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Processing speed in first-epidose of psychosis and first degree relatives: a candidate endophenotype of schizophrenia spectrum disorders

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Processing speed in first-episode of psychosis and first-degree relatives: a candidate an endophenotype of spectrum schizophrenia disorders

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Conflict of interest

The authors have no conflict of interest to declare.

Contributors

All the authors have participated and have made substantial contributions to this paper.

AYR: writing – original draft, conceptualization, methodology, formal analysis, Investigation, validation, visualization.

RMH and NMG: validation, visualization.

RAA: writing – review and editing, conceptualization, methodology, supervision, Investigation, resources, validation, visualization.

Data availability statement

The data supporting the findings of this article is available upon request from the corresponding author, RAA.

Abstract

Objective: The processing speed (PS) is highly impacted in individuals experiencing their first episode of psychosis (FEP). Conducting family studies can help determine whether PS can serve as an endophenotype of schizophrenia spectrum disorders (SSDs), offering valuable insights into the prevention and diagnosis of SSDs. **Method:** A comprehensive cognitive battery, encompassing tests for PS, verbal memory, visual memory, working memory, executive functions, motor dexterity, and attention, was administered to a sample consisting of 133 FEP patients, 146 parents, 98 siblings, and 202 healthy controls (HC). Univariate analyses (ANCOVA) were conducted to compare the different cognitive domains between groups, utilizing sex, age, and years of education as covariates and Bonferroni corrections. Effect sizes were calculated for estimating the magnitude of differences between groups. **Results**: Group comparisons revealed significant differences in all cognitive domains. PS was the most impaired function in patients. Parents and siblings had intermediate PS performance between FEP patients and HC. Large effect sizes were observed in PS between FEP vs siblings, FEP vs controls, parents vs controls, and parents vs siblings. **Conclusions:** Despite not meeting all the necessary criteria, the PS observed in FEP patients and their first-degree relatives suggest its potential as a promising endophenotype for SSDs.

Keywords: First-episode, first-degree relatives, psychosis, processing speed, endophenotype.

Keypoints

Question: Is processing speed (PS) a candidate endophenotype of schizophrenia spectrum disorders (SSDs)? Findings: While PS meets most of the criteria to be considered an endophenotype, the findings of the study do not fully support this conclusion. Importance: Identifying cognitive markers, such as PS, can contribute to the recognition of at-risk populations, facilitating prevention, early diagnosis, and the development of personalized treatment and intervention strategies. Next Steps: Further studies are needed to explore the endophenotype criteria that were not fully met in the current research, providing additional insights into the potential role of PS as an endophenotype for SSDs.

Introduction

Individuals who have experienced a first-episode of psychosis (FEP) often exhibit cognitive impairments across multiple domains (1,2). One of the greatest degrees of impairment is observed in the domain of processing speed (PS), wherein patients show performance 1.5 deviations below healthy subjects (3,4). Importantly, PS deficits persist over time, being present in the premorbid phase, during the first episode, and in chronic schizophrenia(5–7). PS refers to the rate at which various cognitive operations can be executed (8) and it is considered a fundamental domain underlying general cognition (9–11), while also playing an important role in higher-order processes (9). Low PS scores have been associated with poor quality of life and poor functioning (12–14),which is particularly important to day-to-day functioning.

Several proposals have been made regarding the status of endophenotypes of schizophrenia spectrum disorders (SSDs), specifically in terms of cognition. Cognitive endophenotypes must be: (i) associated with illness in the population; (ii) be heritable; (iii) state-independent; (iv) co-segregated within families along with the disease; (v) found in affected family members and unaffected family members at a higher level than in the general population; and vi) a trait that can be measured reliably, and ideally to be more strongly associated with the disease of interest than with other psychiatric conditions (15,16).

PS is a confirmed measurable trait in SSDs, being the Wechsler Digit Symbol Coding Test (DSCT) the gold standard assessment tool (3,17,18).The DSCT is a multimodal test that involves other cognitive processes, such as visual scanning, sustained attention, coordination, and psychomotor speed (PSM).PSM has been considered the motor subcomponent of the PS, differentiating it from speed-related tests with higher cognitive demand, prevailing cognitive subcomponent, such as is the case in DSCT and TMT A (19). It is important to clarify this

distinction, as many studies use the terms PS and PSM indistinctly (20,21). DSCT has been suggested as a screening tool in FEP (18). FEP patients have consistently shown poor performance on the DSCT (5,9,10,22–24), as well as have their first-degree relatives (25–30), indicating a relationship between PS deficits and familial kinship. The presence of PS impairments in both patients and their relatives suggests a potential genetic risk factor for PS deficits and highlights the possibility of PS as an endophenotype of SSDs.

The present study aims to explore cognitive performance, with a particular focus on PS, in a cohort consisting of FEP patients, their first-degree relatives (parents and siblings), and healthy controls for considering PS as an endophenotypeof SSDs.

Methods

Participants

Participants were recruited from two projects: 1) Program for Initial Phases of Psychosis (PAFIP)(23) and 2) PAFIP-FAMILIAS (27), both from the University Hospital Marqués de Valdecilla (Cantabria, Spain). The total sample included five hundred and seventy-nine participants: 133 FEP patients, 146 parents, 98 siblings, and 202 HC groups. FEP participants met the following inclusion criteria: 1) 15-60 years of age, 2) living within the area of study (Santander, Cantabria, Spain), 3) were experiencing a first-episode of psychosis, 4) had not received treatment with antipsychotics, or had not taken medication six weeks prior, and 5) met the diagnostic criteria for schizophrenia (N=61), schizophreniform disorder (N=38), brief psychotic disorder (N=15), psychosis not otherwise specified (N=14), and schizoaffective disorder (N=4). Parents, siblings, and HC met the following inclusion criteria: 1) over 15 years of age, 2) good command of the Spanish language, 3) no psychiatric diagnosis, 4) no brain pathology, 5) no intellectual disability (according to DSM-IV), and 6) no substance use disorders (according to DSM-IV).

Design

The study's design cross-sectionally assessed general cognitive performance and PS among FEP patients and their first-degree relatives from the PAFIP (23) and PAFIP-FAMILIAS projects (27). All participants were informed about the characteristics of the study and signed the informed consent document showing their agreement to participate. Both the PAFIP and PAFIP-FAMILIAS projects were approved by the local institutional review committee (CEIm Cantabria) according to international research ethics standards (approval numbers NCT0235832 and 2017.247).

Sociodemographic and clinical assessment

Sociodemographic data for FEP patients, parents, siblings, and HC were collected regarding sex, age, and years of education. For FEP patients, clinical assessments, medical records, and a baseline interview provided information about age at psychosis onset; when first psychotic symptoms began, and whether they were present most of the time; duration of untreated illness (DUI), which was defined as the time from the first unspecific symptoms related to psychosis to initiation of adequate antipsychotic drug treatment; and duration of untreated psychosis (DUP), which was defined as the time from the first continuous psychotic symptom to initiation of adequate antipsychotic drug treatment. Negative symptoms were assessed by the Scale for the Assessment of Negative Symptoms (SANS) (31). Positive symptoms were assessed by the Scale for the Assessment of Positive Symptoms (SAPS)(32). Depression symptoms were assessed by the Calgary Depression Scale for Schizophrenia (CDS) (33). The Disability Assessment Scale (DAS) Spanish Version (34) was applied for functional assessment. The Brief Psychiatric Rating Scale (BPRS) was used to assess general psychopathology (35).

Neurocognitive Assessment

Cognitive assessment data were obtained by trained neuropsychologists. The chosen battery evaluated several cognitive domains: PS (Digit Symbol Coding Test from WAIS-III) (17), verbal memory (Rey Auditory Verbal Learning Test, RAVLT)(36), visual memory (Rey Complex Figure, RFC) (37), working memory (Digits Backward subtest, WAIS-III) (17), motor dexterity (The Grooved Pegboard test) (19), and attention (Continuous Performance Test, CPT) (38). The executive function domain in this study makes specific reference to set-shifting (TMT B) (19), a term that will be used below. The WAIS-III vocabulary subtest (17) was used to estimate premorbid IQ. Z-scores were calculated for each cognitive domain based on the performance of 221 healthy volunteers who took the same neuropsychological battery as the FEP patients (39). In order to calculate a measure of Global Cognitive Functioning (GDS), raw cognitive scores were reversed when appropriate for standardization so that directionality was consistent (i.e. higher scores indicated better performance). According to the previous methodology (40), the GDS was calculated as T-scores (M=50, S.D.=10), using raw scores from a healthy comparison sample. T scores were converted to deficit scores that reflected the presence and severity of cognitive impairment. Deficit scores on all tests were then averaged to create the GDS score.

Data analysis

Statistical Package for Social Science version 19.0 SPSS (41) was used to analyze socio-demographic, clinical, and neurocognitive data. Univariate analyses (ANCOVAs), with Bonferroni corrections, were used to compare neurocognitive variables in all groups with sex, age, and years of education as covariates. We applied the effect size to assess the magnitude of the differences in PS between the groups analyzed.

Secondary analyses were conducted to further explore the relationship between PS and the fulfillment of the criteria to be considered an endophenotype of SSDs. In the FEP group, Pearson correlation analyses were conducted to examine the relationship between PS and clinical variables and to explore the socio-demographic and clinical characteristics associated with SSDs. In addition, given the multi-component nature of the DSCT test, we examined Pearson correlations between PS and the other cognitive domains in FEP patients, their first-degree relatives, and HC. ANCOVAs were conducted to assess the influence of covariates such as attention and motor dexterity domains on PS, considering their involvement in DSCT performance.

Transparency and Openness

We disclose the process we used to determine our sample size, any data exclusions, manipulations, and measures taken in the study. The study's design and analysis were not preregistered. Any data not provided in the article will be shared upon request from other investigators.

Results

Sociodemographic and clinical information

Ninety-eight percent of the FEP patients were identified as Caucasian. Significant differences were found for age (p<0.001), years of education (p<0.001), and premorbid IQ (p<0.001) (**Table 1**). FEP patients were younger than their siblings and their parents. Siblings completed more years of education than FEP patients, parents, and HC. Within the FEP group, those with a diagnosis of schizophrenia showed more severe negative (SANS) and positive (SAPS) symptoms (**Supplementary 1 and 2**).

Table 1.

Demographic and clinical variables for FEP patients, parents, siblings, and HC.

								ANOVA		
	N	A= FEP N = 133	*N*	B= Parents N = 146	*N*	C= Siblings N = 98	*N*	D= HC N = 202	Stadistics	*p* -value	Pairs comparisons
Sociodemographic variables											
Age, mean (SD)	133	26.79 (8.40)	146	61.66 (7.73)	98	40.29 (13.16)	202	29.71 (8.16)	F=446.820	<0.01	A<D *; A<C, A<B, D<C, D<B, C<B ***
Males, N	133	82 (61.65)	146	55 (37.67)	98	33 (33.67)	202	123 (60.89)	X^2= 36.05	<0.01	C<D, B<D, C<A, B<A ***
Years of education	132	10.60 (3.38)	145	10.26 (3.54)	98	12.56 (3.62)	201	10.84 (2.72)	F= 10.75	<0.01	D<C, B<C, A<C ***
Premorbid IQ	133	39.77 (8.52)	146	41.71 (9.67)	98	42.01 (8.28)	200	41.01 (11.61)	F= 1.403	0.241	
Clinical variables											
GAF	101	51.97 (30.44)									
GDS	130	2.16 (1.59)									
BPRS	131	65.67 (15.09)									
DUP	132	12.72 (28.42)									
DUI	130	19.67 (31.59)									
SAPS	132	14.62 (4.87)									
SANP	131	6.57 (6.24)									
CDS	130	1.65 (1.58)									
DAS	123	2.16 (3.14)									

GAF= Global Functioning, CDS= Global Deficit Score, BPRS= The brief Psychiatric Rating Scale , CDS= Calgary Depresion Scale, DAS=Disability Assessment Scale, SANP= Scale for the Assesment Negative Symptoms, SAPS= Scale for the Assesment Positive Symptoms, DUI= Duration of Untreated Illness, DUP= Duration of Untreated Psychosis. Premorbid IQ covariated with sex, age and years of education. p<0,05*; p<0,01**; p<0,001***

Neurocognitive comparison

Table 2 provides the results obtained from the neuropsychological assessment. Group comparisons, displayed in **Figure 1**, revealed significant differences in all cognitive domains: PS (F=69.384, *p*<0.01); attention (F=14.463, *p*<0.01); motor dexterity (F=12.740, *p*<0.01); verbal memory (F=9.424, *p*<0.01); visual memory (F=7.994, *p*<0.01), and working memory (F=6.208, *p*<0.01). FEP patients obtained lower scores in all cognitive domains except on set-shifting. Parents performed significantly worse in PS in comparison with the other domains, and between siblings, parents, and HC groups. FEP patients with a diagnosis of brief psychotic disorder showed better PS. Large effect sizes (ES: Cohen's d effect size) were observed in PS in pair-wise comparisons: FEP vs HC (ES=1.30 to 0.00), FEP vs siblings (ES=1.08 to 0.01), parents vs HC (ES=1.57 to 0.01), parents vs siblings (ES=1.33 to 0.01). Small effect sizes were observed between FEP vs parents (ES=0.32 to 0.003) and siblings vs HC (ES=0.17 to 0.16) (**Table 3**).

Secondary analyses to examine the influence of attention (F=50.845, p<0.01) and motor dexterity (F=55.055, p<0.01) as covariates on PS showed significant differences between groups in PS. In **Figure 2** we show the Pearson correlations found between PS and the other cognitive domains. Only moderate and large correlations (above 0.30) were taken into account. Among siblings, there was a moderate correlation between PS and the motor dexterity domain (r=.438). Among parents, motor dexterity (r=.342), verbal memory (r=.339), attention (r=.320), and set-shifting (r=.412) showed moderate correlations with PS. Among FEP patients, correlations with PS were found for the domains set-shifting (r=. 405), attention (r=. 406), and verbal memory (r=.369). Pearson correlations and scatter plotswith different trend lines for each group between PS and motor skills can be found in **Supplementary 3 and 4**.

Table 2.

Comparison of cognitive variables for FEP patients, parents, siblings, and HC.

	A= FEP		B= Parents		C= Siblings		D= HC		ANCOVA		Pairs comparisons
	N	Means (SD)	*N*	Means (SD)	*N*	Means (SD)	*N*	Means (SD)	F	*p*	
Neurocognition (Z score)											
Processing Speed											
DSCT	132	-0.61 (0.76)	146	-0.19 (0.90)	98	0.24 (0.85)	200	0.43 (0.77)	69.384	<0.01	A<B **; A<D, B<D, A<C ***
TMT A	132	-1.40 (1.75)	144	-0.96 (2.26)	98	-0.80 (1.21)	201	-0.23 (1)	21.059	<0.01	A<D, A<C ***; B<C*
Verbal Memory	133	-0.26 (0.97)	146	-0.07 (0.93)	98	0.03 (0.97)	202	0.21 (0.89)	9.424	<0.01	A<D ***
Visual Memory	132	-0.32 (0.88)	144	0.01 (1.11)	98	0.24 (0.77)	201	0.08 (0.89)	7.994	<0.01	A<D, A<C ***
Working Memory	133	-0.34 (0.84)	146	0.13 (0.96)	98	0.14 (0.95)	201	0.06 (1.05)	6.208	<0.01	A<D **; A<C ***
Executive Functions	131	-0.29 (0.86)	142	-0.26 (1.39)	97	0.12 (0.71)	202	0.32 (0.52)	11.114	<0.01	B<D **, A<D ***;
Motor Dexterety	132	-0.31 (1.30)	145	-0.16 (1.18)	98	0.19 (0.57)	201	0.24 (0.43)	12.740	<0..01	A<D, A<C ***
Attention	129	-0.43 (1.23)	139	-0.01 (1.22)	98	0.05 (0.87)	182	0.27 (0.30)	14.463	<0.01	A<C **, A<D ***
GDS	125	-0.99 (0.86)	136	-1.08 (0.86)	97	-0.4 (0.55)	181	-0.28 (0.43)	35.196	<0.01	A>D, A>B, A>C*** B>C, B>D *

Group differences, with the covariates, sex, age, and years of education, were assessed with Bonferroni corrected post hoc tests with significance at p<0.05. GDS: Global Deficit Score. p<0,05*; p<0,01**; p<0,001***

Table 3.

Cohen's d effect sizes for the differences in PS performance between FEP patients, parents, siblings, and HC.

Groups pairs	Means (SD)	t-student	*p* value	Δ Cohen
FEP Parents	-0.42 (0.76) -0.72 (0.90)	-3.02	0.003	0.362
FEP Siblings	-0.42 (0.76) 0.45 (0.85)	8.12	p<0.01	1.08
FEP HC	-0.42 (0.76) 0.58 (0.77)	11.65	p<0.01	1.30
Parents HC	-0.72 (0.90) 0.58 (0.77)	-14.50	p<0.01	1.57
Parents Siblings	-0.72 (0.90) 0.45 (0.85)	-10.18	p<0.01	1.33
Siblings HC	0.45 (0.85) 0.58 (0.77)	-1.39	0.165	0.171

FEP: First Episode of Psychosis; HC: Healthy Control

Discussion

This study aimed to explore the cognitive domain of PS in a sample of FEP patients, their first-degree relatives, and HC, for considering its potential as an endophenotype of the disorder. We found that in FEP patients, PS was the most affected cognitive domain. First-degree relatives revealed an intermediate PS performance between FEP patients and HC, such that parents were more affected than siblings(42). A small-moderate effect size suggests that FEP patients underperformed significantly their parents on PS, although to a lower extent than other groups. On the other hand, siblings obtained values similar to those of HC.

The present results on PS partially fulfill the conditions for being considered as a cognitive endophenotype, attending Gottesman (10) and Lenzeweger (11) criteria necessary for the classification of endophenotypes of SSDs. About criterion (i), related to association with a population, our results confirm the presence of cognitive deficits in SSD supported in extensive literature (43,44). Concerning criterion (ii), the presence of a deficit in PS among first-degree relatives reinforces the potential genetic association between cognitive deficits and familial heritability, as supported by existing literature (45–47). Furthermore, our results showed that first-degree relatives are situated in an intermediate performance on PS between FEP patients and HC (25,30,48–51). Regarding criterion (iii), state independence, the cross-sectional nature of our study did not allow us to explore this circumstance. Assuming this limitation, our results provide partial information on the independence between the deficit in PS and other clinical variables such as SANS, SAPS, and BPRS in the FEP group, which matches other studies supporting the independence between symptomatology and cognitive deficits (23).Other studies show the stable presence of PS deficits in FEP patients over the years (5–7). About

criterion (iv), co-segregation, it cannot be verified due to we do not have clinical data on the first-degree relatives. Psychiatric diagnosis was an exclusion criteria in all but FEP samples. However, the moderate observed deficits in PS in parents are in coincidence with previous studies in families composed with at least one parent (52) and multiple members affected (53–56), suggesting the possible influence of genetic load on PS. Criterion (v), impairment in affected and unaffected family members at a higher level than in the general population, is partially fulfilled. Several studies support that our data reveals a lower performance in PS among unaffected first-degree relatives compared to HC (25,30,48–51). Lastly, the criterion (vi), to be a reliably measurable trait that is more strongly associated with the specific disease of interest than with other psychiatric conditions, is partially fulfilled. On the one hand, PS assessed thought DSCT in SSDs presented well reliably in several studies (3,22,57–59), and can therefore be considered a reliable measure. On the other hand, our results showed that when we compared the PS between the different diagnoses in the FEP patients, all but the brief psychotic disorder subgroup showed deficits in PS, as previously published by our group (24). We cannot be certain that PS is unique to SSDs, but, for instance, comparative studies with other diagnoses, such as bipolar disorder, have shown that PS is most impaired in SSDs than in bipolar patients (60,61).

Attending to its multi-component condition, DSCT as a measure of PS deserves further discussion (57,62,63), which in turn implies the necessary consideration of cognitive functions other than PS. Andersen et al.(9) proposed that PS underlies other speed-dependent cognitive domains. If certain higher-order processes depend on PS, better performance in PS would lead to better performance in speed-dependent domains (9,57). This speed-dependence could explain the differences in PS between groups, such that observed in the brief psychotic disorder subgroup, in which the PS deficits are attenuated or compensated with other cognitive domains.

Brief psychotic disorder, considered a less severe diagnosis, had better performance in PS than those with other diagnoses within SSDs(24,64). They also had a better recovery and prognosis, suggesting that PS could be exerting some kind of influence. This was suggested in a recent meta-analysis conducted by Hedges and colleagues (65), wherein patients at high clinical risk of schizophrenia were studied longitudinally in different cognitive domains. Their results showed that those patients who did not develop the disease performed better over time in PS than those who did develop the disease. In our data, siblings obtained similar scores compared to HC on the DCST. This is consistent with the meta-analysis specific to those patients who did not develop symptoms, suggesting that PS may be exerting some influence on those subjects at high clinical risk of developing FEP.

In addition to PS, PSM was recently proposed as an endophenotype of schizophrenia(66). Although both domains measure speed, in terms of the time taken to execute a task, PSM provides information differentiated between two subcomponents, the cognitive and the motor(67). The cognitive subcomponent of PS, evaluated through DSCT, TMT A, and TMT B (68), is defined as the time taken before the initiation of a movement, such as in the selection of responses to a particular stimulus that entails decision making, inhibition of competing responses, volition, motor planning, and sequencing. The motor subcomponent of PS, evaluated through tests such as Grooved Pegboard and Finger Tapping (20), is involved in the initiation, coordination, and execution of a response. Both tests that measure the cognitive subcomponent (DSCT and TMT A for PS) and the motor subcomponent (Grooved Pegboard for motor dexterity) of PS were used in this study. Our results show, supporting the literature, that while patients present deficits in both subcomponents of PS (cognitive and motor)(20,67,69), siblings presented deficits exclusively in the cognitive subcomponent in DSCT but not in TMT A, showing good performance on the motor subcomponent (29,67,70). The differences between

DSCT and TMT A in siblings would be because TMT A assessment does not need the fine psychomotor component (drawing symbols) and working memory (stablising number-symbols relations) implication, in comparison with multi-component cognitive activation used to complete DSCT. On the other hand, parents showed significant deficits compared to the HC group in the two tasks of the cognitive subcomponent. Given the close relationship between PS and PSM, particularly concerning motor dexterity, it is important to consider our correlation results. Patients and parents shared correlations between PS and most cognitive domains, except for motor dexterity. Siblings meanwhile shared no correlations with patients in any cognitive domain, while correlating with parents only in the domain of motor dexterity. The correlation between parents and siblings in motor dexterity may indicate that good performance in this domain may be related to DSCT scores. Therefore, PSM may be a "bridging" domain between more severe cognitive impairments. Studies on PSM in children with motor abnormalities (40,71), and subjects with psychotic experiences (72) point in this direction.

A potential biological explanation for our results concerning PS in FEP patients and their first-degree relatives is based on Andreasen's theory of cognitive dysmetria (73), in which she proposes that altered connectivity between the prefrontal cortex, thalamus, and cerebellum may be behind the psychotic and cognitive symptoms of schizophrenia (73,74). Recent studies relate cerebellar functional connectivity to cognitive and motor deficits in schizophrenia (75) and specifically in PS (76). The results obtained on the relationship between motor dexterity and PS in our sample seem to be in line with these findings. Furthermore, cerebellar dysfunctions have also been observed in siblings of patients with schizophrenia (77,78), such that deficits in PS as a function of first-degree relatives may have biological support.

Limitations and strengths

One of the limitations of the present study lies in the use of a single test for each of the cognitive domains. Although the DSCT test is positioned by MATRICS (18) as the gold standard in the evaluation of PS for schizophrenia patients, several authors have pointed out its limitations. Cepeda and colleagues(79)showed that speed-dependent behavior could be influenced by which test is selected and by the age of the participants. Meanwhile, as mentioned above, researchers have proposed that DSCT is multi-component (57,62,63). Research that focuses on other tests of PS with a lower multi-component level and a small range of patient characteristics, such as age, could provide more specific information about possible endophenotype for SSDs.The use of tests that dispense with the motor aspect of DSCT could provide more accurate results on PS deficits among patients with an FEP, and their relatives. Another limitation is the lack of relatives with psychotic related disorders. Psychiatric diagnoses tended to be used as exclusion, not inclusion, criteria. This should be reconsidered in the future. Additionally, we do not have longitudinal data that could provide answers to the unmet endophenotypes in the present study.

One of the strengths of the present study is the characteristics of the rather large sample of FEP patients along with their siblings, parents, and HC participants, bringing the opportunity to understand the endophenotypic relationships underlying SSDs. Another strength of this study can be found in the FEP patients, who were not conditioned by the long use of pharmacological treatments or by circumstances derived from the chronicity resulting from the course of the disease itself (80).

Future directions

In order to fulfil all the criteria to be considered and endophenotype for SSDs, longitudinal designs could provide information on the trait versus state circumstance of PS deficits in FEP patients, and the follow-up of PS performance in affected and unaffected relatives. In addition, the incorporation of patients with other diagnoses could confirm a specific association between PS deficits and SSDs. Finally, investigations into cerebral electrical activity, brain structure, genetic markers, and biochemical factors, potentially yield insights into endophenotypes of SSDs.

Conclusion

PS is a good candidate for consideration as an endophenotype of SSDs. Further studies are needed to consider that it meets all the criteria for this. In addition, other PS-related cognitive domains, such as motor dexterity, might not only be a fruitful area of future research, but a target for prevention, early intervention, and treatment plans.

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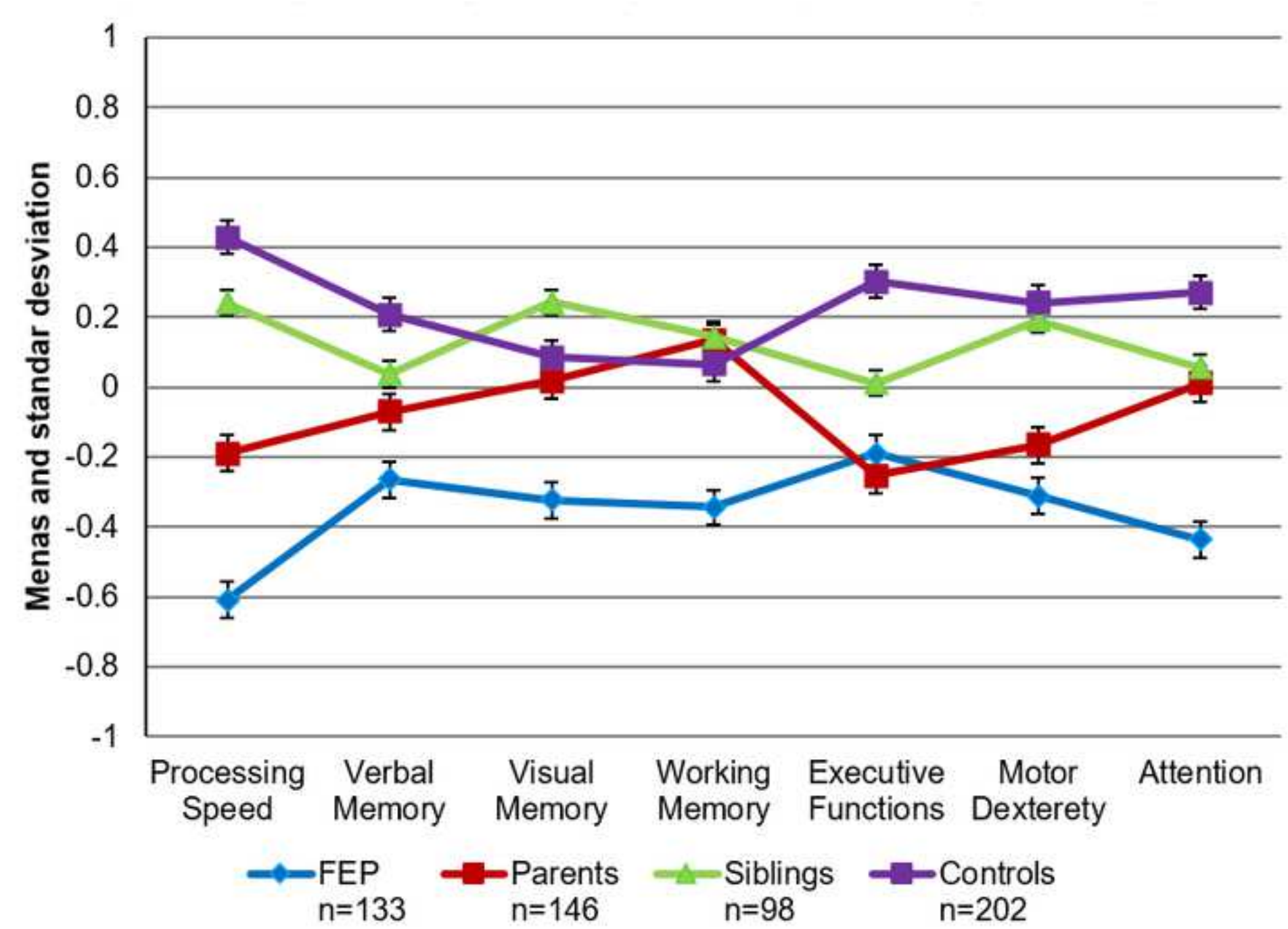
Figure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Menas and standar desviation
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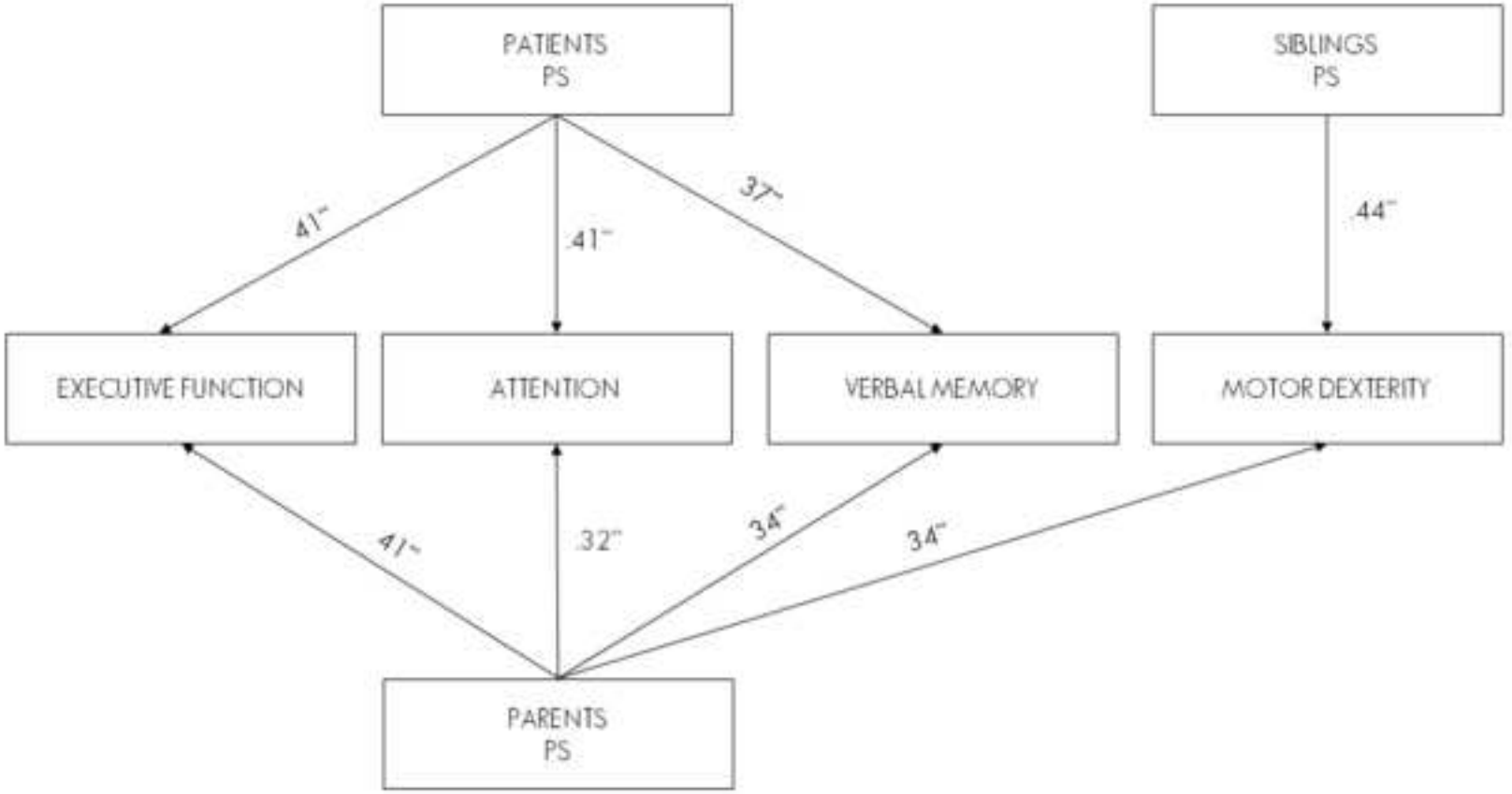
Executive Functions
Motor Dexterety
Attention
FEP n=133
Parents n=146
Siblings n=98
Controls n=202

Figure



Pearson correlations between processing speed and other cognitive domains for patients, parents, and siblings