. During the UG, the more negative mean amplitude of the MFN in medium and unfair offers in comparison with fair offers would be modulated by the negative motivational/affective impact or social pain caused by unfairness (Alexopoulos et al., 2012; Boksem and De Cremer, 2010; Ma et al., 2015) and would reflect a binary classification of the offers in good-vs-bad social situations (Alexopoulos et al., 2012; Boksem and De Cremer, 2010; Fabre et al., 2015; Kaltwasser et al., 2016; Osinsky et al., 2013; Polezzi et al., 2008; Riepl et al., 2016).

The MFN has also been related to prediction errors (Alexopoulos et al., 2013, 2012; Boksem and De Cremer, 2010; Chen et al., 2019a; Fernandes et al., 2019; Ma et al., 2017; Wu et al., 2011; Zhong et al., 2019). Some authors have argued that during the UG the participants would expect to receive fair offers and when they are faced with the unexpected medium and unfair offers then an error signal emerges, which could be reflected in the MFN (Wu et al., 2011; Zhong et al., 2019).

Importantly, our study provides evidence that the MFN elicited during the UG is responsive to fairness and not to monetary gains, given that the offers were balanced by material utility. This was not controlled in most of the reports of the MFN during the UG (Boksem and De Cremer, 2010; Campanha et al., 2011; Chen et al., 2019a; Fabre et al., 2015; Falco et al., 2019; Hewig et al., 2011; Kaltwasser et al., 2016; Luo et al., 2014; Ma et al., 2015, 2017; Mussel et al., 2014; Osinsky et al., 2013; Polezzi et al., 2008; Qu et al., 2013; Riepl et al., 2016; Wu et al., 2011; Zhong et al., 2019). To our knowledge, only few studies have balanced the offers by material utility (Van Der Veen and Sahibdin, 2011).

This result would indicate that early stages of evaluation of social situations (at a latency as early as 250-350 ms after the presentation of a social stimuli), would provide a quick and semi-automatic appraisal of the situation in a good-vs-bad basis, differentiating fair offers from medium and unfair offers. This effect is consistent with the decision-making of the participants, who responded with a higher rejection rates for unfair and medium offers than fair offers. It is also consistent with the emotional reports, where participants reported feeling more negative emotions (sadness, anger, betrayal and devaluation) and less positive emotions (happiness) in unfair and medium offers than in fair offers. Taking all into account, our results suggest that medium and unfair offers were experienced as more negative social situations than fair offers.

### 5.3.2 Influence of major depression and social anxiety on the the Medial Frontal Negativity

We found a borderline main effect of group in the mean amplitude of the MFN, suggesting that the MD/SA group was associated with a more negative mean amplitude of the MFN than the Control group. This result is in line with previous reports that found a more negative MFN in all the conditions of a gambling task in volunteers with symptoms of MD (Tucker et al., 2003) or SA (Judah et al., 2016) in comparison with healthy volunteers. Moreover, Riepl et al. (2016) analysed the MFN during the UG in relation to state and trait, positive and negative affects. They reported that volunteers high in negative affect showed a more negative MFN than volunteers low in negative affect across all offers (under mood induction of anger, in comparison with mood induction of happiness or fear). The authors related this result with the distress and rumination that people experience in association with negative affect.

As the MFN is considered to be related to the negative motivational/affective impact of the stimuli and with rewarding processes, we consider that the strengthened negative emotions and weakened positive emotions experienced during social interactions in people with symptoms of MD and SA could be reflected in a more negative mean amplitude of MFN in all offers, in comparison with the Control group. However, this interpretation should be taken with precautions given that it is a borderline effect.

### 5.3.3 The Medial Frontal Negativity is modulated by fairness and group along the duration of the task

Our results indicate that, in the Control group, the mean amplitude of the MFN associated with fair offers increased as the task advanced. Moreover, in the Control group the slope associated with fair offers was significantly different from the slope associated with unfair offers. These results are in line with a previous study about the neural activation associated with rewards during a gambling task. Brush et al. (2018) reported that the MFN became more positive as the task advanced in control volunteers, suggesting that this would be the expected response of the MFN to rewards (Brush et al., 2018).

Interestingly, our results indicated that the slopes for fair offers along the duration of the task were different between the Control and the MD/SA groups. In agreement with that, (Brush et al., 2018) reported that the MFN increased over trials only in a control group, but not in a group with symptoms of MD. This blunted response to rewards in MD was interpreted in relation to a dysfunction in the reward processing in the dopaminergic system in MD (Brush et al., 2018). Dysfunctions in the reward system in MD during the UG have also been reported using fMRI (Gradin et al., 2015). This study reported that people with MD fail to activate the striatum in fair offers, in comparison with healthy volunteers (Gradin et al., 2015).

However, the lack of studies analysing the modulation of ERPs along the tasks makes it difficult to compare these results in light of previous reports. More studies are needed to test the replicability of these results. It would be advisable that future studies analyse the effect of the advancement of the task in the neural signals.

### 5.3.4 The Late Positive Potential/P300 is modulated by fairness

Our results showed that the LPP/P300 is associated with a more positive mean amplitude in fair than unfair and medium offers, and that in turn it is associated with a more positive mean amplitude in unfair than medium offers. This result is in line with previous studies reporting a more positive amplitude in fair than unfair (Hu et al., 2014; Ma et al., 2015, 2017; Qu et al., 2013; Riepl et al., 2016; Wang et al., 2017) and medium offers (Fabre et al., 2015; Hewig et al., 2011; Hu et al., 2014; Riepl et al., 2016; Wang et al., 2017), and a more positive amplitude in unfair than medium offers (Fabre et al., 2015; Hewig et al., 2011; Hu et al., 2014). However, Luo et al. (2014) found a more positive LPP/P300 in unfair than fair offers.

This result has been interpreted in relation to the different motivational significance or arousal associated with the different levels of fairness (Hu et al., 2014; Ma et al., 2015, 2017; Riepl et al., 2016). Also, the different levels of fairness would be associated with different allocations of attentional resources (Hu et al., 2014; Ma et al., 2015, 2017). This would indicate that fair offers would be more valuable and arousing than unfair (Ma et al., 2015) and medium offers, and would receive more attentional resources. In turn, unfair offers would be associated with higher arousal and motivational significance, and with the allocation of more attentional resources, in comparison with medium offers. Medium offers would be the ones associated with less arousal (Hu et al., 2014) and with less attentional resources.

Another interpretation of the modulation of the LPP/P300 by fairness in our study is related to the cognitive conflict associated with the stimuli. The relation of the LPP/P300 with conflicting decision-making was reported before. Previous studies have linked the more negative amplitudes of the LPP/P300 with more conflicting decisions that require more mental efforts and higher depth of processing of the information (Cui et al., 2019; Heeren et al., 2016). In accordance with this, our results showing a more negative LPP/P300 in medium offers are congruent with an interpretation related to the difficulty/conflict associated with the response of these offers. As previously discussed, fair offers are the easiest to respond because the desire to maximize own gains and the positive emotions triggered by them both lead to the acceptance of these offers. In line with this, fair offers are associated with the shortest reaction times. Responding to unfair offers presents a conflict between the maximization of own gains (accepting the offer) and the punishment of unfair behavior (rejecting the offer). Unfair offers are usually rejected and are associated with longer reaction times than fair offers. In agreement with that, some authors interpreted that responses to fair and unfair offers would be associated with the activation of semi-automatic and fast decision-making processes (system 1) (Polezzi et al., 2008; Zhong et al., 2019). Medium offers are the most conflicting because they are not at any extreme of the fairness continuous and are also associated with the longest reaction times. The higher cognitive conflict experienced in medium offers would require more deliberative processes in order to make a decision, which consumes more cognitive resources and time (system 2) (Fabre et al., 2015; Polezzi et al., 2008; Zhong et al., 2019). This processes would modulate the LPP/P300 amplitude during the medium offers of the UG.

The two interpretations presented here seem contradictory, given that if medium offers would be more conflicting, then should require more cognitive resources. However, it is possible that the LPP/P300 would be modulated by two processes, one related to more arousal of the stimuli and another related to the conflict of the situation. The experimental design of our study does not allow to disentangle the effects of arousal/attention and cognitive conflict on the LPP/P300. Further studies are needed to clarify the existence of these two processes underlying the LPP/P300.

### 5.3.5 The Late Positive Potential/P300 is modulated by symptoms of major depression and social anxiety

Our results showed that the LPP/P300 was associated with a more negative mean amplitude in the MD/SA group in comparison with the Control group. In line with that, Riepl et al. (2016) studied the effect of negative affects in the modulation of the LPP/P300, reporting that this component was more negative as the negative affects increased. Given that MD and SA are associated with more negative affects, this result is in agreement with our finding.

As the LPP/P300 amplitude has been related to the amount of attentional resources allocated to the stimuli, the less positive mean amplitude of this component in the MD/SA group in comparison with the Control group could be related to less attentional resources allocated to the task in the MD/SA group. Other cognitive processes in the MD/SA group could be active during the task, such as for instance rumination. These processes would compete for the cognitive resources available to allocate to the task in the MD/SA group. Moreover, a lack of motivation to engage in the task in the MD/SA group in comparison with the Control group would modulate the LPP/P300 (Riepl et al., 2016).

Another plausible explanation of this result is related to the conflict associated with the decision-making of each level of fairness. Less positive amplitudes in the LPP/P300 would be related to more conflicting situations, as suggested by the modulation by fairness in this component. In line with this, a more negative mean amplitude in the LPP/P300 would be related to more conflict experienced in all the offers in the MD/SA group in comparison with the Control group.

# 6 Limitations

The sample analysed in this study has some characteristics that might limit the generalization of the results. For instance, this sample is mainly composed by women between 18-35 years old. In addition, the volunteers included in this study were students with subclinical symptoms. These characteristics difficult the generalization of these results to men, people in other age ranges or volunteers with clinical symptoms. We decided to include a sample with these characteristics because it facilitates the exclusion of masked variables such as impairments in cognitive functions or psychiatric medication consumption.

Another limitation is the use of psychological questionnaires that are not validated in Uruguay. Future studies might aim to validate psychological questionnaires in Uruguay. Also, future studies might aim to use psychological questionnaires validated in the region or in our country. In addition, the emotional report questionnaires have some limitations. For instance, they require that the volunteers indicate the emotions they felt by self-report at the end of the task, which could bias the results. Moreover, as the emotional reports are provided at the end of the task, they does not allow to test if the emotions reported are evoked by the task. Future studies might aim to include tools that could allow to test this modulation, such as for instance providing measures at the beginning and at the end of the task.

# 7 Perspectives

### Research Domain Criteria

Although there have been some advances in the knowledge about mental disorders, research in this field faces some difficulties, for instance related with the diagnosis of the disorders. For that reason, in the last few years there have been efforts to study mental disorders from a transdiagnostic approach (Saris et al., 2017). One example of this is the Research Domain Criteria (RDoC), created by the National Institute of Mental Health of the United States of America in 2009 (Clark et al., 2017; Sanislow et al., 2014). RDoC is an alternative frame to guide research in mental disorders, putting the focus on the overlapping multidimensionality of mental disorders (Clark et al., 2017; Sanislow et al., 2014).

The aim of RDoC is to provide a useful framework to advance the knowledge of the underlying mechanisms associated with mental disorders (Clark et al., 2017). The RDoC framework does not incorporate the classification of mental disorders included in previous manuals (Clark et al., 2017). Rather, it proposes the study of mental disorders focusing on symptoms or risk factors and integrating knowledge from molecular biology, cellular biology, pharmacology, behavior and neuroscience (Sanislow et al., 2014). RDoC aims to identify relevant dimensions that in the future could be used for the classification of mental disorders (Clark et al., 2017).

The RDoC framework is based on the definition of domains and constructs, based on psychological and biological knowledge about the underlying mechanisms relevant for the functioning of individuals (Sanislow et al., 2014). The domains included in RDoC are *Negative Valence Systems* (responses to aversive stimuli), *Positive Valence Systems* (reward-related processes), *Cognitive Systems*, *Systems for Social Processes* and *Arousal/Regulatory Systems* (such as circadian rythms) (Clark et al., 2017; Sanislow et al., 2014). These constructs are psychological and biological measures and are organized in areas of study, such as genes, molecules, cells, neural circuits, physiology, behavior, self-reports and paradigms (Sanislow et al., 2014). For instance, the domain of *Positive Valence System* includes constructs related to approach motivation, initial responsiveness to rewards, sustained responsiveness to rewards, reward learning and habit (Sanislow et al., 2014). The aim of this framework is to characterize the symptoms produced by impairments in each dimension (Clark et al., 2017).

The RDoC framework is useful to study social impairments in mental disorders in a transdiagnostic manner (Kupferberg et al., 2016) and for the identification of biomarkers associated with mental disorders (Sanislow et al., 2014).

### Prediction of behavior

It would be possible to analyse if signals at a given trial predict the decision-making in the following trials. For instance, it is possible to study if the mean amplitudes of the MFN or the LPP/P300 at a given trial, or if power at a specific region of the time-frequency spectra at a given trial, are different taking into account if the participant accepted or rejected the offer in the following trial. Also, it would be interesting to study if these potential predictive signals are different between the MD/SA and the Control groups.

### Time-frequency

Studying the time-frequency spectra could shed light about processes reflected in different frequency bands and about processes that are not locked to the stimuli (Total Power or Induced Power) (San Martín, 2012). Some authors consider that the theta oscillations would underlie the MFN. During the UG, in healthy volunteers, power in the theta band was found to be modulated by fairness (Wang et al., 2017). During a very similar task about fairness, the authors also found an effect of fairness in theta oscillations (Massi and Luhmann, 2015). Moreover, this study found an effect in the delta band, which is related with the LPP/P300

(Massi and Luhmann, 2015).

### Event-Related Potentials associated to the response to the offers

The data acquirement was designed in order to be able to analyse the ERPs associated to the execution of the response to accept or to reject the offers. It would be possible to compare the ERPs associated to acceptances or rejections between the groups. Moreover, this signal could also be analysed in terms of the time-frequency spectra.

# 8 Conclusion

Mental disorders are prevalent and cause severe impairments in the quality of life of patients. Importantly, mental disorders severely affect social interactions. Given the relevance of social interactions in health and well-being, these impairments cause suffering and complicate the recovery of the patients. The treatments available today for mental disorders are only partially effective and the diagnosis of these disorders has several difficulties. This is in part because of the lack of understanding of the neural basis associated with these disorders. Major depression and social anxiety are within the most prevalent mental disorders.

This study aimed to contribute to the understanding of the neural activation during fair and unfair social interactions in major depression and social anxiety. With this objective, we analysed event-related potentials during the ultimatum game in healthy volunteers and volunteers with symptoms of major depression and/or social anxiety.

The decision-making, reaction times and emotional reports found here were the expected. We found higher rejection rates, more negative emotions reported, and less positive emotions reported as unfairness increased. Also, reaction times were longer in medium offers than in unfair offers, and in turn longer in unfair offers than in fair offers. Interestingly, we found that volunteers in the MD/SA group reported more sadness in all the offers, and especially in medium and unfair offers, in comparison with the Control group. Regarding the neural activation, our results showed two of the expected components during this task, the MFN and the LPP/P300.

We found that the fairness modulated the MFN and the LPP/P300. The MFN was associated with more negative mean amplitudes in medium and unfair offers in comparison with fair offers. This effect would be related with the emotional/motivational impact of unfairness. Alternatively, this result could be related to prediction errors associated with the unexpected medium and unfair offers. In addition, the amplitudes of the LPP/P300 were more positive in fair in comparison with unfair offers, and in turn more positive in unfair in comparison with medium offers. This effect would be related with a higher arousal or motivational significance for fair in comparison with unfair offers, and in turn higher arousal or motivational significance for unfair in comparison with medium offers. Alternatively, this modulation could be related with the conflict associated with the decision-making, with more positive amplitudes of the LPP/P300 in the less conflicting, fair offers and with less positive amplitudes in more conflicting, medium offers.

Interestingly, our results showed a borderline main effect of group in the MFN, indicating that this component was associated with a more negative mean amplitude in the MD/SA group in comparison with the Control group across all offers. The more negative mean amplitude of the MFN in the MD/SA group could be related to a strengthened negative emotional reaction during social interactions, in comparison with the Control group. In addition, the LPP/P300 was associated with a more negative mean amplitude in the MD/SA group in comparison with the Control group across all offers. The more negative mean amplitude in the LPP/P300 in the MD/SA group could be related to less attentional resources available to allocate to the task and/or with higher levels of conflict experienced during social decision-making in the UG, in comparison with the Control group. In addition, we found that the MFN is differently modulated during fair offers along the duration of the task between the MD/SA and the Control groups. This result would indicate dysfunctional reward processing in the MD/SA group.

Although we did not find evidence indicating different behavior during the UG in healthy volunteers and volunteers with symptoms of major depression and/or social anxiety, the emotional reports and neural activations indicate that they experience social interactions in a different manner. We hope to contribute to the understanding of the neural basis associated to social interactions in these disorders.

# 9 Scientific communications

The results or partial results of this work have been presented in regional and international conferences:

- September 2016: *Activación neural asociada a interacciones sociales durante el ultimatum game: un estudio con electroencefalografía.* Poster presented in the IV Jornadas en Biología Humana in Montevideo, Uruguay.
- March 2017: *Neural activation associated to social interactions in major depression: a study using event-related potentials during the ultimaum game*. Poster presented in the 2nd Latin American Brain Mapping Network Congress in Buenos Aires, Argentina.
- June 2019: *Event-Related potentials during fair and unfair social interactions in Depression/Social Anxiety* Poster presented in the 25th Annual Meeting of the Organization for Human Brain Mapping in Rome, Italy.

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# Appendices

## Additional statistical reports

We performed additional statistical reports to test if the subgroups included in the MD/SA group were different in psychological variables, behavior during the UG, emotional reports and ERPs associated to the offers.

### Psychological questionnaires

In order to test differences in psychological variables between the subgroups, for the scores of each psychological questionnaire we performed a one-way ANOVA with the group factor including 4 levels: Control, volunteers with symptoms of Major Depression (MD), volunteers with symptoms of Social Anxiety (SA) and volunteers with symptoms of both disorders (Both MD&SA). Post-hoc comparisons were performed to determine the significance of pairwise contrasts using the Bonferroni correction procedure.

The main effect of group was significant for the scores on depressive symptoms (BDI-II applied in the experimental session, $F_{3,113} = 168, p < 0.000$), social anxiety symptoms (LSAS applied in the experimental session, $F_{3,112} = 144, p < 0.000$, for the subscale of fear/anxiety of the LSAS ($F_{3,112} = 127, p < 0.000$) and avoidance ($F_{3,112} = 79.1, p < 0.000$)), social avoidance and distress (SAD, $F_{3,130} = 281, p < 0.000$), state and trait anxiety (STAI subscale state, $F_{3,113} = 58.4, p < 0.000$, STAI subscale trait $F_{3,129} = 183, p < 0.000$), fear of negative evaluation (FNE, $F_{3,130} = 110, p < 0.000$) and negative affects (PANAS negative, $F_{3,112} = 57.4, p < 0.000$) with the Control group scoring lower than the SA group, the MD group and the Both MD&SA group ($p < 0.000$). Moreover, the main effect of group was significant for the scores on anhedonia (SHAPS, $F_{3,113} = 39.5, p < 0.000$), with the Control group scoring lower than the Both

MD&SA and the MD groups ($p < 0.000$). In addition, the main effect of group was significant for the scores on social comparison orientation (INCOM, $F_{3,129} = 9.59, p < 0.000$), with the Control group scoring lower than the MD and the SA groups ($p < 0.000$).

The main effect of group was also significant for positive affects (PANAS positive, $F_{3,112} = 92.6, p < 0.000$), anticipatory and consummatory interpersonal pleasure (ACIPS, $F_{3,130} = 38.5, p < 0.000$) and self-esteem (RSES, $F_{3,129} = 95.2, p < 0.000$), with the Control group scoring higher than the MD, the SA and the Both MD&SA groups.

Moreover, post-hoc tests showed that the MD and the Both MD&SA groups scored higher than the SA group on depressive symptoms (BDI-II applied in the experimental session, $p < 0.000$), anhedonia (SHAPS, $p < 0.000$) and state anxiety (STAI subscale state, $p < 0.032$). Moreover, post-hoc tests showed that the SA and Both MD&SA groups scored higher than the MD group on social anxiety symptoms (LSAS applied in the experimental session, total score ($p < 0.04$) and subscale of fear/anxiety ($p < 0.000$)). Also, post-hoc tests showed that the Both MD&SA group scored higher than the MD group on the subscale of avoidance of the LSAS ($p = 0.048$) and on social avoidance and distress (SAD, $p < 0.000$), and higher than the SA group on negative affects (PANAS negative, $p = 0.001$). The SA group scored higher than the MD group on social avoidance and distress (SAD, $p < 0.000$). In addition, the MD group scored higher than the SA group on trait anxiety (STAI subscale trait, $p = 0.002$).

In addition, the main effect of group was significant for the total score of interpersonal problems ($F_{3,121} = 69.2, p < 0.000$). The main effect of group was significant in the subscales non-assertive ($F_{3,121} = 62.4, p < 0.000$), cold/distant ($F_{3,121} = 50.8, p < 0.000$), socially inhibited ($F_{3,121} = 86.4, p < 0.000$), vindictive/self-centered ($F_{3,121} = 9.46, p < 0.000$), overly accommodating ($F_{3,121} = 20.8, p < 0.000$) and self-sacrificing ($F_{3,121} = 16.2, p < 0.000$), with the Control group scoring lower than the MD, SA and Both MD&SA groups ($p < 0.023$). The main effects of group in the remaining subscales were non significant ($p < 0.48$).

Post-hoc tests showed that the Both MD&SA group scored higher than the MD group on the total score of interpersonal problems ($p = 0.008$), on the socially inhibited subscale ($p < 0.000$) and on the non-assertive subscale ($p = 0.022$). Post-hoc tests also showed that the Both MD&SA group scored higher than the MD and the SA groups on the subscale of cold/distant ($p < 0.01$). Moreover, the SA group scored higher than the MD group on the subscale of socially inhibited ($p < 0.001$).

## Behavior during the task

We performed two-way ANOVAs to test if the rejection rates and reaction times were different between the subgroups. The ANOVAs included the factors of fairness (fair, medium, unfair) and group (4 levels: Control, MD, SA, Both MD&SA) and the fairness*group interaction. We found that the main effect of group was non significant neither for the rejection rates nor for the reaction times ($p > 0.13$) (Fig. A3 and Table A3).

## Emotional reports

We performed two-way ANOVAs to test if the emotions reported were different between the subgroups. We performed an ANOVA for each of the emotions reported (happiness, anger, sadness, betrayal and devaluation), including the factors of fairness (fair, medium, unfair) and group (4 levels: Control, MD, SA, Both MD&SA) and the fairness*group interaction (Fig. A4 and Table A4). We found that the main effect of group and the fairness*group interaction were non significant for the reported emotions of happiness, anger, betrayal and devaluation ($p > 0.33$).

For the reported sadness, the main effect of group was significant ($F_{3,112} = 3.08, p = 0.03, \eta_p^2 = 0.08$). Post-hoc tests showed that the MD group reported significantly more sadness than the Control group across all offers ($p = 0.035$), while the comparison between the other pairs of groups were non significant ($p > 0.76$). The fairness*group interaction was also significant for the reported sadness ($F_{6,224} = 2.46, p = 0.025, \eta_p^2 = 0.06$). Post-hoc analyses showed that the MD group reported significantly higher sadness in medium ($p = 0.011$) offers and marginally higher sadness in unfair offers ($p = 0.076$) in comparison with the Control group. The comparisons between the other groups were non significant ($p > 0.32$).

## Event-Related Potentials

### Medial Frontal Negativity

In order to test for differences between subgroups, we implemented a MLM. This model included the mean voltage as response variable, the subject as random effect, and the fairness, the group, the trial and all their interactions (fairness*group, fairness*trial, group*trial and fairness*group*trial) as fixed effects. The group factor had 4 levels: healthy volunteers (Control), volunteers with symptoms of Major Depression (MD), volunteers with symptoms of Social Anxiety (SA) and volunteers with symptoms of Major Depression and Social Anxiety (Both MD&SA). Details are shown in Table A5 and in Figure A5.

The results showed that the main effect of group was non significant ($\chi^2(3, N = 96) = 4.63, p = 0.201$). The main effects of fairness and of trial were non significant ($p > 0.15$). The interactions group*fairness, group*trial, fairness*trial and group*fairness*trial were non significant ($p > 0.076$).

### Late Positive Potential / P300

In order to test for differences between the subgroups, we implemented a MLM. This model included the mean voltage as response variable, the subject as random effect, and the fairness, the group, the trial and the fairness*group interaction as fixed effects. The group factor had 4 levels: healthy volunteers (Control), volunteers with symptoms of Major Depression (MD), volunteers with symptoms of Social Anxiety (SA) and volunteers with symptoms of Major Depression and Social Anxiety (Both MD&SA). Details are shown in Table A5 and in Figure A6.

The results showed that the main effect of group was non significant ($\chi^2(3, N = 96) = 4.81, p = 0.186$). Also, the fairness*group interaction was non significant ($p = 0.753$). The main effect of fairness ($p = 0.0018$) and the main effect of trial ($p < 0.0000$) were significant.

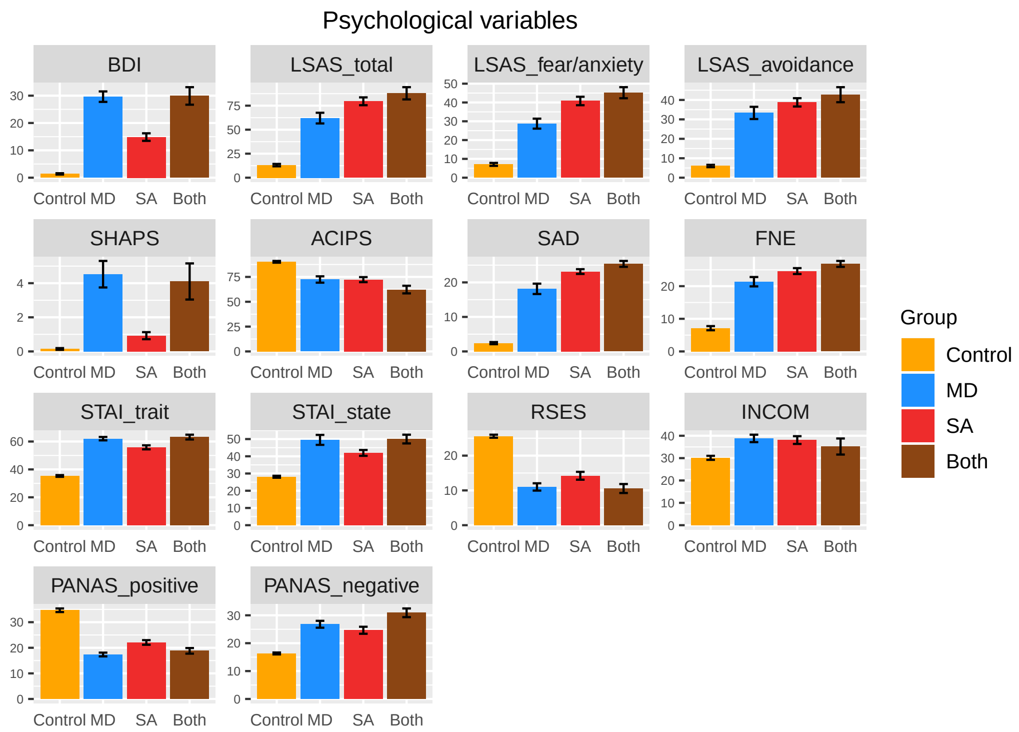


**Figure A1:** Scoring of psychological variables in healthy volunteers (Control), volunteers with symptoms of Major Depression (MD), with symptoms of Social Anxiety (SA) and with symptoms of Major Depression and Social Anxiety (Both MD&SA). BDI-II: "Beck Depression Inventory-II" / LSAS: "Liebowitz Social Anxiety Scale" / SHAPS: "Snaith-Hamilton pleasure scale" / STAI: "State-trait anxiety inventory" / PANAS: "Positive and negative affect schedule" / ACIPS: "Anticipatory and consummatory interpersonal pleasure scale" / SAD: "Social avoidance and distress" / FNE: "Fear of negative evaluation" / RSES: "Rosenberg self-esteem scale" / INCOM: "Iowa-Netherlands comparison orientation scale". Error bars depict one standard error. For more details see Table A1.

**Table A1:** Part 1: Scoring of psychological variables in healthy volunteers (Control), volunteers with symptoms of Major Depression (MD), with symptoms of Social Anxiety (SA) and with symptoms of Major Depression and Social Anxiety (Both MD&SA).

| Questionnaire | Group | n | Mean | Std. Deviation |
|---|---|---|---|---|
| BDI-II | Control | 62 | 1.39 | 1.93 |
| | MD | 19 | 29.63 | 8.34 |
| | SA | 26 | 14.85 | 7.07 |
| | Both MD&SA | 10 | 29.90 | 10.14 |
| LSAS-total | Control | 62 | 13.06 | 9.82 |
| | MD | 19 | 62.05 | 24.21 |
| | SA | 25 | 79.56 | 20.36 |
| | Both MD&SA | 10 | 87.90 | 20.15 |
| LSAS-fear/anxiety | Control | 62 | 7.06 | 6.13 |
| | MD | 19 | 28.74 | 11.53 |
| | SA | 25 | 40.80 | 11.25 |
| | Both MD&SA | 10 | 45.20 | 9.31 |
| LSAS-avoidance | Control | 62 | 6.00 | 4.76 |
| | MD | 19 | 33.32 | 13.72 |
| | SA | 25 | 38.76 | 10.69 |
| | Both MD&SA | 10 | 42.70 | 12.24 |
| ACIPS | Control | 72 | 90.21 | 7.50 |
| | MD | 22 | 72.41 | 14.92 |
| | SA | 29 | 72.28 | 13.67 |
| | Both MD&SA | 11 | 62.27 | 12.73 |
| SAD | Control | 72 | 2.40 | 2.64 |
| | MD | 22 | 18.14 | 7.05 |
| | SA | 29 | 23.14 | 3.70 |
| | Both MD&SA | 11 | 25.36 | 2.84 |
| FNE | Control | 72 | 7.13 | 5.42 |
| | MD | 22 | 21.36 | 6.72 |
| | SA | 29 | 24.62 | 4.87 |
| | Both MD&SA | 11 | 26.82 | 3.03 |
| RSES | Control | 72 | 25.58 | 3.70 |
| | MD | 21 | 11.00 | 4.82 |
| | SA | 29 | 14.21 | 6.08 |
| | Both MD&SA | 11 | 10.55 | 4.27 |

Table A1: BDI-II: "Beck Depression Inventory-II" / LSAS: "Liebowitz Social Anxiety Scale" / SHAPS: "Snaith-Hamilton pleasure scale" / STAI: "State-trait anxiety inventory" / PANAS: "Positive and negative affect schedule" / ACIPS: "Anticipatory and consummatory interpersonal pleasure scale" / SAD: "Social avoidance and distress" / FNE: "Fear of negative evaluation" / RSES: "Rosenberg self-esteem scale" / INCOM: "Iowa-Netherlands comparison orientation scale". For more details see Fig. A1.

**Table :** A1: Part 2: Scoring of psychological variables in healthy volunteers (Control), volunteers with symptoms of Major Depression (MD), with symptoms of Social Anxiety (SA) and with symptoms of Major Depression and Social Anxiety (Both MD&SA).

| Questionnaire | Group | n | Mean | Std. Deviation |
|---|---|---|---|---|
| INCOM | Control | 72 | 30.13 | 7.65 |
| | MD | 21 | 38.81 | 7.63 |
| | SA | 29 | 38.07 | 9.35 |
| | Both MD&SA | 11 | 35.18 | 11.91 |
| SHAPS | Control | 62 | 0.15 | 0.40 |
| | MD | 19 | 4.53 | 3.39 |
| | SA | 26 | 0.92 | 1.06 |
| | Both MD&SA | 10 | 4.10 | 3.35 |
| STAI-trait | Control | 72 | 35.31 | 5.27 |
| | MD | 21 | 62.05 | 5.55 |
| | SA | 29 | 55.83 | 7.80 |
| | Both MD&SA | 11 | 63.18 | 5.69 |
| STAI-state | Control | 62 | 28.13 | 4.52 |
| | MD | 19 | 49.53 | 12.62 |
| | SA | 26 | 41.96 | 8.63 |
| | Both MD&SA | 10 | 50.00 | 8.01 |
| PANAS-positive | Control | 62 | 34.66 | 5.55 |
| | MD | 19 | 17.37 | 3.22 |
| | SA | 25 | 22.08 | 4.53 |
| | Both MD&SA | 10 | 18.80 | 3.46 |
| PANAS-negative | Control | 62 | 16.32 | 2.74 |
| | MD | 19 | 26.79 | 5.39 |
| | SA | 25 | 24.64 | 6.29 |
| | Both MD&SA | 10 | 30.90 | 4.93 |

Table A1: BDI-II: "Beck Depression Inventory-II" / LSAS: "Liebowitz Social Anxiety Scale" / SHAPS: "Snaith-Hamilton pleasure scale" / STAI: "State-trait anxiety inventory" / PANAS: "Positive and negative affect schedule" / ACIPS: "Anticipatory and consummatory interpersonal pleasure scale" / SAD: "Social avoidance and distress" / FNE: "Fear of negative evaluation" / RSES: "Rosenberg self-esteem scale" / INCOM: "Iowa-Netherlands comparison orientation scale". For more details see Fig. A1.

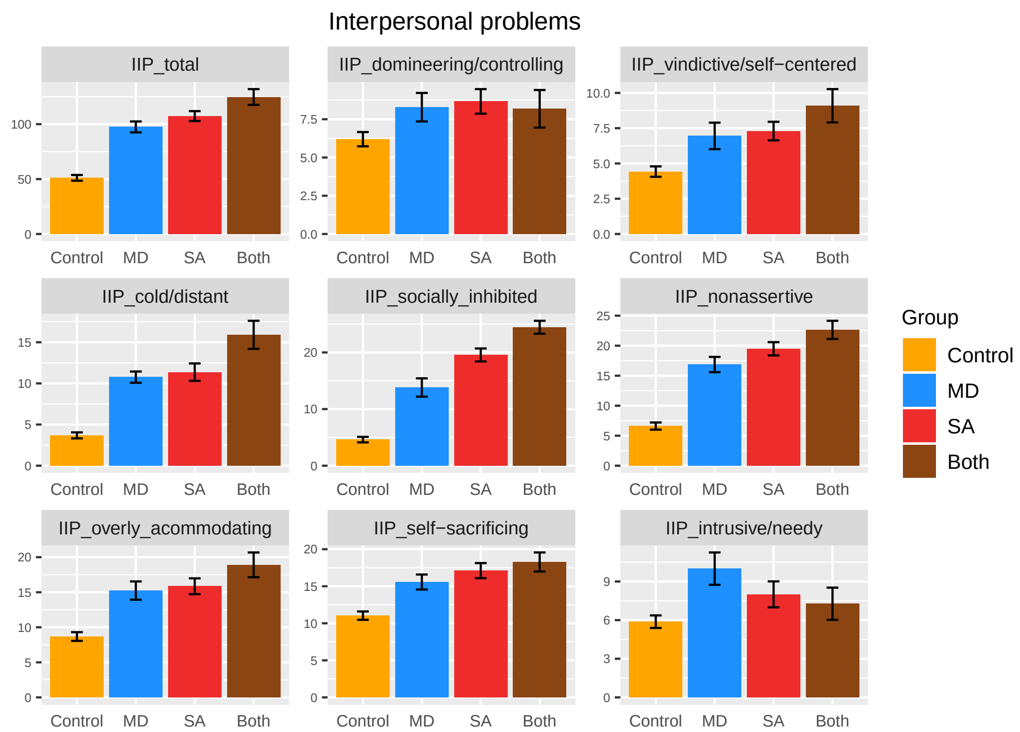


**Figure A2:** Scoring of inventory of interpersonal problems in healthy volunteers (Control), volunteers with symptoms of Major Depression (MD), with symptoms of Social Anxiety (SA) and with symptoms of Major Depression and Social Anxiety (Both MD&SA). Error bars depict one standard error. For more details see Table A2.

**Table A2:** Scoring of inventory of interpersonal problems in healthy volunteers (Control), volunteers with symptoms of Major Depression (MD), with symptoms of Social Anxiety (SA) and with symptoms of Major Depression and Social Anxiety (Both MD&SA).

| Questionnaire | Group | n | Mean | Std. Deviation |
|---|---|---|---|---|
| IIP-total | Control | 66 | 51.11 | 21.35 |
| | MD | 21 | 97.48 | 22.81 |
| | SA | 27 | 107.33 | 23.43 |
| | Both MD&SA | 11 | 124.73 | 23.79 |
| domineering/controlling | Control | 66 | 6.20 | 3.78 |
| | MD | 21 | 8.29 | 4.27 |
| | SA | 27 | 8.67 | 4.17 |
| | Both MD&SA | 11 | 8.18 | 4.07 |
| vindictive/self-centered | Control | 66 | 4.42 | 3.00 |
| | MD | 21 | 6.95 | 4.31 |
| | SA | 27 | 7.30 | 3.42 |
| | Both MD&SA | 11 | 9.09 | 3.91 |
| cold/distant | Control | 66 | 3.68 | 2.98 |
| | MD | 21 | 10.76 | 3.13 |
| | SA | 27 | 11.37 | 5.50 |
| | Both MD&SA | 11 | 15.91 | 5.65 |
| socially inhibited | Control | 66 | 4.61 | 3.98 |
| | MD | 21 | 13.81 | 7.40 |
| | SA | 27 | 19.56 | 5.95 |
| | Both MD&SA | 11 | 24.45 | 3.78 |
| nonassertive | Control | 66 | 6.61 | 4.84 |
| | MD | 21 | 16.86 | 5.84 |
| | SA | 27 | 19.48 | 5.75 |
| | Both MD&SA | 11 | 22.64 | 5.03 |
| overly acommodating | Control | 66 | 8.68 | 5.05 |
| | MD | 21 | 15.24 | 5.97 |
| | SA | 27 | 15.85 | 5.87 |
| | Both MD&SA | 11 | 18.91 | 5.86 |
| Self-sacrificing | Control | 66 | 11.03 | 4.59 |
| | MD | 21 | 15.57 | 4.63 |
| | SA | 27 | 17.11 | 5.29 |
| | Both MD&SA | 11 | 18.27 | 4.27 |
| intrusive/needy | Control | 66 | 5.88 | 3.96 |
| | MD | 21 | 10.00 | 5.75 |
| | SA | 27 | 8.00 | 5.24 |
| | Both MD&SA | 11 | 7.27 | 4.15 |

Table A2: For more details see Fig. A2.

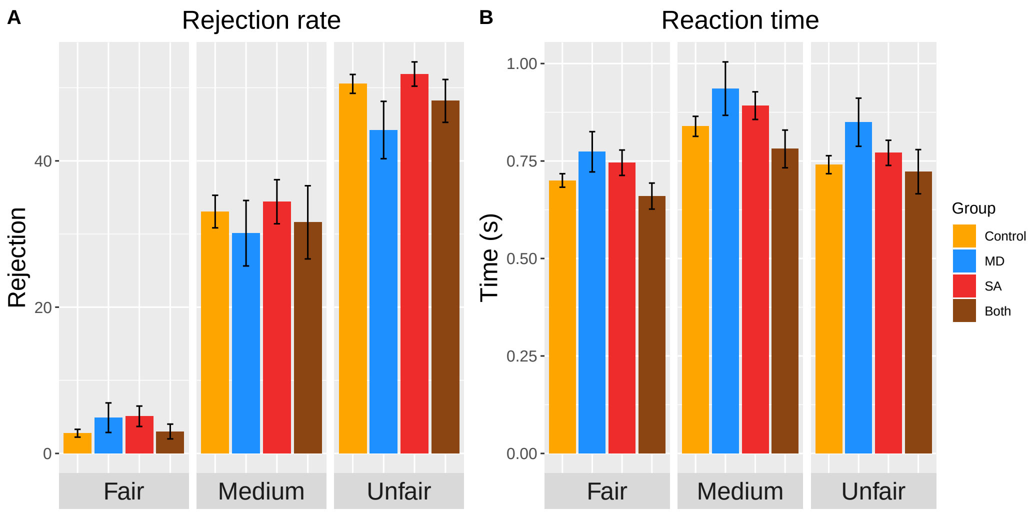


**Figure A3:** Rejection rates and reaction times during the Ultimatum Game in healthy volunteers (Control), volunteers with symptoms of Major Depression (MD), with symptoms of Social Anxiety (SA) and with symptoms of Major Depression and Social Anxiety (Both MD&SA). Error bars depict one standard error. For more details see Table A3.

**Table A3:** Rejection rates and reaction times in subgroups.

| Measure | Group | n | Fair | | Medium | | Unfair | |
|---|---|---|---|---|---|---|---|---|
| | | | Mean | Std. Deviation | Mean | Std. Deviation | Mean | Std. Deviation |
| Rejection rate | Control | 55 | 2.76 | 3.96 | 33.07 | 16.51 | 50.53 | 9.58 |
| | MD | 18 | 4.89 | 8.57 | 30.11 | 18.99 | 44.22 | 16.63 |
| | SA | 24 | 5.08 | 6.84 | 34.42 | 14.75 | 51.87 | 8.13 |
| | Both MD&SA | 10 | 3.00 | 3.20 | 31.60 | 15.82 | 48.20 | 9.27 |
| Reaction times | Control | 55 | 0.70 | 0.13 | 0.84 | 0.19 | 0.74 | 0.17 |
| | MD | 18 | 0.77 | 0.22 | 0.94 | 0.29 | 0.85 | 0.26 |
| | SA | 24 | 0.75 | 0.16 | 0.89 | 0.17 | 0.77 | 0.16 |
| | Both MD&SA | 10 | 0.66 | 0.11 | 0.78 | 0.15 | 0.72 | 0.18 |

Table A3: For more details see Fig. A3.

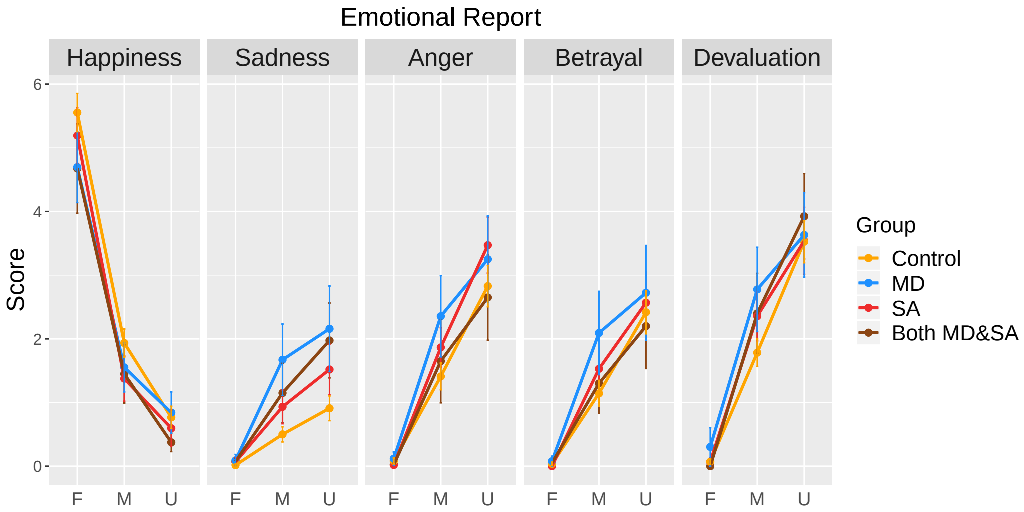


**Figure A4:** Emotions reported after playing the Ultimatum Game in healthy volunteers (Control), volunteers with symptoms of Major Depression (MD), with symptoms of Social Anxiety (SA) and with symptoms of Major Depression and Social Anxiety (Both MD&SA). Error bars depict one standard error. For more details see Table A4.

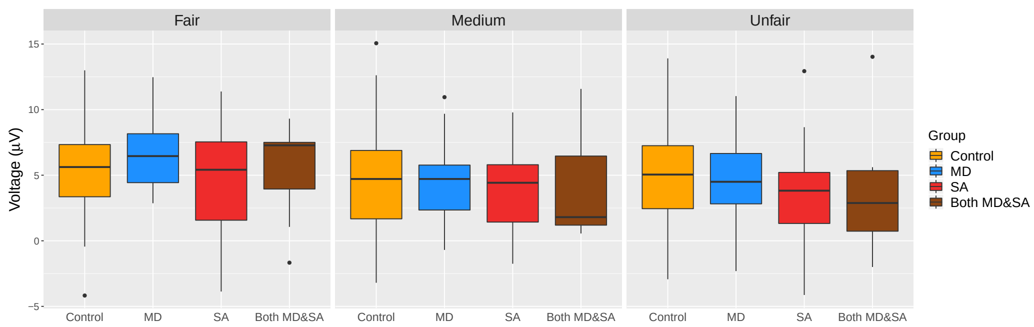


**Figure A5:** Medial Frontal Negativity in healthy volunteers (Control), volunteers with symptoms of Major Depression (MD), with symptoms of Social Anxiety (SA) and with symptoms of Major Depression and Social Anxiety (Both MD&SA). For more details see Table A5.

**Table A4:** Reported emotions in subgroups.

| Emotion | Group | n | Fair | | Medium | | Unfair | |
|---|---|---|---|---|---|---|---|---|
| | | | Mean | Std. Deviation | Mean | Std. Deviation | Mean | Std. Deviation |
| Happiness | Control | 61 | 5.55 | 2.34 | 1.93 | 1.72 | 0.77 | 1.37 |
| | MD | 19 | 4.70 | 2.43 | 1.55 | 1.68 | 0.84 | 1.41 |
| | SA | 26 | 5.19 | 2.23 | 1.38 | 1.81 | 0.60 | 1.45 |
| | Both MD&SA | 10 | 4.68 | 2.22 | 1.45 | 1.45 | 0.38 | 0.46 |
| Anger | Control | 61 | 0.08 | 0.36 | 1.41 | 1.63 | 2.83 | 2.53 |
| | MD | 19 | 0.12 | 0.46 | 2.36 | 2.78 | 3.25 | 2.96 |
| | SA | 26 | 0.02 | 0.10 | 1.87 | 1.58 | 3.47 | 2.24 |
| | Both MD&SA | 10 | 0.03 | 0.08 | 1.65 | 2.07 | 2.65 | 2.13 |
| Sadness | Control | 61 | 0.02 | 0.13 | 0.50 | 0.93 | 0.91 | 1.52 |
| | MD | 19 | 0.09 | 0.40 | 1.67 | 2.45 | 2.16 | 2.93 |
| | SA | 26 | 0.07 | 0.34 | 0.93 | 1.35 | 1.52 | 2.01 |
| | Both MD&SA | 10 | 0.08 | 0.17 | 1.15 | 1.47 | 1.98 | 1.86 |
| Betrayal | Control | 61 | 0.04 | 0.21 | 1.14 | 1.60 | 2.42 | 2.65 |
| | MD | 19 | 0.08 | 0.34 | 2.09 | 2.85 | 2.72 | 3.24 |
| | SA | 26 | 0.00 | 0.00 | 1.53 | 1.72 | 2.57 | 2.45 |
| | Both MD&SA | 10 | 0.05 | 0.11 | 1.30 | 1.49 | 2.20 | 2.11 |
| Devaluation | Control | 61 | 0.07 | 0.34 | 1.78 | 1.69 | 3.52 | 2.57 |
| | MD | 19 | 0.30 | 1.32 | 2.78 | 2.89 | 3.63 | 2.89 |
| | SA | 26 | 0.07 | 0.34 | 2.36 | 1.98 | 3.54 | 2.68 |
| | Both MD&SA | 10 | 0.00 | 0.00 | 2.40 | 1.99 | 3.93 | 2.12 |

Table A4: For more details see Fig. A4.

**Table A5:** Event-Related Potentials in subgroups.

| ERP | Group | n | Fair | | Medium | | Unfair | |
|---|---|---|---|---|---|---|---|---|
| | | | Mean | Std. Deviation | Mean | Std. Deviation | Mean | Std. Deviation |
| MFN | Control | 47 | 5.53 | 3.73 | 4.79 | 4.27 | 4.79 | 3.77 |
| | MD | 17 | 6.59 | 2.82 | 4.86 | 3.23 | 5.10 | 3.26 |
| | SA | 23 | 4.61 | 3.91 | 4.07 | 3.47 | 3.52 | 3.57 |
| | Both MD&SA | 9 | 5.31 | 3.72 | 3.99 | 3.78 | 3.57 | 4.63 |
| LPP/P300 | Control | 47 | 10.42 | 4.09 | 7.36 | 3.34 | 8.49 | 3.80 |
| | MD | 17 | 9.41 | 4.46 | 6.05 | 3.99 | 6.44 | 4.40 |
| | SA | 23 | 9.00 | 3.32 | 5.99 | 3.95 | 6.77 | 3.97 |
| | Both MD&SA | 9 | 8.91 | 6.18 | 5.47 | 3.39 | 7.76 | 4.62 |

Table A5: For more details see Fig. A5 and Fig. A6.

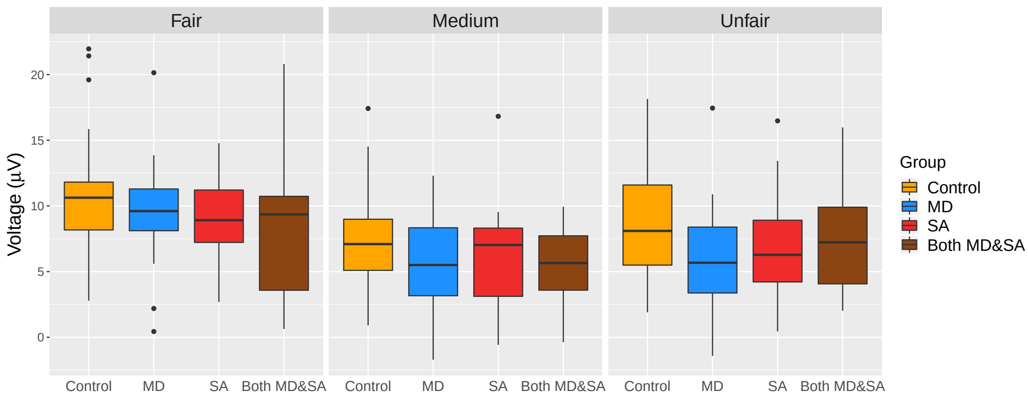


**Figure A6:** Late Positive Potential/P300 in healthy volunteers (Control), volunteers with symptoms of Major Depression (MD), with symptoms of Social Anxiety (SA) and with symptoms of Major Depression and Social Anxiety (Both MD&SA). For more details see Table A5.