

Assessment of Brain Pre-frontal Cortex in Adolescents with Single Ventricle Heart Disease



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Introduction

- Single ventricle heart disease (SVHD) adolescents with Fontan circulation show brain injuries in sites that are associated with cognitive deficits, in particular executive function.
- The brain prefrontal cortex (PFC) is associated with cognition and executive function, but has not been well studied in the SVHD population.
- Analysis of the PFC could elucidate structural brain development in SVHD with considerable clinical implications for treatment and improvement in neurocognitive outcomes.

Purpose

- To compare cognitive status [Montreal Cognitive Assessment (MoCA) and Wide Range Assessment of Memory and Learning Second Edition (WRAML2)] and prefrontal cortex tissue changes in SVHD adolescents compared to age-, gender-matched healthy controls.
- To examine the relationship between prefrontal cortex, cognitive scores [MoCA and WRAML2], and clinical variables [e.g., SV function, ventricle type, oxygen saturation] in SVHD patients.

Methods

- Design:** Cross-sectional, comparative design via secondary data analysis.
- Sample:** 63 adolescents, ages 14 to 18, enrolled [25 SVHD and 38 controls]
- Measures:** MoCA [normal > 26] and WRAML2 [mean 100 SD 15]
- Data Acquisition:** High-resolution T1-weighted Brain MRIs were collected using 3.0-Tesla MRI scanner (Siemens, Tim-Trio, Prisma)
- Tracings:** Manual Region of Interest (ROI) tracings of PFC on T1 weighted images using MRIcron software by single, blinded investigator & PFC volume calculated by voxel approach [Figure 1]
- Analysis:** Chi-squared for categorical data and independent samples t-test for continuous data based on normality distribution. Pre-frontal volumes were assessed using ANCOVA with covariates of age, sex, and total brain volume (TBV). Partial correlations between cognitive scores, clinical variables and pre-frontal volumes were assessed using partial correlations with covariates of age, sex, and TBV

Results

No significant differences between groups except for income and TBV [Table 1]. The majority were single right ventricle, had an extracardiac Fontan with 26% residual cyanosis [Table 2]. All cognitive measures were statistically significant with SVHD group worse than controls [Table 3]. SVHD group had a significant increase in PFC volumes [left, and total] compared to controls [Table 4]. There were no significant correlations between clinical [ventricle type, fenestration, saturation, # meds and surgery, SES and BMI] and cognitive measures compared to PFC volumes [Table 5].

Table 1. Characteristics of SVHD vs Control Groups

Subject Characteristics	SVHD [n=25]	Controls [n=38]	P Value
Age [median / IQR]	16 (15-17)	16 (15-17)	0.67
Gender [Male] (%)	15 (60%)	19 (50%)	0.44
Ethnicity (%)			0.91
White	13 (52%)	20 (50%)	
Hispanic	10 (40%)	16 (42%)	
Other	2 (8%)	2 (8%)	
Socioeconomic Status [median /IQR] [Annual Household Income]	\$73,167.5 [n=24] (\$54068-\$96,758)	\$85,696.0 [n=37] (\$74,317-\$116,633)	0.02
Handedness [Right] (%)	23 (92%)	34 (92%)	0.74
BMI [kg/m2] [median / IQR]	21.1 (19.7-3.0)	21.9 (19.6-24.9)	0.45
Total Brain Volume [L]	1.14 ± 0.14	1.23 ± 0.11	0.005

Table 3. Cognitive Scores in SVHD vs Control Groups

Variables	SVHD [n=25]	Controls [n=38]	p-value
MoCA Total [< 26 abnormal]	23 (20.5-25)	29 (27.8-30)	<0.001
Visuospatial / EF [MoCA]	4.0 (3.0-5.0)	5.0 (5.0-5.0)	<0.001
Attention [MoCA]	4.0 (3.0-5.0)	6.0 (6.0-6.0)	<0.001
Naming [MoCA]	3.0 (3.0-3.0)	3.0 (3.0-3.0)	0.03
Language [MoCA]	2.0 (1.0-2.0)	3.0 (2.0-3.0)	<0.001
Abstraction [MoCA]	1.0 (1.0-2.0)	2.0 (2.0-2.0)	<0.001
Delayed Memory [MoCA]	2.0 (0.5-3.0)	4.0 (4.0-5.0)	<0.001
WRAML2 [GMI]	83.0 (79-92.5)	111 (104.8-118)	<0.001
Attention / Concentration [GMI]	83.5 ± 11.4	109.6 ± 10.0	<0.001
Working Memory Index [GRI]	88 (79.5-97.5)	113.5 (102-122)	<0.001

Figure 1. PFC Tracing Example.

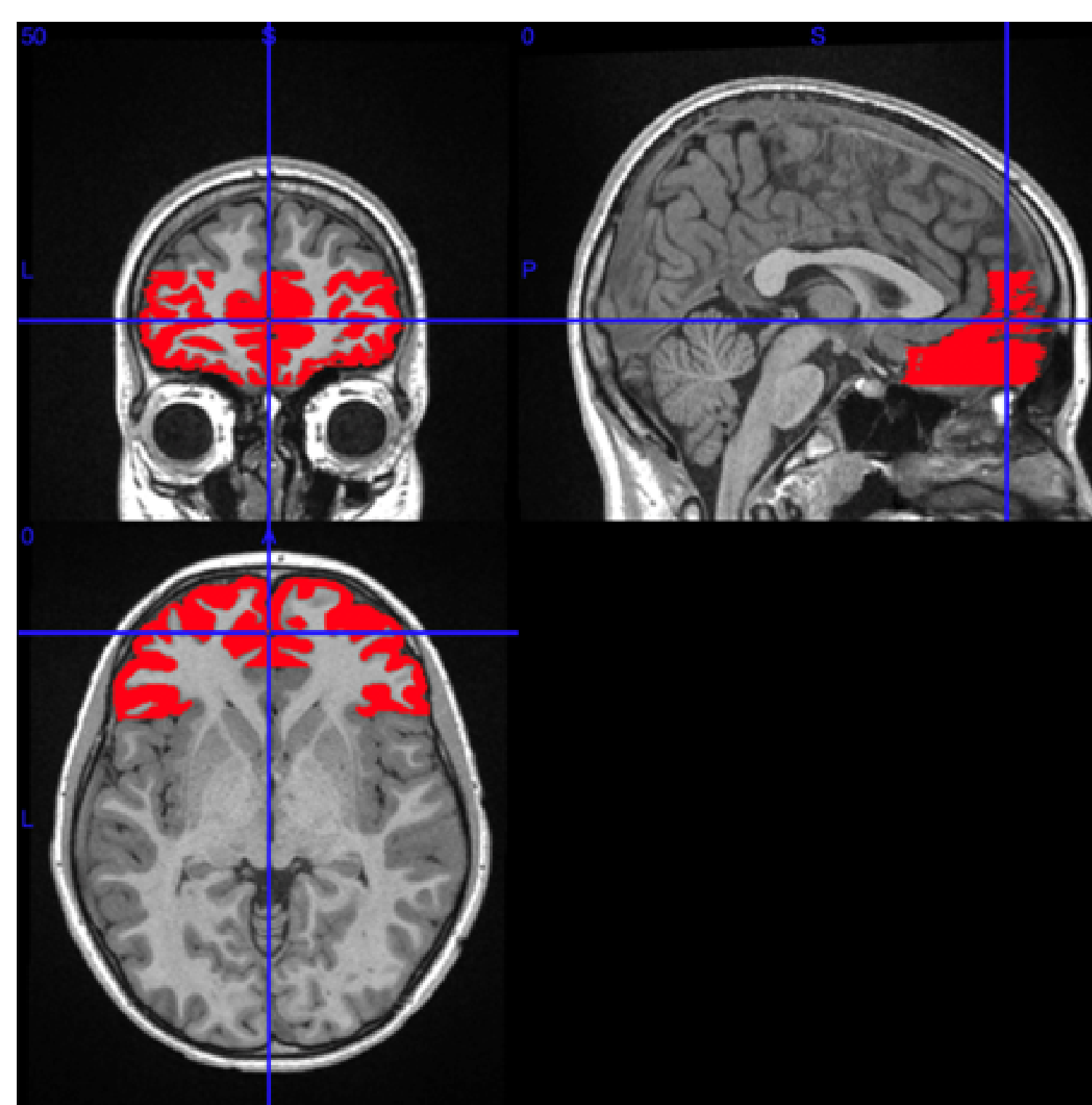


Table 2. Clinical Variables of SVHD Group

Clinical Variables	n (%)
Single Ventricle Diagnosis	
HLHS	6 (24%)
DORV / Unbalanced AVC	6 (24%)
Tricuspid Atresia	4 (16%)
PA / Unbalanced AVC	4 (16%)
PA/IVS/Hypoplastic RV	3 (12%)
DILV	2 (8%)
Ventricle Type (Right)	16 (67%)
Fontan Type (Extracardiac)	21 (78%)
Fontan Fenestration (Yes)	7 (26%)
Residual Cyanosis [sat < 93]	7 (26%)
Number of Surgeries	3 [range 3-4]
Number Medications	3 [range 1-5]

Table 4. PFC Volume in SVHD vs. Controls

PFC Volume	SVHD [n=25] Mean ± SD	Control [n= 38] Mean ± SD	P Values
Left [mm3]	30,697.0 ± 9,943.9	25,153.9 ± 9,686.6	0.043
Right [mm3]	31,265.4 ± 11,130.9	25,536.4 ± 10,842.9	0.061
Total [mm3]	62,831.7 ± 20,297.1	52,261 ± 19,771.9	0.039

ANCOVA; covariates Age, Gender, TBV

Table 5. Partial Correlations between Cognitive Scores and PFC Volumes

Variables	Left PFC Volumes r value (P-value)	Right PFC Volumes r value (P-value)	Total PFC Volumes r value (P-value)
MoCA Total [< 26 abnormal]	-0.08 (0.74)	-0.21 (0.35)	-0.15 (0.51)
Visuospatial / EF [MoCA]	-0.25 (0.27)	-0.34 (0.13)	-0.30 (0.18)
Attention [MoCA]	0.12 (0.59)	0.09 (0.68)	0.11 (0.63)
Naming [MoCA]	0.08 (0.72)	-0.07 (0.78)	0.005 (0.98)
Language [MoCA]	0.002 (0.99)	-0.18 (0.43)	-0.09 (0.69)
Abstraction [MoCA]	-0.13 (0.58)	-0.28 (0.21)	-0.21 (0.35)
Delayed Memory [MoCA]	0.10 (0.66)	0.12 (0.59)	0.11 (0.61)
WRAML2 [GMI]	-0.06 (0.80)	-0.01 (0.96)	-0.03 (0.88)
Attention / Concentration [GMI]	-0.31 (0.16)	-0.27 (0.23)	-0.30 (0.18)
Working Memory Index [GRI]	-0.006 (0.98)	-0.08 (0.73)	-0.04 (0.86)

Covariates, Age, Gender, and TBV

Results cont.

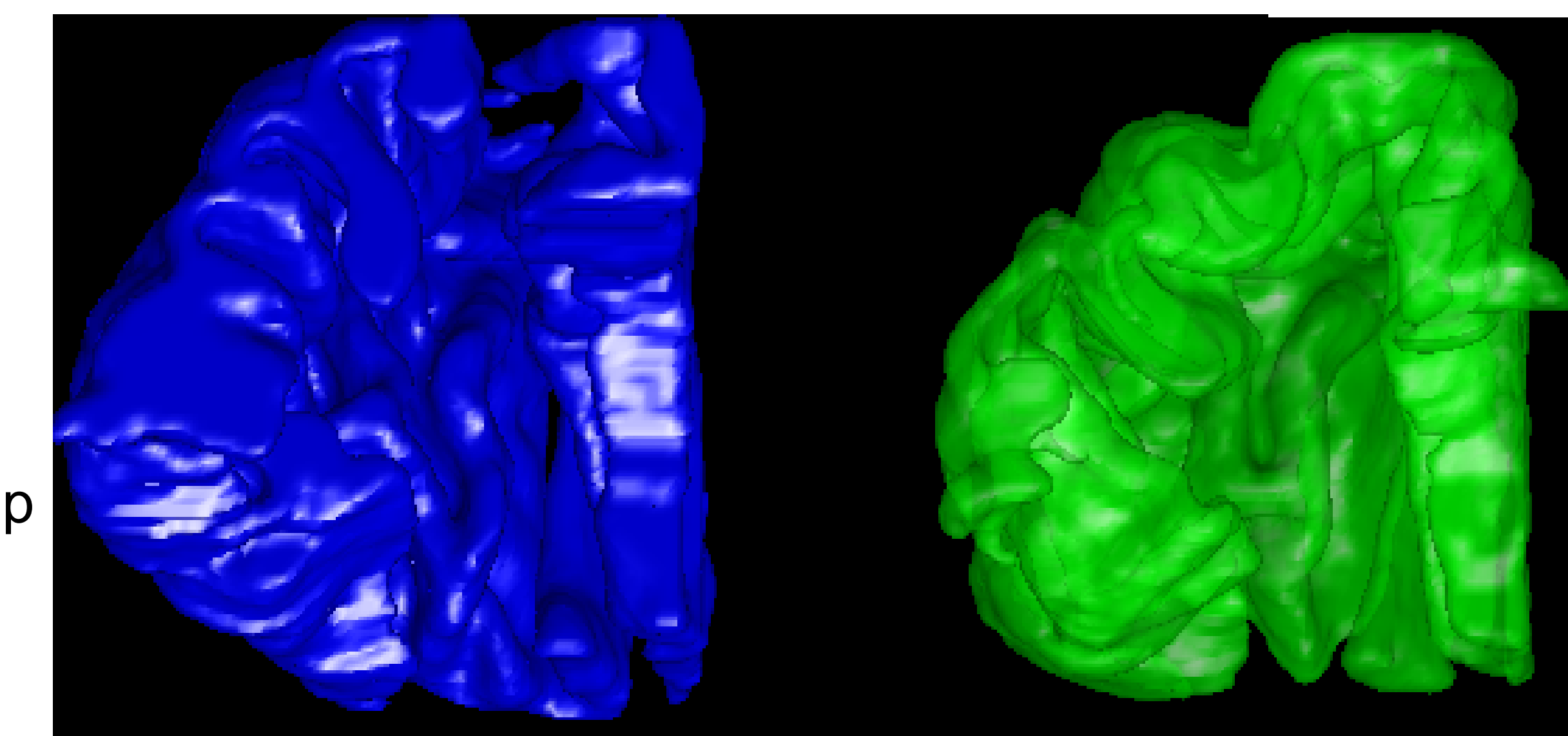


Figure 2. 3D view of left PFC in an 18 year old male with SVHD (blue) appears larger in comparison to age- and gender - matched control (green).

Conclusions

- SVHD group had significant cognitive deficits and reduced total brain volume compared to controls
- However, pre-frontal cortex volume in SVHD was greater than controls
- There were no significant associations between PFC volumes, neurocognitive indices and clinical variables in the SVHD group
- Potential causes may include delayed pruning, chronic low cardiac output state and hypoxic tissue injury leading to regional inflammation, and altered cerebral blood flow.

References

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