DOES CHILDHOOD TRAUMA IMPACT ON COGNITIVE PERFORMANCE IN ADULTHOOD?

A comparative study between patients with First Episode of Psychosis (FEP), their siblings and healthy control subjects.

Trabajo Fin de Máster

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Certificado de aprobación

El siguiente Trabajo de Fin de Máster titulado "Does childhood trauma impact on cognitive performance in adulthood? A comparative study between patients with first episode of psychosis (FEP), their siblings and healthy control subjects" realizado y presentado por Laura Sánchez Sierra, como parte del cumplimiento de los requisitos para el Máster "Iniciación a la Investigación en Salud Mental "de la Universidad de Cantabria, ha sido examinado y se recomienda su aceptación y aprobación para su presentación oral.

Dra. Rosa Ayesa Arriola

Santander, Junio 2020

Declaración de originalidad

Mediante este texto declaro que el proyecto titulado "Does childhood trauma impact on cognitive performance in adulthood? A comparative study between patients with first episode of psychosis (FEP), their siblings and healthy control subjects" presentado por mí como parte del cumplimiento del Máster "Iniciación a la Investigación en Salud Mental" de la Universidad de Cantabria, es un trabajo original y no ha sido presentado anteriormente en ninguna otra Universidad o Institución como cumplimiento o requisito para cualquier curso académico.

Laura Sánchez Sierra

Santander, Junio 2020.

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Abstract

Several studies suggest that First Episode of Psychosis (FEP) patients show cognitive deficits and more trauma exposure than their siblings and healthy control subjects. However, literature about the influence of childhood trauma on cognition is scarce. In the present study, the impact of childhood trauma on cognitive domains (verbal memory, visual memory, processing speed, working memory, executive functions, motor dexterity and attention) and GCF (Global Cognition Functioning) has been explored in a sample formed by 51 FEP patients, their 68 siblings and 65 Healthy control (HC) subjects using a neuropsychological battery and Childhood Traumatic Events Scale (CTES). Results suggested no significant influences of childhood trauma on cognitive functioning by itself. However, it was found that childhood trauma exposure, along with the genetic vulnerability to FEP have a negative impact on attention, executive functions and GCF.

Key words: Childhood Trauma, Cognition, First Episode Psychosis, Global Cognitive Functioning

1 Introduction

Schizophrenia Spectrum disorders (SSD) are known as mental illnesses which notably compromise cognitive abilities in patients who suffer it, being associated with poorer performance on cognitive domains than non-clinical population (Mollon & Reichenberg, 2018).

There is evidence that SSD patients show cognitive deficits prior to the onset of First Episode of Psychosis (FEP) (Mollon & Reichenberg, 2018). Furthermore, it has been suggested that low premorbid cognitive functioning is associated with increased risk for psychotic disorders (Sheffield et al., 2018).

Additionally, studies which explore differences between patients and siblings are very valuable because they make it possible to explore why, having shared the same environment in their childhood, some subjects developed psychotic symptoms and some of them did not. Most studies which compare cognitive performance between SSD patients, their siblings and Healthy Controls (HC) conclude that generally, patients show mild to severe deficits (Islam et al., 2018).

Other studies try to explore whether childhood trauma has any influence on the onset of psychotic disorders and on cognitive deficits, concluding that trauma and adverse childhood experiences have a relevant role in psychotic symptoms in patients with SSD (Sheffield et al., 2018), including cognitive deficits as part of its symptoms.

1.1 Cognitive symptoms in FEP patients and their relatives

FEP patients are characterized by the presence of overall cognitive deficits which are present from early stages of the psychotic disorders (Sheffield et al., 2018). There are some controversial results based on what cognitive domains are affected in SSD. A well-known neuropsychological battery employed on the assessment of these schizophrenic patients is the MATRICS Consensus Cognition Battery (MCCB) (Nuechterlein et al., 2008), which evaluate seven cognitive domains (processing speed, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, reasoning and problem solving, and social cognition) with different validated tests. This battery has been employed in several studies around the world to explore many aspects which characterize FEP patients. One of the most popular results obtained in research is that processing speed has been noted as one of the most impaired domains in these patients (Cella et al., 2015; Sheffield et al., 2018).

Several studies which compare cognitive performance between SSD patients, their siblings and HC subjects conclude that, generally, siblings of patients show an

intermediate performance, showing HC the best performance (Chu et al., 2019; Hou et al., 2016; Islam et al., 2018). Hence, several studies in this area have focused on finding risk factors of psychosis among families with a psychotic patient member and HC subjects (Scala et al., 2012).

In *table 1* it can be observed some studies found on the PubMed database which have reported results about cognitive deficits in FEP patients, as well as the performance of FEP siblings and HC subjects.

Table 1 Previous studies about psychosis and cognition

STUDY	N	ASSESSMENT	VARIABLES	RESULTS	CONCLUSIONS
(McIntosh et al., 2005)	200 (50 C, 74 P, 76 R)	PSE, SADS-L, PANSS, HRDS, YMRS, NART, E-RBMT, HSCT, DSST	Intellectual functions, Memory, Executive functions, Psychomotor performance	Current and premorbid IQ and Memory are impaired in SZ patients and their relatives. Psychomotor performance and IQ were deteriorated in patients.	Cognitive deficits are associated with SZ, affecting patients and relatives.
(Barrantes-Vidal et al., 2007)	169 (68 SZ P, 38 S, 63 C)	SCID-II, WAIS-III, WSMR, Annett handedness Questionnaire, LNS, CPT, WCST	IQ, Attention, Verbal Memory, Working Memory, Executive Functions, Psychotic symptoms.	Sibling showed intermediate performance between patients and controls on IQ, LNS, animal naming, backwards spatial span, phonemic fluency, numbers d' and forward spatial span.	Working memory differed significantly between siblings and controls. No deficits in Verbal Memory were found.
(Kuha et al., 2011)	263 (91 SSD P; 105 S; 67 C)	SCID-I, SCID-II, WAIS-R Vocabulary subtest, DSST, Digit Span, CVLT, TMT	General ability, learning and memory, executive functions, and performance speed	Schizophrenia spectrum disorder was associated with poorer performance in all cognitive domains.	Belonging to the group of unaffected siblings is associated with poorer performance on tasks requiring speeded performance, visual scanning, and executive control in comparison to the control group.
(Meijer et al., 2012)	4445 (1903 FEP P, 1044 S, 911 parents, 587 C)	PANNS, WLT, CPT, RST, DIGIT SYMBOL CODING, DFAR, BFRT, INFORMATION ARITHMETIC, BLOCK DESIGN, HINTING TASK	Psychotic symptoms, Verbal learning and memory, attention, working memory, Theory of mind	Impairments in Verbal learning, processing speed, reasoning, problem solving, working memory, and knowledge acquisition are cognitive phenotypes that could be related to schizophrenia.	Family predisposition to psychotic disorders is associated to verbal learning, processing speed, reasoning, problem solving, knowledge acquisition and working memory impairments.
(Scala et al., 2012)	110 (55 FDR, 55 C)	SANS, GAF, TMT, WCST, VPF, BFT, STROOP, DST, WAIS-R.	Negative symptoms, Global Functioning, Executive Function, memory and attention, IQ.	Controls outperformed SZ Relatives in immediate recall and executive functions.	Adult non-psychiatric Schizophrenia Relatives showed signs of cognitive vulnerability to the disorder.

STUDY	N	ASSESSMENT	VARIABLES	RESULTS	CONCLUSIONS
(Cella et al., 2015)	42 (21 S, 21 C)	MINI, Social Scene Perception Test, Projective Imagination Test, Theory of Mind Vignettes, Facial Affect Identification Assessment, WAIS-R, Hayling sentence completion task, TMT, Six simplified elements test, LNS, RAVLT, Visual Reproduction Test	Social Cognition, IQ, Executive Function, Memory	Siblings underperformed on processing speed, executive functions, and IQ.	This study suggests that these domains should be considered as interdependent rather than independent.
(Hill et al., 2015)	1737 (289 SZ P, 227 BD P, 165 SZaffective P, 315 SZ R, 259 BD R, 193 SZaffective R, 289 C)	BACS, WMS-III, PANSS, YMRS, MADRS	Working Memory	All patient groups were impaired compared to controls	Working memory impairment in probands with schizoaffective disorder and FDR of schizophrenia probands extend beyond deficits predicted by generalized neuropsychological impairment
(Andric et al., 2016)	158 (52 SZ P, 55 S, 51 C)	BFRT, DFAR, WAIS-R, GAF	Facial emotion recognition, IQ	Patients showed lower IQ and performance in BFRT and DFAR than their siblings and controls.	Emotional processing and IQ in schizophrenia patients are notably impaired in comparison to their siblings and controls. In patients, low facial recognition scores were predictors of lower IQ. Siblings of highly cognitive impaired patients presented more difficulties in facial recognitions tasks.
(Hochberger et al., 2016)	2066 (323 SZ P, 260 BD P, 200 SZaffective P, 349 SZ R, 301 BD R, 237 SZaffective R 396 C)	SCID, BACS	Verbal Memory, Processing Speed, Reasoning, and problem solving, Working Memory.	There were not significant differences in cognitive deficits between P, their FDR and C.	Cognitive deficits were similar among the sample.

STUDY	N	ASSESSMENT	VARIABLES	RESULTS	CONCLUSIONS
(Islam et al., 2018)	2764 (1119 SZ P, 1059 S, 586 C)	CPT, WLT, DSST, WAIS-III, CASH, SCAN, PAS, SIS-R, CAPE, PANSS	Sustained attention, Memory and Verbal learning, GCF (Processing Speed, Verbal Comprehension, Working Memory, Visuospatial ability, Problem Solving)	Controls outperformed patients and siblings in cognitive performance.	Patients performance were positively related to the cognitive performance of their siblings. Siblings showed an intermediate performance between patients and controls, getting the last one better results.
(Sheffield et al., 2018)	Review			Verbal memory and processing speed were most robustly impaired FEP P, consistent with findings in both ultra-high risk and chronic stages.	Cognitive impairment is present across the psychosis spectrum. The presence of or vulnerability to psychotic experiences confers risk for cognitive deficits. Assessment of domain specificity within psychotic disorders reveals the largest deficit in processing speed in schizophrenia.
(Chu et al., 2019)	258 (69 P, 71 Risk R, 50 non-risk R and 68 C)	CB-SCID-I, IRAOS, CAARMS, LNS, DSCT, monotone counting test, WMS-R	Psychiatric disorders, Risk mental state, Premorbid IQ, Processing Speed, Executive Functioning, Verbal Fluency, Logical Memory, Visual Memory)	HR Relatives were younger, and the years of education level was lower than in the other groups and were more likely to get higher general psychopathology scores than patients. Healthy controls outperformed patients and relatives in all cognitive domains.	Controls outperformed patients and relatives in all domains, being the group of patients the most impaired one.
(Oertel et al., 2019)	77 (27 C, 27 SZ P, 23 FDR)	SCID-II, SCID-II, RHS, MWT-B, TMT, PANSS	Psychiatric disorders, hallucinatory predisposition, premorbid intelligence, psychomotor speed.	No significant differences were found in motor speed between groups. Patients needed more reaction time.	Patients showed lower scores in immediate and long-term memory tasks and needed more execution time.
(Liu et al., 2019)	267 (72 C, 44 HR R, 73 prodromal, 44 FEP, 34 Chronic SZ)	SIPS, SOPS, POPS, Mini-SCID, PANSS, MCCB	Prodromal symptoms, psychotic symptoms, Processing Speed, Attention, Spatial Working memory, Verbal learning, Visual learning, Reasoning/Problem Solving, Social cognition	FEP P obtained significantly lower scores that controls in Processing Speed, Visual Learning, Problem Solving, Social Cognition and Attention.	No statistically significant differences between chronic SZ and FEP patients.

STUDY	N	ASSESSMENT	VARIABLES	RESULTS	CONCLUSIONS
(Hou et al., 2016)	160 (40 high-risk FDR, 40 non-risk R, 40 P y 40 C)	MATRICS (TMT, Stroop, DST, HVLT-R), SIPS, PANSS	Psychomotor Functions, Attention, Processing Speed, Working Memory, Verbal Memory.	HR Relatives showed an intermediate performance accuracy between patients and non-risk relatives. Patients showed lowest scores in all cognitive domains.	Processing Speed, Attention, Verbal memory and Working memory impairments were found in both relatives with and without risk. Better cognitive performance was found in Healthy Control subjects, followed by Non-Risk relatives. Cognitive impairments were lower in HR relatives than in the group of patients, being the most impaired ones.
(Bora, 2017)	2741 (1314 R, 1427 C)	TMT, WCST, STROOP, RAVLT	IQ, verbal memory, visual memory, processing speed, sustained attention, executive functions, working memory and verbal fluency	Relatives obtained lower IQ scores than Healthy Control Subjects, showing cognitive impairments in all domains.	Deficits in general intellectual ability, verbal learning, planning, and working memory might be associated with risk for schizophrenia.
(Gkintoni et al., 2017)	204 (66 SZ R, 36 BD R, 102 C)	MTCF, COWAT, STROOP, TMT, DST, WCST, Raven's Progressive Matrices, IGT	Visual memory, Verbal Fluency, Inhibition, processing speed, working memory, Cognitive flexibility, Abstract reasoning, Emotional decision making.	Controls outperformed SZ Relatives in all domains except from Emotional decision-making test.	SZ and BD relatives showed cognitive impairments in contrast to the control group.
(Moreno-Samaniego et al., 2017)	92(48 FEP R y 44 C)	SCAN, SPQ, SCID-II, O-LIFE, EPQ-R, CPT-II, WCST, TMT, DSCT, STROOP.	Psychiatric disorders, Schizotypal traits, Vigilance/Sustained attention, cognitive flexibility, signal detection, Selective attention, interference control, working memory.	Relatives showed worse performance than controls in sustained attention, selective attention, interference control and working memory.	Negative schizotypal traits and low education could lead siblings of patients with psychosis to present deficits on vigilance/sustained attention tasks.

STUDY	N	ASSESSMENT	VARIABLES	RESULTS	CONCLUSIONS
(Buck et al., 2020)	573 (299 FEP males, 136 FEP Females, 96 C males, 42 C Females)	WAIS-R, SAPS, SANS, CDSS, SOFAS, WMS-III, CSRB	IQ, Positive and Negative Symptoms, Depression, Social and Occupational Functioning, DUP, Verbal Memory, Visual Memory, Working Memory, Attention, Executive Function, Processing Speed	Males performed more poorly than females in Verbal memory. Patients were more impaired than nonclinical controls across all 6 neurocognitive domains assessed.	Patients were impaired on all neuropsychological domains, with deficits most pronounced in Verbal Memory. Females outperformed males in both groups in this domain.

Abbreviations: P: Patients; S: Siblings; C: Controls; R: Relatives; SZ: Schizophrenia; BD: Bipolar Disorder; FDR: First Degree; HR: High Risk, FEP: First Episode Psychosis; SSD: Schizophrenia Spectrum Disorder

1.2 Trauma and cognition in FEP patients and their relatives

Research about trauma and cognition in FEP patients is scarce. However, it has been reported that FEP patients tend to have been exposed to more traumatic situations than their non ill siblings (Heins et al., 2011), suggesting that experiencing childhood trauma and adverse childhood experiences is a risk factor in developing psychosis (Barrigón et al., 2015).

Besides that, some studies suggest that childhood trauma is related to cognitive deficits, especially in FEP population (Van Os et al., 2017) and that childhood adversity and early cognitive impairment could be associated (Wells et al., 2020). Additionally, a previous study in PAFIP group (Ayesa-Arriola et al., 2020) with a sample formed by 290 FEP patients and 52 HC, reported that besides that FEP patients showed deficits in cognitive performance compared to HC, FEP patients showed differences among them according to the scores obtained in the Childhood Traumatic Events Scale (CTES) questionnaire. Patients with childhood trauma reported deficits in verbal memory.

Therefore, it would be interesting to explore the relation between childhood trauma exposure, cognitive performance/deficits, and the onset of FEP. In *Table 2* it can be seen some studies related to these three points.

Table 2Previous studies about psychosis, trauma and cognition

TITLE	N	ASSESSMENT	VARIABLES	RESULTS	CONCLUSIONS
(Heins et al., 2011)	757 (272 P, 258 S, 227 C)	CASH, CTQ, PANSS, SIS-R	Lifetime psychotic disorder, Childhood trauma, Positive and Negative symptoms.	Positive symptoms were associated with trauma, but not negative symptoms. Patients diagnosed with a psychotic disorder within the first 10 years of their illness reported significantly more childhood trauma compared to not only healthy comparison subjects but also the patients' siblings. the rates of reported trauma were higher for the patients' siblings than for the healthy comparison subjects.	Siblings reported significantly less abuse and neglect compared to their ill relatives. This suggests that discordance in psychotic illness among siblings may be associated with discordance in trauma exposure.
(Barrigón et al., 2015)	120 (60 P: 35 SZ, 1 SZphrenif orm, 9 SZaffectiv e, 12 psychotic features; 60 S)	SCID-I, FIGS, PANSS, CIDI, EPQ	Family History, Psychopathology, Childhood trauma, Cannabis use, Premorbid temperament	The odds of developing psychosis for subjects who experienced childhood trauma were 7,3 times higher than the odds for subjects who did not experienced it.	Childhood trauma was significantly associated with an increased risk of developing psychosis.
(Berthelot et al., 2015)	1500 (184 SZ P, 221 BD P, 1095 R)	CALEC, K-SADS, SCID, GAF, WISC-III, WAIS-III, RCFT, TVFT	Childhood Stressful events, psychiatric disorder, global functioning, IQ, Visual memory, Verbal memory, Executive functions, Working memory	Exposed sample reflected lower scores in IQ, visual episodic memory, and executive functions of initiation, but not in verbal memory or working memory.	In high risk young participants, childhood and adolescent maltreatment had a negative impact on cognitive domains which are usually impaired in adult population with psychosis.
(van Os et al., 2017)	2764 (1119 P, 1059 S, 586 C)	CASH, SCAN, CAPE, WAIS-III; CTQ,	Psychic experiences, IQ, cannabis use, childhood trauma	Siblings reported intermediate values compared to patients and controls in childhood trauma, cannabis use and IQ. Patients showed the highest scores in trauma and cannabis use and the lowest on IQ.	Impact of childhood trauma did not differ between the three groups, so the differences might be associated with another factors, but not with trauma.

TITLE	N	ASSESSMENT	VARIABLES	RESULTS	CONCLUSIONS
(Morales-Muñoz et al., 2018)	137 (75 FEP P, 62 C)	WAIS-III, WMS-III, TMT	Childhood adversities, verbal fluency, Memory, Processing Speed, Execuive Functions, Attention.	In the FEP group, the childhood factor scores significantly predicted the CPT-IP score, whereas no significant results were found for the rest of the cognitive variables. Fluency, Vocabulary, Logical immediate memory, and CPT-IP were significantly correlated with bullying. No significant regressions were found between cognitive variables and childhood adversities in controls.	Patients with some specific childhood adversities, like conflicts within the family, parental problems, severe illness, or bullying also showed some cognitive deficits when tested as adults after FEP. More specifically, these adverse experiences in childhood were associated with attention impairment. Any significant associations within the control group were found.
(Schalinski et al., 2018)	218 (168 FEP P, 50 C)	MACE, MCCB	Adverse childhood experiences, Processing speed, Attention, Working memory, Verbal learning, Visual learning, Reasoning, social cognition.	83,3% of patients and 44% of the controls group reported the exposure to at least one type of childhood adversity. Childhood adversity measures were negatively related to general cognitive performance.	Patients demonstrated impaired cognitive performance and higher severity of childhood adversities compared to controls.
(Wells et al., 2020)	836 (635 C, 448 SZ P, 86 SZaffective P)	WTAR, RBANS, LNS, CAQ	Premorbid IQ, Pronunciation of English words, Neuropsychological status, Attention, Immediate memory, current cognitive function, childhood adversity	Schizophrenia patients showed more childhood adversity than healthy control subjects. Women showed higher scores at CAQ than males in all items.	Family history of Schizophrenia is related to the odd to suffer psychosis, but not with cognitive impairment. Childhood adversity was related to early cognitive impairment in schizophrenia patients.
(Mørkved et al., 2020)	78 SSD P	SCID, PANSS, CTQ-SF, WAIS-III, D-KEFS, Rey Complex Figure, CVLT, CPT, TMT, WCST, Stroop, LNS, Grooved Pegboard	Psychotic disorders, Childhood trauma, Verbal abilities, Executive function, visuospatial abilities, Memory, Attention, Working memory, processing speed.	Childhood trauma group reported significantly higher levels of positive and negative psychotic symptoms. No significant differences were found in cognitive measures between trauma and no-trauma groups.	No significant differences in cognitive functioning between CT and no CT groups.

Abbreviations: P: Patients; S: Siblings; C: Controls; R: Relatives; SZ: Schizophrenia; BD: Bipolar Disorder; FDR: First Degree; HR: High Risk, FEP: First Episode Psychosis; SSD: Schizophrenia Spectrum Disorder

In the present study, siblings were included due to the possibility to explore trauma and cognitive function in FEP patients and their siblings could give clues about why, sharing the same childhood environment, some of them developed psychosis in adulthood and some of them did not.

2 Hypotheses and Objectives

2.1 Objectives

The aim of this study is to explore the relationship between childhood trauma and cognitive performance in FEP patients, their siblings and healthy control subjects.

2.2 Hypotheses

From the present study, due to the results and limitations observed in previous studies, the next hypotheses were tested:

-Hypothesis 1: FEP patients will report more traumatic childhood events during childhood than their siblings and HC subjects.

-Hypothesis 2: FEP patients will show cognitive deficits while their siblings will report worse cognitive performance than HC subjects.

-Hypothesis 3: Among the groups of patients, siblings and HC subjects, participants with a history of childhood trauma will show more severe cognitive deficits.

3 Methods

3.1 Study Design

Data were obtained from the Program of Attention First-Episode of Psychosis (PAFIP and PAFIP-FAMILIAS: un estudio del funcionamiento neuropsicológico y variantes genéticas asociadas en familiares de pacientes con trastornos del espectro de la esquizofrenia (PI17/00221)), an epidemiological and longitudinal program at the University Hospital Marqués de Valdecilla in Cantabria, Spain, approved by the

hospital's review board. In accordance with international standards for research ethics, this program, which is fully funded through public funds by the regional Mental Health Services, was approved by the local institutional review board (Ethics Committee of Cantabria, CEIC-C).

Participation in PAFIP and PAFIP-FAMILIAS was voluntary and participants meeting the inclusion criteria signed an informed consent and were free to withdraw from the program at any time if requested.

3.2 Participants

The patient group consisted of 51 patients diagnosed with FEP (age Range: 17-59, mean: 29.75), 30 males and 21 females, included in the PAFIP program from January 2001 to 2018. Patients included had siblings who accepted participating in the study "PAFIP-familias" and met the following criteria: 1) 15-60 years of age; 2) living in the catchment area; 3) experiencing their first episode of psychosis; 4) no prior treatment with antipsychotic medication or, if previously treated, a total life time of adequate antipsychotic treatment of less than 6 weeks; and 5) DSM-IV criteria from brief psychotic disorder, schizophreniform disorder, schizophrenia, not otherwise specified (NOS) psychosis or schizoaffective disorder. The diagnosed were confirmed by the Structured Clinical Interview for DSM-IV (SCID-I) (First et al., 1996) conducted by an experienced psychiatrist, 6 months from the baseline visit.

A group of 68 siblings from the previous patients (age range: 18-70, mean: 40.75, 17 males and 51 females) participated in this study. Inclusion criteria consisted in: age range 15 to 60 (legal responsible parent or guardian authorized participation in less than 18 cases); good command of Spanish language; Being able and having a good willing to sign a written informed consent; not having a history of psychiatric or organic brain injury diagnosis; not having an intellectual disability according to DSM-IV

criteria; and not having a diagnosis related to substances abuse according to DSM-IV criteria.

A group of 65 healthy volunteers (age range: 14-49, mean: 31.15), 39 males and 26 females, were initially recruited from the community through advertisements. They agreed to provide childhood trauma information and they had no current or past history of psychiatric, neurological or general medical illnesses, including substance abuse and significant loss of consciousness, as determined by using an abbreviated version of the Comprehensive Assessment of Symptoms and History (CASH)(Andreasen et al., 1992).

3.3 Assessments

3.3.1 Socio-demographic variables

Gender, age and years of education were the sociodemographic variables collected from all the participants. This information was provided by patients, relatives, and medical record at admission.

3.3.2 Premorbid variables

Premorbid variables considered were estimated IQ and premorbid adjustment. Estimated IQ was calculated for all participants based on the vocabulary subtest from WAIS-III (Weschler, 1997). Ratings were converted into standard scores and the correspondent centiles were used to estimate the IQ variable.

Premorbid adjustment and psychiatric family background information was only recorded from the patients' group. Premorbid adjustment variable was measured with the Premorbid Adjustment Scale (PAS) (Cannon-Spoor et al., 1982), with ratings from 0 (adjusted) to 6 (least adjusted). This information was fragmented in five subtests corresponding to different stages of life (childhood, early adolescence, late adolescence, adulthood and general adjustment). Information about Duration of Untreated Illness (DUI) and Duration of Untreated Psychosis (DUP) were recorded by interviews to

relatives of the patients. DUI is the time in months from the first unspecific symptom related to psychosis to initiation of adequate antipsychotic drug treatment, and DUP is defined as the time in months from the first continuous psychotic symptom to initiation of adequate antipsychotic drug,

3.3.3 Clinical variables

Psychotic symptoms in patients were measured with the Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham, 1962), the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983) and the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984).

3.3.4 Trauma variables

Childhood Traumatic Events Scale (CTES) (Pennebaker & Susman, 1988) is a questionnaire which assesses childhood traumatic events experienced prior to the age of 17 and recent stressful events experienced in the last three years. In this study, it was only employed the first part to explore childhood trauma information. This questionnaire includes various domains related to death, parental divorce, traumatic sexual experiences, violence, illnesses/ accidents, and other traumas. The subject is required to express having experienced each trauma or not. In case of trauma, the subjects will tell the situation, the age when that occurred, and the intensity of trauma perceived in a Likert scale from 1 (not traumatic) to 7 (very traumatic).

A subject was considered to have “experienced a childhood trauma” if he or she scored at least one kind of trauma as >4, or “not experienced a childhood trauma” if all kinds of traumas were scored <=4 .

3.3.5 Neuropsychological assessment

Trained neuropsychologists carried out the neuropsychological assessments when patients’ clinical status permitted and when siblings and HC were willing and

available to participate. The measures selected from different test to evaluate cognitive performance have been detailed below:

-Rey Auditory Verbal Learning Test (RAVLT) (Rey, 1964): A list of 15 words is read out loud by the examiner and the subject has to say as many words as he/she can remember. The process is repeated four more times. Then, the examiner says a new list with 15 different words and the subject has to say as many words as he can remember. After that and 30 minutes later, the subject is requested to recall the words of the first list. Finally, from 50 words, the participant must select the words of the first list which he could recognize.

-WAIS-III Digit Symbol subtest (Weschler, 1997): The instrument consists in a paper with a box on the top including different symbols associated to numbers from 1 to 9. Next, there are 7 lines of 20 numbers and the subject must write the correspondent symbol below the numbers as fast as he can for 2 minutes.

-Grooved Pegboard Handedness test (Lezak, 1994): The instrument is composed of a board with twenty-five holes with randomly positioned slots and pegs. Pegs must be rotated to match the hole before they can be inserted. First, the subject will perform the task with his dominant hand and then, with the non-dominant hand.

-Rey Complex Figure(Osterrieth, 1944): In this test examinees are asked to reproduce a line drawing. In the first phase, they must copy it. In the second and third phase, 3 and 30 minutes later respectively, subjects must draw it again by recall.

-Trail Making Test (Reitan & Wolfson, 1985): This test if formed by two parts, A and B. In part A, subjects must connect 25 circles drawn in a paper that includes numbers from 1 to 25 in ascendant order. In part B, the examinee must repeat the same process, but with the difficulty that there will be numbers from 1-13 and letters from A

to L. The sequence of connection will be number-letter in ascendant and alphabetical order (1-A, 2-B, 3-C…). It should be done as fast as possible.

-WAIS-III Vocabulary subtest (Weschler, 1997): A list of 33 words is read aloud and the subject must give a definition of each one. As mentioned, estimated IQ was calculated from all participants based on this test. Ratings were converted into standard scores and the correspondent centiles were used to estimate the IQ variable.

-WAIS-III Digits subtest (Weschler, 1997): This test has two parts. In the first part, examiner says a sequence of digits (from 2 to 9 digits, adding one digit each two sequences) and the subject must repeat them forward. In the second part, the process is similar, but the sequences are formed from 2 to 8 digits and the examinee must repeat in backward.

-Cognitive Performance Test (CPT) computerized version (Cegalis & Bowlin, 1991): The participant is exposed to a computer screen with black distorted background and white letter appears randomly in the middle of it. The subject must click the left button of the mouse when the letter was an X.

According to published literature, a Global Cognitive Functioning was estimated using different measures to determine the following cognitive domains (Ayesa-Arriola et al., 2016) : verbal memory was assessed with the Rey Auditory Verbal Learning Test (RAVLT long term recall) (Rey, 1964); Visual memory was assessed with the Rey Complex Figure (RCF long term recall) (Osterrieth, 1944); Executive functioning was assessed with the Trail Making Test (TMT; time to complete TMT-B minus TMT-A) (Reitan & Wolfson, 1985); Working memory was assessed with the WAIS-III Backward Digits scale (total subscore) (Weschler, 1997); Processing speed was measured with the WAIS-III Digit Symbol subtest (standard total score)(Weschler,

1997); Motor dexterity was assessed with the Grooved Pegboard Handedness (GP; time to complete with dominant hand) (Lezak, 1994); Attention was assessed with the Continuous Performance Test (CPT; total correct responses) (Cegalis & Bowlin, 1991); and premorbid IQ was determined using the WAIS-III vocabulary subtest (standard total score) (Weschler, 1997).

In order to calculate a measure of global cognitive functioning (GCF), prior to standardization, raw cognitive scores were reversed when appropriate, so they were all in the same direction (i.e., the higher the score, the better the performance). In line with previous methodology (Reichenberg et al., 2009), the GCF was calculated as T-scores (M = 50, SD = 10), with raw scores from a healthy comparison sample (n = 187) (Arabzadeh et al., 2014). T-scores were converted to deficit scores that reflected presence and severity of cognitive impairment. Deficit scores on all tests were then "averaged" to create the GCF score (Ayesa-Arriola et al., 2016).

3.4 Statistical Analysis

The Statistical Package for Social Science, version 19.0 (*IBM SPSS Statistics for Windows,* 2010) was used for statistical analysis. A p value<0.05 was considered statistically significant.

3.4.1 Sociodemographic, premorbid and clinical analysis

Descriptive statistics (sample size, mean, standard deviation, ANOVA, and chi-squared test) were applied to the three main groups of the sample (patients, siblings and HC). The variables included in this analysis consisted in gender, age, years of education and estimated IQ. Moreover, premorbid adjustment (childhood, early adolescence, late adolescence, adulthood and general premorbid adjustment), psychiatric family history,

SAPS score, SANS score, BPRS score, DUI and DUP were explored on the patient's group.

3.4.2 Neuropsychological, trauma and GCF analysis

First, trauma frequencies were obtained to run a chi-squared test and explore trauma differences between patients, siblings and HC by a pair-wise analysis. Then, the sample was structured in two different sample divisions. At first, the sample was divided in three groups (patients, siblings and HC). Then, the sample was divided in six groups according to having experience childhood trauma or not (patients with trauma, patients without trauma, siblings with trauma, siblings without trauma, HC with trauma and HC without trauma). For both structures, it was run the same statistical analysis procedure. For cognitive tests, GCF and cognitive domains, mean differences between groups were estimated with ANCOVA Bonferroni corrected, using sex, age, and years of education as covariates. Post-Hoc analysis was used to compare the main effects of the different groups. To explore further information, Pearson correlations were run in the significant variables to ascertain the type of correlation existing with the variables age and years of education.

4 Main results

4.1 Sample characteristics

Out of 184 participants, 51 were patients, 68 siblings and 65 HC subjects. 86 (46.7%) of them were male participants (total mean: age 34.3, years of education 11.53 and estimated IQ 102.9). Sociodemographic variables of the different groups will be shown in *Table 3*. In addition, several moments of premorbid adjustment were obtained in the PAS questionnaire, SAPS and SANS score, BPRS, DUP, DUI and the presence or not of psychiatric family history in the group of patients are detailed in *Table 3* too.

Table 3 Sociodemographic measures

	Patients		Siblings		HC				
	N=51	Mean(SD)	N=68	Mean(SD)	N=65	Mean(SD)	F/χ2	p	Post-Hoc Paired compairisons
Male Gender(%)	30(58,8%)		17(25%)		39(60%)		20,493	<0,001**	1>2; 2<3
Age	51	29,75(10,353)	68	40,75(13,196)	65	31,15(8,588)	18,8	<0,001**	1<2; 2>3
Years of education	42	10,90(3,267)	68	12,56(3,691)	61	10,80(2,657)	5,711	0,004*	1<2;2>3
Estimated IQ	50	97,8(13,06)	68	108,16(11,683)	65	101,31(11,329)	11,717	<0,001**	1<2;2>3
Psychiatric Family History (%)	10(20%)		16(24,2%)		0 (%)		17,429	<0,001**	1>3;2>3
General Premorbid adjustment	49	3,17(2,438)							
PAS (Childhood)	49	1,9(1,206)							
PAS (Early Adolescence)	49	2,35(1,239)							
PAS (Late Adolescence)	49	2,41(1,523)							
PAS (Adulthood)	45	1,59(2,160)							
DUI	50	15,98(23,83)							
DUP	51	10,52(21,19)							
SAPS	50	14,47(4,512)							
SANS	49	6,37(6,254)							
BPRS	50	66,92(16,72)							

*Group differences significant at p<0.05

**Group differences significant at p<0.001

PA: Premorbid Adjustment

4.2 Trauma comparison between groups

As it can be seen in *Table 4*, the group of siblings was the one that reported higher exposure to childhood trauma in all measures assessed, except from illness/accidents, where patients showed a higher percentage. Accordingly, HC was the group which showed having exposure to less childhood adversities. However, these differences were only significant in death, showing siblings more trauma than patients; illness, where patients and siblings reported more trauma than HC; and total trauma, showing siblings more trauma than HC.

Table 4 Type of Trauma Percentages

Trauma	Patients	Siblings	HC	χ2	p	Paired comparisons
Death	7(13,7%)	20(29,4%)	10(15,4%)	5,86	0,053*	1<2
Parental Divorce	8(15,7%)	14(20,6%)	6(9,2%)	3,335	0,189	
Sexual	1(2%)	4(5,9%)	2(3,1%)	1,37	0,504	
Violence	3(5,9%)	5(7,4%)	0(0%)	4,72	0,094	
Illness	6(11,8%)	5(7,4%)	0(0%)	7,4	0,025**	1>3;2>3
Others	11(21,6%)	15(22,1%)	9(13,8%)	1,752	0,416	
Total trauma	23(45,1%)	37(54,41%)	22(33,85%)	5,698	0,058*	2>3

*Group differences close to significance at p<0.05

**Group differences significant at p<0.05

4.3 Neuropsychological comparisons between groups

Based on the ANCOVA results (*Table 5*), considering age, sex and years of education as covariates, significance differences were found between the three groups in

WAIS-III Digit symbol (raw Score), TMT-A and TMT-B (time), CPT (reaction time and corrects), Grooved Pegboard (dominant Hand), RAVLT (trials 1-5, short term recall and long term recall) and Rey Figure (short and long term recall). In all test, differences were due to the low performance of the group of patients. Moreover, the group of HC significantly outperformed siblings in Grooved Pegboard (dominant hand).

Table 5 Three groups cognitive comparison

Test	Patients(N=51) X (SD)	Siblings(N=68) X (SD)	HC(N=184) X (SD)	F	p	Post-Hoc Paired compairisons
Premorbid IQ						
WAIS-III vocabulary[1]	40,10(9,207)	44,85(8,537)	41,77(8,077)	2,182	0,116	
Processing speed						
WAIS-III Digit Symbol[1]	58,69(15,606)	76,38(18,091)	78,09(16,832)	25,679	<0,001**	1<2;1<3
TMT-A (seconds)	44,76(18,033)	32,04(12,117)	34,40(11,153)	17,745	<0,001**	1<2;1<3
CPT (reaction time)	536,38(61,773)	488,79(52,832)	486,36(49,290)	16,372	<0,001**	1<2;1<3
Motor Dexterity						
Grooved pegboard (sec)[2]	71,75(14,067)	60,93(11,926)	57,75(7,471)	30,521	<0,001**	1<2;1<3;2<3
Working Memory						
WAIS-III Digits forward[1]	9,06(2,403)	9,12(2,236)	9,86(2,318)	2,17	0,17	
WAIS-III Digits backward[1]	6,14(1,732)	6,49(1,824)	7,06(2,221)	2,756	0,066	
Verbal memory						
RAVLT trials 1-5	44,00(10,210)	49,13(9,983)	49,65(9,880)	4,919	0,008*	1<3
RAVLT short term recall	8,67(3,217)	10,01(2,707)	10,22(3,130)	3,628	0,029*	1<3
RAVLT long term recall	8,41(3,119)	9,74(3,006)	10,11(3,312)	4,592	0,011*	1<3
Visual memory						
Rey Figure short term recall	20,05(6,528)	20,99(5,88)	21,26(6,942)	3,282	0,04*	1<2
Rey figura Long term recall	20,10(6,911)	21,25(6,01)	21,75(6,571)	3,217	0,043*	1<2
Attention						
CPT (corrects)	73,40(9,431)	75,71(7,107)	77,80(3,284)	6,385	0,002*	1<3
Executive Function						
TMT-B (sec)	86,14(30,170)	76,99(39,559)	62,89(22,510)	10,523	<0,001**	1<3

Using sex, age and years of education as covariates.
*Group differences significant at p<0.05
**Group differences significant at p<0.001
[1]Raw Score
[2]Dominant Hand

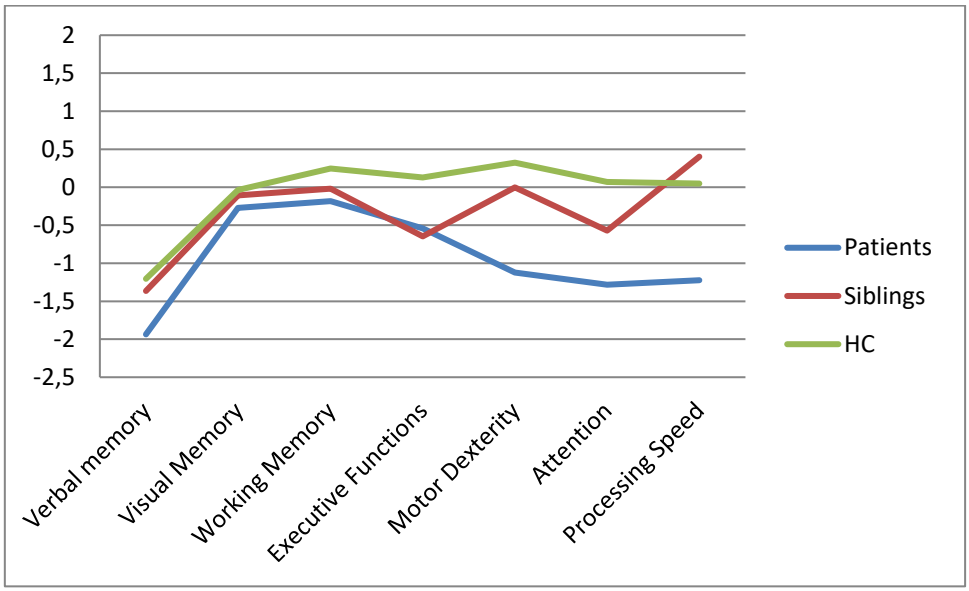
Comparing the three groups in *Table 6*, patients got significantly lower GCF score than siblings and HC, as well as HC significantly outperformed the group of siblings. Moreover, patients significantly underperformed siblings on visual memory, processing speed and motor dexterity. Moreover, they showed significantly lower scores than HC on all domains except from visual memory and working memory. In addition, HC outperformed siblings on executive functions and motor dexterity.

Table 6 Three groups GCF comparison

Domain	Patients(N=51) X (SD)	Siblings(N=68) X (SD)	HC(N=184) X (SD)	F	p	Post-Hoc Paired compairisons
Verbal Memory	-1,936(1,345)	-1,366(1,297)	-1,205(1,429)	4,592	0,011*	1<3
Visual Memory	-0,273(0,994)	-0,107(0,864)	-0,036(0,945)	3,217	0,043*	1<2
Processing speed	-1,225(1,199)	0,402(0,950)	0,050(0,969)	27,154	<0,001**	1<2;1<3
Working Memory	-1,183(0,806)	-0,021(0,849)	0,247(1,034)	2,756	0,066	
Executive Functions	-0,541(1,034)	-0,648(1,586)	0,130(0,862)	7,351	0,001*	1<3;2<3
Motor Dexterity	-1,121(1,452)	-0,004(1,231)	0,324(0,771)	30,521	<0,001**	1<2;1<3;2<3
Attention	-1,282(2,898)	-0,573(2,184)	0,070(1,009)	6,385	0,002*	1<3
GCF	0,973(0,640)	0,614(0,725)	0,436(0,477)	13,921	<0,001	1<2;1<3; 2<3

Using sex, age and years of education as covariates.
*Group differences significant at p<0.05
**Group differences significant at p<0.001

Graph 1 Three Group GCF Domains



4.4 Neuropsychological comparisons between trauma groups

ANCOVA results using sex, age and years of education (*Table 7*) to compare means between the six groups of patients, siblings and HC with or without trauma revealed significant differences in all tests except from WAIS-III vocabulary raw score, WAIS-III digits forward score and Rey Figure long term recall. Comparing both groups of patients, no significant differences were found. The group of patients with trauma significantly underperformed both groups of siblings and HC on WAIS-III Digit Symbol raw score, TMT-A and CPT (reaction time). In addition, they showed more deficits than HC with trauma and both groups of HC in Grooved pegboard. According to patients without trauma, they reported significantly lower scores than both

groups of siblings and HC in WAIS-III Digit symbol raw score, CPT (reaction time) and Grooved Pegboard. Furthermore, they underperformed siblings without trauma and both groups of HC in TMT-A. Additionally, it was found that HC without trauma significantly outperformed patients with trauma in WAIS-III Digits backward, RAVLT trials 1-5, CPT corrects and TMT-B. They also got higher scores than patients without trauma in RAVLT short term recall and TMT-B and better scores thar siblings without trauma in RAVLT trials 1-5 and long-term recall. Finally, HC with trauma outperformed patients in CPT (corrects) too.

Table 7 Cognition by trauma groups comparisons

Test	P T (N=23) X (SD)	P NT (N=28) X (SD)	S T(N=37) X (SD)	S NT(N=31) X (SD)	HC T(N=22) X (SD)	HC NT(N=43) X (SD)	F	p	Post-Hoc Paired compairisons
Premorbid IQ									
WAIS-III vocabulary[1]	38,48(9,629)	41,43(8,796)	44,84(9,642)	44,87(7,154)	41,27(9,755)	42,02(7,186)	1,484	0,238	
Processing speed									
WAIS-III Digit Symbol[1]	53,04(14,421)	63,32(15,237)	76,76(16,073)	75,94(20,507)	80,41(15,610)	76,91(17,482)	11,412	<0,001**	1<3;1<4;1<5;1<6;2<3;2<4;2<5;2<6
TMT-A (seconds)	47,74(20,028)	42,32(16,175)	31,38(11,660)	32,84(12,915)	37,64(11,270)	32,74(10,852)	8,585	<0,001**	1<3;1<4;1<5;1<6;2<3;2<4;2<6
CPT (reaction time)	528,86(49,077)	542,29(70,496)	489,73(51,755)	487,68(54,929)	475,19(49,952)	492,53(48,474)	7,061	<0,001**	1>3;1<4;1<5;1<6;2<3;2<4;2<5;2<6
Motor Dexterity									
Grooved Pegboard (sec)[2]	71,83(11,664)	71,68(15,986)	59,70(9,789)	62,39(14,092)	57,05(7,723)	58,09(7,412)	12,904	<0,001**	1<3;1<5;1<6;2<3;2<4;2<5;2<6
Working Memory									
WAIS-III Digits forward[1]	8,83(2,588)	9,25(2,271)	9,14(2,507)	9,10(1,904)	9,32(1,961)	10,14(2,455)	1,424	0,218	
WAIS-III Digits backward[1]	5,83(1,969)	6,39(1,499)	6,84(2,048)	6,06(1,436)	6,41(1,894)	7,40(2,321)	3,35	0,007	1<6
Verbal memory									
RAVLT trials 1-5	42,39(10,530)	45,32(9,933)	51,24(10,087)	46,61(9,405)	48,95(9,489)	50,00(10,165)	4,188	0,001*	1<6;4<6
RAVLT short term recall	8,78(2,860)	8,57(3,532)	10,65(2,276)	9,26(3,011)	10,00(3,101)	10,33(3,175)	3,496	0,005*	2<6
RAVLT long term recall	8,39(2,658)	8,43(3,501)	10,38(2,520)	8,97(3,381)	10,00(3,008)	10,16(3,491)	3,424	0,006*	4<6
Visual memory									
Rey figure short term recall	20,935(6,499)	19,297(6,580)	20,446(6,160)	21,629(5,560)	19,386(6,548)	22,221(7,015)	1,942	0,09*	
Rey figure Long term recall	21,065(6,945)	19,278(6,905)	20,973(6,485)	21,581(5,477)	20,477(5,793)	22,395(6,917)	1,611	0,16	
Attention									
CPT (corrects)	72,05(11,374)	74,46(7,623)	76,73(5,521)	74,48(8,567)	78,43(1,964)	77,45(3,804)	3,715	0,003*	1<5;1<6
Executive Function									
TMT-B (sec)	93,95(31,366)	79,78(28,143)	79,25(41,608)	74,35(37,547)	72,18(26,216)	58,14(18,978)	5,751	<0,001**	1<6;2<6

Using sex, age and years of education as covariates.
*Group differences significant at p<0.05
**Group differences significant at p<0.001
[1]Raw Score
[2]Dominant Hand

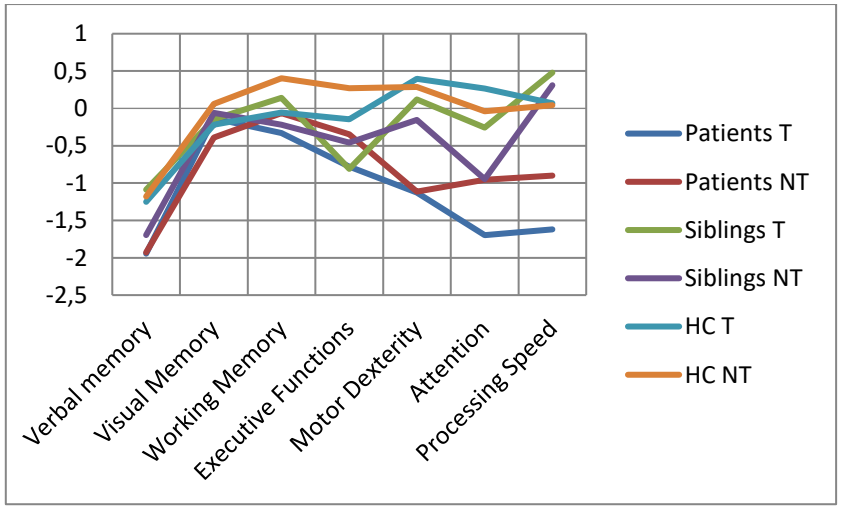
Attending GFC, patients with trauma reported significantly lower scores than siblings with trauma and lower scores than both groups of HC with and without trauma; patients without trauma and siblings without trauma significantly underperformed HC without trauma. Siblings with trauma got lower GCF than siblings without trauma. Furthermore, significant differences were found in all domains, except from visual memory (*Table 8*). In processing speed, patients with and without trauma got significantly lower scores than both groups of siblings and HC. Due to motor dexterity, both control groups and siblings with trauma outperformed the two groups of patients and siblings without trauma got significantly better scores than patients without trauma. Moreover, HC with trauma referred significantly better results than patients with trauma on attention. Finally, HC without trauma outperformed patients with trauma on all domains except from visual memory, as well as they outperformed siblings with trauma on executive functions.

Table 8 Trauma groups GCF comparison

Domain	P T (N=23) X (SD)	P NT (N=28) X (SD)	S T(N=37) X (SD)	S NT(N=31) X (SD)	HC T(N=22) X (SD)	HC NT(N=43) X (SD)	F	p	Post-Hoc Paired compairisons
Verbal Memory	-1,945(1,147)	-1,929(1,510)	-1,088(1,087)	-1,696(1,459)	-1,251(1,298)	-1,180(1,506)	3,424	0,006*	4<6
Visual Memory	-0,134(0,999)	-0,391(0,993)	-0,147(0,933)	-0,060(0,788)	-0,218(0,833)	0,058(0,994)	1,611	0,16	
Processing speed	-1,621(1,136)	-0,900(1,170)	0,479(0,905)	0,310(1,007)	0,068(0,986)	0,041(0,972)	11,909	<0,001**	1<3;1<4;1<5;1<6;2<3;2<4;2<5;2<6
Working Memory	-0,328(0,916)	-0,064(0,698)	0,143(0,953)	-0,217(0,668)	-0,056(0,881)	0,403(1,080)	3,35	0,007*	1<6
Executive Functions	-0,781(0,957)	-0,346(1,071)	-0,809(1,714)	-0,460(1,429)	-0,144(1,139)	0,270(0,652)	3,894	0,002*	1<6;3<6
Motor Dexterity	-1,129(1,204)	-1,114(1,650)	0,122(1,010)	-0,155(1,454)	0,396(0,797)	0,288(0,765)	12,904	<0,001**	1<3;1<5;1<6;2<3;2<4;2<5;2<6
Attention	-1,698(3,496)	-0,954(2,343)	-0,258(1,697)	-0,948(2,633)	0,264(0,604)	-0,038(1,169)	3,715	0,003*	1<5;1<6
GCF	1,082(0,732)	0,885(0,554)	0,456(0,547)	0,797(0,862)	0,449(0,434)	0,429(0,505)	8,317	<0,001	1<3;1<5;1<6;2<6;3<4; 4<6

Using sex, age and years of education as covariates.
*Group differences significant at p<0.05
**Group differences significant at p<0.001

Graph 2 GCF domains by Trauma Groups



5 Secondary results

5.1 The influence of covariates in neuropsychological comparison between groups

Females outperformed males in verbal memory (p=0.001) and motor dexterity (p=<0.001), while male outperformed in visual memory. Furthermore, significant differences were found due to age in GCF (p=0.036), verbal memory (p=0.028), visual memory (p=<0.001), processing speed (p=0.004), executive functions (p=0.032) and motor dexterity (p=0.005). According to years of education, GCF and all domains excepting working memory were influenced by this variable: GCF (p<0.001); verbal memory (p=0.028), visual memory (p=0.004), processing speed (p=<0.001), executive functions (p=0.001); motor dexterity (p=<0.001), attention (p=0.048). A Pearson correlation test referred a positive correlation between age and processing speed and negative correlation between visual memory and executive functions. On the other hand, the same test proved a significant positive correlation between years of education and all domains except from working memory.

5.2 The influence of covariates in neuropsychological comparison between trauma groups

In addition, it is remarkable that females significantly outperformed males in verbal memory (p=0.001) and motor dexterity (p=<0.001). age had a significant influence on GCF (p=0.019), verbal memory (p=0.021), processing speed (p=0.007), working memory (p=0.02), executive functions (p=0.031) and motor dexterity (p=0.005). In the case of years of education, it had a significant influence on: GCF (p<0.001), verbal memory, processing speed, working memory and motor dexterity (p=<0.001); executive functions (p=0.002); and attention (p=0.042). In all these domains, Pearson correlation test reported al positive correlation with years of education. Nevertheless, the same statistical test showed a negative relation between age

and working memory or executive functions, while the relation with processing speed was positive.

6 Discussion

6.1 The impact of trauma on FEP

As reported in previous studies, it has been supported that HC subjects have suffered less childhood trauma and adversities than FEP patients and their siblings (Cella et al., 2015; Scala et al., 2012; Sheffield et al., 2018). However, no significant differences were found between patients and siblings in the present study.

This finding made us wonder what factor could have been protecting siblings against FEP. An overall overview of the results obtained suggested that IQ could be involved in that question, as reported in other studies (Bora, 2017; McIntosh et al., 2005). The group of siblings reported significantly higher scores on this variable than patients and HC. This may suggest that, on the one hand, a higher IQ plays a protective role on siblings in contrast to patients. On the other hand, HC also reported lower IQ, however, this group was protected by having been exposed to less childhood trauma, which is considered as a risk factor of FEP (Barrigón et al., 2015).

6.2 Deficits on verbal memory, processing speed and motor dexterity as cognitive symptoms of FEP

Verbal memory has been noted to be deteriorated in FEP patients (Buck et al., 2020) compared to HC. However, siblings' performance showed no differences neither with patients nor with HC in our study. This could mean that psychotic symptoms influence on these domains, but it should be further explored as a FEP vulnerability factor, since siblings obtained a performance as close to patients as to HC.

According to processing speed, patients significantly underperformed siblings and HC, as reported in published literature, which means that this domain is one of the

most impaired in FEP patients (Sheffield et al., 2018). Maybe, processing speed could be a consequence of the illness and not a predictor, which would explain why siblings showed no differences between them and HC.

Due to motor dexterity, patients showed worse performance than both siblings and HC (McIntosh et al., 2005), meaning that motor dexterity could be a consequence of the illness. Additionally. HC significantly outperformed siblings, which could be influenced by age, being siblings significantly older than patients and HC.

6.3 The impact of Trauma X Group interaction on GCF, attention and executive functions

GCF significant differences were found between patients and both siblings and HC, as well as between siblings and HC. This may suggest the existence of three levels of performance in GCF, showing patients the most severe deficit and HC the best performance. Hence, it may be interesting to explore why siblings showed and intermediate performance. The two statements below may give some clues: 1) Compared to patients, siblings could be protected against FEP because of a higher IQ.; 2) Siblings may not reach HC performance because they are genetically vulnerable to the deficits usually impaired in psychotic population, as shown in other studies (Morales-Muñoz et al., 2018). Considering that significant differences were found between siblings with trauma and siblings without trauma, it could be concluded that siblings with trauma are close to the patients' performance and siblings without trauma are closer to HC. This statement supports a study which suggest that vulnerability to FEP along with trauma have a negative impact on GCF (Kuha et al., 2011).

Previous studies have suggested that childhood trauma is related to attention deficits (Morales-Muñoz et al., 2018). This statement has been supported in our study because significant differences were found between patients and HC in attention

domain. However, considering trauma, these differences were significant only comparing the two HC groups to patients with trauma. Therefore, attention is only affected when patients have experienced childhood trauma.

Furthermore, in executive functions, HC significantly outperformed patients and siblings, supporting previous results (Kuha et al., 2011). Paying attention to the results obtained in trauma, no differences were found between the three trauma groups. In contrast, differences were found between patients and siblings, both with trauma, and the group of HC without trauma. Then, having experienced trauma and belonging to the groups genetically vulnerable to FEP have a negative influence on this domain. On the other hand, considering that no differences were found between patients and siblings in executive functions, it could be interesting to explore why, growing in the same childhood environment, some of these subjects developed psychosis and others did not. Therefore, the higher IQ could be considered once again as a protector against psychosis.

7 Limitations and Conclusions

The first limitation of the present work was that sample was not large enough to make a study by type of trauma and then, determine whether any kind of trauma influence specifically on cognition functioning among the sample. Furthermore, trauma variable was transformed into a dichotomous variable according to having experienced at least one type of trauma or not. Nevertheless, it has not been explored if continuous exposure to one type of trauma or even if more than one type of trauma makes any difference in the assessment of cognitive functioning. In addition, considering that covariates employed in the statistical analysis (sex, age and years of education) have influenced on our results, other covariates such as substance abuse or the influence of pharmacological treatment in cognition, could be explored in future studies.

In conclusion, the five highlights of this work will be shown below:

1. HC tend to outline having experienced less childhood trauma than siblings and no differences were found between patients and siblings.
2. Verbal memory, processing speed and motor dexterity use to be impaired in FEP patients compared to siblings and HC.
3. Childhood trauma, along with the genetic vulnerability to psychosis have a negative impact on attention, executive functions and GCF.
4. Childhood trauma relationship with cognitive performance seems to be relevantly mediated by other variables such as age, sex and years of education.
5. Higher IQ may be protecting siblings of FEP patients against the illness onset.

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