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DEFICIT IN CO-REPRESENTATION IN MAJOR DEPRESSIVE DISORDER:

EVIDENCE FROM THE JOINT SIMON EFFECT

DEFICIT DI CO-RAPPRESENTAZIONE NEL DISTURBO DEPRESSIVO MAGGIORE:

UNO STUDIO SULL'EFFETTO SIMON SOCIALE

Relatore:

Chiar.mo Prof. CARLO MARCHESI

Correlatore:

Chiar.ma Prof.ssa CHIARA DE PANFILIS

Tutor:

Chiar.ma Dr.ssa MARIA LIDIA GERRA

Laureanda:

MARIANGELA CASELLA

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A nonna Angelina

Scusa se non ho fatto in tempo

Spero che tu sia orgogliosa di me

Mi manchi

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SUMMARY

Background

Social cognitive deficits are importantly involved in the pathogenesis and the consequences of Major Depressive Disorder (MDD). Deficit in "reading" social interactions has been found in acutely depressed patients, but it is still unknown whether it persists in the remission phase, contributing to psychosocial impairment. In this study, we hypothesize deficit in *action co-representation*, an automatic and dedicated social process, which reflects the ability to represent one's own and another person's actions, both in the acute and in the remission phase of depression. We also expect a positive and significant correlation between the deficit in co-representation and social functioning.

Materials and Methods

The sample included 35 patients with MDD, evaluated during the acute phase of depression; 25 patients with remitted MDD, re-evaluated during the euthymic phase (ET) and 38 healthy controls (HC). Participants completed the Joint Simon task (JST), which consists in the distribution of the complementary go-nogo parts of the standard Simon task across two participants. Subsequently, as control condition, they were administered the Standard Simon task (SST), which is a behavioural measure of conflict resolution. Participants are asked to respond to visual stimuli (shapes) by making a rightward response to one stimulus and a leftward response to another. The side of the display on which the shapes appear influences participants' speed of responding by either matching (i.e., corresponding trials) or not matching (i.e., non-corresponding trials) the side (left or right) associated with the shape. Psychometric tests were used to assess social and global functioning.

Results

Considering the JST, although we found a significant main effect of the Condition (Within subject effect: F1,95=1.09, p=.03), only HC displayed a Joint Simon effect, with significant difference between corresponding and non-corresponding trial (MDD: F1, 95=4.39 p=.25; ET: F1, 95=.63 p=.43; HC: F1, 95=4.39 p=.04). By contrast, in the SST corresponding stimuli were processed faster as compared to non-corresponding stimuli (Within subject effect: F1, 95=125.81, p<.001) in each diagnostic group (MDD: F= F1,95= 69.32, p<.01; ET: F1,95= 16.48, p<.01; HC: F1,95=58.04, p<.01), with significant Simon Standard effect. Considering both tasks patients with MDD, also in phase of remission, reported greater reaction times as compared with HC (Between subject effect: SST: F2,95=14.58, p<.01; JST: F2,95=20.68, p<.01). The 'missed-JSE', only for the ET group, was positive correlated with the social functioning scale (r =, 4; p <, 05) with a tendency towards significance with the global functioning scale (r =, 4; p <, 07)

Conclusion

Patients with MDD did not perform the social task with a relevant JSE, either in the acute phase of the disease or after symptom remission, presenting a "missed-JSE". The absence of a JSE in patients, as compared with HC, could be interpreted as a deficit of action co-representation, which seems to represent a stable element in MDD related with social dysfunction, regardless of symptoms remission.

1. INTRODUCTION

1.1. Major Depressive Disorder

Major Depressive Disorder (MDD), also called endogenous depression or unipolar depression, is a mood disorder defined by one or more major depressive episodes (MDE) and the lifetime absence of mania and hypomania.

To meet criteria for an MDE, five of nine symptoms are required to be present during the same 2-week period. One of these symptoms has to be depressed mood or anhedonia (loss of interest or pleasure). The required frequency and pervasiveness during the 2-week period somehow varies according to the symptom, but most of them have to be present "nearly every day".

The DSM-5 criteria for the diagnosis of major depressive disorder (DSM-5, 2013) are:

- Depressed mood
- Loss of interest or pleasure
- Change in weight or appetite
- Insomnia or hypersomnia
- Psychomotor retardation or agitation
- Loss of energy or fatigue
- Worthlessness or guilt
- Impaired concentration or indecisiveness
- Thoughts of death or suicidal ideation or attempt

The subject may have a single episode of Major Depressive Disorder or a recurrence of multiple episodes. In this case, we speak of Recurrent Major Depressive Disorder, where major depressive

episodes alternate with phases of total well-being (euthymic phase), distinctive of each individual. Over 2/3 of patients have been reported to have relapses; in particular, the probability of a relapse is 50%, after a first episode; whereas the probability of a third may be superior 90% after the second episode (DSM-IV-TR. ICD-10 / ICD-9-CM, 2007).

MDD is reported to be made a frequent and debilitating medical condition, associated with significant mortality and high costs for the public health system, due to its elevated recurrence and epidemiological features (World Health Organization, 2001; Kessler et al., 2003). Despite this, its pathophysiology remains an open chapter with many aspects yet to be understood.

1.2 Social functioning in Major Depressive Disorder

Clinically, MDD presents itself as a complex and heterogeneous disorder, characterized by depressed mood and anhedonia together with the involvement of various other dimensions such as sleep, appetite, endocrine functioning, motor skills and, last but not least, attention and cognitive abilities (Nelson and Charney, 1981). The latter would show an association with depressive symptoms (McDermott and Ebmeier, 2009), negatively affecting the patient's social functioning (Murrough et al., 2011; Evans et al., 2014).

The motivational and affective profile associated with depression could also influence the ability to perceive the sense of social belonging (Steger and Kashdan, 2009); in fact, patients reduce their social relationships and feel less interest in interpersonal situations (Nezlek et al., 2000).

Overall, depression has a close correlation with the expression of community behaviour, making inter-relational skills more deficient and secondarily reducing the patients' social support. Thus, it follows that stress increases, symptoms worsen and the healing period is prolonged. (Tse and Bond, 2004).

The social dysfunction could be underlying several psychopathological components of MDD. A prominent role could be played by the decrease in concentration with the tendency to orient thoughts

towards oneself (Mor and Winquist, 2002), following the persistent thinking pattern called rumination: "thoughts that focus the person's attention on their depressive symptoms and on the implications of these symptoms "(Nolen-Hoeksema et al., 2008). Social anhedonia, the loss of interest and pleasure in societal contacts, would also play an essential role in determining the social dysfunction of depressed patients (Gurtman, 1987; Clark and Watson, 1991; Watson et al., 1992; Tse and Bond, 2004).

1.2.1 Social functioning in Recurrent Major Depressive Disorder

Social and interpersonal functioning has always played an effective role in the clinical fields of various psychopathological contexts; as a matter of fact, it is greatly influenced in major depressive and anxiety disorders, also after remission (Saris et al., 2017).

Santini et al. (2015) demonstrated that affective indicators, such as perceived support, are more important for social functioning in depression than behavioural indicators, such as received support. Actually, increased levels of perceived are influential in the onset of depression. It has been noted that the quality of life and well-being in social and subjective interactions is lower in anxious patients compared to healthy controls. (Cramer et al., 2005).

Moreover, social functioning is highly affected in depressive disorder patients and, specifically, in those with comorbid anxiety and depression, notwithstanding the little accurate literature. Residual impairments have been recorded to remain, even after complete remission, and social dysfunction to be a predictor of future psychopathology. (Saris et al., 2017).

A specimen of people with MDD, Dysth or DD has been analysed by Rhebergen et al. (2009) over a three-year period of differences in social and physical functioning after remission, compared to people without diagnosis. The results illustrate the long-term debilitating effects of psychopathology. Damaged recovery of functioning is associated with long-term symptoms; in fact, a slower and less

functional recovery has been manifested in subjects with dysthymia (with or without superimposed DCS), even after three years.

In a study by Furukawa et al. (2010), a moderate to extremely large social dysfunction was found in major depressed patients at the point of treatment starting. A rapid decrease was noted in the first six months of treatment; however, consecutively, fluctuating patterns were showed up to 10 years of follow-up.

1.3 Theory of Mind in MDD

Taking into consideration a broader and not necessarily pathology-oriented vision, we may talk of "social cognition" to mean the set of processes that allows an individual to interact with members of the same species. Such processes include the understanding of other people's experiences, intentions and, therefore, actions, favouring the ability to act in the community context (Adolphs, 1999; Ochsner and Lieberman, 2001), through the multidimensional concept made up of affective and cognitive processes (De Jaegher et al., 2010).

One of the main components that make up social cognition is the Theory of Mind (ToM; Green et al., 2008), i.e. the ability to understand the intentions, dispositions and perspectives of the other (Frith, 1992; Baron-Cohen, 2001). ToM is significantly impaired in affective disorders, both in unipolar and bipolar depression (Bora et al., 2016; Bora and Berk, 2016), in both acute and sub-acute phases. Numerous evidence is found that, even during complete remission of symptoms, therefore when patients are in euthymia, ToM remains considerably altered (Mitchell and Young, 2016; Dalkner et al., 2019). The general functioning of the patients, measured with the VGF scale (DSM-IV-TR, 2000) is substantially correlated with the ToM abilities of the patients themselves (Vlad et al., 2018) and the same is true for the affective symptomatology with the ToM (Bora and Berk, 2016). It is, therefore, likely that alterations in ToM have important findings in the lives of depressed patients, with repercussions on their life quality, thus being able to predict possible relapses (Inoue et al., 2004;

Inoue et al., 2006). Understanding cognitive deficits related to the social dimension, defined as an independent dimension from affective symptoms, could allow new therapeutic strategies in the treatment of depression (Murrough et al., 2011). Socio-cognitive deficits should be identified in patients to ensure a treatment path that is more efficient in obtaining a complete stabilization of the psychopathological picture (Hoertnagl et al., 2014).

Nowadays, the ToM is usually measured through tests involving the observation of faces' images or videos of people; the subject is subsequently asked to deduce the emotions and thoughts of the people depicted. This method is quick, practical and inexpensive, but requires the conscious participation of the subjects involved into the evaluation, since data could be influenced by the will of the participants in the study (Baron-Cohen et al., 2001; Dziobek et al., 2006; McDonald et al., 2006; Stone et al., 1998). Other researchers on ToM have been carried out independently of the subjects' will, however using an expensive optical reader of the ocular position and quite elaborate experimental situations (Keysar et al., 2003).

Another possibility, still under research, and so far not used on people suffering from affective disorders, comes from the study by Humphreys and Bedford (2011). The Authors pointed out that the neurobiological processes of ToM were also involved in another phenomenon, called the Joint Simon Effect.

1.4. The Simon effect and its social variant

Simon's standard task consists in presenting a subject with two different stimuli (e.g., a high-pitched sound and a low-pitched sound or a rhombus and a circle). The two stimuli are presented individually and in random succession or to the right or left of the median line of the subject. Regardless of the spatial localization of the stimulus, (irrelevant component of the stimulus) the subject has to respond (e.g., press a button or move a lever) to the right or left of his own midline. The specific response to

that side of the subject is given only in relation to the specific stimulus (relevant component of the stimulus; e.g., if the symbol is the circle or the rhombus; Simon, 1969; Simon and Craft, 1970).

For example, participants have to move a lever to the right when they hear a high-pitched sound; instead, they have to respond with a movement to the left when the sound is lower, regardless of whether the sound is to the left or right.

In this type of task, the responses are typically faster when the side where the stimulus is presented corresponds with the side where the response is performed. At the same time, the performance turns out to be lower when there is no spatial Stimulus-Response (SR) correspondence: this phenomenon is known as Simon Effect (SE; Simon, 1990).

It has been possible to reproduce the SE also using other types of stimuli, for example somatic-sensory as well as acoustic and visual, and different spatial organizations of SR such as horizontal and vertical (these works have been reviewed by Proctor and Vu, (2006) and Hommel, 2011).

Several explanations have been proposed for the SE; some Authors (e.g., Kornblum et al., 1990; De Jong et al., 1994) explain that the SR spatial correspondence facilitates response performance by means of direct association. Other authors argue that the spatial correspondence between stimulus and response prepares attention to other events with spatial correspondence (e.g., Nicoletti and Umiltà, 1989; Nicoletti and Umiltà, 1994). Another hypothesis (Hommel, 1993; Hommel et al, 2001) is that the stimulus and the response are coded on a cognitive level in the same representative domain of perceived event and acted event, when these are in the same position, thus favouring a more immediate response.

The so-called dual-route model (De Jong, 1994) describes the SE as an interaction between two different codes: a code which is activated automatically by the position of the stimulus (irrelevant component of the stimulus); and a code which is activated by the information provided to the subject (relevant component of the stimulus). The non-corresponding position of the stimulus, even if

irrelevant for the purpose of the task, cannot be ignored by the cognitive system of the subject that automatically activates a corresponding spatial response, which has to be corrected to comply with the instructions of the task. The consequence is an interference that causes a delay in response (Umiltà et al, 1999).

Actually, it is interesting to note that SE is lost as soon as the spatial coding of the response is eliminated (Hommel, 1996). For this purpose, it is sufficient to ask the subject to carry out the task by answering a single symbol; then executing the answer even from one side only (e.g., pressing only the button on the right and only when the diamond appears and doing nothing when the circle appears). This type of task is called go-nogo: the subject has to give only one type of response (so-called 'go') when only one specific stimulus appears and not perform any action when the other stimulus appears (so-called 'nogo'). Since there is only one response modality, its spatial coding is lost and so is the SE (Liepelt et al., 2011; Hommel, 2013). Only a response that is encoded in the subject's space can be automatically activated by a stimulus encoded in the subject's space (Ansorge and Wöhr, 2004).

However, when the same go-nogo task is administered to two participants simultaneously, where each responds from one side only to a specific symbol assigned to him (joint / social go-nogo Simon task), it is possible to observe an SE (Sebanz et al., 2003) known as the Social Simon Effect or Joint Simon Effect (JSE).

In the go-nogo task with two participants, each of them responds more quickly when the stimulus to which he has to respond appears on the same side where he himself is. Similarly, an SR non correspondence is associated with a latency in the response (about 11 ms; Sebanz et al., 2003) which consists of an interference (Ferraro et al., 2011) similar to what occurs in the standard task of Simon.

The concept that it is not possible to observe an SE in a go-nogo task carried out individually (Kornblum et al., 1990; Umiltà and Nicoletti, 1990) is well established. However, the debate is still

open regarding what generates the JSE, which is documented when the same task is no longer carried out individually (Mussi et al., 2015).

Some authors see in the JSE the existence of a cognitive co-representation of the action of others. Therefore, the subject would carry out a standard SE within his own cognitive representations. On the one hand, he has the cognitive representation of what he himself does; on the other hand, he has the representation of what the other close subject (co-actor) has to do in a social and interactive context between the participants. (Sebanz et al., 2003; Knoblich and Sebanz, 2006; Sebanz et al., 2006, Sebanz and Knoblich, 2009, Tsai and Brass, 2007; Vesper et al., 2010; Möller et al., 2011a, b; Kiernan et al., 2012). In this context of co-representation, the subject becomes one with the co-actor, his own hand and the hand of the other being a single body (Welsh, 2009).

Other authors explain the JSE as a representation of the same person sitting next to him (Lugli, 2015), rather than his own action. Consequentially, the interference would not be determined by a conflict in the SR spatialisation (spatiality), but something more inherent to the discernment between oneself and the other. *"The symbol appeared on the other side: is it my turn to answer now?* (Philipp and Prinz, 2010; Wenke et al., 2011; Karlinksy, 2017).

Yamaguchi et al. (2018) hypothesize that the subject is influenced both by the action that the other has to perform and by the stimuli referred to the latter. Stenzel et al. (2014) showed that the JSE was markedly influenced by the co-actor's actions and less by their intentionality to answer, with a JSE more expressed when the co-actor acted in responding as an expression of his intentionality.

Some studies have questioned the purely social origin of the JSE, proposing it as the consequence of sharing one's own peripersonal space (Guagnano et al., 2010); however, the results are not always replicable and the non-social origin of the JSE might be an anomaly (Welsh et al., 2013). In favour of the non-social hypothesis, the JSE was induced in an individual go-nogo task by accentuating the spatialization of the stimuli. Through a specific preparation towards spatial stimuli, the effect was also reduced until it disappeared in a subsequent social task, thus making the Authors lean towards a

spatial origin (Dittrich et al., 2013), however without excluding that the latter might be in the cases influenced by social parameters (Dittrich et al., 2012; Porcu, 2016). The effect has also been understood as the product of an attentional phenomenon, which sees the close subject as a distraction that induces a spatial coding in the responses (Milanese et al., 2010; Milanese et al., 2011; Dolk et al., 2011; Dolk et al., 2013; Dolk and Liepelt 2018; Liepelt, 2014; Klempova and Liepelt, 2015; Doneva and Cole, 2014). Then a JSE was documented when, instead of another human being, the subject performed the task with a metronome next to him (JSE = 8 ms), a vintage table clock with spheres rotating under the dial (10 ms) or the small Japanese statue of the cat waving with its paw (19 ms; Dolk et al., 2013). Similar results were also offered by Stenzel and Liepelt (2016), with a task between human subject and object or digital image. The study was replicated with the statue of the Japanese cat; the JSE was documented as long as the object was visible, had something moving and emitted a sound when moving (JSE = about 10 ms) or if the movement was audible with the object out of the visual field (about 5 ms; Puffe et al., 2017). However, these results need to be interpreted with care, given that minimal task execution parameters can pollute the results and create a JSE attributable to a nearby researcher, rather than to the Japanese cat statue (Michel et al., 2018).

A JSE was also documented when the experiment was performed with the silent and immobile image of a wooden hand (JSE = approximately 14 ms), and in the same subjects only a minimal JSE (approximately 4 ms) was recorded when the test was performed. Instead, when performed with the representation of a human hand, the minimal JSE was only valid for subjects who had just watched a Pinocchio film with touching scenes related to the wooden puppet. Candidates who had just watched a normal love comedy with human actors had a JSE of 11 ms with the human hand image and 5 ms with the wooden hand image (Mölller et al., 2011a). Under neutral experimental conditions, only the image of a human hand moving, and not that of a wooden hand, is capable of evoking a significant JSE (9 ms; Tsai and Brass, 2007).

Even when the test was performed only among humans, the results were quite inconsistent.

If the participants were sex-matched couples, a JSE was documented between 7 and 15 ms; the effect sometimes reached 0 instead, and lost significance when the participants were a male and a female (Mussi et al., 2015; van der Weiden et al., 2016).

In another study, the subjects were all recruited together, placed in a room, and then divided into two groups; the members of each group were motivated towards their belonging to the newly invented group and, in the meantime, they experienced (induced) emotions that were not free from rivalry towards the other group. Once called to do the task, a JSE of about 8 ms was observed when both subjects belonged to the same group and no JSE if they belonged to two different groups (McClung et al., 2013). Previously (2011) Iani et al. demonstrated that, actually, it is not the belonging to a defined group that made the JSE significant, but rather the interdependence understood as cooperation between the subjects (Iani et al., 2014). However, the results can also be interpreted in terms of attention: towards oneself in competition, towards the other in cooperation (Mendl et al., 2018).

Consistent with the interdependence hypothesis, when subjects played tetris together before the task, those who previously played competitive tetris then performed the task with a 10 ms JSE, with a significant difference (15 ms JSE) compared to those who previously played cooperatively (Ruissen and de Bruijn, 2016). Those who experienced social inclusion occurrences carried out the Joint Simon task with a JSE (9 ms); on the contrary, the effect was not significant for those who experienced social exclusion (Costantini and Ferri, 2013). Lavender, with a scent capable of relaxing and stimulating attention towards inclusion, increases the JSE; on the other hand, a smell associated with restless and exclusionary attention states, such as peppermint, reduces the effect (Sellaro et al., 2015).

When the go-nogo task took place between two people, who had been dating in friendship for at least six months, the JSE turned out to be about 9 ms, but it became only 3 ms when the two participants were two strangers (Ford and Aberdein, 2015). In another go-nogo task there was a higher JSE between two partners in love (about 8 ms) than between two friends (about 4 ms; Quintard et al., 2018).

Subjects receiving oxytocin administration had a marked and significant increase in JSE compared to those receiving placebo, without this resulting in any difference in standard SE (Ruissen and de Bruijn, 2015).

In Buddhist subjects, therefore belonging to a collectivistic culture, a significantly higher JSE (18 ms) was recorded, than in atheistic subjects (10 ms; Colzato et al., 2012b). In other subjects, a collectivistic awareness was induced by asking them to circle in a text pronouns of the first person plural. They performed the task with a significantly higher JSE than subjects who had to search for pronouns of the first person singular in the text, and who had carried out an activity that would develop individualistic awareness (Kiihnen and Oyserman, 2002; Colzato et al., 2012a).

Another study found that the JSE (17 ms) was documentable in individuals who perceived themselves to be of low social class and who performed the test with perceived individuals of high social class, but not vice versa (Aquino et al., 2015).

Those who performed the task with friendly and reassuring individuals had a JSE of 16 ms; whereas, if the task partner was intimidating, and therefore the subject experienced emotions of insecurity and irritation, it was not possible to register a JSE (Hommel et al., 2009). The JSE was modulated by emotions even when induced by a film that had been watched shortly before. Those who had just watched "Harry and Sally" were in a good mood (7.6 points on the scale of Russell et al., 1989) and had a JSE of over 15 ms; those who had just watched "The Champ" were in a bad mood (4.7 points) and did not have a significant JSE (Kuhbandner et al., 2010).

The JSE is, therefore, sensitive to the modulation of both social and non-social factors (Dolk et al., 2011), such as moving and playing objects which attract attention, or people towards whom emotional closeness, cooperation and similarity are experienced. The same also applies to images or representations charged with these values. Perhaps it is possible to think of a multifactorial origin of the JSE, in case it would be reasonable to consider this effect as a sensitive parameter rather than a specific indicator.

The study by Wen and Hsieh (2015) does not disconfirm this perspective. The subjects performed the go-nogo task alone but with always-false awareness, without knowing that the task was shared with another person in another room; or with a computer connected remotely. In both cases, a significant and superimposable JSE was documented; the researchers went further and also measured the brain activity of the subjects. Although the JSE was always present, the activated brain areas were different. Only when the subjects thought they were sharing the task with a human being, could an activity in the median pre-frontal cortex be documented, "an area dedicated to understanding the thoughts and intentions of others and which could reflect a cognitive social aspect in the discrimination between self and other during the Joint Task". The results were not fully reproduced in the study by Sahai et al. (2019).

The meta-analysis by Karlinsky, Lohse and Lam (2015) offers numerous original contributions to the field of joint action. First of all, the significant work emerging since the introduction of the Joint Simon Task has been evaluated thanks to the application of quantitative methods (Sebanz et al., 2003). Second, the size of: (1) the overall JSE, (2) the JSE, with replicated original conditions (see Sebanz et al., 2003), and (3) the JSE, with anticipated elimination or reversal of the effect, have been explored. Third, an analysis of the individual go/no-go (IGNG task), considered as an important control when investigating the JSE and interpreting its joint effects, has been included (e.g., Sebanz et al., 2003). Such meta-analysis suggests the reliable although small effect of JSE (summary d = 0.26). However, it also showed considerable data asymmetry, thus indicating potential publication bias. In detail, due to the fact that data are positively inaccurate, more small “positive” than negative result studies are being published. The “real” effect size revealed itself to be even smaller than it first appeared (d = 0.17) when reducing the analysis to great samples. Consequentially, (1) an adequate sample size is needed to achieve statistical power; (2) a limited “practical” significance of such effect might be observed. It has also been noticed that the IGNG random-effects model is reinforced by the small JSE effect size.

No significant JSE was documented if the task was done with a computer instead of a person. In the work of Sellaro et al. (2013) no JSE was documented when the task was shared with an individual who was in another room, therefore not physically next to him.

In conclusion, it can be assumed that when the task is performed in 'traditional' ways and, among other things, between two people, the literature offers solid documentation that social factors, co-representation of the other, emotional and affective resonance compared to the above-said other, play an important role in the genesis and modulation of the JSE. Such factors represent the cognitive abilities of the Theory of Mind and they confirm what documented by Humphreys and Bedford (2011; Introduction, § 1.1.). Compared to the JSE evaluation in the psychiatric field, a vast literature is not available today. Sebanz et al. (2005) recruited eight high-functioning autism patients who performed the task with a significant JSE. Liepelt et al. (2012) recruited patients with schizophrenia and did not document any JSEs. De la Asuncion et al. (2015) obtained a significant effect in patients suffering from schizophrenia (17 ms) and even greater than in healthy controls (7 ms). In the study by Van der Weiden et al. (2016), the JSE was not influenced by sub-clinical psychotic symptoms or by interpersonal distress, as measured by the Interpersonal Reactivity Index scale (IRI; Davis, 1980; Davis, 1983).

1.5. The present study

To date no previous studies evaluated patients with MDD Simon or Joint Simon paradigms. Searching PubMed (www.ncbi.nlm.nih.gov/pubmed) for the following words (without quotes): "social simon effect", "social simon task", "social simon paradigm", "social simon action "," joint simon effect "," joint simon task "," joint simon paradigm "," joint simon action ", it was not possible to find any work that included depressed and / or bipolar patients in both acute and euthymic phases.

This study intends to evaluate the basis of the social functioning of patients during the acute and remission phase of MDD, using the JSE paradigm (Sebanz et al., 2003). The results are compared

with a group of sex- and age-matched healthy controls. Each subject is also administered a standard Simon task as a confounding variable of general cognitive and attentional performance.

To understand the results of the behavioural tasks properly, several clinical variables described in the next chapter have also been taken into consideration.

The hypothesis is that patients show a reduced JSE compared to controls, as a consequence of an alteration in ToM.

2. MATERIALS AND METHODS

2.1. Participants

The protocol of this research work was approved by the Ethics Committee of Parma. The patients taking part in this study were recruited while they were being treated at the Integrated Welfare Department of Mental Health and Pathological Addictions (DAI-SMDP) in Parma, and subsequently contacted by telephone to perform the evaluation in euthymic phase. Healthy controls are people who have never suffered from any psychiatric pathologies; therefore, they belong to a non-clinical population and have been selected through word of mouth. No participant received any monetary or other compensation.

The subjects agreed to participate in a research work aimed at evaluating "Individual characteristics, depressive symptoms and attention skills". In order to safeguard the ecological validity of the research, no mention was made of the aims inherent to mutual social co-representation. In this way, possible bias induced by the awareness of the participants were eliminated.

During the first meeting, the purpose of the study was explained to the subjects, with the above-said precautions; their interest in participating as well as their ability to express valid informed consent were evaluated. Each consent form was signed in the presence of the recruiting physician, who made himself available to provide any further explanations and clarifications.

The complete description of the purposes of the study (including the interest in possibly documenting the social capacities to co-represent the other) was always provided for the Healthy controls at the end of the experimental measurements. The same happened for patients at the end of the experimental measurements performed in the euthymic phase or by telephone a few months after, when the patients already identified in the depressive phase were contacted and did not make themselves available for the subsequent evaluation in euthymic phase.

All subjects underwent an initial diagnostic screening to determine their eligibility for the study. Only those who met the following criteria were chosen.

Exclusion criteria for the whole participant sample group:

- Diagnosis of any psychotic disorder (past or present);
- Substances addiction;
- Cognitive impairment (based on clinical judgment);
- Left-handedness, identified by Edinburgh Handedness Inventory (Oldfield, 1971).

General inclusion criteria for the whole sample:

- Age between 18 and 60 years;
- Good understanding of the Italian language;
- Good visual capacity possibly also by means of correction.

Inclusion criteria for the patients group with Major Depressive Disorder (MDD):

- Diagnosis of MDE by the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I; First et al., 2002).

Inclusion criteria for the patients group in euthymic phase (ET):

- Having previously been recruited and therefore belonging to the group with MDD;
- Complete remission of symptoms for at least two continuous months.

Inclusion criteria for the healthy control group (HC):

- Absence of previous or current psychiatric illnesses, as reported by the subject and verified through an interview with the recruiting doctor;

- Score < 4 for each personality disorder at the Structured Clinical Interview for DSM-IV Axis II Disorders. (SCID-II; First et al., 1997).

The final participant sample group was selected in a period between 1 September 2015 and 1 February 2019. The sample includes 35 patients evaluated during the acute phase of an MDE (20 females, 57%; age group average: 50 years), 25 patients evaluated in euthymic phase (13 females, 52%; age group average: 51 years) and 38 healthy controls (22 females, 58%; age group average: 50 years).

Two patients were excluded and, consequentially, not reported above and in subsequent analyses due to the fact that they performed behavioral tasks with a high number of errors, which compromised the effective recording of responses.

Out of the group of 35 patients evaluated in acute phase (MDD), 23 patients (66%) suffered from a Major Depressive Episode (MDE) in the context of MDD; out of the 23 patients, 13 had already suffered from the same pathology in the past. Other 10 (29%) suffered from MDE in the context of Bipolar Disorder type 1 and this was not the first MDE. The remaining two patients (5%) faced MDE in the context of Bipolar Disorder type 2, even though it was not their first depressive episode. Out of the 35 patients evaluated in T0, two suffered from Obsessive Compulsive Disorder (OCD), one had formerly suffered from Psychotic Disorder Not Otherwise Specified, and another one had previously suffered from Dysthymia.

In 25 patients re-evaluated in euthymic phase (ET), 14 patients (56%) had earlier suffered from MDE in the setting of unipolar depression. Other eight patients (32%) had suffered from MDE in the setting of Bipolar Disorder of type 1, and the remaining two had suffered from MDE in the context of type 2 bipolar disorder. In the 25 patients re-evaluated in Tl, two suffered from OCD and one had once suffered from Psychotic Disorder Not Otherwise Specified. As can be seen, not all patients evaluated during the acute phase were later evaluated also in euthymic phase. As a matter of fact, 10 of them could not be recruited for the second evaluation: eight patients refused the re-evaluation in euthymic

phase, due to transport difficulties and problems in reaching the place of task execution. Two patients had serious clinical conditions and were therefore unable to participate in the subsequent evaluation.

2.2. Pre-experimental measurements

- *Demographic questionnaire*: it collects the personal data of the subjects, such as gender, age, educational qualification, marital status, employment status, nationality.
- *Structured Clinical Interview for DSM-IV Axis I Disorders, Patient edition* (SCID-I / P; First et al., 2002): it is a semi-structured interview conducted by the doctor to investigate Axis I disorders according to the DSM-IV. It is used to ensure compliance with the inclusion and exclusion criteria.
- *Global Assessment of Functioning* (GAF): it is a hetero-administered scale based on clinical judgment to evaluate social, occupational and psychosocial functioning in adults on a directly proportional numerical scale from zero to 100 (DSM-IV-TR, 2000).
- *Social Adaptation Self-Evaluation scale* (SASS; Bosc et al., 1997): it was developed to assess social motivation and behavior. It investigates different areas of social functioning, including work, leisure, environmental organization and coping skills. It is a self-administered test of 20 items, ranging from zero (no social adaptation) to three (maximum social adaptation). The total score on the scale can range from zero to 60; the social malfunction is defined by a score < 35.
- *Hamilton Depression Rating Scale* (HAM-D; Hamilton, 1960): it is a test that evaluates the severity of depressive symptoms using a hetero-administered scale composed of 21 items whose scores are directly proportional to severity. The threshold that excludes the presence of depressive symptoms is equal to seven points.

- *Hamilton Anxiety Rating Scale* (HAM-A; Hamilton, 1959): it is like the previous one but made up of 14 items, to evaluate the severity of anxious symptoms.
- *Physical Anhedonia Scale and Social Anhedonia Scale* (PAS and SAS; Chapman et al., 1976): they aim to measure hedonic abilities as personal trait features, both in relation to sensory experiences (e.g., tactile, gustatory, auditory, visual, sexual, motor) and to social interpersonal situations. They are self-administered tests in the form of questionnaires with "true or false" answers, respectively composed of 61 and 40 items. Higher scores indicate higher levels of anhedonia. II cut -off to define an anhedonia-affected subject is a higher score than 12 in the SAS and greater than 18 in the PAS.
- *Temporary Experience of Pleasure Scale* (TEPS; Gard et al., 2006): this scale also investigates pleasure; the hedonic aspects of experiences are divided into two dimensions: the anticipatory (10 items) and the consumer (8 items) for 18 items in the form of a self-administered quiz where the scores are inversely proportional to the levels of anhedonia.
- *Ruminative Response Scale short form* (RRS; Treynor et al., 2003): it measures the ruminative activity of the subject through a self-administered questionnaire consisting of 10 items, which distinguish the ruminative aspects in "reflection" (R) and "brooding" (B). With a neutral value, the former refers to the ability to reflect in order to react to problems and solve them; whereas, the second refers to a gloomy and anxious meditation on one's own difficulties. The scores are directly proportional

2.3. Experimental measurements

2.3. a. Joint Simon Task

The task takes place in a quiet room and dimly lit with two participants at a time, one of which is the subject to be examined (Figure 1, represented in black) and the other a co-actor of the same sex and similar age of the subject (Figure 1, represented in gray). The co-actor is usually a person who works in the clinic, playing an equal participant role to the subject, having minimal circumstantial interactions with the subject and maintaining a neutral attitude. The two participants do not know each other and have not met previously; after a brief greeting, they sit at a table next to each other, the subject always being seated to the right of the co-actor. Both rest their heads on a height-adjustable chin rest. On the table and about 57 cm from the faces of the participants is located a 28-inch screen, where the stimuli of the task will appear. The chin guards are adjusted so that the height of the participants' pupils coincides with the height of the screen center. Opposite each subject, central to the participant's midline, an Italian keyboard is also located, used to respond to the stimuli presented.

The subject and co-actor are assigned a specific symbol to respond to, either a circle or a rhombus; each symbol on the screen occupies a viewing angle of 1 ° in height and 1 ° in width. The assignment of the symbol to the participant is random and based on the numeric ID that makes the subject's participation anonymous (e.g., all subjects with an even ID number always respond to the circle).

In the center of the screen there is a white cross that the participants have to fix during the task without making eye movements; the participants must perceive the stimuli with peripheral vision. The rhombus and the circle appear one at a time, alternating or repeating in a random sequence; they appear randomly arranged in a specific position or to the right or left of the central cross, and the position has a distance from the central cross of 6.5° of the viewing angle.

The participant sitting on the right is always the evaluated subject; he responds to the assigned stimulus regardless of the position where it appears; to respond he uses the index finger of his right hand and presses a key located on the right of the keyboard in front of him (the letter "L"). The other participant, sitting on the left, is always the co-actor; he always responds to his assigned symbol by pressing a key located on the left of the keyboard in front of him with the index finger of his left hand (the letter "A"). Even in this case, the position of appearance of the stimulus is irrelevant for the response.

The lateral position of appearance of the symbol and the lateral position where the response is given replicate the spatial coding of the response as expected for the detection of a Simon effect, which, in this specific task, would be called "Joint Simon Effect" (Introduction; § 1.2.).

Each symbol appears with a variable latency between 600 and 1000 ms and remains visible on the screen until a participant presses an answer key; if no one responds, the symbol remains visible for 1000 ms, then it disappears, and any subsequent response is not recorded. If one participant responds to the symbol assigned to the other subject, the symbol disappears; the response is internally recorded as an "error" and the computer emits a short warning sound for the error made. Participants are carefully trained to respond as quickly as possible, and making as few mistakes as possible.

The task begins with a test session; the participants know that the responses are not recorded and they become familiar with the experimental dynamics described above; the test presents 51 stimulations to be answered. Subsequently, 408 stimulations are presented divided into 24 units of 17 stimuli each. Each unit of 17 stimuli is separated from the next by a pause screen; participants freely decide how long the pause will last. Each stimulus can be "corresponding" if it appears on the same side where the response is given, or "non corresponding" if it appears on the affixed side (e.g., if the patient responds to the circle, a non corresponding stimulus is a circle appearing on the left).

The collection of responses and the presentation of stimuli is performed by the "E-Prime" program, version 2.0 (Psychology Software Tools, Inc.).

In this way, the assessed subject performs a go-no go task (Introduction, §1.2.). Healthy control group is expected to show a significant difference in response times between corresponding and non corresponding stimuli; if this difference is noteworthy, it takes the name of Joint Simon Effect (JSE). As already described (Introduction, §1.2.), if measured under classical and neutral experimental conditions, this effect could reflect the social capacity of the individual to co-represent and, therefore, to mentalize others' actions and intentions (Theory of Mind, ToM). This would allow spatial coding of the response because the healthy control group would perform the task with its right hand and with the mental representation of the co-actor's left hand (Introduction, §1.3.). On the other hand, lower social capacities of co-representation (i.e. a reduction or absence of the JSE) are expected in patients both in the acute phase and in the remission phase, having these documented alterations in the performance of ToM (Introduction, § 1.3.).

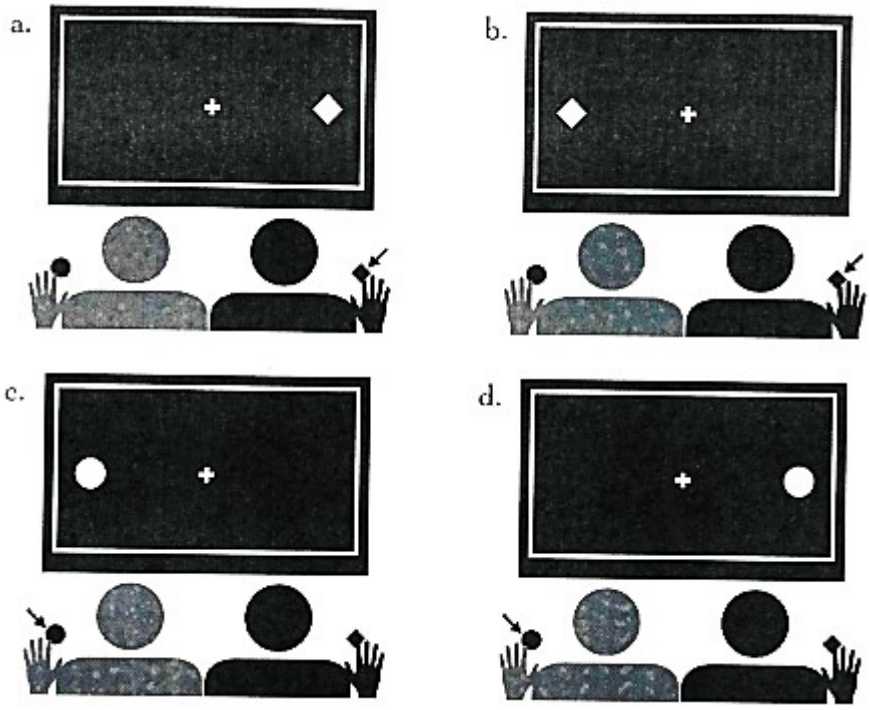


Figure 1: a schematic representation of the experimental situation of the Joint Simon Task is provided. For major clarity, the keyboard is not shown; only the answer key can be seen, which is shown with the symbol it is associated with during the task. An arrow represents the participant's correct response action to the stimulus. In gray and to the left is the co-actor, black and right of the rated entity.

The images show the following:

a) The assessed subject responds to a corresponding stimulus.

b) The assessed subject responds to a non corresponding stimulus.

c) The co-actor responds to a corresponding stimulus.

d) The co-actor responds to a non corresponding stimulus.

2.3. b. Standard Simon Task

At the end of the first part (Joint Simon Task § 2.3.a.), the co-actor leaves; it is explained to the subject that the co-actor has already played the part individually or that he will play it later. The subject is asked whether he perceived the interaction with the co-actor as friendly / goliardic, neutral / conscientious, competitive / tense.

Now the subject sits alone at the table, the co-actor's keyboard is put away.

The task is restarted, this time in standard modality; it is explained to the subject that he will have to do what he did before, but this time by also answering the other symbol (to which the co-actor previously replied) using the index finger of his left hand and pressing the leftmost key on his own keyboard (the letter "A"). The experimental conditions are faithfully repeated; in fact, since the response to the symbol is assigned according to the numeric ID of the participant, he will respond with the index finger of the right hand to the same symbol to which he previously responded during the social task. Obviously, he responds with the index of the left hand to the same stimulus to which the co-actor previously responded.

In this way, the subject performs a standard Simon task; all the participants evaluated are expected to perform the task with a significant Simon effect, showing the usual ease and interference in providing responses to stimuli that have a respectively corresponding and non corresponding spatialization. (Introduction, § 1.2.).

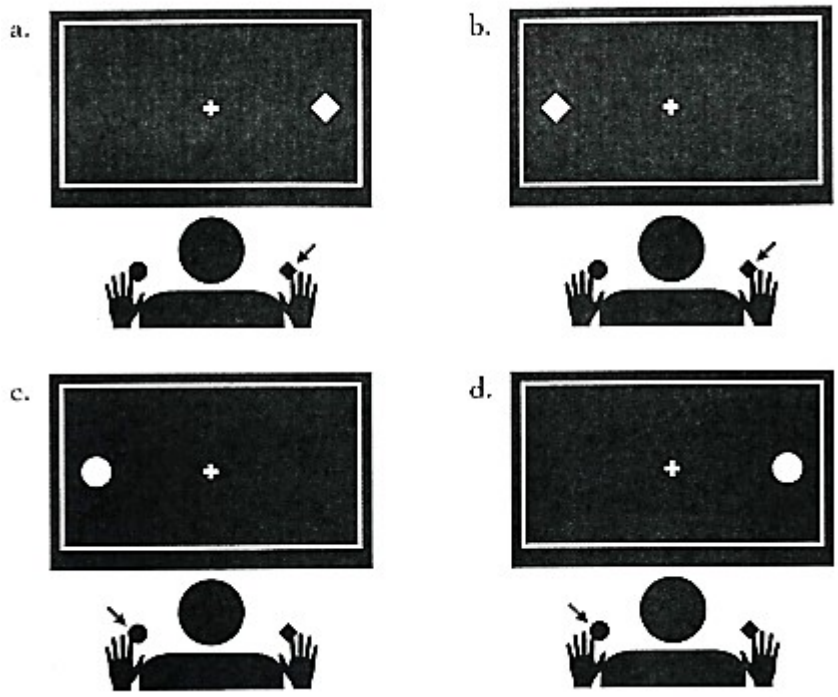


Figure 2: as in Figure 1, a schematic representation of the task is provided, in this case the Standard Simon Task. The assessed subject answers alone and is depicted in black.

The pictures show the following:

a) The subject responds with the right index finger to a corresponding stimulus.

b) The subject responds with the right index finger to a non corresponding stimulus.

c) The subject responds with the left index finger to a corresponding stimulus.

d) The subject responds with the left index finger to a non corresponding stimulus.

2.4. Statistic analysis

Univariate ANOVA was used to compare the continuous socio-demographic and clinical variables between the healthy control group and the clinical groups. As regards the categorical variables, the χ^2 test was applied.

A paired-sample t test was used to compare clinical variables between the subsample of patients during the acute phase, which were re-evaluated in euthymic phase (in this case, continuous variables only).

To evaluate the presence of the Simon effect and of the Joint Simon effect, two Repeated Measure ANOVA X 2 (Conditions: reaction time in Corresponding trial vs. reaction time in Non corresponding trials) X 3 (Group: MDD vs. ET vs. HC) were performed, with the reaction times in Corresponding and non Corresponding trials as within subject factor and the group as between subject factor.

Finally, Pearson correlations were used to look for an association between JSE range and clinical variables.

3. RESULTS

3.1. Sample description

The results were compared between the healthy control group (HC), the patient group evaluated in the acute phase (MDD), the patient group in euthymic phase (ET), and the same patients previously evaluated in the acute phase (MDD); the latter was a subset of the MDD group.

Sex, age and marital status of the patient groups were not different from those in the healthy control group. Healthy controls displayed advance education, and, unlike the patient group, all had jobs.

The MDD group, compared to the HC group, has significant differences in all the clinical variables taken into consideration (Table 1): their global and social functioning is lower (GAF, SASS), while the expression of symptoms of depression and anxiety is greater (HAM-D, HAM-A). There is a lower predisposition to experiences of pleasure, both in a global sense and as regards the anticipatory and consumer aspects (TEPS tot., TEPS ant., TEPS cons .), as well as sensory and social factors; there is also a greater inclination for rumination in all its aspects (RRS tot, RRS b., RRS r.).

Compared to the HC group, the ET group shows some relevant differences in the various skilled clinics. The global and social functioning has lower scores (GAF, SASS), such as to suggest a social dysfunction, depressive symptoms (HAM-D) are more expressed: nevertheless, they appear not to have a clinically significant score. The consumer anhedonia is only slightly more manifested (TEPS cons.); on the contrary, trait personological anhedonia, in relation to both sensory experiences and social situations (PAS, SAS) is evident in a marked way in both scales to the point of identifying euthymic patients as subjects affected by anhedonia. In ET group, they highlight relevant scores both as regards rumination in a general sense (RRS tot.), and as regards the ability to ponder about their difficulties in a gloomy and anxious way (RRS b.)

From the comparison of the ET group with the same samples evaluated during the acute phase, it is possible to deduce that all the clinical variables of the patients in euthymic phase were significantly improved compared to the acute phase (Table 2).

According to the prediction of the experimental conditions, all participants recognized that the interaction with the co-actor was neutral / courteous.

No Speed Accuracy Trade- off (SAT) was detected in any of the three groups; in fact, no remarkable negative correlation between the timing of response and the mistakes made either during the standard task, nor during the social, was noticed.

Compared to the first evaluation during the acute phase, the ET group was re-evaluated after an average of 16.4 months (SD = 12.6 months).

3.2. Reaction times, SE and JSE

For the Simon task we found a significant between-subject effects ($F_{2,95}=14.58$, $p<.01$, η^2 partial=.24), indicating that in HC reaction times were faster compared to both patients with MDD in the acute phase ($p<.01$, CI=-121.53,-43.34) and patients with MDD in remission ($p<.01$, CI=-108.85, -22.90). Moreover we found a significant main within-subject effect of Condition ($F_{1,95}=125.81$, $p<.001$, η^2 partial=.57), without Group by Condition interaction ($F_{2,95}=2.65$, $p=.08$, η^2 partial=.05), indicating that in both groups reaction times in the corresponding trials were faster than those in non corresponding trials (Graph 1).

Considering the post-hoc comparisons, we observed that each group features a Simon effect:

- The HC group has a Simon effect equal to 27.0 ms, SD ± 21.9 ms, with a significant difference between corresponding and non corresponding trials ($F_{1,95}=58.04$, $p<.01$, CI=-34.02, -19.96)

- The MDD group has a Simon effect equal to 30.7 ms, SD ± 24.9 ms; with a significant difference between corresponding and non corresponding trials ($F_{1,95}$= 69.32, p<.01, CI=-38.06, -23.4)
- ET group has a Simon effect equal to 17.7ms, SD ± 16.3ms, with a significant difference between corresponding and non corresponding trials ($F_{1,95}$= 16.48, p<.01, CI=-24.40, -9.06)

With regard to the Joint task (Graph 2), again we found a significant between-subject effects ($F_{2,95}$=20.68, p<.01, η2 partial=.30), indicating that in HC reaction times were faster compared to both patients with MDD in the acute phase (p<.01, CI=-116.58,-51.74) and patients with MDD in remission (p<.01, CI=-91.09, -19.82).

We found a significant main within-subject effect of Condition ($F_{1,95}$=1.09, p=.03, η2 partial=.05), without Group by Condition interaction ($F_{2,95}$=.31, p=.74, η2 partial=.01). We realised that even in the Joint task participants were faster in the responses to corresponding trials (mean reaction times=463,49±6.06 msec) as compared to non corresponding trials (mean reaction times=469.17±5.87 msec). However, the post-hoc comparisons revealed that the non corresponding response times are different in a significant manner compared to corresponding times only in the HC group.

Consequently, it turns out to be the HC group is the only one to exhibit a Joint Simon effect: 8.3 ms, SD 21.0 ms; $F_{1, 95}$=4.39 p=.04, η2 partial=.04

During task execution, the MDD group reported no crucial differences between non corresponding and corresponding response times (Joint Simon Effect 4.8 ms; SD ± 29.6 ms; $F_{1, 95}$=4.39 p=.25, η2 partial=.01); the same is true for the ET group (3.9 ms; SD ± 21.6 ms; $F_{1, 95}$=.63 p=.43, η2 partial=.01).

It follows that the patients did not perform the task with a relevant JSE, either in the acute phase of the disease or during the symptom remission period: in this case, it is a "missed-JSE" for both groups.

3.3. Correlations between JSE range and clinical variables

It is possible to note that only in the group of healthy controls is a JSE present. No correlations emerged between the latter and the variables, both demographic and clinical.

Looking for a correlation between the patients' 'missed-JSE' and the clinical variables, a remarkable positive correlation with SASS (r =, 4; p <, 05; Graph 3) is observed. Moreover, a positive correlation with a tendency towards significance (r =, 4; p <, 07, Graph 4) is showed only for the ET group with GAF.

No other significant correlations between missed-JSE of patient groups with other demographic and clinical variables have been found.

Table 1. Socio-demographic and psychometric characteristics.

	MDD	HC	ET	Between-groups differences	
	n=35	n= 38	n=25	Main effect of factor Group	Post-hoc comparisons
Age	49.8±9.1	49.7±9.7	51.0±8.4	F=.162, p=.85; η^2_p=13.74	
Sex (F)	20 (57%)	22 (58%)	13 (52%)	χ 2 =.236, p =.89	
Education (years)	12.2±3.8	14.1±3.0	10.8±3,7	F=6.9, p<.01; η^2_p=83.06	HC > ET, ET = MDD
Family status (single)	9 (26%)	6 (16%)	3 (12%)	χ 2 =11.7, p =.30	
Occupation (employed)	31 (89%)	38 (100%)	21 (84%)	χ 2 =12.7, p =.123	
GAF	51.2±8.0	85.3±4.6	76.9±7.8	F=244.41, p<.01; η^2_p=11198.14	HC > ET > MDD
SASS	29.5±9.0	39.3±5.4	33.1±8.3	F=15.71, p<.01; η^2_p=892.204	HC > ET > MDD
HAM - D	21.8±7.7	1.5±1.5	2.5±2.0	F=190.84, p<.01; η^2_p=4482.362	MDD > ET > HC
HAM - A	17.3±8.3	1.7±1.7	1.9±1.8	F=101.29, p<.01; η^2_p=2717.04	MDD > ET > HC
PAS	27.6±8.4	11.3±5.8	20.4±10.6	F=36.96, p<.01; η^2_p=2435,37	MDD > ET >HC
SAS	20.6±7.2	11.5±5.4	17.5±8.1	F=16.82, p<.01; η^2_p=772.176	MDD > HC, ET > HC
TEPS					
Ant.	33.6±5.2	41.4±6.4	39.4±6.9	F=15.36, p<.01; η^2_p=580.27	HC > MDD, ET > MDD
Cons.	31.9±7.1	39.1±5.8	38.1±6.4	F=13.08, p<.01; η^2_p=534.29	HC > MDD, ET > MDD
Total score	65.5±11.2	80.5±11.0	77.6±11.7	F=17.66, p<.01; η^2_p=2221.165	HC > MDD, ET > MDD
RRS					
B.	14.1±2.5	9.5±3.0	11.3±3.1	F=24.07, p<.01; η^2_p=193.27	MDD > HC > ET
R.	12.6±2.8	9.4±3.2	10.7±2.8	F=10.61, p<.01; η^2_p=95.31	MDD > HC > ET
Total score	26.8±4.7	18.9±5.4	22.0±5.3	F=21.22, p<.01; η^2_p=559.93	MDD > HC > ET

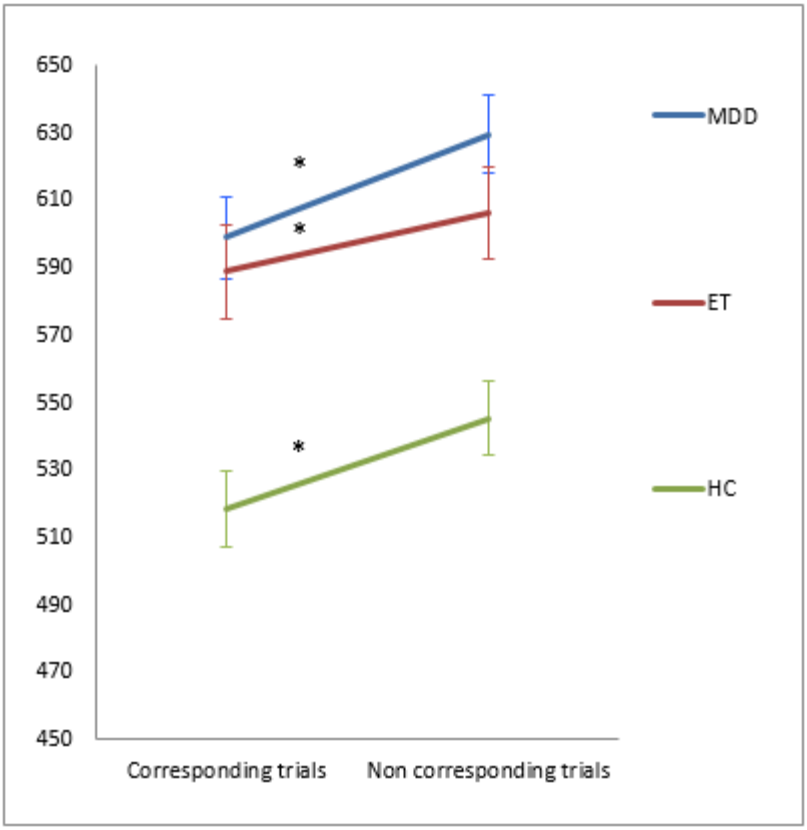
MDD = patients with Major Depressive Disorder; HC = Healthy Controls; ET= patients with Major Depressive Disorder re-evaluated in euthymic phase; GAF = Global Assessment of Functioning; SASS = Social Adaptation Self-Evaluation scale; HAM – D = Hamilton Depression Rating Scale; HAM – A = Hamilton Anxiety Rating Scale; PAS = Physical Anhedonia Scale; SAS = Social Anhedonia Scale; TEPS = Temporary Experience of Pleasure Scale; RRS = Ruminative Response Scale.

Table 2: Clinical variables of the patient group evaluated during MDE (n = 25) compared with the same patients re-evaluated in euthymic phase (n = 25).

	MDD	**ET**	**TEST**	***p***
VARIABLES	**MEAN ± SD**	**MEAN ± SD**	***t***	
GAF	50,8 ± 8,0	76,9 ± 7,8	14,2	< ,001
SASS	27,9 ± 8,0	33,1 ± 8,3	3,0	< ,01
HAM-D	22,8 ± 8,0	2,5 ± 2,0	- 13,8	<, 001
HAM-A	17,8 ± 8,7	1,9 ± 1,8	- 9,2	< ,001
TEPS *Tot.*	65,1 ± 12,1	77,6 ± 11,7	4	< ,01
TEPS *Ant.*	33,4 ± 5,3	39,4 ± 6,9	3,8	< ,01
TEPS *Cons.*	31,7 ± 7,7	38,1 ± 6,4	3,4	< ,01
PAS	28,2 ± 7,7	20,4 ± 10,6	- 3,1	< ,01
SAS	21,4 ± 6,8	17,5 ± 8,1	- 2,3	< ,05
RRS *Tot.*	27,7 ± 4,5	22,0 ± 5,3	- 4,3	< ,001
RRS *B.*	14,7 ± 2,3	11,3 ± 3,1	- 4,7	< ,001
RRS *R.*	13,0 ± 3,0	10,7 ± 2,8	- 3,0	< ,01

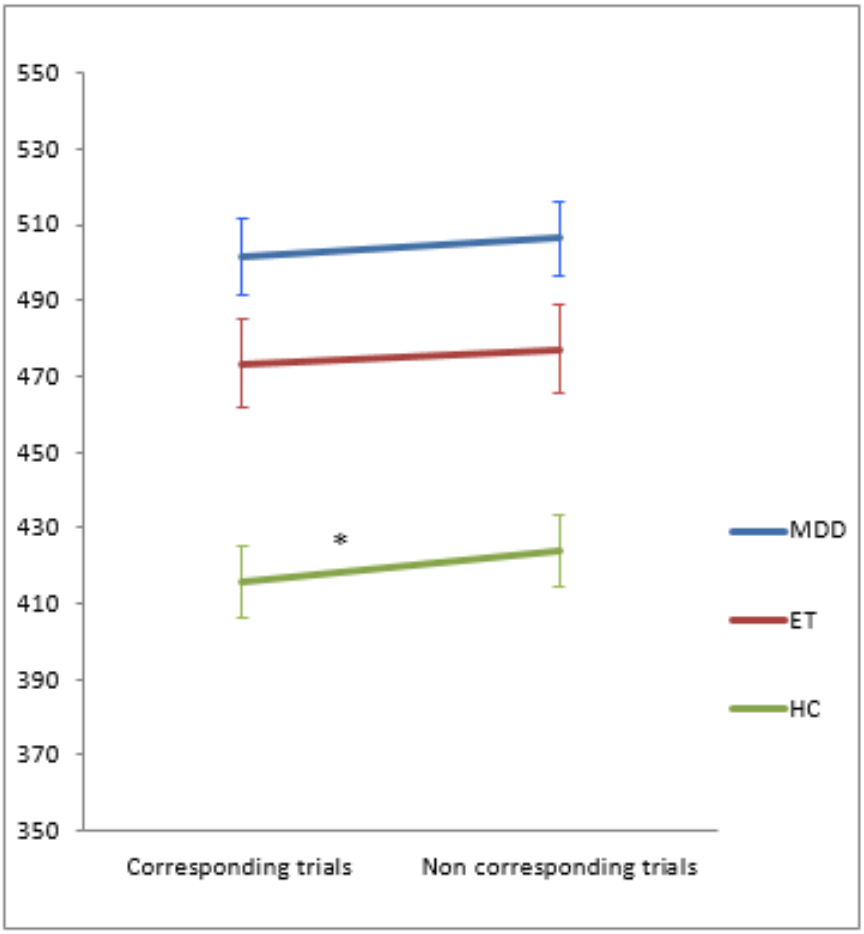
MDD = patients with Major Depressive Disorder; ET= patients with Major Depressive Disorder re-evaluated in euthymic phase; GAF = Global Assessment of Functioning; SASS = Social Adaptation Self-Evaluation scale; HAM – D = Hamilton Depression Rating Scale; HAM – A = Hamilton Anxiety Rating Scale; TEPS = Temporary Experience of Pleasure Scale; PAS = Physical Anhedonia Scale; SAS = Social Anhedonia Scale; RRS = Ruminative Response Scale.

Graph 1: Reaction times (milliseconds) for corresponding and non corresponding trials during the Standard Simon Task are shown.



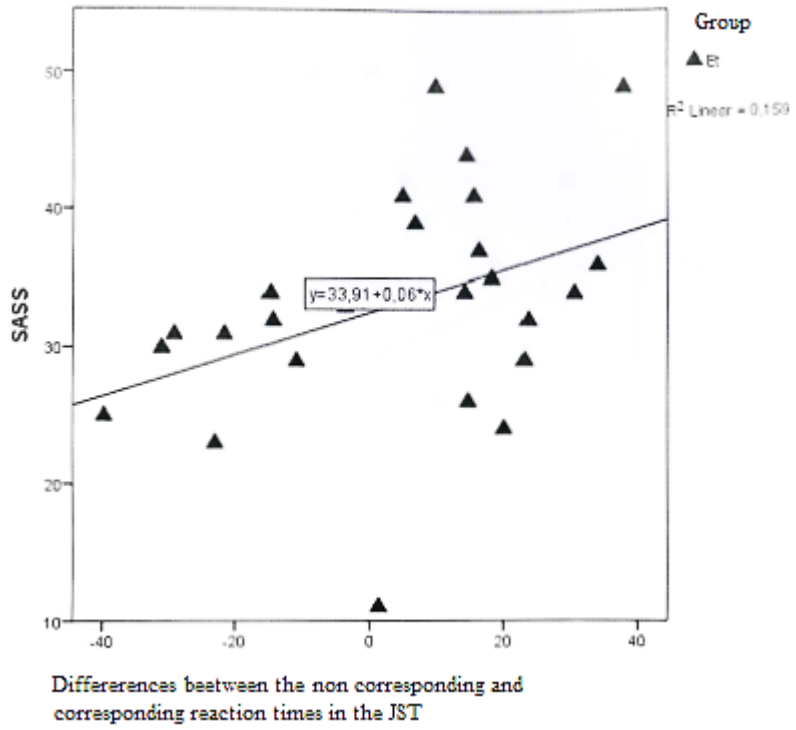
MDD = patients with Major Depressive Disorder; ET= patients with Major Depressive Disorder re-evaluated in euthymic phase; HC = Healthy Controls.

Graph 2: Reaction times (milliseconds) for corresponding and non corresponding trials during the Joint Simon Task are shown.



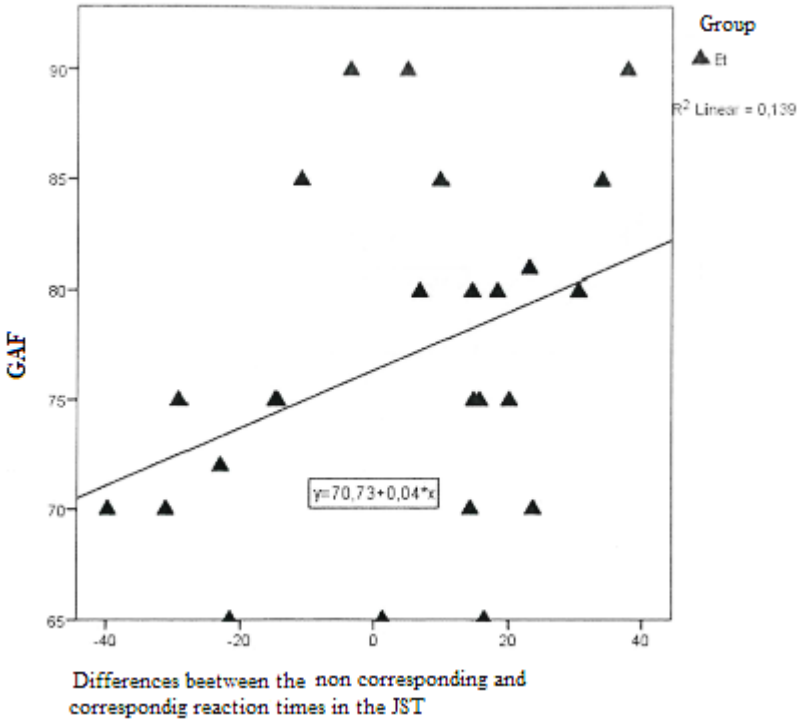
MDD = patients with Major Depressive Disorder; ET= patients with Major Depressive Disorder re-evaluated in euthymic phase; HC = Healthy Controls.

Graph 3: The positive significant correlation between the missed-JSE (abscissa) and SASS (ordinate) is shown in the group of patients evaluated in euthymic phase (ET) r =, 4; p <.05.



ET= patients with Major Depressive Disorder re-evaluated in euthymic phase; SASS= Social Adaptation Self-Evaluation scale.

Graph 4: The positive correlation with a tendency to significance is shown between the missed-JSE (abscissa) and GAF (ordinate) in the group of patients evaluated in euthymic phase (ET) r =, 4; p <, 07.



ET= patients with Major Depressive Disorder re-evaluated in euthymic phase; GAF= Global Assessment of Functioning

4. DISCUSSION

This study aims to evaluate the social aspects of co-representation and ToM using the JSE paradigm in patients with MDD: during the acute phase of an MDE and during complete remission of symptoms through re-evaluation. The clinical groups were compared with a group of healthy individuals of the same sex and age who have never had any diagnosis of psychiatric disorders. The subjects were also administered a standard Simon task in order to distinguish the social meaning of the go-nogo task from the cognitive conflict of the standard task.

Secondly, we try to explain the results of both standard and social behavioural tasks, based on the clinical variables of functioning, anhedonia and rumination.

With regard to the first objective of the study, only in the group of healthy controls a JSE was found. Some authors see in the JSE the existence of a cognitive co-representation of the action of others. Therefore, the subject would carry out a standard SE within his own cognitive representations. On the one hand, he has the cognitive representation of what he himself does; on the other hand, he has the representation of what the other close subject (co-actor) has to do in a social and interactive context between the participants. (Sebanz et al., 2003; Knoblich and Sebanz, 2006; Sebanz et al., 2006, Sebanz and Knoblich, 2009, Tsai and Brass, 2007; Vesper et al., 2010; Möller et al., 2011a, b; Kiernan et al., 2012). In this context of co-representation, the subject becomes one with the co-actor, his own hand and the hand of the other being a single body (Welsh, 2009).

On the contrary, in the group of patients, both in the acute and in the euthymic phase, we did not find a significant JSE. This means that, regardless of the depressive phase, the subjects performed the social task without a statistically significant difference between the non corresponding and the corresponding reaction times. This lack of difference is called 'missed-JSE' (Results, § 3.2.) and indicates that the activation of the spatial coding of the response does not occur in patients.

Several authors (Introduction, § 1.2.) agree that the absence of a JSE in patients can be ascribed to the social deficit of action co-representation, as well as of Theory of Mind, which the healthy participants of the study (HC group) spontaneously adopt towards the co-actor during the joint task. The presence of a JSE in the HC group is a not surprising result; indeed, it offers a demonstration of the fact that the experimental procedures were carried out without mistakes.

Hommel et al., (2009) showed that negative interactions between jointly acting participants eliminated co-representation of action. This means that the action co-representation is a phenomenon that depends on social factors.

In the meta-analysis by Bora and Berk (2015), it is not evident which particular aspects of ToM, such as modality (i.e., verbal vs visual), content of stimuli used in ToM activities (be it cognitive - i.e., inferring of beliefs and motivations, or affective - i.e., inferring what a person is feeling), and ToM processes (decoding vs reasoning) may be compromised in MDD. From the results, we can infer the presence of obvious deficits in ToM with medium effect size dimensions in MDD. The latter suggest that many MDD patients have remarkable difficulties in the aspect of social cognition.

According to some authors, the damage of ToM in MDD corresponds to the severity of depressive symptoms. ToM deficits concern affective and cognitive stimuli, as well as verbal and visual tasks; besides, decoding and reasoning are compromised. The damage to ToM may be related to functional dysconnectivity in brain networks playing a role in ToM, such as ventromedial prefrontal and temporoparietal regions (Bora et al., 2012a; Cusi et al., 2012; Kerestes et al., 2013; Peng et al., 2015).

Protracted ToM deficits after remission of depression may be regarded as a risk factor for relapse of depressive episode (Inoue et al 2006).

The ToM deficiency of patients with depression has not yet clearly and unambiguously been understood. Several authors (Introduction, § 1.1.) hypothesize that social dysfunction during a

depressive episode depends on cognitive aspects inherent to concentration, on the tendency to ruminate on one's depressive symptoms or on social anhedonia.

Notwithstanding the little accurate literature, social functioning has been found to be affected in patients with anxiety, even more so in those with depressive disorders and, specifically, in those with comorbid anxiety and depression. It has been noted that residual impairments have been recorded to remain, even after complete remission, and social dysfunction to be a predictor of future psychopathology (Saris et al., 2017).

Keysar et al., (2003), have shown that the expression of ToM skills does not occur spontaneously; people must engage and focus their attention to co-represent each other's thoughts, intentions, dispositions and perspectives. In fact, concerning the ability to concentrate, the results of the standard task suggest that the patients in the sample do not have difficulties in carrying out the task, which, in this case, is more demanding than the go-nogo social variant as a single individual is responsible for both responses.

It was noted that in the patient groups (MDD, ET) there is no correlation between missed-JSE and RRS b. indicative of the tendency to ruminate on one's depressive symptoms; the same is also found for the anhedonia measurement scales (PAS, SAS, TEPS).

Therefore, the considered hypothesis is that the pathology causes certain mostly negative effects and consequences on the ToM abilities of patients. Actually, the Review by Bora et al. (2016) suggests that some deficits may be traced back to pathological contexts rather than to individual characteristics (Bora et al., 2009).

As regards the relationship with the social functioning of the individual, evaluated in this study with the SASS (Materials and methods, § 2.2.), it is possible to note that, both in the acute phase and in the euthymic phase, patient scores are significantly lower than those of healthy controls; in particular, the ET group reports suggestive results of social dysfunction. The data present in the literature

consider co-representation and ToM skills as a requirement to interact with others in a satisfactory way, to be able to understand the emotions, intentions and actions of others (Preston and de Waal, 2002). A positive and noteworthy correlation between the JSE and SASS would then be expected. This is observable (Results, § 3.3., Graph 3) only in part: in fact, only in the ET group, a positive correlation between SASS and missed-JSE is present. Thus, according to the literature (Preston and de Waal, 2002), a reduced social functioning in the ET group is correlated with the reduced capacity for co-representation.

The above also applies to the global functioning, which in this study was measured with the GAF (Materials and methods, § 2.2.). In fact, a positive correlation with a tendency towards significance exclusively in the ET group is observed (Results, § 3.3., Graph 4).

This could be due to the fact that MDD is a recurrent disorder and risk of recurrence is related to the number of previous episodes (Solomon et al. 2000; Kessing et al. 2004). Such reflection inspired the idea that depressive episodes could lead to permanent residual impairments or scars that confer risk of subsequent episodes (Rohde et al. 1990; Burcusa & Iacono, 2007). Contrastively, individuals who in the past suffered from depression may already have had features that made them vulnerable to recurrent depression beforehand (Just et al. 2001; Christensen & Kessing, 2006; Sowislo & Orth, 2013). The first is called the 'scar hypothesis'; the latter is called the 'vulnerability hypothesis'.

Regarding the standard task, a large and solid SE was documented in all three groups. Such result is very important for statistical purposes; in fact, it excludes the possibility that generic aspects of cognitive-attentional nature may act as confounding factors in the collection of data. In other words, the difference in the JSE does not depend on a cognitive or attention deficit.

In conclusion, this study shows that patients with MDD did not perform the joint task with a relevant JSE, either in the acute phase of the disease or after symptom remission, presenting a "missed-JSE". The absence of a JSE in patients, as compared with HC, could be interpreted as a

deficit of action co-representation, as well as Theory of mind, which seems to represent a stable element in MDD related with social dysfunction, regardless of symptoms remission.

4.1. Limits of the study

Although the JSE is a phenomenon with solid foundations, which can be used as a research tool in the population affected by psychiatric disorders, it still remains to be studied in depth under various aspects. In particular, a greater dissection of the topic would be desirable, because, during the euthymic phase, it has been found that deficits in social skills play a relevant role in hindering the patient's reintegration and rehabilitation (Barrera et al., 2013).

A further factor to take into consideration refers to the compilation of self-administered scales; actually, it may be affected by the participants' personal variables, such as goodwill and understanding, leading to a possible alteration of the accuracy of the data collected.

Finally, the limited sample size, particularly regarding the group of patients re-evaluated in euthymia, raises doubts of statistical power. It would be desirable to replicate the survey on a larger sample, for a further and a more accurate differentiation among the subjects, according to the current and lifetime diagnosis of the disorder.

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