Relations between Neurocognition, Theory of Mind and Functional Outcome in Patients with a First-Episode of Schizophrenia and Gender Differences at 3-year follow-up.

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I cannot avoid thinking about almost four years ago. I had many difficulties with Spanish, but still eager to know more. I chose to do this work without thinking about all the limits. I have been wantingto do it for years, but I did not have the necessary means and neither the necessary preparation.
Although I may have a lot to be a professional, I tried my best to carry out a scientific and useful study. This work was done with a lot of love and dedication.
But even so, all this would be impossible without the support and help of many people.

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On a more personal level, I would like to dedicate this work to my family. The one I am far away from. It has not been easy to be away from them but even so, they have always been by my side. And the one I have nearby, they gave me the chance to accomplish this dream.
Thank you for your support and for trusting in me. I will always be grateful to them.

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Thank you!

Dorela Cika

Abstract

Introduction: Neurocognitive impairments and deficits in theory of mind (understating one`s and other`s mental states) are enhanced in patients with schizophrenia. Such impairments have been observed also in first-episode patients. Inevitably, arises the need to know about the effects that these impairments can cause to patient`s everyday functioning. Also, several studies suggest that there are differences due to gender. The purpose of this work was to study the longitudinal relations (over the course of 3 years) of neurocognition, theory of mind (ToM) and functional outcome in patients who were going through a first-episode of schizophrenia.

Methods: Records from 100 patients with a first episode of schizophrenia, treated at the Marques de Valdecilla Hospital in Santander Spain, were included in this study. The information was provided by the Program of Attention Phases Initial Psychosis (PAFIP) in this hospital. All the data: neurocognition (Neuropsychological Assesment Battery), ToM (Reading the mind in the eyes, Eye-task) and functionality (Disability Assessment Scale, DAS), were collected from professionals. For the statistical analysis, the SPSS-22 computer application was used.

Results: Among neurocognitive variables, at baseline, the Working Memory was the one that has the most significant relation with the DAS items (a total of 7 out of 15). At 3-year follow-up Global DAS is significantly ($p < .05$) related to five variables: Working Memory, Attention, Verbal Memory, Premorbid IQ and Motor Dexterity (positive correlation: $p = .314$). ToM does not present any statistically significant relation with Functional Outcome (DAS). Analysis about gender differences showed significant difference on DAS total score ($p < .05$), with higher scores for men, in comparison to women (2.26 vs. 1.54).

Conclusions: In conclusion, at the 3-year follow-up, patients with a first episode of schizophrenia showed better global functioning than at baseline. Specifically, at follow-up, general outcome functioning is related to Working Memory, Verbal Memory, Attention, Motor Dexterity, and Premorbid IQ. Differently, from ToM, neurocognition was related to functional outcome at both time-points. Regarding gender differences, at baseline women showed better global function than men, but this difference did not appear at the follow-up assessment.The present work could help further investigations or treatment interventions about which domains are strongly related to functional outcome in patients with a first-episode of schizophrenia.

Key Words: First-episode schizophrenia; Functional outcome; Neurocognition; Theory of Mind; Gender differences.

Table of Contents

1. INTRODUCTION

Beuler was the first to identify schizophrenia as a "split personality", referring to their thoughts and a separation or loosed associations and affects. (Moskowitz et al.,2011).

Nadira Khamker (2015), in the article about first episode of schizophrenia, concludes that schizophrenia is a chronic psychiatric condition. Patients with schizophrenia present clinically psychotic, negative and cognitive symptoms, which can become evident late in adolescence or in early adulthood. This condition follows a relapsing-remitting course and eventually results in a chronic state of residual symptoms and functional impairment (Khamker, 2015). It is important an early identification and treatment of the first episode, to help the patients, and their families, to cope with the anxiety that the symptoms produce and also to reduce the risk of suicide (Khamker 2015).

´´The range of studies currently being conducted under the broad umbrella of first-episode psychosis will, before the turn of the century, address and answer many specific questions regarding the etiology and course of schizophrenia. Along the way, we will also learn about the onset of the illness, which symptoms and signs best define it, and their prognostic significance.´´ Keshavan and Schooler (1992).

Several studies provide conclusions that negative symptoms, neurocognition, and social cognition are all important variables in predicting the functional outcome in people with schizophrenia (Meyer and Kurtz,2009; Couture et al 2011).

Also, it is well known that neurocognitive abilities form an important role in the functioning of each one of as in society and also contribute to our relationships with other people. Many other authors have found on their studies neurocognitive domains in which the patients diagnosed with schizophrenia spectrum disorder show impairments. (Cornblat et al., 2009; Mohamed et al.,1999). And, numerous studies have shown that neurocognitive domains affect the functional outcome, even more than symptoms, in patients with schizophrenia (Velligan et al., 2000; Bell and Bryson., 2001; Brekke et al., 1997; Green et al., 2004).

Green and colleagues 2000, defined neurocognition as a constellation of cognitive abilities such as: processing speed, working memory, visual and verbal learning and memory, executive functioning, and showed that has been associated with functional impairments, up to 20%-60% of the variance on the real world functioning (Green et al., 2000). Also, Cornblatt et al 2009, showed that neurocognitive impairments are common in schizophrenia, causing the most of the disturbance that characterizes this disorder.

Nuechterlein et al 2004, examined the identification of separable cognitive factors in schizophrenia. It was recommended the inclusion of six domains in the cognitive battery for clinical trials. Those domains are: Speed of Processing, Attention/Vigilance, Working Memory, Verbal Learning and Memory, Visual Learning and Memory, and Reasoning and Problem Solving (a seventh dimension - verbal comprehension- was valued but not recommended).

In a study about cognitive functioning in first episode schizophrenia Addington J. and Addington D., 2002, comparing first episode patients and controls, concluded that there were no differences in early information processing between the groups. Also, it was found that first episode subjects had superior scores in the domain of verbal memory, indicating impaired performance. In comparison with controls the first episode subjects performed better on the measures of executive functioning, and in visual memory (using WCST and Rey complex figure). This assessment was made after 1 year from the first episode, and the results may have been due to the use of the same measures, thus to learning effect.

Roncone et al 2002, mentioned verbal memory as one of the variables that are associated with work capacity. Meanwhile, Ventura et al 2009, published a model in which is shown the neurocognition as a variable that influences the functional outcome. It was concluded that neurocognition indirectly affects outcome through negative symptoms, so it has direct and indirect effects on functional outcome. Executive functioning was found to have a major influence on the occupational functioning profile of men subjects with schizophrenia spectrum disorder. In their study Tabares- Seisdedos et al 2008, about neurocognitive and clinical predictors of functional outcome in patients with schizophrenia and bipolar disorder (1-year follow up), found that, after 1 year of follow up, the functional outcome was better predicted by three specific domains: Verbal Memory, Motor Speed, and Vocabulary. So, they enhanced the importance of verbal memory, as the most important domain which affects the functional outcome (Tabares-Seisdedos. et al, 2008). Meanwhile, these results differ from the findings in the study of Green et al 2004, (*´´Longitudinal studies of cognition and functional*

outcome in schizophrenia: implications for MATRICS´´), which identifies two different domains as a predictor of functional outcome, such as Executive functioning and Verbal fluency (Green et al., 2004). Meanwhile, Lesson et al 2009 concluded that general intellectual functioning is a better predictor than impairments in specific neurocognitive domains. Milev et al 2005 suggested that the relations between neurocognition and functional outcome are more evident in chronic schizophrenia than in first episode subjects. And both, Milev et al 2005 and Tandberg et al 2011, concluded that attention and processing speed where two important variables to predict employment status in first episode subjects, after studying the importance of neurocognition on the employment status of subjects with a first episode of psychosis during 2 years: the better-sustained attention, the better global functioning (Tandberg et al 2011). Rodriguez -Sanchez and colleagues 2007, investigated the hypothesis of the processing speed in the cognitive dysfunction on first episode psychosis. The cognitive performance of subjects with schizophrenia and controls was compared and they suggested that this domain (speed of processing) is severely impaired in the first episode psychosis subjects. So, a deficit in this domain might support the theories of the neural basis of schizophrenia and may also lead to functional disturbances (Rodriguez-Sanchez et al., 2007). In the same line Gonzalez-Ortega and colleagues 2013, demonstrated the association between neurocognitive functioning and clinical and functional outcome in first episode psychosis subjects, differencing the working memory as the domain which is significantly related with negative symptoms and psychosocial functioning (Gonzalez-Ortega et al., 2013).

It has been also demonstrated that in subjects with schizophrenia, the impact of neurocognitive deficits on functional outcome is mediated through social cognition (Addington etal 2010). In the review of the functional significance of social cognition in schizophrenia, Couture et al 2006 resumed that social cognition and its domains have been found to be related to community, social, and work functioning (Couture et al., 2006).

So, an important factor which affects the functional outcome is social cognition. But, what do we know about social cognition in schizophrenia? There appear to be 3 primary domains of inquiry: emotion perception, theory of mind (ToM), and attributional style (Penn et al., 2008). Green M. F. and colleagues 2008, in their article, presented a summary of the discussion from a workshop supported by the NIMH (National Institute of Mental Health), where they identified five areas of social cognition, Theory of Mind (TOM), Social Perception, Social Knowledge, Attributional bias, Emotional Processing. Also, it's noted that these domains are not absolute (Green et al, 2008). The findings of Sergi et al 2007 suggest that social cognition

forms a distinct domain from neurocognition, although they are closely related. Couture and colleagues 2006 resumed different articles where was suggested a significant association of social cognition with functional outcome.

Cook et al 2013, in a sample of 43 outpatients with serious mental illness studied the relations between neurocognition, ToM and functional outcome, concluding that better cognition and better ToM at baseline was significantly associated with functional outcome. At the moment, it has not been demonstrated a significant relationship between ToM and functional outcome.

The first to mention the term ToM were Premack and Woodruff in 1978, in the famous study: *"Does Shimpaze has a Theory of Mind?"*. They explained it from an evolutionary point of view, arguing that the theory of self and others has been developed as a result of the adaptation in the complex of the social environment (Premack and Woodruf, 1978). Green et al 2008, defined ToM as a *"mental state and an ability to infer intentions, dispositions, and beliefs of others"*, different from empathy. ToM it is a necessary ability to function in the sociability and to maintain relations with other people. It helps to understand intentions, jokes or states of others, for which a misinterpretation of them would lead us to a more anxious and disturbed state. ToM has been associated with poor outcome and clinical insight (awareness of illness) (Rowena et al., 2015). It is shown that ToM impairments are common and occur with a considerable impact on schizophrenia (Bora et al, 2009).

Frith and Corcoran 1996, explored the ToM in patients with schizophrenia. Demonstrating that the subjects had difficulties when they were asked to specify what was going on the minds of other people. These results are not related to medication because other subjects also medicated (patients with symptoms of passivity and patients in remission) did not show an impaired ToM. It has been demonstrated that 80% of patients who represent behavioral symptoms also presented ToM impairments (Harrington et al., 2012). Bright-Paul et al 2008, specified that the identification of ToM its complex because it doesn't involve just the social functions, it also involves personal cognitive functions. According to Roncone and colleagues 2002, ToM is one of the best predictors of social functioning.

Ayesa-Arriola et al 2016, in the article about the relationship between ToM and processing speed in first episode psychosis subjects (3 years follow-up), suggested that patients in comparison with healthy subjects showed significant impairment in ToM task and also showed significant differences in all neurocognitive domains scored. Also, it was specified that, from all the neurocognitive domains, processing speed was the unique significant

contributor to efficient ToM and a trend of significance in visual memory (Ayesa-Arriola et al., 2016).

Clearly, it can be suggested that domains of cognition and ToMaffect occupational functionality in patients with schizophrenia. But, what about gender differences? Analysing the differences between men and women, Grossman et al 2008, carried out a 20 years longitudinal study, questioning the gender differences in schizophrenia and other psychotic disorders, and they showed that women have a tendency for a better functional outcome in comparison with men and also that these differences are not unique for schizophrenia. They also concluded that women have also a better course of illness, hypothesizing that one of the reasons is, the age of onset (the younger the worse). (Grossman et al., 2008). But, Moriarty et al 2001, concluded that there were no differences across gender in the relations between neurocognitive variables, clinical symptoms and adaptive deficit, and just some gender differences in the severity of symptoms were observed. (showing men a higher level of negative symptom severity) (Moriarty et al 2001).

1.1. Hypothesis and Objectives

The present study consists of an analysis of longitudinal relations between Neurocognition, ToM and Functional Outcome in subjects with a first episode of schizophrenia, over the course of 3 years of assessment. It was hypothesized:

1. Neurocognitive domains have a higher significant relation with functional outcome in comparison with ToM (in the two time-points).

2. Subjects would perform a better state in functional outcome measured after 3-year follow-up, in comparison with functional outcome measured at baseline.

The objectives of the present study are:

1. Study of the relations between neurocognitive domains, ToM and functional outcome, at baseline.
2. Study of the relations between neurocognitive domains, ToM and functional outcome, at 3 years follow-up.
3. Study of differences due to gender.
4. Study of the differences/changes during the follow-up (over time).

2. METHODOLOGY

Archival data from 100 patients with a first episode of schizophrenia treated at the Hospital Marques de Valdecilla in Santander Spain were included in this study. The data was provided by the Program of Attention Phases Initial Psychosis (PAFIP) in this hospital. The subjects met the criteria of: 1) An age of 17 to 58 years; 2) Living in the area of Cantabria; 3) They were going through their first episode; 4) Where diagnosed through SCID-1 (Structured Clinical Interview DSM-IV) (First et al.,1996).

2.1. Description of the sample.

The sample that has been collected consists of 100 patients diagnosed with schizophrenia, 50% / 50% of whom are divided according to gender (Figure 1). Their ages are between 17 and 58 years with a median in 30.55 years. The mean age is 32.31. Despite a slight asymmetry, the distribution shows a clear tendency towards the normal bell (Figure 2).

The mean age of women (34.26 years) is somewhat higher than that of men (30.37 years) and although the difference does not reach statistical significance ($p > .05$), it shows a tendency ($p = .060$).

Regarding the level of studies (Figure 3), the majority of the sample (61%) have a medium level, divided between specifications such as Bachelor, ESO, FP; etc…. Only 19% have reached higher university levels. When compared between genders, there are no differences that can be considered as statistically significant (with $p > .05$) although we can see more women with higher education (22% vs 16%) or middle (66% vs 56%) and above all more men who have stayed at the primary stage of studies (28% vs 12%).

Regarding the time that the subjects have been diagnosed, the mean of the sample is 13.37months. The average for men is higher than that for women, without reaching statistical significance ($p > .05$).

Figure 1: Sector diagram. Participants according to their GENDER

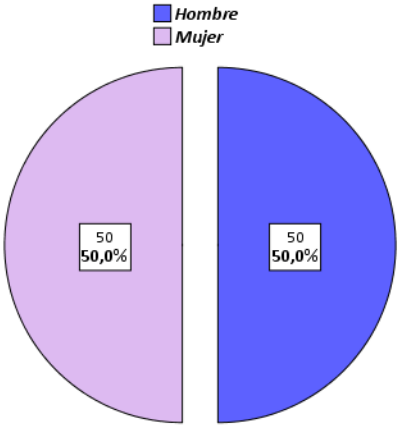

Figure 2: Histogram. Participants according to their AGE

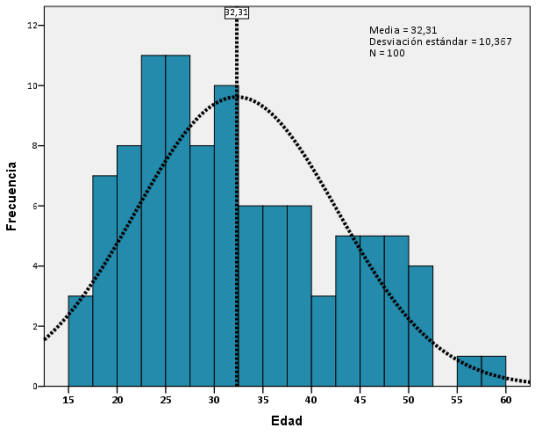

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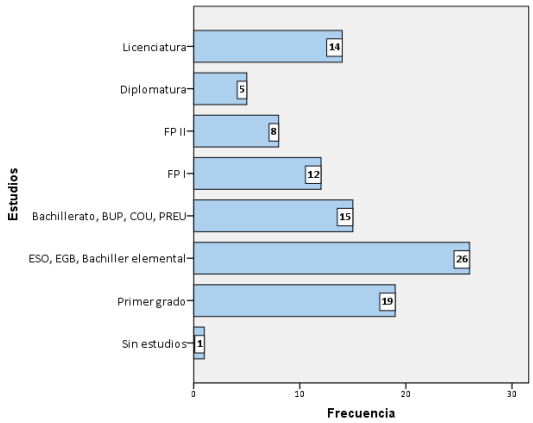
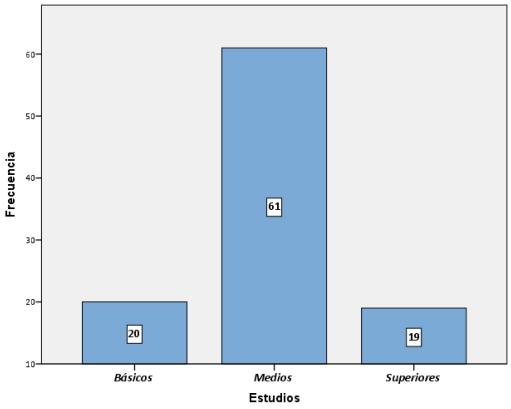
Figure 3: Bar diagram. Participants according to their LEVEL OF STUDIES





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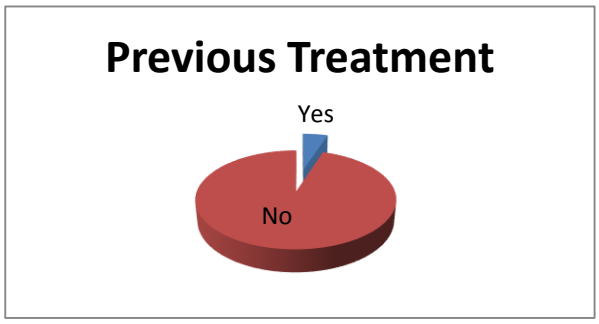
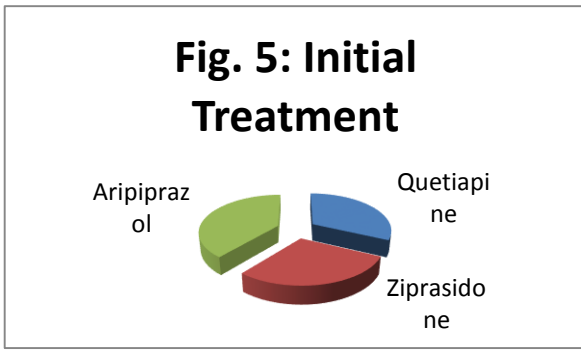
And finally, a total of 95 subjects had not received previous treatment (Figure 4). Regarding its initial treatment: dominated aripiprazole (39), followed by quetiapine (32) and finally ziprasidone (29) (Figure 5).





	Frequency	Percent	Valid Percent	Cumulative Percent
Yes	5	2,6	2,6	2,6
No	95	97,4	97,4	100,0
Total	100	100,0	100,0	

	Frequency	Percent	Valid Percent	Cumulative Percent
Quetiapine	32	32,3	32,3	32,3
Ziprasidone	29	29,7	29,7	62,1
Aripiprazole	39	37,9	37,9	100,0
Total	100	100,0	100,0	

2.2. Measures

- **Neurocognition**

As other studies (Nuechterlein et al., 2004) suggest, neurocognition is measured by 8 domains, which are: Verbal Memory; Working Memory; Motor Dexterity; Visual Memory; Executive Functioning; Attention; IQ and Information Processing Speed. It was used the neuropsychological assessment battery with the following tests:

- **Verbal Memory: Rey's verbal learning test. (Rey., 1964)** In this test, is read a list of 15 words, (list A) that the subject must memorize. The list is read five times and

after each of the times, the subject should try to repeat it as exhaustively as possible, regardless of the order. After this, the professional reads (only once) a second list (list B with 15 different words) whose function is to exert an interference effect. Immediately afterward the subject was asked to try to remember the first list again. After 30 minutes of delay, the participants were asked again for the first list, to evaluate the long-term memory. Finally, the subject is presented with a written page in which a total of 50 words appear, among which are the fifteen words of the first list. Here the subject must recognize what the words of the first list are. *To measure the verbal memory the delay responses have been used.*

- **Working Memory: "Letters and Numbers" is a subtest of the WAIS-III (Wechsler Intelligence Scale for Adults- III, 1997) battery**. It consists in reading to the subject a combination of letters and numbers. The subject's task is to repeat the sequence, first the numbers in ascending order and then the letters in alphabetical order.
- **Motor Dexterity: (Grooved Pegboard Test (Lafayette Instrument Company) (Lezak., 1995).** It is a test that evaluates fine motor ability. The task is to place metal pins in the 25 holes of a perforated board (that are randomly rotated), using first the dominant hand and then the non-dominant hand. With the right hand, the pins should be inserted from left to right. With the left hand, the pins should be inserted from right to left.
- **Visual Memory: The Rey Complex Figure (FCR) is a memory copy and reproduction task (Osterrieth., 1944)** in which the subject is presented with an abstract linear figure and asked to make a copy as accurately as possible. Three minutes after finishing the copy, they were asked to perform a memory playback. 20 minutes later a new memory playback is requested again. Basically, 18 predetermined parts of the figure are considered. Their level of perfection is valued. This gives a quantitative score for each of the executions over a total of 36 points.
- **Executive Functions: Trail Making Test (form A and B) (Periañez et al., 2007; Reitan and Wolfson., 1985).** The (TMT) is a task that was originally included in the Army Individual Test Battery. It is a very sensitive test, of simple use and helps to differentiate healthy individuals from individuals with brain damage. This task is made up of two parts. In the first part (TMT-A) the subject is presented with a sheet in which 25 numbered circles are distributed; the subject has to join them with a

continuous path following the order of the numbers. In the second part (TMT-B) the circles contain numbers and letters; the subject has to join them, alternating numbers and letters and respecting the respective numerical and alphabetical orders alternately (1-A-2-B-3-C ...).

- **Attention: The Continuous Performance Test (CPT) (Cegalis and Bowlin., 1991).** In the task, the subject is presented in front of a computer screen in which letters are followed. The subject must respond by pressing a key on the computer each time the indicated stimulus appears. The test presents a total of 360 stimuli consisting of letters. The stimuli occur on the screen approximately every second and are presented on a noisy background, that difficulties their perception.
- **Processing Speed (Wechsler.,1997):** Number key of the WAIS-III is one of the subscales of the WAIS-III battery. A table with numbers from 1 to 9, it is presented to the subjects, below each number comes a meaningless symbol that "represents" the number. Under that table, which serves as a sample, a larger one appears with a distribution of numbers. The task is, to place under each of these numbers the corresponding symbol according to the sample table. The task is prolonged for two minutes and the subject is asked to complete as many symbols as possible.
- **Premorbid IQ (IQ): "Vocabulary" is a subtest of the WAIS-III battery (Wechsler Intelligence Scale for Adults- III, 1997).** The subject is asked to define (orally) some words, that the professional reads aloud.

- **ToM measures**

Reading the mind in the eye (revised version Baron-Cohen, 2001), was used to measure the social cognition as Theory of Mind. It is included in the neuropsychological assessment battery, consisting in the presentation, on the screen of a computer, of 36 blackand white photographs of the region of the eyes collected from magazines. Each pair of eyes has been standardized to the same size by picking up the region between the eyebrows and the bridge of the nose. The subjects are asked to choose between four adjectives (the correct one and three distractors) that describe what the person in the photograph may be thinking or feeling.

- **Functional Outcome measures**

The data to measure the functional outcome was obtained from **the Disability Assessment Scale (DAS)**(Maña et al., 1998), measuring the global functioning and also separated items, which are: Personal Care; Low Activity; Slowness; Isolation; Participation in Home; Affective- Spouse; Sexual - Spouse; Children; Opposite Sex Relations; Social Contacts; Work Performance; Interesting to Get a Job; Information Interest; Emergency Behaviour.

All these measures were obtained from the PAFIP program at the Hospital Marques de Valdecilla and each one was administrated by trained professionals.

3.Statistical Analyses

For the statistical analysis, the SPSS-22 computer application was used. In order to assess associations between neurocognition and ToM with functional outcome, a longitudinal design was used.

The techniques and statistical tests used have been: Data exploration with QQ graph of adjustment to normality, histogram, asymmetry coefficients and kurtosis/height together with the Kolmogorov-Smirnov goodness of fit test and description with the usual tools of centrality (mean, median) and variability (standard deviation, range, and interquartile range). Spearman's correlation coefficient, for the associative study between variables. And for the longitudinal changes test U of Mann-Whitney and W test of Wilcoxon.

The statistical analysis has been structured in its usual two parts.

The first is where was proceed to make a descriptive approximation of the study population, in all the variables that have been collected, both those of result (VD) and those that can be considered as predictors (VI) of these. Likewise, the Kolmogorov-Smirnov Goodness of Fit Test has been used with them to verify the normality of the distribution of these variables (it is considered significant deviation only if $p < .01$) together with their descriptive indices of asymmetry and kurtosis. (height).

In the second part, it proceeded to carry out a bivariate study of the relations of each I.V. with each of the D.V. items, using the appropriate tests for the type of variables that cross. When both variables are quantitative, and in view of the way in which they are distributed, it was opted for the Spearman correlation method and the Wilcoxon Test W. And for the crossing of a variable with 2 independent case categories with a quantitative variable, the Mann-Whitney U-test was chosen. In all these inferential statistical tests, significance is considered when p <.05.

3.1. Descriptive analysis

3.1.1. Neurocognitive domains

In this section, are described the 8 variables that form the domains of neurocognition, both at baseline and in the evaluation performed at 3 years of follow-up. The results are summarized in Tables 1 and 2 below.

In the baseline measurements (table 1), the exploration allowed us to verify that in 5 of the variables: verbal memory, working memory, and visual memory, premorbid IQ, and processing speed (both WAIS variables), the data presented a good fit to the model of the Gaussian normal (p> .05) without the presence of any value out of range. On the other hand, in the variables: motor dexterity, executive functioning, and attention, are presented great asymmetries, that are appreciated by the appearance of anomalous values (of outlier far out type) on the opposite side, provoking their removal in a highly significant way (p <.001). With regard to these same variables measured at 3 years (Table 2), the exploration is very similar in terms of the adjustment or not of the data to the Gaussian bell. Except one: premorbid IQ (WAIS vocabulary), where is observed a deviation from the significant normality (p <.01) that in the basal measurement did not exist and that occurs again due to the existence of a clear outlier far out value.

The aforementioned tables also contain the values of the classic descriptive indexes (mean, standard deviation, etc ...). Although the possible changes are analyzed in the inferential part

of the present study, significant differences in the average values of the variables are already appreciated here. On the other hand, variability statistics seem to indicate that the sample covers interindividual differences quite well and that therefore the sample is not concentrated in a single part of the continuum of values.

Although the possibility of converting all these values into standardized Zscore was considered, this only achieves the homogenization of the scoring, but, since it is a linear transformation, it does not lead to the normalization of those variables that do not conform to it (above already commented).

Table 1: Exploratory and descriptive analysis. Neurocognitivel variables. (N = 100). Basal measurement.

		Exploration: Form			Centrality		Range	Variability	
Variable	N	Asymmetry	Kurtosis	Test SW: p -value	Mean	Median	(Min. / Max.)	Standard deviation	Interquartile range
Verbal Memory	99	0.296	-0.559	.061 NS	7.62	7.00	2.00 / 15.00	2.85	5.00
Working Memory	99	-0.025	-0.723	.453 NS	6.56	7.00	1.00 / 13.00	3.14	5.00
Motor Dexterity	99	3.758	20.692	.002**	73.77	69.00	41.00 / 229.00	23.03	16.00
Visual Memory	99	-0.238	-0.657	.717 NS	17.39	18.00	2.00 / 32.50	7.09	10.50
Executive Functions	96	-2.146	7.064	.000**	-63.92	-49.00	-335.00 / 68.00	52.47	54.50
Attention	93	-1.680	2.113	.000**	67.62	74.00	7.00 / 80.00	16.22	15.50
Premorbid IQ: WAIS vocabulary	98	-0.103	-0.549	.075 NS	9.36	10.00	5.00 / 15.00	2.36	4.00
Processing Speed	99	-0.228	-0.632	.243 NS	7.78	8.00	1.00 / 14.00	3.32	4.00

NS = Non-significant deviation (p> .05) the variable is normally distributed

** = Significant serious deviation (p <.01) the variable does not adjust to normal

Table 2: Exploratory and descriptive analysis.Neurocognitive variables. (N = 100). Follow-up at 3 years.

		Exploration: Form			Centrality		Range	Variability	
Variable	N	Asymmetry	Kurtosis	Test SW: p-value	Mean	Median	(Min. / Max.)	Standart deviation	Interquartile range
Verbal Memory	90	-0.148	-0.576	.332NS	8.67	9.00	0.00 / 15.00	3.41	5.00
Working Memory	90	0.039	0.039	.278NS	8.12	8.00	1.00 / 17.00	3.03	4.00
Motor Dexterity	90	2.258	2.258	.002**	67.80	63.00	42.00 / 158.00	17.68	18.00
Visual Memory	90	-0.268	-0.268	.603NS	18.01	19.00	4.00 / 31.00	6.82	11.00
Executive Functions	87	-4.108	21.03	.001**	-53.61	-39.00	-372.00 / -9.00	53.04	38.00

Attention	90	-2.151	4.269	.000**	72.36	77.00	28.00 / 80.00	11.35	7.50
Premorbid IQ: WAIS vocabulary	90	4.863	36.595	.002**	10.34	10.00	4.00 / 40.00	3.92	4.00
Processing Speed	89	-0.169	-0.162	.334 NS	8.74	9.00	2.00 / 15.00	2.82	3.00

NS = Non-significant deviation (p> .05) the variable is normally distributed

** = Significant serious deviation (p <.01) the variable does not adjust to normal

3.1.2. ToM

Table 3 describes this variable both in the baseline situation and in the evaluation of the 3-year follow-up. The exploration helped to verify that there is no outlier far out value. The KS Test indicates that none of the two variables do deviate significantly (p> .05) from the normal model (they are normally distributed). And as for the descriptive ones, the average values are very similar in both measurement moments; while the indices of variability seem to indicate that the group is well distributed along a large part of the continuum of empirical values.

Table 3: Exploratory and descriptive analysis. Variable of TOM. (N = 100). Basal measurement and follow-up at 3 years.

		Exploration: Form			Centrality		Range	Variability	
Variable	N	Asymmetry	Kurtosis	Test SW: p-value	Mean	Median	(Min. / Max.)	Standart deviation	Interquartile range
EYE-Task - basal	95	-0.524	0.746	.205^{NS}	21.37	22.00	7.00 / 33.00	4.53	5.00
EYE-Task at 3 years	901	-0.352	0.228	.244^{NS}	21.36	21.00	7.00 / 33.00	5.09	7.25

NS = Non-significant deviation (p> .05) the variable is normally distributed

3.1.3. Functional OutcomeSmirnov Goodness of Fit Test

The DAS generates 15 variables: 14 particular items, plus a total score. The results of its exploration and description are summarized in Tables 4 and 5.

All of them, both in one measurement and in the other, move away in a highly significant way ($p < .001$) from the normal curve.

Regarding the descriptive indexes, and although most of the variables cover all or almost the entire range of possible values in each scale, clear asymmetries are observed due to the concentration of values at one or the other end of the continuum. This contributes to the lack of normality mentioned above. And with regard to averages values, some changes are observed between the basal state and that seen at 3 years, whose significance will have to be determined in the inferential part of the study.

Table 4: Exploratory and descriptive analysis. Variables of the Functional Outcome: DAS. (N = 100). Basal measurement.

		Exploration: Form			Centrality		Range	Variability	
Variable	N	Asymmetry	Kurtosis	Test SW: p-value	Mean	Median	(Min. / Max)	Standart deviation	Interquartil range
Personal care	100	2.162	4.525	.000**	0.41	0.00	0.00 / 4.00	0.82	0.75
Low Activity	100	0.759	-0.708	.000**	1.05	1.00	0.00 / 4.00	1.18	2.00
Slowness	100	1.700	1.892	.000**	0.39	0.00	0.00 / 3.00	0.71	1.00
Isolation	100	0.408	-1.025	.000**	1.37	1.00	0.00 / 4.00	1.26	2.00
Participation in home	100	1.093	0.353	.000**	0.64	0.00	0.00 / 3.00	0.82	1.00
Affective-Spouse	98	-1.679	0.866	.000**	7.41	9.00	0.00 / 9.00	3.38	0.00
Sexual-Spouse	98	-1.696	0.953	.000**	7.47	9.00	0.00 / 9.00	3.26	0.00
Children	99	-1.521	0.343	.000**	7.25	9.00	0.00 / 9.00	3.50	0.00
Opposite sex relations	99	1.033	0.048	.000**	0.58	0.00	0.00 / 3.00	0.76	1.00
Social contacts	99	2.651	6.705	.000**	0.14	0.00	0.00 / 2.00	0.38	0.00
Work performance	99	0.340	-1.863	.000**	3.95	1.00	0.00 / 9.00	4.22	9.00
Interest in getting a job	99	-0.494	-1.658	.000**	6.06	9.00	0.00 / 9.00	3.64	7.00
Interest information	99	4.280	29.887	.000**	0.79	1.00	0.00 / 9.00	1.11	1.00
Emergency behavior	99	1.440	1.177	.000**	0.31	0.00	0.00 / 2.00	0.53	1.00
Global DAS (F.O.)	100	0.043	-1.390	.006**	1.90	2.00	0.00 / 4.00	1.49	3.00

NS = Non-significant deviation (p> .05) the variable is normally distributed

** = Significant serious deviation (p <.01) the variable does not adjust to normal

Table 5: Exploratory and descriptive analysis. Variables of the Functional Outcome: DAS. (N = 100). Follow-up at 3 years.

		Exploration: Form			Centrality		Range	Variability	
Variable	N	Asymmetry	Kurtosis	Test SW: p-value	Mean	Median	(Mín. / Máx.)	Standart deviation	Interquartil Range
Personal care	92	2.176	4.001	.000**	0.30	0.00	0.00 / 3.00	0.0.66	0.00
Low Activity	92	0.968	-0.154	.000**	0.65	0.00	0.00 / 3.00	0.83	1.00
Slowness	92	1.356	0.566	.000**	0.41	0.00	0.00 / 3.00	0.67	1.00
Isolation	92	1.106	0.341	.000**	0.67	0.00	0.00 / 3.00	0.87	1.00
Participation in home	91	1.988	3.504	.000**	0.37	0.00	0.00 / 3.00	0.71	1.00
Affective-Spouse	91	-1.238	-0.466	.000**	6.86	9.00	0.00 / 9.00	3.823	0.00
Sexual-Spouse	91	-1.263	-0.378	.000**	6.89	9.00	0.00 / 9.00	3.781	0.00
Children	91	-1.290	-0.289	.000**	6.96	9.00	0.00 / 9.00	3.685	0.00
Opposite sex relations	91	1.646	1.577	.000**	0.51	0.00	0.00 / 3.00	0.89	1.00
Social contacts	91	8.185	71.989	.000**	0.16	0.00	0.00 / 2.00	0.99	0.00
Work performance	91	0.356	-1.877	.000**	3.82	1.00	0.00 / 9.00	4.31	9.00
Interest in getting a job	91	-1.191	-0.463	.000**	6.88	9.00	0.00 / 9.00	3.60	6.00
Interest information	91	4.035	24.841	.000**	0.64	0.00	0.00 / 9.00	1.21	1.00
Emergency behavior	90	3.571	13.353	.000**	0.10	0.00	0.00 / 2.00	0.34	0.00
Global DAS (F.O.)	93	0.497	-1.316	.000**	1.23	1.00	0.00 / 4.00	1.34	4.00

NS = Non-significant deviation (p> .05) the variable is normally distributed

** = Significant serious deviation (p <.01) the variable does not adjust to normal

3.2. INFERENTIAL ANALYSIS

The main intention of the previous exploratory / descriptive part of the variables is to know the way in which the quantitative variables are distributed since this influences the choice the right tests when testing the objectives mentioned above.

The 15 variables of the Functional Outcome (DAS) are the main variables (according to the objectives of the work). Its lack of adjustment to the bell of Gauss is decisive for the aforementioned election. Given this situation, it is advisable to use non-parametric statistical procedures that, while statistically less powerful, do not have such adjustment among their conditions and are also more appropriate (Krzywinski, M. and Altman, N., 2014).

In conclusion, for this inferential part the following non-parametric tests have been chosen:

- Spearman's correlation coefficient, for the associative study between pairs of quantitative variables.

- Test U of Mann-Whitney, for the crossing of a categorical factor with 2 independent categories, with quantitative variables.

- Test W of Wilcoxon, for the longitudinal study of the changes in quantitative variables.

4. Results

4.1. Study of the relations between Neurocognitive variables, ToM and DAS, at baseline.

In this objective, the study of the relations between all the neurocognitive variables (as factors, or I.V), as well as the variable ToM (also as I.V) with all the variables of the Functional Outcome (DAS) is proposed (considered as D.V.). The reasons given above suggest using the Spearman coefficient.

The results are summarized in table 6. It shows the values of the coefficients (scale: 0 - 1) and if they are statistically significant (1% or 5%) unilaterally. As can be seen in this table, there are few correlation coefficients that reach statistical significance (marked in bold) and those that are, show values with low intensity/magnitude. So, in particular:

- Global DAS score correlates with: Working Memory ($p < .05$, moderate intensity and inverse direction) and the Processing Speed ($p < .05$; light

intensity). According to this, the patients with higher values (worse state) in the Occupationalionality, tend to have lower scores in both factors (Working Memory and Processing Speed).

The Low Activity itemhas a highly significant relation (p <.01) of moderate and inverse intensity, again with the Working Memory. The Slowness itempresents a significant association (p <.05) also moderate and inverse, with the Executive Function. The Isolation is also significantly related (p <.05) moderately and inversely with the Working Memory. The affective-spouse itemhas a significant relation (p <.05) of a milder and more direct intensity, with visual memory. That is, in this case, it is patients with lower values in the item(better state) who tend to have higher scores in this memory factor. The Sexual-Spouse itembehaves very similarly to the previous one. And in the same line, we can see a relation in Children itemwith Verbal Memory.

Opposite sex relations reaches significant association with 3 factors, in order of more to less intensity, are: Verbal Memory (p <.01), Working Memory (p <.05) and Attention (p <. 05). The magnitudes are, like almost all, moderate. And the sense, inverse. The Social Contacts correlate significantly, moderately and inverse with the Working Memory (p <.05) and also but directly with the Motor Dexterity (p <.05). The Work Performance itemis significantly related (p <.05) moderate and inverse with Working Memory. The Interest in Getting a Job, with the Motor Dexterity (p <.05), again in moderate intensity and inverse (like most of the observed relations). And finally, Interest for Information is associated significantly with three factors that in order of more to less magnitude, are: Verbal Memory (p <.01), Premorbid IQ (p <.05) and Working Memory (p <.05) once again in the opposite direction.

Consequently, the Working memory factor is the one that has the most significant relation with the DAS items(a total of 7 out of 15). The verbal memory follows (with 3 meanings). ToM does not present any statistically significant relation with Functional Outcome items (DAS).

Table 6: *Inferential analysis Association between neurocognitive variables and TOM with the variables of DAS. Basal situation.*

Variables	*Verbal Memory*	*Working Memory*	*Motor Dexterity*	*Visual Memory*	*Executive Functioning*	*Attention*	*Premorbid IQ.:WAIS vocabulary*	*Processing Speed*	*TOM EYE-Task*
Global DAS (F.O.)	-.117	**-.208** *	.072	.061	-.092	-.100	-.011	**-.172** *	-.005

Personal Care	-.073	-.029	.052	.020	.111	-.083	.013	-.092	-.013
Low Activity	-.107	**-.293** **	.011	.133	-.097	-.104	-.097	-.159	.055
Slowness	-.165	-.125	.078	.068	**-.206** *	-.075	-.041	-.051	-.126
Isolation	-.083	**-.218** *	.059	.065	-.083	-.106	-.034	-.156	-.021
Participationn at home	-.088	-.129	.053	.062	-.023	.024	-.158	-.143	-.012
Affective-Spouse	.091	.009	.057	**.189** *	-.003	.024	.082	.089	.101
Sexual-Spouse	.099	.014	.055	**.200** *	-.001	.030	.082	.087	.120
Children	**.180** *	-.030	-.054	.155	.169	.044	-.035	.073	.098
Oppostie sex relations	**-.242** **	**-.191** *	.087	.023	-.149	**-.183** *	-.055	-.089	-.104
Social contacts	.040	**-.210** *	**.211** *	.083	-.105	-.087	-.044	-.157	.033
Work performance	-.098	**-.211** *	.080	.082	-.146	.008	.012	-.144	.000
Interest in getting a job	.105	.189 *	**-.202** *	.038	.133	.076	.001	.112	.068
Interest information	**-.257** **	**-.168** *	.211 *	.001	-.168	-.167	**-.174** *	-.203	-.124
Emergency behavior	-.030	-.017	.016	.070	-.086	-.039	-.095	-.040	-.135

* = Significant at 5% (P <.05) ** = Highly significant at 1% (P <.01)

To complete the study, the relation between the independent factors (ToM and Neurocognitive domains) has been calculated (table 7).

It has been found that ToM is significantly directly related to, in order: Attention (p <.01, high intensity), Verbal memory (p <.01, high), Premorbid IQ (p <.01 ; high),Visual Memory (p <.01, already moderate) and Executive Functioning (p <.05, moderate). And it also has a significant but inverse relation (p <.01) with Motor Dexterity.

On the other hand, almost all of the neurocognitive domains correlate significantly between them.

Table 7: *Inferential analysis Association of the neurocognitive variables among themselves and with the Theory of Mind (TOM). Basal situation.*

Variables	***Verbal Memory***	***Working Memory***	***Motor Dexterity***	***Visual Memory***	***Executive Functioning***	***Attention***	***Premorbid IQ: WAIS vocabulary***	***Processing Speed***
TOM	**.375** **	.088	**-.383** **	**.255** **	**.218** *	**.429** **	**.322** **	.153
Memoria Verbal	---							
Memoria de Trabajo	**.197** *	---						

Destreza Motriz	-.383 **	-.194 *	---					
Memoria Visual	.315 **	.076	-.433 **	---				
Memoria Visual	.309 **	.230 *	-.426 **	.287 **	---			
Atención	.350 **	.294 **	-.482 **	.292 **	.318 **	---		
Inteligencia: WAIS vocabul.	.222 *	.423 **	-.211 *	.180 *	.190 *	.209 *	---	
Vel. Procesam.: WAIS núm.	.363 **	.400 **	-.213 *	.180 *	.286 **	.190 *	.452 **	---
Vel. Procesam.: WAIS digitos	.365 **	.313 **	-.265 **	.225 *	.358 **	.304 **	.331 **	.715 **

* = Significant at 5% (P <.05) ** = Highly significant at 1% (P <.01)

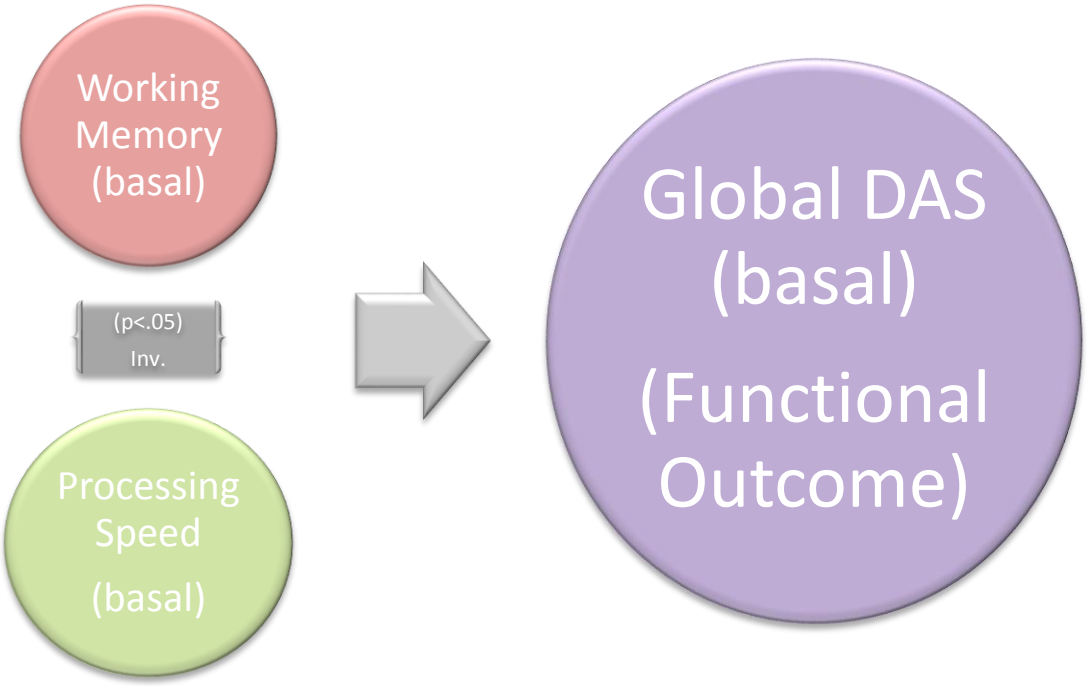


Illustration 1

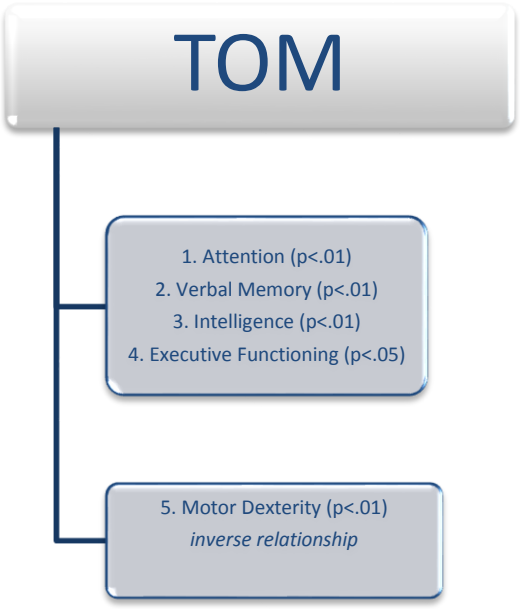


Illustration 2

4.2. Study of the relations between Neurocognitive domains, TOM and DAS, at 3 years.

The second objective raises the same question as the previous one, but with the values obtained by the subjects in the third year of follow-up. Logically, the same statistical procedure has been used

The results can be seen in table 8.

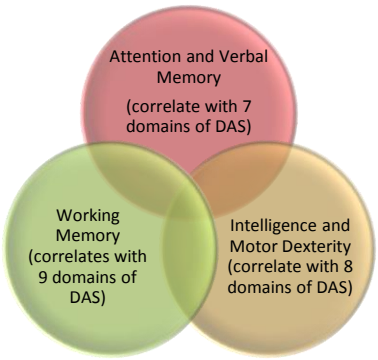
- Global DAS is significantly (p<.05) related to five variables: Working Memory, Attention, Verbal Memory, and Premorbid IQ. With Motor Dexterity it is showed a positive significant correlation (p=.314). It is not shown a correlation with Processing Speed (differently from basal measures).

Very interesting issues are appreciated, such items as Low Activity and Slowness, are associated with almost all variable (all these correlations inversed, except with Motor Dexterity). The same happens with Interest for Information, correlates significantly with all neurocognitive variables. Whereas, on the contrary, the itemsAffective-Spouse and Sexual-Spouse hardly have significant (positive) relation, only with Premorbid IQ. At baseline, they

presented a positive significant correlation with Visual Memory. And in addition, they have almost equal coefficients in all the crosses.

Interest for Information, Low Activity, and Children ($p<.01$) domain are the only ones which correlate with ToM. This relation was not observed at baseline.

Seen from the other side, the independent factors most related to the DAS itemsare: Working Memory (with 9), Motor Dexterity (8), the Premorbid IQ (another 8), the Verbal Memory (with 7) and Attention (other 7).



From a general point of view, the situation has changed quite a lot, as long as there are many more significant correlation coefficients. The most of these correlations are, still, inverse.

Table 8: *Inferential analysis Association between neurocognitive variables and TOM with the DAS total score and items. Follow-up at 3 years.*

Variables	***Verbal Memory***	***Working Memory***	***Motor Dexterity***	***Visual Memory***	***Executive Functioning***	***Attention***	***Premorbid IQ: WAIS vocabulary***	***Processing Speed***	***TOM EYE-Task***
Global DAS (F.O.)	**-.207** *	**-.324** **	**.314** **	-.118	-.174	**-.211** *	**-.197** *	-.125	-.074
Personal care	-.082	**-.208** *	**.317** **	-.117	-.143	-.015	**-.273** **	-.119	**-.201** *
Low acctivity	**-.243** **	**-.406** **	**.317** **	**-.197** *	**-.217** *	**-.194** *	**-.308** **	-.164	-.146
Slowness	**-.190** *	**-.336** **	**.244** *	-.151	**-.217** *	**-.209** *	**-.314** **	**-.245** *	-.150
Isolation	-.119	**-.276** **	**.193** *	-.040	-.110	**-.200** *	-.126	-.116	-.001
Participation in the home	-.140	**-.276** **	**.183** *	-.030	-.040	-.118	-.123	-.025	-.069
Affective-Spouse	.082	.131	-.160	.193	.007	.055	**.223** *	.121	.120
Sexual-Spouse	.082	.131	-.160	.193	.007	.057	**.223** *	.122	.120
Children	**.214** *	-.026	-.179	.114	**.201** *	.113	.054	-.090	**.254** **
Opposite sex relations	**-.188** *	**-.186** *	.176	-.058	-.158	**-.293** **	.001	-.091	-.052

Social contacts	.060	-.123	.097	-.073	-.022	**-.237** *	.006	-.121	-.007
Work performance	**-.277** **	**-.305** **	**.277** **	**-.216** *	-.161	-.017	**-.225** *	**-.186** *	-.039
Interest on getting a job	.196 *	.149	-.180	**.252** *	-.014	-.101	.020	.077	-.047
Interest information	**-.246** *	**-.433** **	**.390** **	**-.313** **	**-.239** *	**-.287** **	**-.365** **	**-.228** *	**-.233** *
Emergency behavior	-.139	-.158	.177	-.067	-.042	-.090	-.117	-.052	-.076

* = Significant at 5% (P <.05) ** = Highly significant at 1% (P <.01)

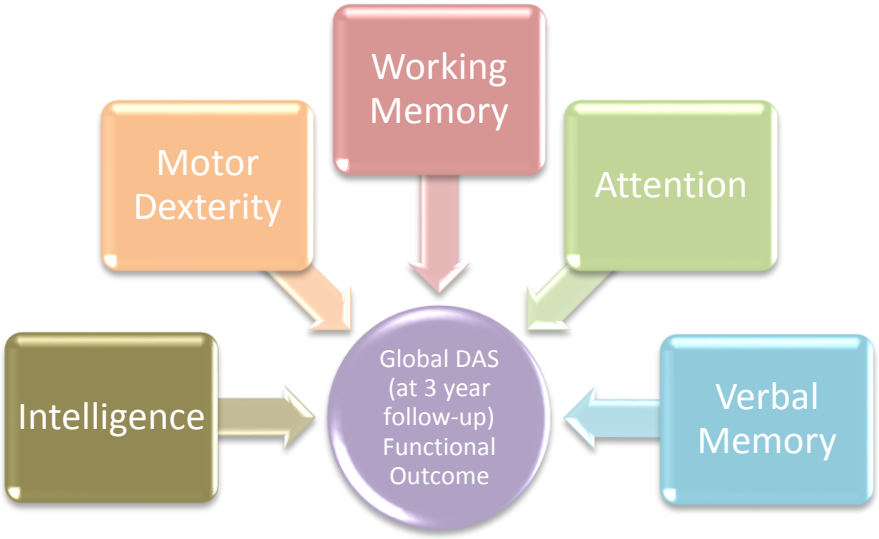
Regarding the correlations of I.V. between them (table 9), it is noticeable a similar situation with the one mentioned above, because the majority of the correlation coefficients have increased in intensity, although some do not. Therefore, now the variable ToM already correlates significantly with all neurocognitive variables. It is now seen a correlation with Working Memory (that did not exist at the beginning). And another interesting change is that in baseline Verbal Memory and ToM had a significantly positive correlation (p=.375) and now it is observed a significant negative correlation (p= -.296)

As much as these among themselves.

Table 9: *Inferential analysis. Association of the neurocognitive variables among themselves and with the TOM. Follow-up at 3 years.*

Variables	***Verbal Memory***	***Working Memory***	***Motor Dexterity***	***Visual Memory***	***Executive Functioning***	***Attention***	***Premorbid IQ: WAIS vocabulary***	***Processing Speed***
TOM (EYE task)	**-.296** **	**.387** **	**-.386** **	**.404** **	**.351** **	**.392** **	**.336** **	**.328** **
Verbal Memory	---							
Working Memory	**.383****	---						
Motor Dexterity	**-.378****	**-.476** **	---					
Visual Memory	**.364****	**.336** **	**-.397** **	---				
Executive Functioning	**.433****	**.327** **	**-.305** **	**.358** **	---			
Attention	**.233***	**.394** **	**-.337** **	**.344** **	**.291** **	---		
Premorbid IQ:WAIS vocabulary.	**.238***	**.529** **	**-.243** *	**.333** *	**.306** **	**.221** *	---	
Processing Speed	**.294****	**.568** **	.171	**.341** **	**.364** **	**.350** **	**.516** **	---

* = Significant at 5% (P <.05) ** = Highly significant at 1% (P <.01)



4.3. Gender differences

This objective was set out to determine if there exist differences between men and women and if these are maintained in both evaluation points. For this, although it would have been desirable to use the parametric tests of Student, the reasons repeatedly mentioned advise to use one of their non-parametric alternatives, such as the Mann-Whitney U-test of differences between two independent groups.

Table 10 summarizes the results of all variables in baseline. As can be seen, there are not many differences that reach statistical significance.

Among the neurocognitive ones, signification appears ($p < .05$) only in Verbal Memory and in Working Memory. In both, women obtain mean values (both mean and median) higher than men. Respectively, 8.37 vs 6.88 words and 7.22 vs 5.90 numbers.

In Occupational Functionality, is shown a significant difference ($p < .05$) in the total DAS score, with higher scores for men (2.26 vs 1.54). Highly significant differences ($p < .01$) are seen in: Low activity, Participation at home and in Interest for Information. In all three, the values reached by males are higher (worse state) than the values of women.

In the rest, including the variable of ToM, the gender differences are not significant (p> .05); although it is true that some of them could have become (p <.10): Premorbid IQ (higher score in women), and in Isolation, and Opposite sex relations (higher scores in men).

Table 10: *Inferential analysis Transversal study. Basal measurement. Differences in terms of Gender. All variables: Neurocognitive, ToM and Functional Outcome.*

	Men		**Women**		*Test M-W*	
Variable	Mean (D.E.)	Median	Mean (D.E.)	Median	**Value**	**P-Sig**
Verbal Memory	6.88 (2.55)	7.00	8.37 (2.96)	9.00	2.38	.017 *
Working Memory	5.90 (3.25)	5.50	7.22 (2.91)	7.00	2.16	.031 *
Motor Dexterity	72.44 (15.74)	69.50	75.12 (28.75)	68.00	0.44	.664 NS
Visual Memory	18.39 (7.25)	20.00	16.37 (6.85)	16.50	1.55	.123 NS
Executive Functioning	-57.98 (44.91)	-47.00	-70.37 (59.45)	-53.00	0.72	.473 NS
Atenttion	69.52 (14.61)	76.00	65.77 (17.44)	73.00	1.17	.243 NS
Premorbid IQ: WAIS vocabulary	8.94 (2.20)	9.00	9.78 (2.47)	10.00	1.88	.060 NS
Processing Speed	7.52 (3.23)	8.00	8.04 (3.43)	8.00	0.80	.430 NS
TOM (EYE task)	61.67 (4.82)	22.00	21.06 (4.25)	22.00	0.94	.351 NS
Global DAS (F.O.)	2.26 (1.50)	3.00	1.54 (1.40)	1.00	2.41	.017 *
Personal care	0.52 (0.95)	0.00	0.30 (0.65)	0.00	1.18	.244 NS
Low activity	1.42 (1.23)	1.00	0.68 (1.02)	0.00	3.19	.001**
Slowness	0.48 (0.79)	0.00	0.30 (0.61)	0.00	1.18	.253 NS
Isolation	1.60 (1.24)	2.00	1.14 (1.25)	1.00	1.92	.055 NS
Participation in the home	0.84 (0.84)	1.00	0.44 (0.76)	0.00	2.77	.006**
Affective-Spouse	7.59 (3.23)	9.00	7.22 (3.56)	9.00	0.58	.572 NS
Sexual-Spouse	7.67 (3.05)	9.00	7.27 (3.48)	9.00	0.63	.514 NS
Children	7.63 (3.13)	9.00	6.88 (3.82)	9.00	1.16	.246 NS
Opposite sex relations	0.73 (0.84)	1.00	0.42 (0.64)	0.00	1.94	.055 NS
Social contacts	0.20 (0.46)	0.00	0.08 (0.27)	0.00	1.54	.124 NS
Work performance	4.65 (4.33)	2.00	3.26 (4.04)	1.00	1.43	.153 NS
Interest in getting a job	5.63 (3.52)	9.00	6.48 (3.75)	9.00	0.82	.415 NS
Interest information	1.18 (1.35)	1.00	0.40 (0.61)	0.00	4.35	.000**
Emergency Behavior	0.37 (0.53)	0.00	0.26 (0.53)	0.00	1.28	.235 NS

N.S. = NOT significant (p> .05) * = Significant at 5% (p <.05) ** = Highly significant at 1% (p <.01)

Table 11 summarizes the results from the data obtained at 3-year follow-up. And as can be seen, there are less significant relations than in baseline. In fact, only the significance (p <.05) of the difference in Verbal Memory is maintained, where women still have the highest scores. In all the others there is no significance (p> .05). It should be mentioned trends toward significance in three variables (p <.10): Visual Memory, Participation in Home and in Interest for Information (with higher values, in all three, in men).

Table 11: *Inferential analysis Transversal study. Follow-up at 3 years. Differences in terms of Gender. All variables: Neurocognitive, ToM and DAS.*

	Men		**Women**		*Test M-W*	
Variable	Mean (D.E.)	Median	Mean (D.E.)	Median	**Value**	**P-Sig**
Verbal Memory	7.87 (3.38)	8.00	9.50 (3.29)	9.00	2.14	.032 *
Working Memory	7.57 (3.11)	7.50	8.70 (2.87)	9.00	1.84	.066 NS
Motor Dexterity	67.63 (17.82)	65.50	67.98 (17.73)	62.00	0.57	.575NS
Visual Memory	20.15 (7.22)	20.50	17.82 (6.24)	18.00	1.86	.063NS
Executive Functioning	-54.76 (48.83)	-40.50	-52.32 (57.99)	-33.00	0.88	.384NS
Attention	73.41 (11.13)	78.00	71.25 (11.60)	77.00	1.29	.200NS
Premorbid IQ: WAIS vocabulary	9.70 (2.20)	10.00	11.02 (5.08)	10.50	1.42	.156NS
Processing Speed.	8.54 (2.86)	9.00	8.95 (2.79)	9.00	0.76	.450NS
TOM (EYE task)	21.72 (5.37)	21.50	20.98 (4.82)	21.00	0.66	.510NS
Global DAS (F.O.)	1.38 (1.44)	1.00	1.08 (1.24)	1.00	0.87	.385 NS
Personal care	0.29 (0.70)	0.00	0.32 (0.63)	0.00	0.57	.588 NS
Low activity	0.78 (0.93)	0.00	0.53 (0.72)	0.00	1.16	.245 NS
Slowness	0.47 (0.69)	0.00	0.36 (0.64)	0.00	0.80	.445 NS
Isolation	0.67 (0.90)	0.00	0.68 (0.84)	0.00	0.24	.820 NS
Participation in the home	0.52 (0.85)	0.00	0.23 (0.52)	0.00	1.74	.087 NS
Affection-Spouse	7.43 (3.38)	9.00	6.32 (4.16)	9.00	1.43	.152 NS
Sexual-Spouse	7.50 (3.27)	9.00	6.32 (4.16)	9.00	1.43	.152 NS
Children	7.55 (3.20)	9.00	6.40 (4.04)	9.00	1.39	.158 NS
Opposite sex relations	0.55 (0.88)	0.00	0.47 (0.90)	0.00	0.75	.467 NS
Social contacts	0.07 (0.33)	0.00	0.26 (1.34)	0.00	0.40	.835 NS
Work performance	4.48 (4.40)	2.00	3.21 (4.18)	2.00	1.36	.176 NS
Interest in getting a job	6.30 (3.87)	9.00	7.43 (3.27)	9.00	1.36	.180 NS
Interest information	0.73 (0.92)	0.00	0.55 (1.43)	0.00	1.67	.096 NS
Emergency behavior	0.16 (0.43)	0.00	0.04 (0.20)	0.00	1.62	.124 NS

N.S. = NOT significant (p> .05) * = Significant at 5% (p <.05)

In conclusion, there has been hardly any differences due to gender at 3-year follow-up (just the differences in verbal memory are maintained).

4.4. Differences in the follow-up.

Finally, this last objective raises the possibility that there have been changes in time from the baseline measurement until those at 3-year follow-up. To do this, a statistical procedure of repeated measures must be used, specifically either ANOVA or Student. But for the same reasons already explained, it was decided to use the non-parametric alternative that corresponds to them: the W Test of Wilcoxon. This procedure has been used both with the complete sample and divided into two groups corresponding their gender. The results of the complete sample are summarized in Table 11 below. It has been found that:

- In the vast majority of neurocognitive variables, there are significant changes ($p < .01$). And in all of them, it has been observed that the scores obtained at 3 years are higher than the scores of the baseline measurement, with the exception of Motor Dexterity in which patients score higher at basal measures.
- In ToM task, there are no changes that can be admitted as significant ($p > .05$)
- In Functional Outcome (DAS) a highly significant change ($p < .01$) was found in the global scores, with the means at baseline being higher (worse). But in the particular items, only a few changes have been found ($p < .01$) in: Low Activity, Isolation, and Emergency Behavior; and also although with less power (only for $p < .05$) in Participation in the home. In all of them, as in the total score, it is observed that the subjects have higher values at baseline measurements.

Table 11: *Inferential analysis Longitudinal study. Changes in the evaluation of follow-up at 3 years with respect to the baseline measurement. Complete sample. All the variables: Neurocognitive, ToM and DAS.*

	Basal Measurement		**Measures at 3 year**		***W test***	
Variable	Mean (D.E.)	Median	Mean (D.E.)	Median	**Value**	**P-Sig**
Verbal Memory	7.56 (2.72)	7.00	8.67 (3.42)	9.00	3.01	.001**
Working Memory	6.57 (3.13)	7.00	8.12 (3.03)	8.00	5.09	.000**
Motor Dexterity	73.98 (23.83)	69.50	67.80 (17.68)	63.00	3.73	.000**
Visual Memory	17.47 (7.29)	18.00	19.01 (6.82)	19.00	2.46	.007**

Executive Functioning	-61.94 (51.48)	-49.00	-53.08 (53.12)	-39.00	2.85	.002**
Attention	67.63 (16.47)	75.00	72.21 (11.55)	77.00	3.12	.001**
Premorbid IQ: WAIS vocabulary	9.34 (2.32)	10.00	10.38 (3.93)	10.00	3.70	.000**
Processing Speed	7.78 (3.26)	8.00	8.74 (2.82)	9.00	3.24	.000**
TOM (EYE task)	21.43 (4.53)	22.00	21.52 (4.93)	21.00	0.32	.377^{NS}
Global DAS (F.O.)	1.83 (1.49)	2.00	1.23 (1.34)	1.00	3.48	.000**
Personal care	0.37 (0.78)	0.00	0.30 (0.66)	0.00	0.64	.269^{NS}
Low activity	0.98 (1.14)	1.00	0.65 (0.83)	0.00	2.47	.007**
Slowness	0.36 (0.69)	0.00	0.41 (0.67)	0.00	0.63	.274^{NS}
Isolation	1.35 (1.25)	1.00	0.67 (0.87)	0.00	4.65	.000**
Participation in the home	0.62 (0.84)	0.00	0.37 (0.71)	0.00	2.27	.012 *
Affective-Spouse	7.34 (3.45)	9.00	6.91 (3.79)	9.00	1.34	.099^{NS}
Sexual-Spouse	7.40 (3.32)	9.00	6.94 (3.75)	9.00	1.59	.058^{NS}
Children	7.18 (3.55)	9.00	7.03 (3.63)	9.00	0.79	.239^{NS}
Opposite sex relations	0.57 (0.75)	0.00	0.51 (0.89)	0.00	0.55	.299^{NS}
Social contacts	0.12 (0.36)	0.00	0.17 (1.00)	0.00	0.42	.353^{NS}
Work performance	3.81 (4.21)	1.00	3.87 (4.32)	1.00	0.12	.452^{NS}
Interest in getting a job	6.17 (3.63)	9.00	6.86 (3.61)	9.00	1.03	.155^{NS}
Interest information	0.74 (1.14)	1.00	0.64 (1.21)	0.00	0.96	.175^{NS}
Emergency behavior	0.30 (0.51)	0.00	0.10 (0.34)	0.00	3.28	.001**

N.S. = NOT significant (P> .05) * = Significant at 5% (P <.05) ** = Highly significant at 1% (P <.01)

As mentioned, the total group was divided into two groups according to their gender. The reduction of the N of subjects, by half in each sex, implies a mathematical increase in the values of the p-sig, so that it is more difficult to prove a significance.

Table 12 contains the results for men. As expected, the p-sig are higher. So, in particular:

- In the neurocognitive variables, it is possible to admit the existence of significant differences in a large part of the variables. The high significance is maintained (p <.01) in: Working Memory, Motor Dexterity, and Premorbid IQ. And it is also significant (only for p.05) for the changes in: Verbal memory, Attention, and Processing Speed. In all of them, the scores are higher in the follow-up evaluation at

three years, with the exception of the aforementioned Motor Dexterity. Significance has been lost in Visual Memory and in Executive Functioning.

- In the ToM variable, the lack of significant changes is also maintained (p >.05).
- In Functional Outcome, there is still a significant difference (p <.01) in the overall score of the DAS, being higher in the basal moment (worse state). And likewise, significant changes have been found in the itemsalready mentioned above: Low activity (p <.01), Isolation (p <.01), Participation in the home (p <.05) and Emergency behavior (p <. 05).

Table 12: Inferential analysis Longitudinal study. Changes in the evaluation of the follow-up at 3 years with respect to the basal measurement. All the variables: Neurocognitive, ToM and DAS.

Group of men

	Basal measurements		**Measurements at 3 year**		***W test***	
Variable	Mean (D.E.)	Median	Mean (D.E.)	Median	**Value**	**P-Sig**
Verbal Memory	6.80 (2.46)	7.00	7.87 (3.38)	8.00	2.01	.022 *
Working Memory	6.07 (3.28)	6.00	7.57 (3.11)	7.50	3.43	.000**
Motor Dexterity	71.87 (15.72)	69.50	67.63 (17.82)	65.50	2.45	.007**
Visual Memory	18.70 (7.28)	20.00	20.15 (7.22)	20.50	1.40	.083 NS
Executive Functioning	-53.93 (41.01)	-45.00	-54.76 (48.83)	-40.50	0.88	.192 NS
Attention	69.57 (14.76)	76.00	73.48 (11.30)	78.00	2.21	.013 *
Premorbid IQ: WAIS vocabulary	9.04 (2.20)	9.00	9.76 (2.19)	10.00	2.65	.003**
Processing Speed	7.61 (3.26)	8.00	8.54 (2.86)	9.00	2.12	.017 *
TOM (EYE task)	21.82 (4.86)	22.00	22.16 (4.94)	22.00	0.54	.296NS
Global DAS (F.O.)	2.22 (1.54)	3.00	1.38 (1.44)	1.00	3.06	.001**
Personal care	0.47 (0.92)	0.00	0.29 (0.70)	0.00	1.21	.137NS
Low activity	1.40 (1.25)	1.00	0.78 (0.93)	0.00	2.77	.002**
Slowness	0.42 (0.75)	0.00	0.47 (0.69)	0.00	0.47	.354NS
Isolation	1.60 (1.27)	2.00	0.67 (0.90)	0.00	3.92	.000**
Participation in the home	0.82 (0.90)	1.00	0.52 (0.85)	0.00	1.87	.036 *
Affective-Spouse	7.58 (3.26)	9.00	7.60 (3.22)	9.00	0.11	.500NS
Sexual-Spouse	7.67 (3.06)	9.00	7.67 (3.09)	9.00	0.08	.500NS
Children	7.65 (3.10)	9.00	7.72 (3.02)	9.00	0.38	.500NS
Opposite sex relations	0.74 (0.85)	1.00	0.56 (0.//)	0.00	1.30	.106NS
Social contacts	0.16 (0.43)	0.00	0.07 (0.34)	0.00	1.03	.219NS
Work performance	4.60 (4.37)	2.00	4.58 (4.40)	2.00	0.10	.466NS
Interest in getting a job	5.67 (3.50)	9.00	6.23 (3.90)	9.00	0.53	.301NS

Interest information	1.16 (1.43)	1.00	0.74 (0.93)	0.00	1.70	.051^{NS}
Emergency behavior	0.38 (0.54)	0.00	0.17 (0.44)	0.00	2.32	.017 *

N.S. = NOT significant (P> .05) * = Significant at 5% (P <.05) ** = Highly significant at 1% (P <.01)

In table 13 the results for women are summarized, suggesting they do not behave like men in some of the variables. Specifically:

- In the neurocognitive variables, there are significant differences in all of them. There are highly significant changes (p <.01) in: Working Memory, Motor Dexterity, Executive Functioning, Premorbid IQ and Processing Speed; while the differences are only significant (p <.05) in: Verbal memory, Visual memory, and Attention. In almost all of these variables, as in the case of men, the scores are higher in the follow-up at three years, with the aforementioned exception of the Motor Dexterity.
- In the task of ToM, significant changes still do not appear (p> .05).
- And in Functional Outcome, the highly significant difference (p <.01) is observed in Global DAS, with higher values (worse state) at baseline. In terms of items, there are significant differences in Isolation (p <.01) and in Emergency Behavior (p <.05). Also, significant changes have been found (that in men was not observed) in: Affective-spouse (p <.05) and Sexual-spouse (p <.05) in which the scores are higher in the basal measure. And in its place, there is no significant difference in Low Activity, as it was for men.

Table 13: Inferential analysis Longitudinal study. Changes in the evaluation of follow-up at 3 years with respect to the baseline measurement. All the variables: Neurocognitive, ToM and DAS.

Group of women.

	Basal measurements		**Measurements at 3 year**		*W test*	
Variable	Mean D.E.)	Median	Mean (D.E.)	Median	**Value**	**P-Sig**
Verbal Memory	8.34 (2.79)	9.00	9.50 (3.29)	9.00	2.21	.013 *
Working Memory	7.09 (2.92)	7.50	8.70 (2.87)	9.00	3.70	.000**
Motor Dexterity	76.18 (30.12)	69.00	67.98 (17.73)	62.00	2.78	.002**
Visual Memory	16.18 (7.16)	16.00	17.82 (6.22)	18.00	2.18	.014 *
Executive Functioning	-71.15 (60.60)	-53.00	-51.15 (58.24)	-32.00)	3.20	.000**
Attention	65.69 (18.00)	73.00)	70.95 (11.79)	76.00	2.19	.014 *

Premorbid IQ: WAIS vocabulary	6.94 (2.44)	10.00	11.02 (5.08)	10.50	2.47	.006**
Processing Speed	7.95 (3.29)	8.00	8.95 (2.79)	9.00	2.51	.006**
TOM (EYE task)	21.02 (4.18)	22.00	20.86 (4.89)	21.00	0.14	.448^{NS}
Global DAS (F.O.)	1.46 (1.37)	1.00	1.08 (1.24)	1.00	1.79	.002**
Personal care	0.28 (0.62)	0.00	0.32 (0.63)	0.00	0.18	.440^{NS}
Low activity	0.57 (0.85)	0.00	0.53 (0.72)	0.00	0.37	.378**
Slowness	0.30 (0.62)	0.00	0.36 (0.64)	0.00	0.47	.354^{NS}
Isolation	1.11 (0.84)	0.00	0.68 (0.64)	0.00	2.51	.006**
Participation in the home	0.43 (0.74)	0.00	0.23 (0.52)	0.00	1.38	.091 ^{NS}
Affective-Spouse	7.11 (3.64)	9.00	6.26 (4.20)	9.00	1.83	.039 *
Sexual-Spouse	7.15 (3.56)	9.00	6.26 (4.19)	9.00	2.09	.018 *
Children	6.74 (3.90)	9.00	6.40 (4.04)	9.00	1.19	.188^{NS}
Opposite sex relations	0.40 (0.61)	0.00	0.47 (0.90)	0.00	0.68	.237^{NS}
Social contacts	0.09 (0.28)	0.00	0.26 (1.34)	0.00	0.35	.414^{NS}
Work performance	3.09 (3.96)	1.00	3.21 (4.18)	0.00	0.10	.463^{NS}
Interest in getting a job	6.62 (3.73)	9.00	7.43 (3.27)	9.00	0.96	.176^{NS}
Interest information	0.36 (0.57)	0.00	0.55 (1.43)	0.00	0.46	.322^{NS}
Emergency behavior	0.23 (0.48)	0.00	0.04 (0.20)	0.00	2.32	.017 *

N.S. = NOT significant (P> .05) * = Significant at 5% (P <.05) ** = Highly significant at 1% (P <.01)

5. DISCUSSION

The purpose of this work was to study the relations of neurocognition, ToM and functional outcome in patients who were going through a first-episode of schizophrenia. Several researchers enhance neurocognitive impairments and deficits in ToM (understating one`s and other`s mental states), in patients with schizophrenia (Fett et al., 2011; Kosmidis et al., 2008; Reichenberg et al., 2010). Findings reveal that these are two different domains but, related between them (Sergi et al., 2007). Such impairments have been observed also in patientswith a first-episode of schizophrenia (Harrington et al., 2012).

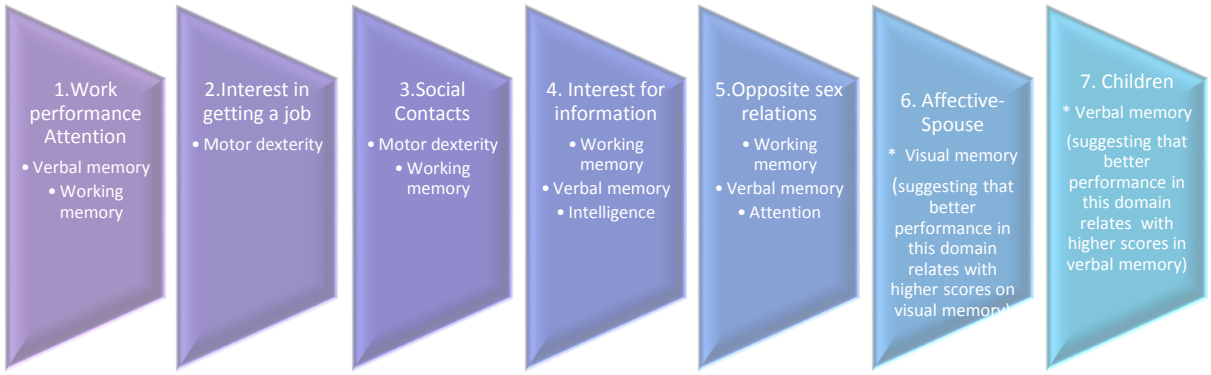
Inevitably, arises the need to know about the effects that these impairments can cause to patient`s daily life, family relationships, social life, performance in work,..etc. Rinaldi et al 2010, in a review about employment and first-episode psychosis, concluded that young people with a first episode start to lose their job, even though they would prefer to work and have a social life. Different investigations studied this impact on functional outcome, such as Velligan and colleagues (2000), where was suggestedthat functionality was affected by neurocognition` -s domains, or, Rowena and colleagues (2015) who concludedthat ToM is related with poor outcome.

So, based on the searched literature and on the purpose of this work, it was hypothesized that neurocognitive domains have a higher significant relation with functional outcome in comparison with ToM (in the two time-points).

It could be said that the first hypothesis was partially proved because global functioning at baseline was significantly related just with two of the neurocognitive domains (from 8), demonstrating a significant (inverse) relation with working memory and processing speed. This indicates that patients with a worse state in functional outcome tend to have lower scores in both aforementioned domains. This finding is in accordance with Gonzalez-Ortega et al 2013, who showed the association of working memory with functional outcome. In the same vein, Reichenberg et al 2010, suggested working memory as the domain with the higher average of impairment in patients with schizophrenia. Other findings mentioned processing speed as the most impaired domain in first-episode patients and as the main predictor of outcome (Rodriguez-Sanchez et al 2007 and Ojeda et al 2008). On the other hand, at this time-point evaluation, ToM didn`t show a significant association either with global

functioning nor with its items. Contrary tothe findings of Couture et al 2006. At this time-point, it was observed a relation of ToM with processing speed (in accordance with Ayesa-Arriola et la 2016), attention, premorbid IQ, verbal memory, and motor dexterity. The data suggested an inverse relation between ToM and motor dexterity. Further research is needed to investigate this result.

Meanwhile, the significative relations between functioning items and neurocognition domains, are shown in the illustration below.



Each one of this findings generates investigations issues

At 3 years follow-up, global functional outcome correlated with more neurocognitive domains, such as: working memory, attention, verbal memory, premorbid IQ, and motor dexterity. In accordance with other investigations (Milev et al., 2005; Bowie et al., 2008; Tandberg et al.,2011; Roncone et al., 2002; Piñon et al., 2018 and Lesson et al.,2009). Other findings mentioned also executive functioning (Ventura et al., 2009 and Green et al., 2004) but in this work didn`t show any significant relations. Bowie and colleagues (2006) also demonstrated that neurocognitive variables are highly associated with functional outcome.

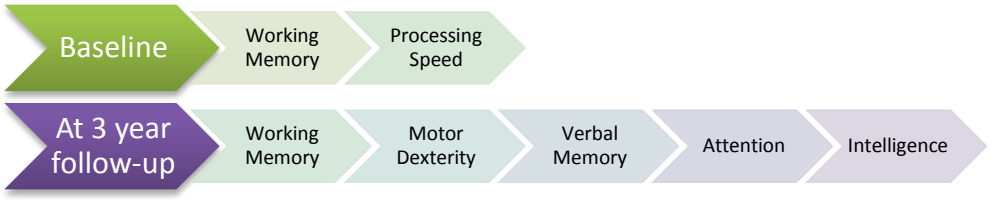
At this second time-point, ToM still doesn`t correlate significantly with the global functional outcome. This result is different from the conclusions of other researchers (Roncone et al., 2002; Rowena et al., 201, Couture et al., 2006 and Fett et al., 2011). Although, relations are observed with some of its items, such as: Interest for information, Personal care, and Children`s dimension. Just the relation with children`s dimension is positive, suggesting that lower scores on ToM are related with poor performance on this domain (and backward).As mentioned above in this work (Green et al., 2008), the importance of ToM is crucial in the relationship with others and this result may be due to this fact.

About its relations with neurocognitive domains, in this second time-point, ToM correlates with all of them (as seen above in Table 9).

In both time-points, neurocognitive domains correlate among them and also do with ToM (except working memory in baseline).

About the functional outcome`s items relations with neurocognition, is important to mention that their correlations after 3-year follow-up have incremented. Just the emergency behavior domain doesn`t show any correlation.

So, partly according to Cook et al 2013, these findings suggest that neurocognition domains, differently from ToM, have a significant relation with functioning**.**



The second hypothesis was that subjects would perform a better state in functional outcome measured after 3-year follow-up, in comparison with functionality measured at baseline. This hypothesis was confirmed. Aforementioned results affirm that in terms of the global functional outcome, it was observed a highly significant change, suggesting that the general state improves at 3 years follow-up. The subjects showed better functioning on items like: low activity, isolation, emergency behavior and participation at home. Also, it`s observed a better performance in all neurocognitive domains. Such result affirms the significant relation between neurocognition and functional outcome because, as it is shown in table 11, are observed higher median scores on neurocognitive domains and lower ones (better) in functional outcome. In accordance with Malla et al., 2005, these findings suggest the importance of early interventions in these domains (among others) to improve functionality.

So, this strong relation of global functioning with neurocognitive domains is important for further research and for treatment plans.

The longitudinal study of the two-time points didn`t show any significant change in ToM. According tothe suggestions of other studies mentioned above, it wasn`t expected this result, although it may be due to the fact that ToM, as a part of social cognition, was measured just with one task.Badgaiyan 2009,concludes that it is not clear if ToM impairments in schizophrenia show impairments on the expressionof what they see or understand, or

impaired ToM, to resolve this issue would be recommended to asses separately this factors. Further research is needed to clarify this vagueness.

Regarding gender differences, the longitudinal study of the follow-up showed that the functional outcome is similar for the two groups, with the difference that women show a significantly better in two aspects: Affective-Spouse and Sexual-Spouse. In accordance with the findings of Usall and colleagues (2007), DAS differ in gender. Although it is worth to mention that at baseline women showed a better global functioning, this significant relation was not maintained. Grossman et al 2008, also conclude that women show a tendency for a better outcome, and it is concluded that this may lead to a better course of illness. ToM remains with insignificant changes, without showing differences due to gender. This finding leads to thinking that ToM is a trait, implying a more stable and permanent performance it is not a state (a momentary reaction). Further investigations are needed to clarify this result on first-episode patients.

For the neurocognitive domains, differences between men and women are also seen in working memory, verbal memory (showing women higher scores). Except for the difference in verbal memory, all the other differences are not maintained at 3-year follow-up. This result is different from the findings of Moriarty et al 2001, who concluded that there are no gender differences in neurocognitive variables. Reviewing the literature about gender differences in first-episode schizophrenia, Ochoa et al., 2012 concluded that one of the reasons for these differences may be due to the higher age of onset in women, which may provide women patients a better adaptation with functionality in their daily life. In accordance with this conclusion, in the present study, patients had an average age higher in women. Or, this small differences may be due to the gender occupation role in the society? Future research is needed to resolve many questions.

5.1. Limitations

The present study has several limitations. A multidimensional study and analysis would be needed to investigate in depth these relations and to see which variable affects each other. Without forgetting that providing some of the subject`s personal characteristic, would be really interesting. Also, it was used just one task to measure ToM (EYE task), and this resulted in a relatively limited assessment of ToM. Remaining in the same line, it would be helpful to assess more social cognition domains, apart from ToM. This would enrich the present`s study results and conclusions. As another important limitation is also the

medication that the patients were taking during the 3 years follow-up. It has been included descriptive information about their initial treatment (antipsychotic), but their side effects were not assessed, and also were not investigated the impact that they may have on all the neurocognitive domains, ToM and also on functional outcome. Also, it would be helpful to include more data such as stressful life events, self-attitudes, personality traits, interest in working based on their material need to work..etc. Another important limitation is that to obtain more generalized conclusions, a larger sample would be needed.

6. Conclusions

Resuming the findings of the present study it could be said that it provides important information about how neurocognition, ToM and functional outcome relate to each other. In conclusion, at the first time-point, the patients with a first episode of schizophrenia showed worse functioning in comparison with the results at the second time-point (3 year follow-up). Women performed significantly better than men, but this difference did not appear at the follow-up.

Differently, from ToM, neurocognition relates with functional outcome at both time-points. Specifically, at baseline global functioning is related to working memory and processing speed. And, at the three years follow up it is related to working memory, verbal memory, attention, motor dexterity, and premorbid IQ. Different aspects of functioning related to domains of neurocognition, which on the other hand, correlate among them. ToM does not relate significantly to the global functioning, and doesn't differ from gender, but relates to almost all neurocognitive variables. The present work could help further investigations or treatment interventions about which domains are strongly related to functional outcome in patients with a first-episode of schizophrenia.

7. References*:*

1. Addington, J., & Addington, D., (2002). Cognitive functioning in first-episode schizophrenia. *Journal of Psychiatry and Neuroscience, 27*(3), 188–192.

2. Addington, J., Girard, T. A., Christensen, B. K, Addington, D. (2010). Social cognition mediates illness-related and cognitive influences on social function in patients with schizophrenia-spectrum disorders. *Journal of Psychiatry and Neuroscience*: JPN, 35(1), 49-54. http://doi.org/10.1503/jpn.080039

3. Ayesa-Arriola, R., Setién-Suero, E., Neergaard, K. D., Ferro, A., Fatjó-Vilas, M., Ríos-Lago, M., … Crespo-Facorro, B. (2016). Evidence for Trait Related Theory of Mind Impairment in First-Episode Psychosis Patients and Its Relationship with Processing Speed: A 3 Year Follow-up Study. *Frontiers in Psychology*, 7, 592. http://doi.org/10.3389/fpsyg.2016.00592

4. Badgaiyan, R. D., (2009). Theory of mind and schizophrenia. *Consciousness and Cognition*, 18(1), 320–324. http://doi.org/10.1016/j.concog.2008.10.008

5. Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y., and Plumb, I. (2001). The "Reading the Mind in the Eyes" Test revised version: a study with normal adults, and adults with Asperger syndrome or high-functioning autism. *J. Child Psychol. Psychiatry* 42, 241–251. http:/doi.org/10.1111/1469-7610. 00715

6. Bell, M. D., Bryson, G., (2001). Work rehabilitation in schizophrenia: does cognitive impairment limit improvement? *Schizophr Bull*. 27(2): 269–279

7. Bora, E., Yucel, M., Pantelis, Ch., (2009). Theory of mind impairment in schizophrenia: meta-analysis. *Schizophr Res.* 109(1-3): 1–9. http://doi.org/10.1016/j.schres.2008.12.020

8. Bowie, C. R., Leung, W. W., Reichenberg, A., McClure, M. M., Patterson, T. L., Heaton, R. K., & Harvey, P. D. (2008). Predicting Schizophrenia Patients' Real World Behavior with Specific Neuropsychological and Functional Capacity

Measures. *Biological Psychiatry*, 63(5), 505–511. http://doi.org/10.1016/j.biopsych.2007.05.022

9. Bowie, Ch. R., Reichenberg, A., Patterson, Th. L., Heaton, R. K., Harvey, Ph. D., (2006). Determinants of real-world functional performance in schizophrenia subjects: correlations with cognition, functional capacity, and symptoms. *Am J Psychiatry*. 163(3): 418–425. http://doi.org/10.1176/appi.ajp.163.3.418

10. Brekke, J. S., Raine, A., Ansel, M., Lencz, T., Bird, L., (1997). Neuropsychological and psychophysiological correlates of psychosocial functioning in schizophrenia. *Schizophr Bull.* 23(1): 19–28.

11. Bright-Paul, A., Jarrold, Ch., Wright, D. B., (2008). Theory-of-mind development influences suggestibility and source monitoring. *Dev Psychol*.; 44(4): 1055–1068. http://doi.org/10.1037/0012-1649.44.4.1055

12. Cegalis, J., and Bowlin, J. (1991). Vigil: Software for the Assessment of Attention. Nashua, *NH: Forthought*.

13. Cook, E. A., Liu, N. H., Tarasenko, M., Davidson, C. A., & Spaulding, W. D. (2013). Longitudinal Relationships between Neurocognition, Theory of Mind, and Community Functioning in Outpatients with Serious Mental Illness (SMI). *The Journal of Nervous and Mental Disease*, 201(9), 10.1097/NMD.0b013e3182a2140b. http://doi.org/10.1097/NMD.0b013e3182a2140b

14. Cornblatt, B. A., Green M. F., Walker E. F., Mittal V. A., (2009). Schizophrenia: Etiology and neurocognition. In: Blaney PH, Millon T, editors. *Oxford Textbook of Psychopathology*. Oxford University Pres. 298–332.

15. Couture, S. M., Granholm, E. L., & Fish, S. C. (2011). A Path Model Investigation of Neurocognition, Theory of Mind, Social Competence, Negative Symptoms and Real-World Functioning in Schizophrenia. *Schizophrenia Research*, 125(2-3), 152–160. http://doi.org/10.1016/j.schres.2010.09.020

16. Couture, Sh. M., Penn, D. L., Roberts, D. L. (2006). The Functional Significance of Social Cognition in Schizophrenia: A Review. *Schizophrenia Bulletin (*Volume-1, Suppl-32), S44-S63. http://dx.doi.org/10.1093/schbul/sbl029

17. Fett, A. K. J., Viechtbauer, W., Dominguez, M. G., Penn, D. L., van Os, J., Krabbendam, L., (2011). The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: a meta-analysis. *Neurosci Biobehav Rev.* 35(3): 573–588. http://doi.org/10.1016/j.neubiorev.2010.07.001

18. First, M. B., Spitzer, R. L., Gibbon, M., and Williams, J. B. W. (1996). Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-CV). Washington, DC: *American Psychiatric Press, Inc.*

19. Frith, C.D., Corcoran, R.,(1996). Exploring 'theory of mind' in people with schizophrenia. *Psychol Med.* 26(3): 521–530.

20. González-Ortega, I., De Los Mozos, V., Echeburúa E., Mezo, M., Besga, A., Ruiz de Azúa, S., González-Pinto, A., Gutierrez, M., Zorrilla, I., González-Pinto, A., (2012). Working memory as a predictor of negative symptoms and functional outcome in first episode psychosis. *Psychiatry Res.* 206(1): 8–16. http.//doi.org/10.1016/j.psychres.2012.08.025

21. Green, M. F., Kern, R. S., Heaton, R. K., (2004). Longitudinal studies of cognition and functional outcome in schizophrenia: implications for MATRICS. *Schizophr Res.* 72(1): 41–51. http://doi.org/10.1016/j.schres.2004.09.009

22. Green, M. F., Penn, D. L., Bentall, R., Carpenter, W. T., Gaebel, W., Gur, R. C., Heinssen, R., (2008). Social cognition in schizophrenia: An NIMH workshop on definitions, Assessment and research opportunities. *Schizophrenia Bulletin,* 34(6), 1211-1220. http:/doi.org/10.1093/schbul/sbm145

23. Grossman, L. S., Harrow, M., Rosen, C., Faull, R., Strauss, G. P., (2008). Sex differences in schizophrenia and other psychotic disorders: A 20-year study of psychosis and recovery. *Comprehensive Psychiatry,* 49(6), 523-529. http://doi.org/10.1016/j.comppsych.2008.03.004

24. Harrington, L., McClure, J., Siegert, R. J., Langdon, R.,(2012) Schizophrenia, theory of mind, and persecutory delusions. *Cognitive Neuropsychiatry*, 10:2, 87-104, http://doi.org/10.1080/13546800344000327

25. Keshavan, M. S., Schooler, N. R., (1992). First-episode studies in schizophrenia: criteria and characterization. *Schizophr Bull.* 18(3): 491–513.

26. Khamker, N., (2015). First episode schizophrenia. *South African Family Practice,* 57(5), 29–33.

27. Kosmidis, M. H., Aretouli, E., Bozikas, V. P., Giannakou, M., & Ioannidis, P. (2008). Studying Social Cognition in Patients with Schizophrenia and Patients with Frontotemporal Dementia: Theory of Mind and the Perception of Sarcasm. *Behavioral Neurology*, *19*(1-2), 65–69. http://doi.org/10.1155/2008/157356

28. Krzywinski, M., Altman, N., (2014). Points of significance: Nonparametric tests.*Nat Methods.*11(5): 467–468. http://doi.org/10.1038/nmeth.2937

29. Lesson, V. C., Barnes, T. R. E., Hutton, S. B., Ron, M. A., Joyce, E. M., (2009) IQ is a predictor of functional outcome in schizophrenia: A longitudinal four-year study of first-episode psychosis. *Schizophrenia Research,* 107(1), 55-60. http://doi.org/10.1016/j.schres.2008.08.014

30. Lezak, M. (1995). Neuropsychological Assessment. New York, NY: *Oxford University Press*

31. Mañá, S., Ivorra, J., Girón, M., 1998. Adaptación y fiabilidad de la entrevista para la evaluación de la discapacidad social en pacientes psiquiátricos (OMS). vol. 25(2). Revista de Psiquiatría de la Facultad de Medicina de Barcelona, pp. 43–48.

32. Meyer, M. B., & Kurtz, M. M., (2009). Elementary Neurocognitive Function, Facial Affect Recognition, and Social-skills in Schizophrenia. *Schizophrenia Research*, *110*(1-3), 173–179. http://doi.org/10.1016/j.schres.2009.03.015

33. Mohamed, S., Paulsen, J. S., O`Learly, D., Arndt, S., Andreasen, N., (1999). Generalized cognitive deficits in schizophrenia. Study of first-episode patients. *Arch Gen Psychiatry*: 56(8): 749-754. http://doi.org/10.1001/archpsyc.56.8.749

34. Milev, P., Ho, B. Ch., Arndt, S., Andreasen, N. C., (2005). Predictive values of neurocognition and negative symptoms on functional outcome in schizophrenia: a longitudinal first-episode study with 7-year follow-up. *Am J Psychiatry.* 162(3): 495–506. http://doi.org/10.1176/appi.ajp.162.3.495

35. Moriarty, P. J, Lieber, D., Bennett, A., White, L., Parrella, M., Harvey, P. D., Davis, K. L., (2001). Gender differences in poor outcome patients with lifelong schizophrenia. *Schizophr Bull.*; 27(1): 103–113.

36. Moskowitz, A., Heim, G., (2011). Eugen Bleuler's *Dementia Praecox or the Group of Schizophrenias*(1911): A Centenary Appreciation and Reconsideration, *Schizophrenia Bulletin*, 37 (3), 471-479, https://doi.org/10.1093/schbul/sbr016

37. Nuechterlein, K. H., Barch, D. M., Gold, J. M., Goldberg, T. E., Green, M. F., Heaton, R. K., (2004). Identification of separable cognitive factors in schizophrenia. *Schizophr Res.* 72(1): 29–39. http://doi.org/10.1016/j.schres.2004.09.00

38. Ochoa, S., Usall, J.,Cobo, J., Labad, X.,Kulkarni, J., (2012). Gender Differences in Schizophrenia and First-Episode Psychosis: A Comprehensive Literature Review. *Schizophr Res Treatment.* 2012; 2012: 916198.. http:/doi.org/10.1155/2012/916198

39. Ojeda, N., Peña, J., Sánchez, P., Elizagárate, E., Ezcurra, J., (2008). Processing speed mediates the relationship between verbal memory, verbal fluency, and functional outcome in chronic schizophrenia. *Schizophr Res.*101(1-3): 225–233. http://doi.org/ 10.1016/j.schres.2007.12.483

40. Osterrieth, P. A. (1944). Contribution an l'étude de la perception et de la memoire (The test of copying a complex figure: a contribution to the study of perception and memory). *Arch. Psychol.* 30, 286–350.

41. Penn, D. L., Sanna, L. J., Roberts, D. L., (2008). Social Cognition in Schizophrenia: An Overview, *Schizophrenia Bulletin*, 34 (3), 408–411, https://doi.org/10.1093/schbul/sbn014

42. Periáñez, J. A., Ríos-Lago, M., Rodríguez-Sánchez, J. M., Adrover-Roig, D., Sánchez-Cubillo, I., Crespo-Facorro, B., et al. (2007). Trail Making Test in traumatic brain injury, schizophrenia, and normal ageing: sample comparisons and normative data. *Arch. Clin. Neuropsychol*. 22, 433–447. doi: 10.1016/j.acn.2007.01.022

43. Piñon, A., Alvarez, M. C., Torres, T., Vaazquez, P., Otero, F., (2018). Neuropsychological profile of patients diagnosed with schizophrenia spectrum disorder. *Revista de Discapacidad, Clínica y Neurociencias* (RDCN). 5.1. 1-14.

44. Premack, D., Woodruff, G. (1978). Does the chimpanzee have a theory of mind? *Behavioral and Brain Sciences*, 1(4), 515-526. http://doi.org/10.1017/S0140525X00076512

45. Reichenberg, A. (Avi). (2010). The assessment of neuropsychological functioning in schizophrenia. *Dialogues in Clinical Neuroscience*, *12*(3), 383–392.

46. Reitan, R. M., and Wolfson, D. (1985). The Halstead–Reitan Neuropsychological Test Battery: Therapy and Clinical Interpretation. Tucson, AZ: *Neuropsychological Press.*

47. Rey, A. (1964). L'Examen Clinique en Psychologie. Paris: *Presses Universitaires de France.*

48. Rinaldi, M., Killackey, E., Smith, J., Shepherd, G., Singh, S. P., Craig, T., (2010). First episode psychosis and employment: A review. *Int Rev Psychiatry*. 22(2): 148–162. http://doi.org/10.3109/09540261003661825

49. Rodríguez-Sánchez, J. M., Crespo-Facorro, B., González-Blanch, C., Perez-Iglesias, R., Vázquez-Barquero, J. L., (2007). Cognitive dysfunction in first-episode psychosis: the processing speed hypothesis. PAFIP Group Study *Br J Psychiatry Suppl*. 51: s107- s110. http://doi.org/10.1192/bjp.191.51.s107

50. Roncone, R., Falloon, J. R. H., Mazza, M., De Risio, A., Pollice, R., Necozione, S., Morosini, P. L., Casacchia, M., (2002). Is theory of mind in schizophrenia more strongly associated with clinical and social functioning than with neurocognitive deficits?. *Psychopathology*. 35(5): 280–288. http://doi.org/10.1159/000067062

51. Rowena, Ng., Fish, S., & Granholm, E. (2015). Insight and theory of mind in schizophrenia. *Psychiatry Research*, *225*(0), 169–174. http://doi.org/10.1016/j.psychres.2014.11.010

52. Sergi, M. J., Rassovsky, Y., Widmark, C., Reist, Ch., Erhart, S., Braff, D. L., Marder, S. R., Green, M. F., (2007). Social cognition in schizophrenia: Relationships with neurocognition and negative symptoms. *Schizophrenia Research*, (Volume 90,Issue 1). 316 - 324. http://doi.org/10.1016/j.schres.2006.09.028

53. Tabarés-Seisdedos, R., Balanzá-Martínez, V., Sánchez-Moreno, J., Martinez-Aran, A., Salazar-Fraile, J., Selva-Vera, G., Rubio, C., Mata, I., Gómez-Beneyto, M., Vieta, E., (2008). Neurocognitive and clinical predictors of functional outcome in patients with schizophrenia and bipolar I disorder at one-year follow-up. *J Affect Disord.* 109(3): 286–299. http://doi.org/10.1016/j.jad.2007.12.234

54. Tandberg, M., Ueland, T., Sundet, K., Haahr, U., Joa, I, Johannessen, J. O., Larsen, T. K., Opjordsmoen, S., Rund, B. R., Røssberg J. I., Simonsen, E., Vaglum, P., Melle, I., Friis, S., ., (2011). Neurocognition and occupational functioning in patients with first-episode psychosis: a 2-year follow-up study. *Psychiatry Res.*188(3): 334–342. http://doi.org/10.1016/j.psychres.2011.04.021

55. Usall, J., Haro, J. M., Araya, S., Moreno, B., Muñoz, P. E., Martínez, A., & Salvador, L.,(2007). Social functioning in schizophrenia: what is the influence of gender?. *The European Journal of Psychiatry*, *21*(3), 199-

205.http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S0213616320070003000 04&lng=es&tlng=en.

56. Velligan, D. I., Bow-Thomas, C. C., Huntzinger, C., Ritch, J., Ledbetter, N., Prihoda, T. J., Miller, A. L., (2000). Randomized controlled trial of the use of compensatory strategies to enhance adaptive functioning in outpatients with schizophrenia. *Am J Psychiatry.* 157(8): 1317–1323. http://doi.org/10.1176/appi.ajp.157.8.1317

57. Ventura, J., Hellemann, G. S., Thames, A. D., Koellner, V., & Nuechterlein, K. H. (2009). Symptoms as mediators of the relationship between neurocognition and functional outcome in schizophrenia: A meta-analysis. *Schizophrenia Research*, *113*(2-3), 189–199. http://doi.org/10.1016/j.schres.2009.03.035

58. Wechsler (1997). Wechsler Adult Intelligence Scale-III. San Antonio, TX: *The Psychological Corporation.*