

Familiarity of the Intelligence Quotient in First Episode Psychosis: Is the Degree of Family Resemblance Associated With Different Profiles?

Nancy Murillo-García ^{1,2}

Jordi Soler ³

Victor Ortiz-García de la Foz ^{1,4}

Margarita Miguel-Corredera ¹

Sara Barrio-Martinez ¹

Esther Setién-Suero ⁵

Sergi Papiol ^{4,6,7}

Mar Fatjó-Vilas ^{3,4,8}

Rosa Ayesa-Arriola ^{1,2,4,*}

1. Research Group on Mental Illnesses, Valdecilla Biomedical Research (IDIVAL), Santander 39011, Spain.

2. Department of Molecular Biology, School of Medicine, University of Cantabria, Santander 39011, Spain.

3. Department of Evolutionary Biology, Ecology and Environmental Sciences, University of Barcelona, Barcelona 08028, Spain.

4. Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Instituto de Salud Carlos III, Madrid 28029, Spain.

5. Department of Psychology, Faculty of Health Sciences, University of Deusto, Bilbao, Basque Country 48014, Spain.

6. Institute of Psychiatric Phenomics and Genomics (IPPG), University Hospital, LMU Munich, Munich 80336, Germany.

7. Department of Psychiatry and Psychotherapy, University Hospital, LMU Munich, Munich 80336, Germany.

8. FIDMAG Germanes Hospitalàries Research Foundation, Barcelona 08830, Spain.

*To whom correspondence should be addressed; Cardenal Herrera Oria s/n, 39011, Santander Spain, Research Group on Mental Illnesses, Valdecilla Biomedical Research (IDIVAL); tel: +34 942 203826, fax: +34 942 315517, e-mail: rayesa@humv.es

Abstract

Background and Hypothesis: There is uncertainty about the relationship between the family intelligence quotient (IQ) deviation and the risk for schizophrenia spectrum disorders (SSD). This study tested the hypothesis that IQ is familial in first episode psychosis (FEP) patients and that their degree of familial resemblance is associated with different profiles.

Study Design: The participants of the PAFIP-FAMILIAS project (129 FEP patients, 143 parents, and 97 siblings) completed the same neuropsychological battery. IQ-familiality was estimated through the Intraclass Correlation Coefficient (ICC). For each family, the intra-family resemblance score (IRS) was calculated as an index of familial similarity. The FEP patients were subgrouped and compared according to their IRS and IQ.

Study Results: IQ-familiality was low-moderate ($ICC = 0.259$). A total of 44.9% of the FEP patients had a low IRS, indicating discordancy with their family-IQ. Of these patients, those with low IQ had more schizophrenia diagnosis and a trend towards poorer pre-morbid adjustment in childhood and early adolescence. Whereas FEP patients with low IQ closely resembling their family-IQ were characterized by having the lowest performance in executive functions.

Conclusions: The deviation from the familial cognitive performance may be related to a particular pathological process in SSD. Individuals with low IQ who do not reach their cognitive familial potential show difficulties in adjustment since childhood, probably influenced by environmental factors. Instead, FEP patients with high phenotypic family resemblance might have a more significant genetic burden for the disorder.

Key words: first episode psychosis/schizophrenia spectrum disorders/intelligence quotient/familiality/cognition

Introduction

The familiarity of a trait (also denominated familial aggregation or familial transmission) indicates phenotypic resemblance among family members probably due to shared genetic and environmental factors.^{1,2} Different cognitive traits have shown familiarity in population with Schizophrenia Spectrum Disorders (SSDs), even from the First Episode of Psychosis (FEP). Zhang et al.³ found that relatives of SSD patients underperformed healthy controls in attention, executive functions and intelligence quotient (IQ), and these impairments were greater for families with increased genetic risk for schizophrenia. Executive dysfunctions were reported in first-degree relatives of FEP patients in a previous study by our group.⁴ Moreover, Scala et al.⁵ described that relatives of patients with cognitive deficits showed more impairments in executive functions than relatives of patients cognitively preserved. Goldberg et al.⁶ observed greater familial aggregation for IQ among families of patients with early onset schizophrenia compared to families of patients with adult onset.

The IQ is one of the neuropsychological measures with the highest heritability estimates, ranging from about 40% to 70% from childhood to adulthood.^{7–9} The genetic architecture of IQ is highly polygenic,^{10,11} although is also influenced by environmental factors such as education.⁹ The IQ is a quantitative estimation of the general cognitive ability obtained after administering standardized tests whose main advantage is that allows to measure intelligence in the population. Extensive research has reported that patients with SSDs have a lower IQ than healthy subjects,^{12,13} and that in some cases this feature is present from childhood and adolescence.¹⁴ Based on the strong genetic influence on IQ, one may expect that relatives of patients with SSDs would show similar scores. This would indicate common genetic factors underlying both the risk for the disorder and intellectual deficit, consistent with the neurodevelopmental model of schizophrenia. From this hypothesis, the disorder is consequence of a neurodevelopmental disruption, probably influenced by polygenic risk.¹⁵ There is some evidence in its support,^{16,17} including a family resemblance to the IQ pattern of the proband.^{18–21} However, other studies reported a higher IQ of relatives compared to the patients with SSDs, suggesting that environmental factors predominate in the pathway to the disorder and cognitive outcomes.^{22,23} These last findings correspond with the dual hit hypothesis of schizophrenia, explaining that genetic and environmental factors, such as cannabis consumption or trauma affect brain development, represent synergetic risks for the disorder.²⁴

Throughout this document we will use the term “IQ-familiarity” to refer to the degree of similarity for the IQ among members of the same family. Previous findings on family designs are contradictory,²⁵ indicating different degrees of family resemblance for the IQ in FEP patients. The significance of stratifying FEP patients according to their IQ-familiarity pattern would be to describe different profiles and the treatment needs associated with such characteristics. It is expected that FEP patients more phenotypically like their relatives also are genetically homogenous, thus expressing an increased genetic risk for psychosis. In contrast, FEP patients who bear little resemblance to their relatives might be a subgroup at risk for the disorder conferred by not reaching their potential abilities as proposed by Kendler et al.²⁶ To accomplish this

classification, the intra-family resemblance score (IRS) can be used to estimate the family similarity of each family. Soler et al.^{27,28} have described this statistical method that allows obtaining a quantitative score that indicates whether a family is concordant (high resemblance) or discordant (low resemblance) for the trait. The IRS calculation is based on the mean scores of family members for the trait, taking covariates into account, and providing a unique score for each family. We anticipate that the IQ has a general degree of familiarity, but it may be especially interesting to calculate the similarity of the different families through the IRS method.

Our main objective was to estimate the overall IQ-familiarity in a sample of FEP patients and their first-degree relatives. First, we aimed to confirm that IQ was overall similar among family members, so we tested if the family variable significantly explained a proportion of the IQ variance through a linear mix model. Second, we sought to quantify the specific degree of similarity within each family through the IRS calculation. Third, we explored whether the different patterns of IQ resemblance indicated by the IRS were related to different profiles in the subsample of FEP patients. Thus, we stratified FEP patients according to their IRS and IQ and compared their premorbid, clinical, and neurocognitive characteristics. We hypothesized that 1) the IQ is significantly explained by the family in our sample, 2) the IRS is useful to describe diverse patterns of family resemblance for the IQ, 3) FEP patients with low IRS will show more unfavorable features.

Methods

Study Setting and Sample

Between January 2018 and March 2021, we invited the first-degree relatives of 387 FEP patients to participate in the PAFIP-FAMILIAS project (FIS PI17/00221).⁴ All those patients had been enrolled from 2001 to 2016 in a program for initial phases of psychosis denominated PAFIP at the University Hospital Marqués de Valdecilla (Cantabria, Spain).^{29,30} The local institutional review committee (CEIm Cantabria) approved both projects (PAFIP and PAFIP-FAMILIAS) in accordance with international research ethics standards and all participants gave their written informed consent. In total, 377 subjects from 133 families agreed to participate in the PAFIP-FAMILIAS study (133 FEP patients, 146 parents, and 98 siblings).

Inclusion criteria for FEP patients was age between 15 and 60 years; living in the catchment area; experiencing a first episode of psychosis; and being antipsychotic medication naïve, or, if previously treated, had a total lifetime of adequate antipsychotic treatment of less than 6 weeks. Exclusion criteria was meeting DSM-IV criteria for drug or alcohol dependence; having intellectual disability; having history of neurological disease or head injury. The diagnoses were confirmed through the Structured Clinical Interview for DSM-IV (SCID-I) conducted by an experienced psychiatrist within 6 months of the baseline visit.

First-degree relatives of the FEP patients were included if they were older than 15 years; had good command of the Spanish language; and the ability to give a written informed consent. Exclusion criteria was having any psychiatric diagnosis; organic brain pathology; intellectual

disability; or substance use disorders according to DSM-V criteria. The psychiatric history was explored by a psychologist through the CASH (Comprehensive Assessment of Symptoms and History).³¹

Sociodemographic and Clinical Assessment

We retrieved sex, age, and years of education. The relatives completed a single evaluation session of approximately 2 h. Data of FEP patients were obtained via medical records and interviews at baseline when enrolled in the PAFIP cohort. We recorded the patients' socioeconomic status, derived from the parents' occupation ('low qualification worker' versus 'other'), and whether they lived with their parents. Clinical data included age at psychosis onset (age when the emergence of the first continuous psychotic symptom occurred); duration of untreated illness (DUI, the time from the first nonspecific symptom related to psychosis); duration of untreated psychosis (DUP, time from the first continuous psychotic symptom to initiation of adequate antipsychotics). Positive symptoms at baseline were assessed by the Scale for the Assessment of Positive Symptoms (SAPS),³² and negative symptoms by the Scale for the Assessment of Negative Symptoms (SANS).³³ The premorbid adjustment was evaluated by the premorbid adjustment scale (PAS).³⁴ This tool assess 5 dimensions (sociability, peer relationships, academic performance, adaptation to school, sexual aspects) in different stages of life (child- hood, early adolescence, late adolescence, adulthood).³⁴ Functionality was assessed by the Global Assessment of Functioning scale.³⁵

Neuropsychological Assessment

All the participants underwent the same neuropsychological battery. The FEP patients completed the assessment at their inclusion in the PAFIP cohort, on average 10.5 weeks after their inclusion. Their first-degree relatives completed the evaluation at their inclusion in the PAFIP- FAMILIAS study.

We estimated the IQ by the WAIS-III Vocabulary subtest,³⁶ which has demonstrated to be a valid proxy measure of crystallized intelligence.³⁷ We assessed: 1) verbal memory (Rey Auditory Verbal Learning Test, RAVT)³⁸; 2) visual memory (Rey Complex Figure, RFC)³⁹; 3) processing speed (WAIS-III Digit Symbol subtest)³⁶; 4) working memory (WAIS-III Digits Backward subtest)³⁶; 5) executive function (Trail Making Test part B, TMTB)⁴⁰; 6) motor dexterity (The Gooved Pegboard Test)⁴⁰; 7) attention (Continuous Performance Test, CPT)⁴¹; 8) theory of mind (ToM, The Reading the Mind in the Eyes Task, RMET).⁴² Prior to standardization, raw scores were re- versed when appropriate, so they were all in positive direction. Raw scores were transformed into Z scores to allow direct comparisons between subjects as described in previous studies.^{43,44} We also estimated the Global Deficit Score (GDS), a quantitative value obtained for each individual based on their performance on all neuropsychological tests. According to the method of Reichenberg et al.,⁴⁵ we first converted raw scores of each test into T-scores. Second, we converted these scores into deficit scores

ranging from 0 (no impairment) to 5 (severe impairment). The deficit score of 0 (T score > 40) indicates absence of impairment; a score of 1 (T score = 39–35) for mild impairment, a score of 2 (T score = 34–30) for mild to moderate impairment, a score of 3 (T score = 29–25) for moderate impairment, 4 (T score < 20) a moderate to severe impairment (T score = 24–20), and a score of 5 a severe impairment. Third, we estimated the GDS by averaging the deficit scores of all tests. Based on previous findings, GDS scores greater than or equal to 1 suggest overall impairment.⁴³

Statistical Analysis

We performed the statistical analysis following three main steps (figure 1), using Stata version 14 (StataCorp, 2013) and SPSS version 19 (IBM, 2016).

- 1) We estimated the IQ-familiality through the two-level Linear Mix Model (LMM). Following Soler et al.,^{27,28} we analyzed separately the entire sample and the subsample of unaffected relatives to control for the confounding effect of the disorder. We introduced IQ as the dependent variable; sex, age, and years of education as covariates; and family (subjects nested within families by codes) as random effect. We considered evidence of familiality if the variance of the random effect (family) was >0 by means of the chi-bar-square and calculated the intraclass correlation coefficient (ICC) to measure the strength of the family effect (ICC = 0 no familiality, ICC = 1 total familiality).
- 2) After confirming the IQ-familiality, we calculated the IRS. This is a quantitative value shared by the members of a family and indicates their degree of similarity for the trait. We calculated these scores separately for the total sample and the subsample of unaffected relatives. The IRS was obtained by^{27,28}:
 - i. Creation of a data set that included all possible pairs of relatives within the family. For each family of N members, $N*(N - 1)/2$ pairs of relatives were included.
 - ii. Two-level LMM analysis, wherein the dependent variable was the absolute difference in IQ points between the members of each pair in the families. Sex and age were introduced as covariates, and family as a random effect factor. We applied a family size weight of $2/N$ since each family included only N-1 independent pairs.⁴⁶
 - iii. Random effects estimations (best linear unbiased predictions, BLUP) for each family. The resulting IRS is a continuous variable that was multiplied by -1 to facilitate interpretation. According to previous evidence, the IRS score is, by definition, normally distributed with a mean of 0. Thus, IRS <0 indicates lower intra-family resemblance, and >0 higher intra-family resemblance.^{27,28}
 - iv. Estimation of correlation between IRS and family-IQ (the mean IQ of the members of a family). A significant correlation would suggest that families would only be similar for determined IQ scores; while a nonsignificant correlation would show that there is no specific IQ pattern associated with families with high IRS.

3) We selected the set of FEP patients to subgroup them according to their IRS and individual IQ. We used zero as the cutoff point for the IRS_{27,28} to consider concordant (IRS > 0) or discordant (IRS < 0) scores. We grouped patients depending on whether their IQ was low (<90), average (90–110) or high (>110). We ran univariate analyses (ANCOVA) to compare continuous variables between groups (IQ, age, years of education, SAPS, SANS, etc.), and chi-square for categorical variables (sex, socioeconomic status, living with parents, and diagnosis). Comparisons of neurocognitive data were covariated with sex, age, and years of education. Pairwise comparisons were conducted with Bonferroni correction. All statistical tests were two-tailed and significance was determined at 0.05.

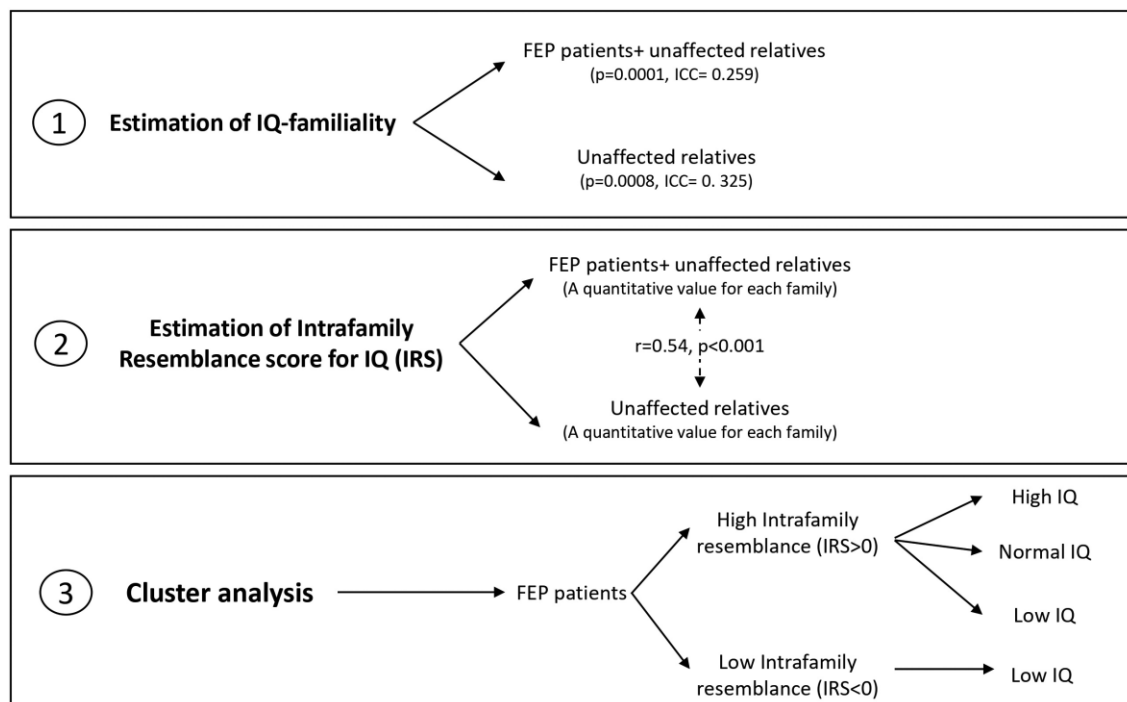


Fig. 1. Process of the statistical analysis.

Results

Sample Characteristics

We included 361 subjects belonging to 129 families (figure 2). The FEP patients had a mean age of 26.67 years (SD = 8.29), had completed on average 10.55 years of education (SD = 3.36) and the 62.59% were male. The parents had a mean age of 61.51 years (SD = 7.76), had completed 10.22 years of education (SD = 3.57), and the 36.42% were fathers. Siblings had a mean age of 39.68 years (SD = 12.84), had completed 12.73 years of education (SD = 3.57) and the 31.9% were male.

We performed the analysis of IQ-familiality on both the full sample and the subsample of unaffected relatives to avoid the potential confounding effect of the disorder. This subsample was composed by families with at least 2 members genetically related (therefore, families composed only by spouses were discarded) without history of psychiatric diagnosis. We included in this subset 137 relatives from 53 families, wherein 77 were siblings, and 60 parents.

IQ-familiality and Intrafamily Resemblance Score (IRS)

We found evidence of IQ-familiality, as the LMM showed that the variance of the random effect “family” was above zero for the full sample ($P < .001$) and for the subsample of unaffected relatives ($P < .001$). The ICC suggested that IQ has a low-moderate degree of familiality both in the full sample ($ICC = 0.259$) and in unaffected relatives ($ICC = 0.325$).

Subsequently, we estimated the IRS value for each family separately for the entire sample and for unaffected relatives. The correlation between the IRS estimated for the 2 datasets was strong ($r = 0.55$, $P < .001$), indicating that this family value is similar even when eliminating the possible confounding effect of the disorder. In the total sample, the IRS had a normal distribution with a mean of 0.042 ($SD = 0.41$).

In the entire sample, we found no significant correlations between IRS scores and family-IQ ($P = .935$) or individual IQ ($P = .880$). However, when selecting only the FEP patients, we observed a positive correlation between their IRS and IQ ($P < .001$, $b = 0.450$).

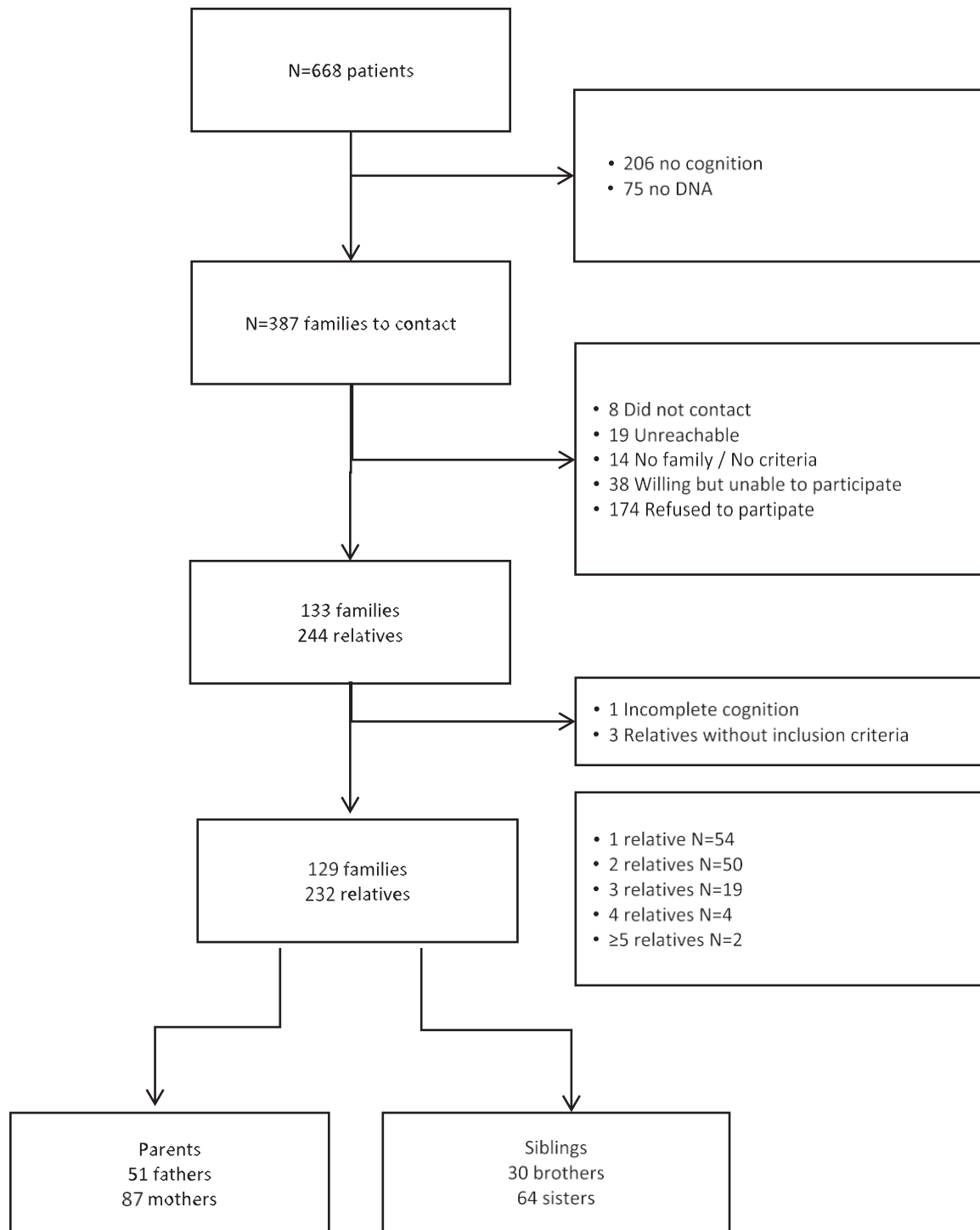


Fig. 2. Flow diagram.

FEP Patients' Subgroups

Two outliers were identified by descriptive statistics and dispersion graphs, one with an IRS of -33.6 and the second with an IQ of 140. After removing them, 127 FEP patients were classified as “discordant” ($IRS < 0$, low resemblance to family-IQ) or “concordant” ($IRS > 0$, high resemblance to family-IQ). The 44.9% of the FEP patients were discordant to their family-IQ. Subsequently, both discordant and concordant FEP patients were subgrouped according to their IQ. The largest subgroup was that of “average IQ concordant” (27.6% of the sample), while the smallest was that of “high IQ discordant” (3.9% of the participants).

The group comparisons are shown in table 1. No difference by diagnosis was found between all subgroups. However, after comparing specifically the subgroups “low IQ discordant” versus “low IQ concordant” the first ones were significantly more frequently diagnosed with schizophrenia ($\chi = 9.492$, $P = .023$). Both subgroups with low IQ had completed fewer years of education ($P < .001$). The patients in the “low IQ discordant” subgroup deviated the most from their family-IQ ($MIRS = -9.30$), showed the lowest IQ ($P < .001$) and had a poorer premorbid adjustment in childhood ($P = .006$) and early adolescence ($P = .009$).

We ran repeated ANOVAS to analyze the different dimensions of the PAS over distinct life stages. For all subgroups, the academic performance significantly declined from childhood to late adolescence ($F = 33.91$, $P < .001$, figure 3). The two subgroups with low IQ had the poorest academic performance in childhood ($P < .010$) and early adolescence ($P < .050$) (supplementary material, figure 1). Also, the dimension of adaptation to school showed a significant decline over time ($F = 23.71$, $P < .001$) for all subgroups, and a tendency toward poorer adjustment for the subgroups “low IQ discordant” and “high IQ discordant”.

The “low IQ discordant” subgroup had a poorer performance in the domains of verbal memory ($P = .031$), processing speed ($P = .017$) and ToM ($P < .001$). The “low IQ concordant” subgroup performed significantly worse in executive functions ($P = .001$) and had a greater global deficit score than the subgroup “high IQ concordant” ($P = .006$) (table 2, figure 4).

Discussion

We found that IQ has low-moderate familiarity in FEP, and that the IRS is useful to identify concordant and discordant families for the trait. FEP patients with low IQ, regardless of their family resemblance, had the poorest academic performance in childhood and adolescence. FEP patients with low IQ and family discordance were more frequently diagnosed with schizophrenia and showed a tendency toward a worse premorbid adaptation to school. Meanwhile FEP patients with low IQ and family concordance presented the poorest performance in executive functions.

Our results on a low-moderate familiarity for the IQ in FEP corresponds with Goldberg et al.,⁶ who reported moderate indexes in SSD population. Other authors have described familial contribution to IQ in SSD using various methodological approaches.^{20,47,48} Evidence of IQ-familiarity in this population has significant implications. It justifies the interest of family

designs to understand the pathological process associated with cognitive deficit in SSD and highlight the potential of intelligence as an endophenotype of the disorder. However, the familiarity analysis does not inform about the basis of the intra-family similarity for the trait, so we must rely on studies of adoptive and biological families to determine the specific contribution of genetic and environmental factors. A recent study estimated that genetic factors account for 42% of IQ.⁹

Through the estimation of the IRS index, we found that FEP patients who closely resemble to their family-IQ (as evidenced by a high IRS) tend to have a higher IQ. Conversely, the less the patient's IQ is like their family, the lower their IQ may be. This corresponds with the study of Kendler et al.,²⁶ who concluded that deviation from family cognitive ability confers risk of developing schizophrenia probably due to qualitative developmental impairments.

To delve into the characteristics associated with family-IQ discordance, we grouped and compared the FEP patients according to their IRS and IQ. Contrary to what we expected, the subgroups were similar on demographic and clinical characteristics. The most striking result was the difference between subgroups in premorbid adjustment, especially in the academic dimension. The two subgroups of patients with low IQ had a poorer scholastic performance in childhood that continued deteriorating to late adolescence, and they had completed fewer years of education at baseline. These findings replicate the known strong link between cognitive abilities and premorbid academic adjustment in patients with SSDs,^{49–51} and inform about a possible neurodevelopmental disruption from early stages in life. Previous evidence has shown that cognitive deficits in patients with schizophrenia are observable from childhood and early adolescence.^{14,16,52}

The subscale of adaptation to school of the PAS assesses aspects such as enjoyment of school, friendships, or participation in school activities. Our results confirmed a deterioration over time in this subscale for all the FEP patients, consistent with previous evidence.^{49,53,54} However, the novelty of our results is that patients with a discordant low and high IQ showed a tendency toward poorer adaptation to school, although not reaching statistical significance (figure 3). A similar trend was observed for the sociability and peer relationships subscales of the PAS for the subgroup “high IQ discordant”. We interpret these tendencies as a possible link between the deviation from familial cognitive potential and a pattern of worse social adjustment that begins early in life. Interestingly, FEP patients in the “low discordant IQ” subgroup were more frequently diagnosed with schizophrenia (73.08%) than the “low concordant IQ” subgroup (40%). Taken together, these findings could indicate a subgroup of FEP patients with a worse premorbid adjustment, more chronic disorder, and greater familial cognitive deviation, probably because of neurodevelopmental disruption. However, this potential profile needs to be further studied in a larger sample to achieve greater statistical power.

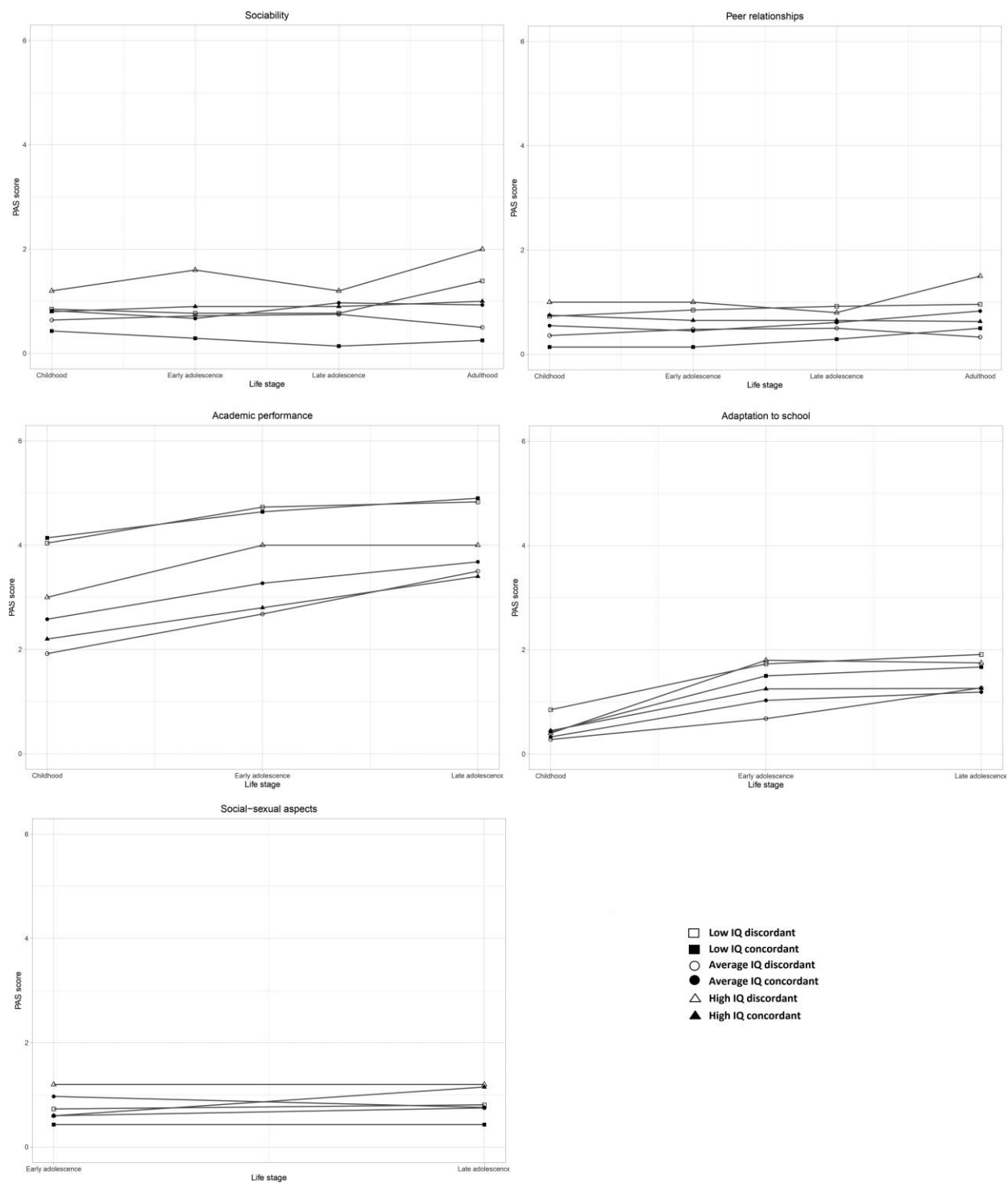


Fig. 3. Subscales of the Premorbid Adjustment Scale for the subgroups of FEP patients. Higher scores suggest worse adjustment.

We observed significant differences between subgroups in the neurocognitive scores. The differential performance in verbal memory, processing speed, and ToM seems to be associated

with IQ but not family IRS, since the 2 subgroups with lower intelligence obtained worse outcomes in such domains. Contrary, the performance in executive functioning might be related to cognitive familiarity because the “low IQ concordant” subgroup performed significantly worse than the “low IQ dis- cordant”. Therefore, the executive dysfunction of FEP patients could be especially heritable, which agrees with previous literature.^{55,56}

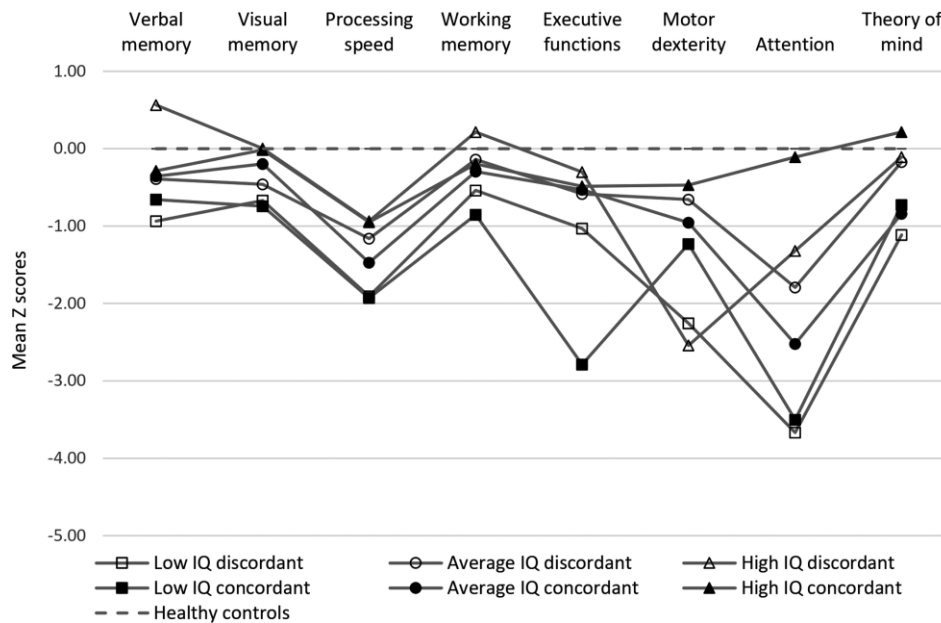


Fig. 4. Neurocognitive profile of FEP patients.

Our results on IQ-familiarity may have different practical implications in the future. The cognitive potential of FEP patients could be estimated from a neuropsychological evaluation of their first-degree relatives. This is a relatively simple and affordable way to plan personalized interventions. For example, FEP patients with high cognitive familial potential may be candidates for cognitive remediation from the onset of psychosis that seeks to improve cognitive outcomes. While patients with less cognitive familial potential might especially benefit from strategies focused on improving instrumental skills and functioning in daily life.

The main strength of this study is the use of neuro- psychological data of FEP patients and their unaffected first-degree relatives, which allowed estimating IQ-familiarity indexes. However, some limitations must be mentioned. Some patients’ subgroups were formed by few members, hindering the statistical power. Future research with more participants should explore if the amount of cognitive family deviation is relevant for the patients’ out- comes, for example comparing those highly discordant vs slightly discordant. Other limitation is not having enough representation of FEP patients with high IQ discordant, so we are unable of generalizing the features of this population. In addition, the statistical model we used indicates the degree of IQ-

familiality but does not inform about the cause of the family resemblance. It is well known that intelligence is malleable by rearing, for example through the parental educational level.⁵⁷ Therefore, future studies should study the genetic factors underlying the familiality of intelligence. Another limitation is the IQ estimate by the WAIS-III Vocabulary subtest. This tool measures crystallized intelligence, leaving aside other types such as fluid intelligence. Limitations regarding the characteristics of the sample must also be considered. Since the participation was voluntary, a subset of FEP patients with better cognitive and functioning outcomes could be enrolled in this study.

Conclusion

The IQ is familial in a low-moderate degree in FEP, although there are several degrees of family resemblance that can be quantified by the IRS. The great deviation from family-IQ in FEP patients might be related to a later schizophrenia diagnosis and premorbid difficulties from childhood. This could inform about a specific path that led to the FEP, but further research on genetic and epigenetic factors are necessary. For instance, a genetic analysis could test whether FEP patients with higher IQ-familiality show higher polygenic risk for schizophrenia, while an epigenetic study could explore potential disruptions of this type in FEP patients with low IQ-familiality. Stratifying patients according to their concordance or discordance to family neurocognition can help to better understand the heterogeneity of manifestations of psychosis to offer better prevention and treatment strategies. In families with high IQ-familiality, prevention strategies could be implemented, for example, with unaffected siblings to potentially avoid the psychotic onset. In families with low IQ-familiality there would be great opportunity to intervene on environmental factors, for example, implementing early cognitive remediation post-FEP to improve long term outcomes.

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Table 1. Sociodemographic, Premorbid, and Clinical Comparisons Among Subgroups of FEP Patients

	Low IQ discordant (LD) n = 26 (20.5%)		Average IQ discordant (AD) n = 26 (20.5%)		High IQ discordant (HD) n = 5 (3.9%)		Low IQ concordant (LC) n = 15 (11.8%)		Average IQ concordant (AC) n = 35 (27.6%)		High IQ concordant (HC) n = 20 (15.7%)		F	P	Post hoc ^a
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)			
Sociodemographic															
Sex (male %)	26	20 (76%)	26	11 (42%)	5	2 (40%)	15	12 (80%)	35	21 (60%)	20	14 (70%)	$\chi^2 = 10.487$	.063	AD<LD [‡] , LC [‡]
Age at inclusion	26	24.65 (4.52)	26	27.04 (8.05)	5	27.60 (17.60)	15	23 (6.83)	35	27.37 (8.60)	20	30.35 (9.35)	1.78	.122	
Age at onset	26	23.65 (5.28)	25	26.57 (8.15)	5	26.51 (15.72)	15	22.52 (6.91)	34	27.05 (8.71)	20	29.54 (8.86)	1.86	.106	
Low socioeconomic status (yes %)	26	14.00 (53.8%)	25	6.00 (24.0%)	5	1.00 (20.0%)	15	9.00 (60.0%)	34	15.00 (44.1%)	20	6.00 (30.0%)	$\chi^2 = 9.059$	.107	
Living with parents (yes %)	26	22.00 (84.6%)	26	16.00 (61.5%)	5	4.00 (80.0%)	15	11.00 (73.3%)	34	18.00 (52.9%)	20	11.00 (55.0%)	$\chi^2 = 8.548$	.129	
Premorbid data															
IQ	26	81.15 (5.35)	26	98.85 (3.82)	5	115.00 (6.12)	15	84.33 (6.51)	35	100.29 (3.63)	20	112.50 (3.80)	150.31	<.001	LD<AD,HC,AC,HC; AD<HD,AC,HC; LC<AD,HD,HC; AC<HD,HC
IRS IQ	26	-9.30 (6.72)	26	-5.39 (5.55)	5	-2.27 (2.10)	15	6.24 (4.31)	35	5.56 (4.19)	20	6.63 (4.52)	42.63	<.001	LD<LC,AC,HC; AD<LC,AC,HC; HD<LC [‡] ,AC [‡] ,HC [‡]
Family-IQ	26	96.81 (5.28)	26	109.76 (5.02)	5	112.70 (4.32)	15	88.83 (8.06)	35	104.15 (6.10)	20	113.00 (6.22)	42.91	<.001	LD<AD,HD,AC,HC; LC<LD [‡] ,AD,HD,AC,HC; AC<AD [‡] ,HD [‡] ,HC
Deviation from family-IQ	26	-15.66 (5.39)	26	-10.91 (5.14)	5	2.30 (8.41)	15	-4.50 (3.79)	35	-3.86 (5.89)	20	-0.50 (3.98)	29.34	<.001	LD<AD [‡] ,HD,LC,AC,HC; AD<HD,LC [‡] ,AC,HC
Years of education	26	8.62 (1.36)	26	12.23 (3.80)	5	11.20 (1.79)	15	8.53 (2.20)	34	11.09 (3.63)	20	11.85 (3.48)	5.76	<.001	LD<AD [‡] ,AC [‡] ,HC [‡] LC<AD [‡] ,HC [‡]
PAS childhood	26	2.69 (1.48)	25	1.33 (1.12)	5	2.33 (1.58)	14	2.14 (0.88)	33	1.78 (1.24)	20	1.75 (1.20)	3.46	.006	LD>AD [‡]
PAS early adolescence	26	2.94 (1.14)	25	1.72 (1.01)	5	3.20 (2.12)	14	2.33 (0.95)	33	2.13 (1.44)	20	2.07 (1.20)	3.23	.009	LD>AD [‡]
PAS late adolescence	26	2.97 (1.50)	24	2.26 (1.18)	5	3.09 (1.80)	14	1.91 (1.34)	33	2.27 (1.90)	20	2.47 (1.86)	1.15	.341	
PAS adult	26	2.37 (2.54)	24	1.04 (1.32)	4	3.47 (3.19)	8	1.04 (0.91)	30	1.75 (2.49)	17	1.80 (2.45)	1.52	.189	
PAS general	25	4.02 (2.41)	25	2.75 (1.63)	5	4.83 (2.91)	14	4.10 (2.16)	33	3.03 (2.24)	20	3.35 (2.35)	1.73	.134	
Clinical and functioning data															
SAPS	26	15.23 (3.89)	26	14.81 (5.28)	4	14.75 (3.69)	15	16.47 (5.91)	35	14.20 (4.92)	20	13.05 (3.62)	1.05	.391	
SANS	26	8.54 (6.62)	26	5.73 (6.19)	4	11.50 (7.94)	15	6.47 (7.43)	34	5.79 (5.95)	20	5.10 (5.22)	1.41	.224	
Schizophrenia diagnosis (yes%)	26	19 (73%)	26	12 (46%)	5	2 (40%)	15	6 (40%)	35	11 (31%)	20	9 (45%)	$\chi^2 = 25.06$	.199	LD>LC [‡]
DUP	26	14.50 (20.32)	26	7.31 (10.00)	5	15.83 (25.08)	15	9.61 (15.74)	34	8.66 (25.88)	20	14.31 (35.35)	0.52	.761	
DUI	25	20.02 (23.67)	26	11.96 (14.52)	4	25.75 (23.84)	15	17.58 (26.50)	34	16.88 (30.09)	20	23.65 (39.53)	0.45	.810	
GAF	20	47.00 (28.16)	22	47.82 (31.17)	3	30.33 (9.24)	10	59.70 (36.96)	28	58.64 (29.61)	14	52.29 (32.89)	0.88	.501	

^aAll post hoc comparisons are Bonferroni corrected and significant at $P < .001$ except when indicated. [‡] $P \leq .010$. [¶] $P \leq .050$. DUI = Duration of Untreated Illness; DUP = Duration of Untreated Psychosis; GAF = Global Assessment of Functioning; IQ = Intelligence Quotient; IRS = Intra-family Resemblance Score; PAS = Premorbid Adjustment Scale; SANS = Scale for the Assessment of Negative Symptoms, SAPS = Scale for the Assessment of Positive Symptoms.

Table 2. Neurocognitive Comparisons Among Subgroups of FEP Patients

	Low IQ discordant (LD)		Average IQ discordant (AD)		High IQ discordant (HD)		Low IQ concordant (LC)		Average IQ concordant (AC)		High IQ concordant (HC)		F	P	Post hoc*
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)			
Verbal memory	26	-0.94 (0.95)	26	-0.39 (0.88)	5	0.57 (0.71)	15	-0.66 (1.04)	34	-0.36 (1.12)	20	-0.29 (0.73)	2.57	.031	LD<HD [¶]
Visual memory	25	-0.67 (0.81)	26	-0.46 (1.00)	5	0.00 (1.11)	15	-0.74 (1.41)	34	-0.20 (0.99)	20	-0.02 (0.82)	1.59	.170	
Processing speed	26	-1.91 (0.92)	26	-1.16 (1.02)	5	-0.94 (0.87)	15	-1.93 (0.80)	34	-1.47 (1.24)	20	-0.95 (1.01)	2.90	.017	LD<HC [¶]
Working memory	26	-0.54 (0.59)	26	-0.14 (0.95)	5	0.22 (0.47)	15	-0.86 (0.61)	34	-0.30 (0.85)	20	-0.20 (0.77)	2.19	.060	
Executive functions	26	-1.03 (1.31)	26	-0.58 (1.12)	5	-0.30 (1.06)	13	-2.79 (2.89)	34	-0.53 (1.63)	20	-0.49 (0.98)	4.52	<.001	LC<LD [¶] ,AD [¶] ,HD [¶] ,AC, HC [¶]
Motor dexterity	26	-2.26 (5.90)	26	-0.66 (1.24)	5	-2.54 (1.09)	15	-1.23 (1.87)	34	-0.96 (1.58)	19	-0.47 (1.09)	1.17	.327	
Attention	24	-3.67 (5.02)	25	-1.79 (3.31)	5	-1.32 (4.21)	15	-3.50 (3.69)	33	-2.52 (4.91)	20	-0.11 (0.61)	1.90	.100	
Theory of Mind	19	-1.11 (0.71)	22	-0.17 (0.81)	4	-0.11 (0.40)	13	-0.73 (0.89)	29	-0.84 (0.91)	14	0.22 (0.91)	5.43	<.001	LD<AD [¶] ,HC [¶] ; AC<HC [¶]
Global Deficit Score	23	-1.32 (0.93)	25	-0.86 (0.58)	5	-0.81 (0.64)	13	-1.52 (1.04)	33	-0.97 (0.96)	19	-0.42 (0.32)	3.45	.006	LD<HC [¶] ; LC>HC [¶]

*All post hoc comparisons are Bonferroni corrected and significant at $p < 0.001$ except when indicated. [¶] $P \leq .010$. ^{¶¶} $P \leq .050$. Note: All cognitive variables were covariated with age, sex, and years of education.

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