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Differential White Matter Maturation from Birth to 8 Years of Age

Q [1,2], P [3], H K [3], Q P [1,2], M O [1], M [1], D H [3], H [4], F F [5,6,7,8] H H [1,2]

[1]D R , C H P , P , PA 19104, A, [2]D R , P M , P , P , PA 19104, A, [3]D R , B C H , C M , N C C H , B 100045, C , [4]D B E , P M , P , PA, A, [5] P B K L B M H , P , B 100871, C , [6]K L M P , P , B 100871, C , [7]P C L , P , B 100871, C , [8]PK -IDG/MG I B R , P , B 100871, C

A H H , D R , C H P , P M , P , PA, A. E : 6@ . F F , P C , P , B , P. R. C . E : @ .
Q P

Abstract

C (M) (D I) 118 (D) 0 8 31 (A D) 2 7 , M D I M M *fast, intermediate,* *slow* 0 8 *fast* *intermediate* D M A D. D M 0 8

Key words: 0 8 , , , (D I), ,

Introduction

D (M) L 1967; H . 2005), M (N . 2004; E . 2012), 2005), (. 2005), (C . 2009; B . 2011; D . 2015), (. 2009), . 2005; H . 2006), (L . 2006). D M . 2001; D . 2007; G . 2008; L 2014), (C . 2010; A . 2014), (F . 2007), (B -G . 2004; K . 2014; O . 2016), (ADHD) (. 2009; E . 2014). M ( ), ( ), ( ), ( ), ( ), ( ), ( ) (. 2004). D M M (D) , (A D) .

D MRI, (D I), M (L B . 2001). M ,

D I, . D I- M . F (FA), 0 1, (. 2002). R (RD) (AD), , , . 2002, 2005). M (MD) (L . 2008).

M (M . 2001; H . 2006; D . 2012; G . 2012; . 2013; . 2014), ,

(L . 2008; . 2010; L B 2011; L . 2012). K M D I D (M . 2001; . 2004; D . 2006, 2008; H . 2006; L . 2008, 2012, 2017; . 2008; . 2010; L B 2011; G . 2012; . 2013, 2015; . 2014). D M (H . 2006, 2009) (M . 2013) D I . A , (D . 2006; . 2008; A . 2010), (M . 2001; . 2004; L . 2008; . 2013), (D . 2012; . 2014), P (L . 2012), (. 2010; L B 2011)

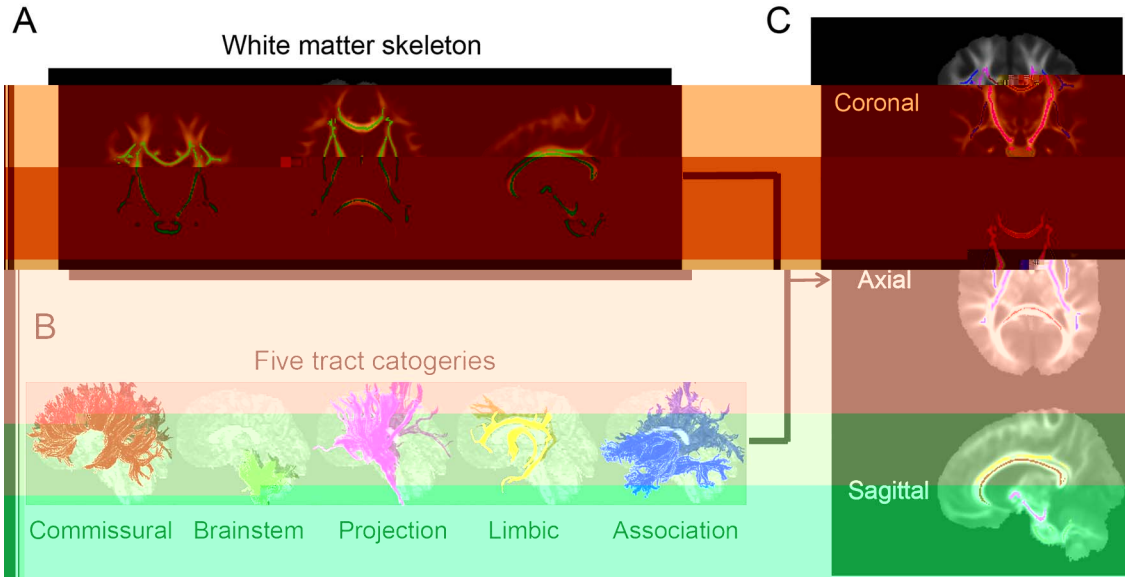

Figure 1. P M . (A) M ( ), ( ), ( ) FA 0.2; (B) 3D ; (C) M. (B).

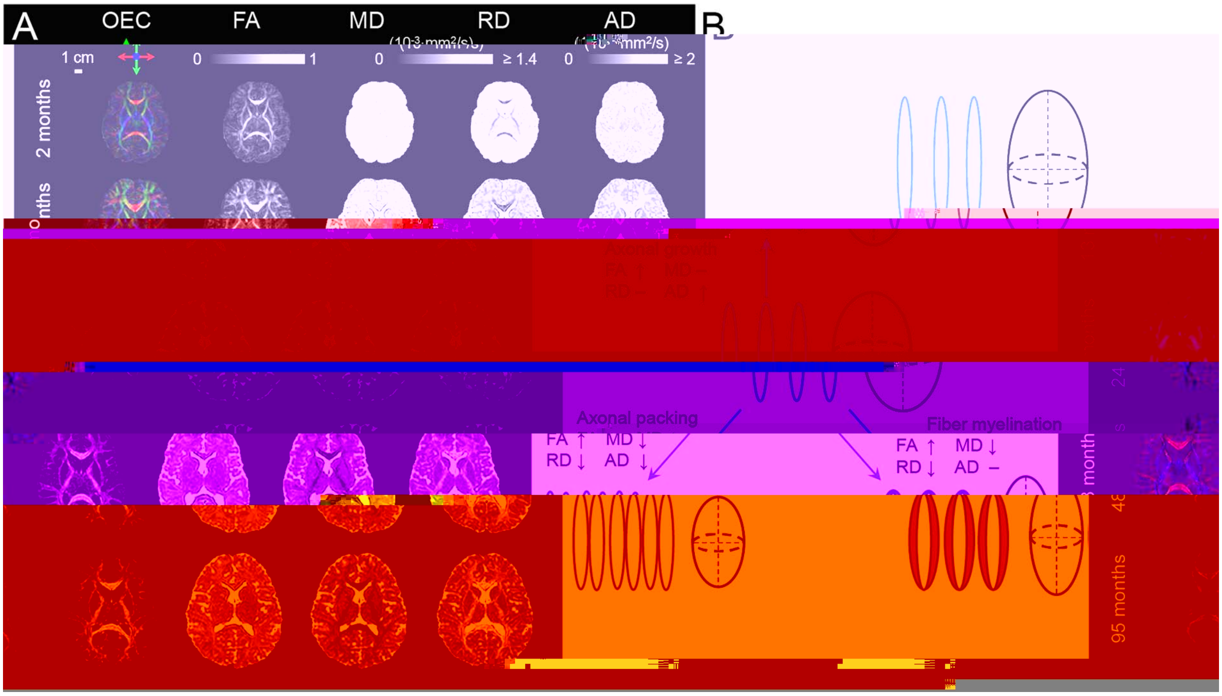

Figure 2. (A) R OEC, FA, MD, RD, AD 2-, 13-, 24-, 48-, 95- . (B) (, ,) D I M .

M FA . M D I (M . 2001; H . 2006; H . 2006; D . 2008; L . 2008, 2012; D . 2012; G . 2012; . 2013; K . 2014; . 2014, 2016) M M . F (0 2) (2 8) M , . I , . D M M . M M . D A (B . 2007; . 2011) (. 2008; . 2012) M A D , A D . D ( ) D I M M A D. I M 0 8 , M . E M ,

M . H , M 118 . D 0.17 7.91 D I (FA, MD, RD, AD) . I , 31 A D M . D M .

Materials and Methods

Pediatric Subjects

H . D (52 M/66F; : 3.36 ± 2.44 ; : 0.17 7.91) 31 A D (31 M; : 4.11 ± 1.42 ; : 2.33 7) B C ' H . . D (H.K. D.H.) / , . D MR , . N MRI . D I R B , D. A D . A D D I . D A D

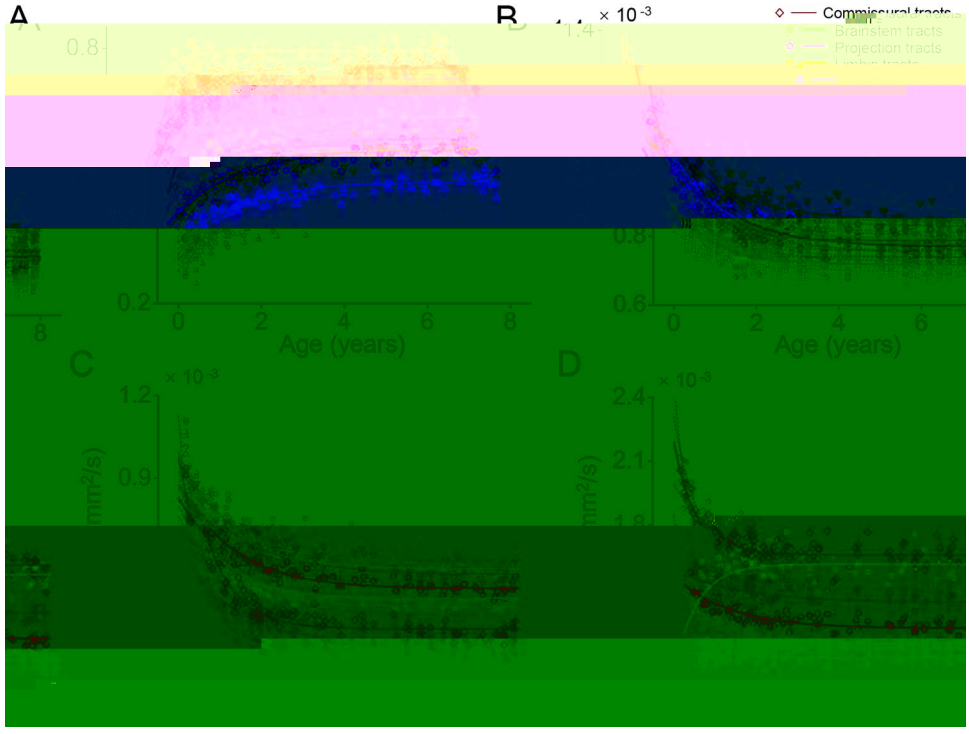

Figure 3. D F M FA (A), MD (B), RD (C), AD (D) . . M I .

DTI Acquisition and Measurement of Tract-Specific and Tract-Group-Specific WM Microstructure

A 3 P A (P , B , N) . D I EPI (EN E, =2). E 128 × 128 256 × 256 2. A 2 - . A 70 9.3 100 , . D 30 (J . 1999), - 1000 s/ 2. - , D I (H.K. P.) . A D I (J . 2006) . H D I . A F 1, D A D 0.5 0.25 (P = 0.41) (P = 0.06) A D D ,

D I - D I- : FA, MD, RD, AD. - M . B , M (JH ICBM-D I-81) (M . 2008), FA 118 D 31 A D - FA - (B) (. 2006) F L (://. . / / / B /) M , (H . 2011, 2012). , FA 0.2 (. 2006) M F 1A. A M JH ICBM-D I-81 (M . 2008) M , M (F . 1B) (. 2004). M : 1) (CC), (BCC), (GCC) ; 2) , (ICP), (MCP), (CP) , (ML); 3) , (C), (CP), ((AIC), (PIC), (RIC)), ((ACR), (CR), (PCR)); 4) , ((CGC) (CGH)), (P); 5)

Table 1 (%) D I (FA, MD, RD, AD) 0 8 D I F 58

	FA	MD	RD	AD
ALL	54.4	−29.9	−44.1	−14.7
Commissural	64.8	−42.5	−63.8	−24.2
CC	92.1	−53	−73.6	−34.6
GCC	54.2	−45.1	−65.9	−29
BCC	71.2	−37.4	−59.5	−15.3
Brainstem	81.9	−22.1	−39	
PC	104	−18.8	−38.9	
MCP	90.1	−26.6	−42.2	−6.9
ICP	69	−20.3	−35.8	
CP	59		−28.9	25.7
ML	48.5	−12.3	−30.1	8
Association	54	−28.3	−38.2	−16.4
LF	63.8	−32.7	−42.9	−19.6
FOF	71.8	−22.2	−34	−8.1
F	59.4	−22.6	−37.8	
EC	41.8	−21.9	−30.9	−11.3
	57.5	−30.3	−40.3	−24.2
Limbic	49.9	−23.5	−37.1	−8.4
P	44.7	−24	−38.7	−9.4
CGC	62.2	−28.2	−42.5	−11.1
CGH	40.6	−17.4	−29.5	
Projection	44.7	−27	−39.5	−13.5
PIC	35.8	−20	−41.9	−6.2
RIC	35.3	−23.1	−34.9	−11.8
AIC	57.1	−22.2	−38.3	−5.2
PCR	51.6	−28.2	−37.8	−16.4
CP	43.8	−28	−51.6	−16.8
CR	46.6	−29.5	−39.1	−18.3

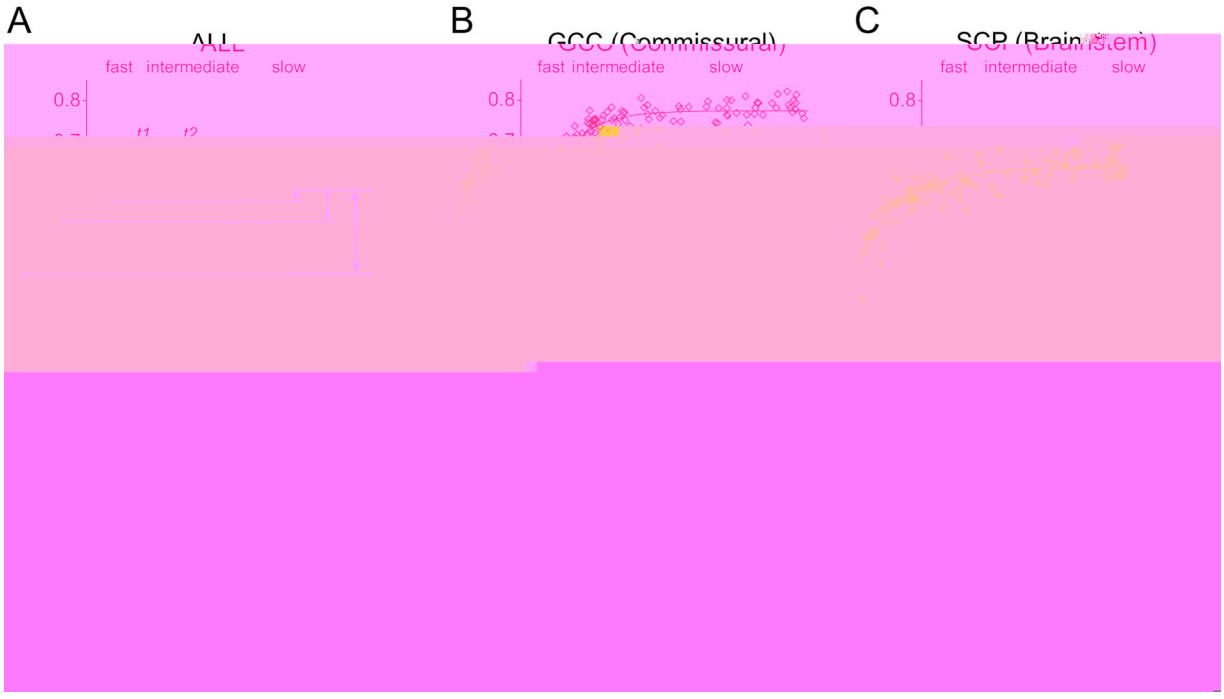

Figure 4. (*fast, intermediate, slow*) GCC (*B*), CP (*C*), (*D*), P (*E*), C (*F*), FA M (*A*) t1 t2 (FÂ( ) FÂ (=0)) 2/3 8/9 (FÂ(=8) FÂ (=0)) M : *fast, intermediate, slow* . P M M M .

M I . D M . F 1. F 2A D I- , - FA, MD, RD, AD - (OEC) , D 2, 13, 24, 48, 95 . A I , M - , . M 8 - F 2A, FA RD MD . A , , - D I- , D I (B 2002; . 2003; H . 2005; D . 2006, 2008; L . 2008; G . 2009) F 2B.

Results

Overview of WM Microstructural Profile Characterized by DTI-Derived FA, MD, RD, AD, and Orientation-Encoded Colormap

A M F 1. F 2A D I- , - FA, MD, RD, AD - (OEC) , D 2, 13, 24, 48, 95 . A I , M - , . M 8 - F 2A, FA RD MD . A , , - D I- , D I (B 2002; . 2003; H . 2005; D . 2006, 2008; L . 2008; G . 2009) F 2B.

Three Phases in the WM Tract Maturational Curve

- FA, MD, RD, AD, , M F 3. FA, MD, RD, AD -

1. I FA 0 8 M GCC, CP, , P, C F 4, FA *fast* , *intermediate* , *slow* . GCC, CP, , P, C M , . M *fast intermediate* . F , *fast inter-mediate* (*t1 t2*) GCC 0.97 1.94 CP (1.49 2.96), (1.98 3.87), P (1.5 2.99), C (2.1 4.08), GCC . M M ($P > 0.05$ K). FA, MD, RD, AD 2. 5., .

Differential Maturation of WM Tracts and Tract Groups

FA, MD, RD, AD , (F 5 8), - (F 5 8). A F 5, M FA 54.4%, FA ( ) (64.8%) (81.9%) FA ( ) (49.9%), (44.7%), (54%) . A F 5 2.,

Table 2 ( ) ( ) FA,
. P M M

	Fast		*Intermediate*		*Slow*	
	0 1	L	1 2	L	2	L
All	0 1.3	1.3	1.3 2.6	1.3	2.6	
Commissural	0 0.9	0.9	0.9 1.79	0.9	1.79	
Brainstem	0 1.08	1.08	1.08 2.15	1.07	2.15	
Association	0 1.61	1.61	1.16 3.19	1.58	3.19	
Limbic	0 1.63	1.63	1.63 3.23	1.6	3.23	
Projection	0 1.64	1.64	1.64 3.25	1.61	3.25	
CC	0 0.49	0.49	0.49 0.97	0.49	0.97	
PC	0 0.87	0.87	0.87 1.74	0.87	1.74	
PIC	0 0.87	0.87	0.87 1.74	0.87	1.74	
GCC	0 0.97	0.97	0.97 1.94	0.97	1.94	
MCP	0 1.03	1.03	1.03 2.06	1.03	2.06	
ICP	0 1.17	1.17	1.17 2.33	1.16	2.33	
BCC	0 1.19	1.19	1.19 2.37	1.18	2.37	
RIC	0 1.2	1.2	1.2 2.39	1.19	2.39	
AIC	0 1.31	1.31	1.31 2.61	1.3	2.61	
LF	0 1.34	1.34	1.34 2.68	1.34	2.68	
CP	0 1.49	1.49	1.49 2.96	1.47	2.96	
P	0 1.5	1.5	1.5 2.99	1.49	2.99	
CGC	0 1.55	1.55	1.55 3.07	1.53	3.07	
PCR	0 1.58	1.58	1.58 3.14	1.56	3.14	
ML	0 1.67	1.67	1.67 3.31	1.64	3.31	
FOF	0 1.72	1.72	1.72 3.41	1.68	3.41	
F	0 1.73	1.73	1.73 3.43	1.69	3.43	
CP	0 1.8	1.8	1.8 3.55	1.75	3.55	
CGH	0 1.83	1.83	1.83 3.6	1.77	3.6	
EC	0 1.83	1.83	1.83 3.6	1.77	3.6	
CR	0 1.96	1.96	1.96 3.83	1.87	3.83	
	0 1.98	1.98	1.98 3.87	1.89	3.87	
ACR	0 2.03	2.03	2. 03 3.96	1.93	3.96	
C	0 2.1	2.1	2.1 4.08	1.98	4.08	

fast *intermediate* (0.9 1.79) (1.08 2.15) (1.63 3.23), (1.64 3.25), (1.61 3.19) , M (1.3 2.6). C FA , MD (0.72 1.44), RD (0.78 1.57), AD (0.56 1.13) , (MD: 1.57 3.12 , RD: 1.53 3.05 , AD: 1.81 3.56), (MD: 1.42 2.84 , RD: 1.41 2.81 , AD: 1.46 2.92), (MD: 1.17 2.34 , RD: 1.24 2.48 , AD: 0.94 1.87) (3. 5.) .

a, *b*, *c* FA F 5. *a*, *b*, *c* / M M (F . 5). F , (*a*), *b*, *c* M (F . 3).

A F 6, *a* *b* . *c* . O , *c* LF CGC FA , LF CGC .

Larger Microstructural Residual Variance in the WM of Children with ASD During Brain Development from 2 to 8 Years of Age

L M A D D M F 4 5.

Discussion

I , D. I- M (*n* = 118) 0 8 . M . M

Table 3 . ( ) ( ) MD, *fast* . P M M M . .

	Fast		*Intermediate*		*Slow*	
	0 1	L	1 2	L	2	L
ALL	0 1.09	1.09	1.09 2.19	1.09	2.19	
Commissural	0 0.72	0.72	0.72 1.44	0.72	1.44	
Brainstem	0 1.15	1.15	1.15 2.31	1.15	2.31	
Association	0 1.17	1.17	1.17 2.34	1.17	2.34	
Projection	0 1.42	1.42	1.42 2.84	1.41	2.84	
Limbic	0 1.57	1.57	1.57 3.12	1.55	3.12	
CC	0 0.39	0.39	0.39 0.79	0.39	0.79	
GCC	0 0.73	0.73	0.73 1.47	0.73	1.47	
C .	0 0.97	0.97	0.97 1.93	0.96	1.93	
PC	0 1.02	1.02	1.02 2.03	1.02	2.03	
MCP	0 1.02	1.02	1.02 2.04	1.02	2.04	
	0 1.05	1.05	1.05 2.09	1.04	2.09	
BCC	0 1.05	1.05	1.05 2.1	1.05	2.1	
ML	0 1.07	1.07	1.07 2.14	1.07	2.14	
LF	0 1.09	1.09	1.09 2.18	1.09	2.18	
ICP	0 1.11	1.11	1.11 2.22	1.11	2.22	
CP	0 1.17	1.17	1.17 2.33	1.16	2.33	
EC	0 1.35	1.35	1.35 2.69	1.34	2.69	
F	0 1.36	1.36	1.36 2.71	1.35	2.71	
AIC	0 1.36	1.36	1.36 2.71	1.35	2.71	
PIC	0 1.36	1.36	1.36 2.71	1.35	2.71	
CGC	0 1.4	1.4	1.4 2.78	1.39	2.78	
F	0 1.4	1.4	1.4 2.79	1.39	2.79	
CR	0 1.45	1.45	1.45 2.89	1.44	2.89	
RIC	0 1.45	1.45	1.45 2.89	1.44	2.89	
PCR	0 1.48	1.48	1.48 2.94	1.46	2.94	
ACR	0 1.52	1.52	1.52 3.01	1.5	3.01	
CGH	0 1.8	1.8	1.8 3.55	1.75	3.55	
FOF	0 2.36	2.36	2.36 4.51	2.14	4.51	
CP						

, *fast, intermediate, slow* 0 8 , . . F , . D M , M A D M - . D I 3 MR , M (D . 2006; . 2008; A . 2010) (M . 2001; . 2004; L . 2008, 2012; . 2010; L B 2011; D . 2012; . 2013; . 2014) M - . O , M -

, . B , M 0 8 M D I . A M D I .

Possible Biological Processes Underlying WM Maturation from 0 to 8 Years

P , , M (B . 1987; K . 1988; H . 1992; H . 2005; C .

Table 4 ( ) ( ) RD,
fast . P M M

	Fast			*Intermediate*			*Slow*	
	0	1	L	1	2	L	2	L

Table 5 . ( ) ( ) AD, *fast* . P M M M . .

	Fast		*Intermediate*		*Slow*	
	0 1	L	1 2	L	2	L
ALL	0 0.97	0.97	0.97 1.94	0.97	1.94	
Commissural	0 0.56	0.56	0.56 1.13	0.56	1.13	
Association	0 0.94	0.94	0.94 1.87	0.94	1.87	
Projection	0 1.46	1.46	1.46 2.92	1.45	2.92	
Limbic	0 1.81	1.81	1.81 3.56	1.75	3.56	
Brainstem						
CP	0 0.27	0.27	0.27 0.55	0.27	0.55	
F						
CC	0 0.35	0.35	0.35 0.69	0.35	0.69	
	0 0.43	0.43	0.43 0.87	0.43	0.87	
ICP						
GCC	0 0.6	0.6	0.6 1.19	0.6	1.19	
CP	0 0.62	0.62	0.62 1.23	0.62	1.23	
PC						
BCC	0 0.98	0.98	0.98 1.96	0.98	1.96	
LF	0 1.04	1.04	1.04 2.08	1.04	2.08	
MCP	0 1.04	1.04	1.04 2.09	1.04	2.09	
EC	0 1.08	1.08	1.08 2.17	1.08	2.17	
P	0 1.11	1.11	1.11 2.21	1.1	2.21	
CR	0 1.39	1.39	1.39 2.77	1.38	2.77	
ACR	0 1.43	1.43	1.43 2.84	1.42	2.84	
CGC	0 1.58	1.58	1.58 3.13	1.55	3.13	
PCR	0 1.68	1.68	1.68 3.33	1.65	3.33	
RIC	0 1.99	1.99	1.99 3.89	1.9	3.89	
AIC	0 2.23	2.23	2.23 4.29	2.06	4.29	
ML	0 2.63	2.63	2.63 4.91	2.27	4.91	
FOF	0 4.13	4.13	4.13 6.43	2.31	6.43	
PIC	0 4.47	4.47	4.47 6.66	2.19	6.66	
CGH						
C .						

Differentiated Maturation Across WM Tracts and WM Tract Groups

D M (G . 2012; K . 2014; . 2016; O . 2019) D I , M M M (F 5 8). (FA: (*a*)↑, *b*↑, *c*↑; RD: *a*↑, *b*↑, *c*↓; AD: *a*↑, *b*↑, *c*↑) M 1) (AD: *c*↑) (FA: *c*↑; RD: *c*↓); 2) (AD: *a*↑) (FA: (*a*)↑; RD: *a*↑); 3) (AD: *b*↑) (FA: *b*↑; RD: *b*↑). O , (FA: (*a*)↓, *b*↓, *c*↓; RD: *a*↓, *b*↓, *c*↑; AD: *a*↓, *b*↓, *c*↓) 1) (AD: *c*↓) (FA: *c*↓; RD: *c*↑); 2) (AD: *a*↓) (FA: (*a*)↓; RD: *a*↓); 3) (AD: *b*↓) (FA: *b*↓; RD: *b*↓). C

, , (L 1967; K . 1988; H 1990; R . 1994; P . 2008, 2011), M F . 5: 1) M . F , CC, PIC, PCR GCC, AIC, ACR, ; 2) M . F , M M M . M M , CC 0 8 . C (. ., . 2018) (. ., R . 1994) , M (. ., FOF LF) . F M M M (. ., CC) M (. .,

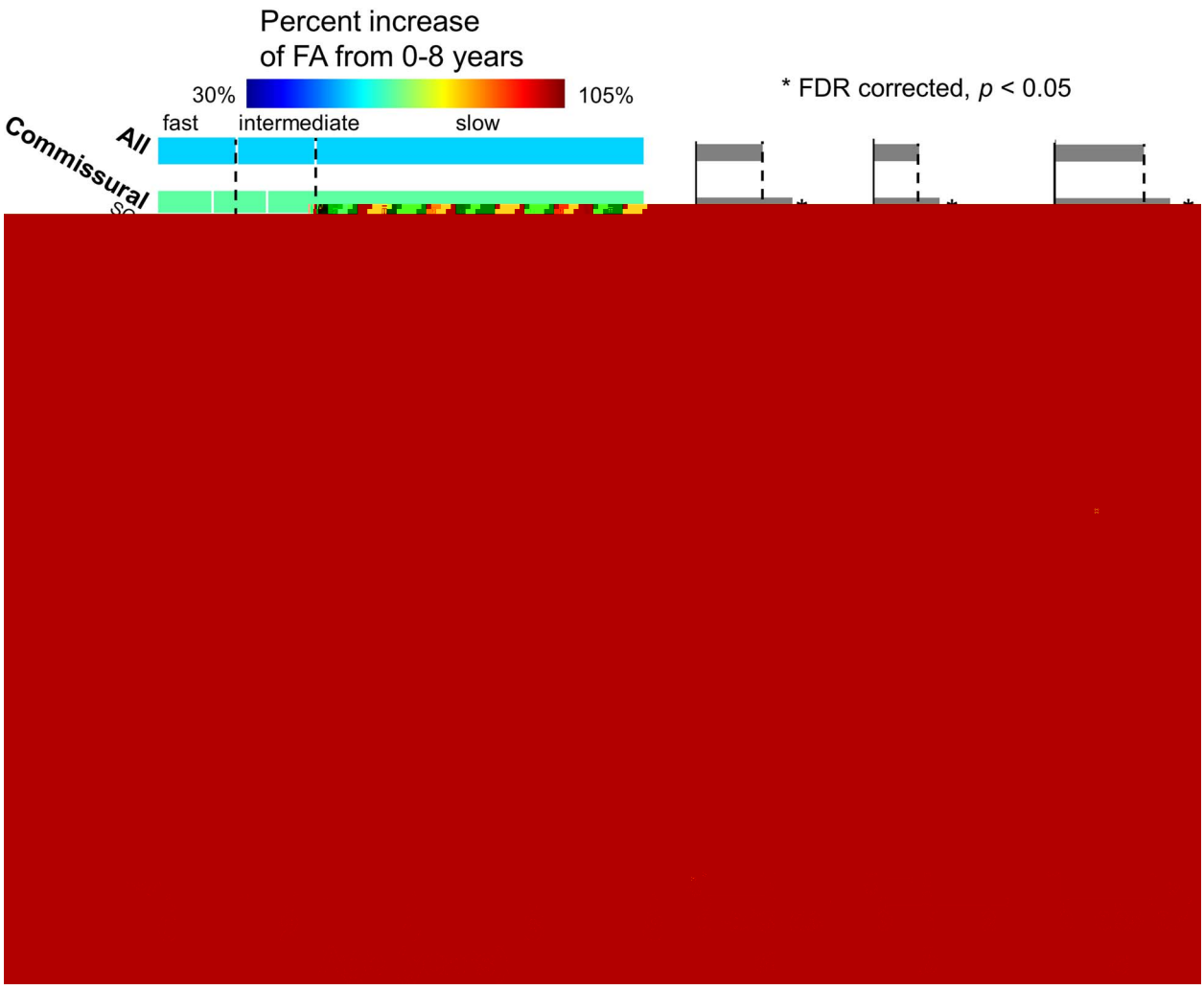

Figure 5. I FA 0 8 (1), (/ 2) *a, b, and c* FA M . M M . O , M M (*fast, intermediate, slow*), 8(148.1( )-69(853 77D E)18.1()-30.9( )-.4( )-2.4(.9(77D E))12.1( )-297.4( ).1(-772.6(8(( )-1)--29 8.1(29)11. (.)-257.)-32

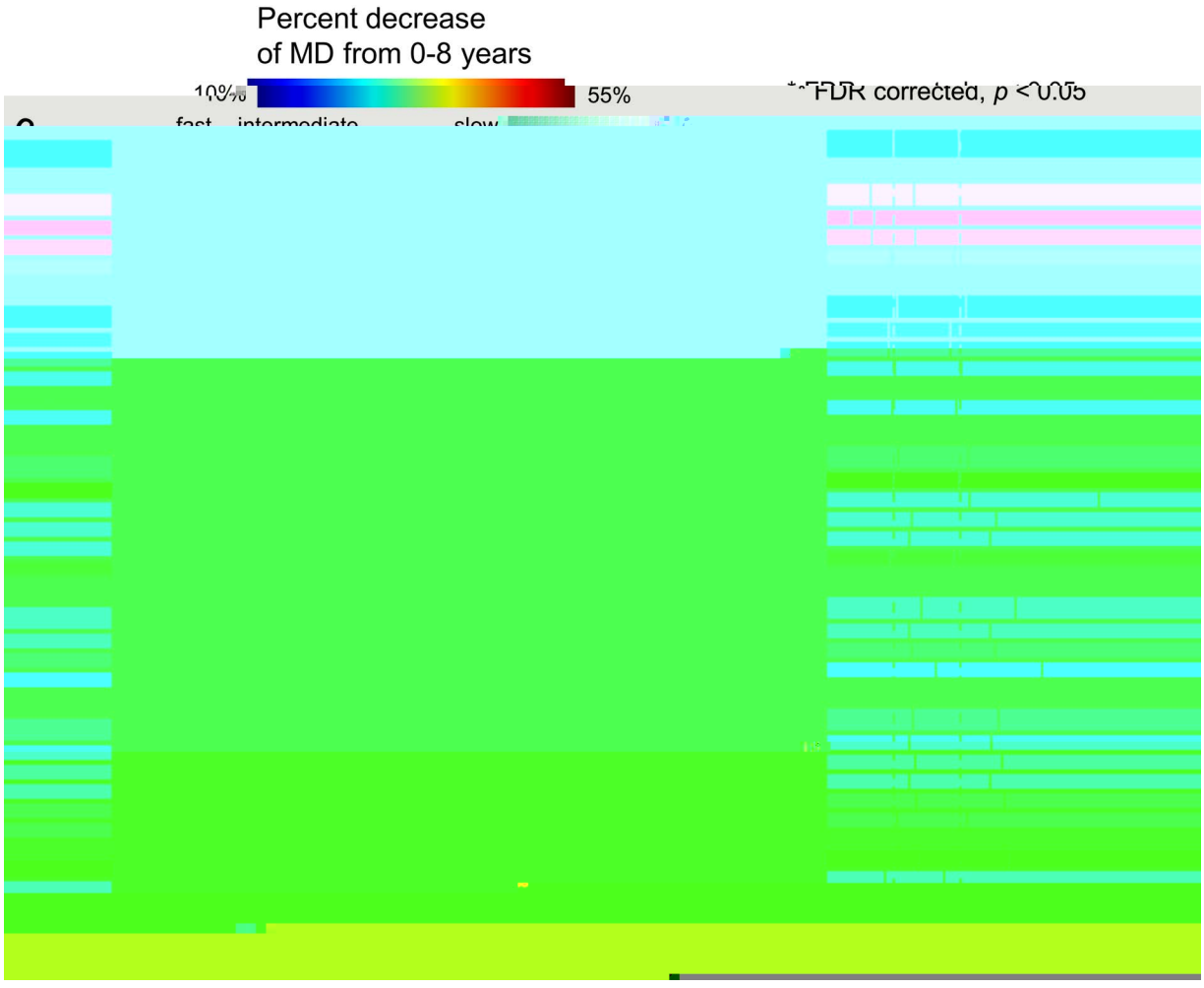

Figure 6. I MD 0 8 (1), (/ 3) a, b, c MD M . M M . O , M M M (, ,), M MD 0 8 . * a, b, c M, . * a, b, c M' , (.) ($R^2 < 0.223$) MD CP, ( ) a, b, c . P F 1 M .

A D (H - 2007; 2007). H (F 4 - - (. ., M . 2015) 5) M A D, D M, (DKI) (J . 2005) (NODDI) (. A . 2012), M D I (. ., O . 2019). D I- M . D M - D I- M . A . A M D I- M 0 8 . . D I- M , C M R^2 . F 0 8 (. ., FA 35 104%), D M M - -

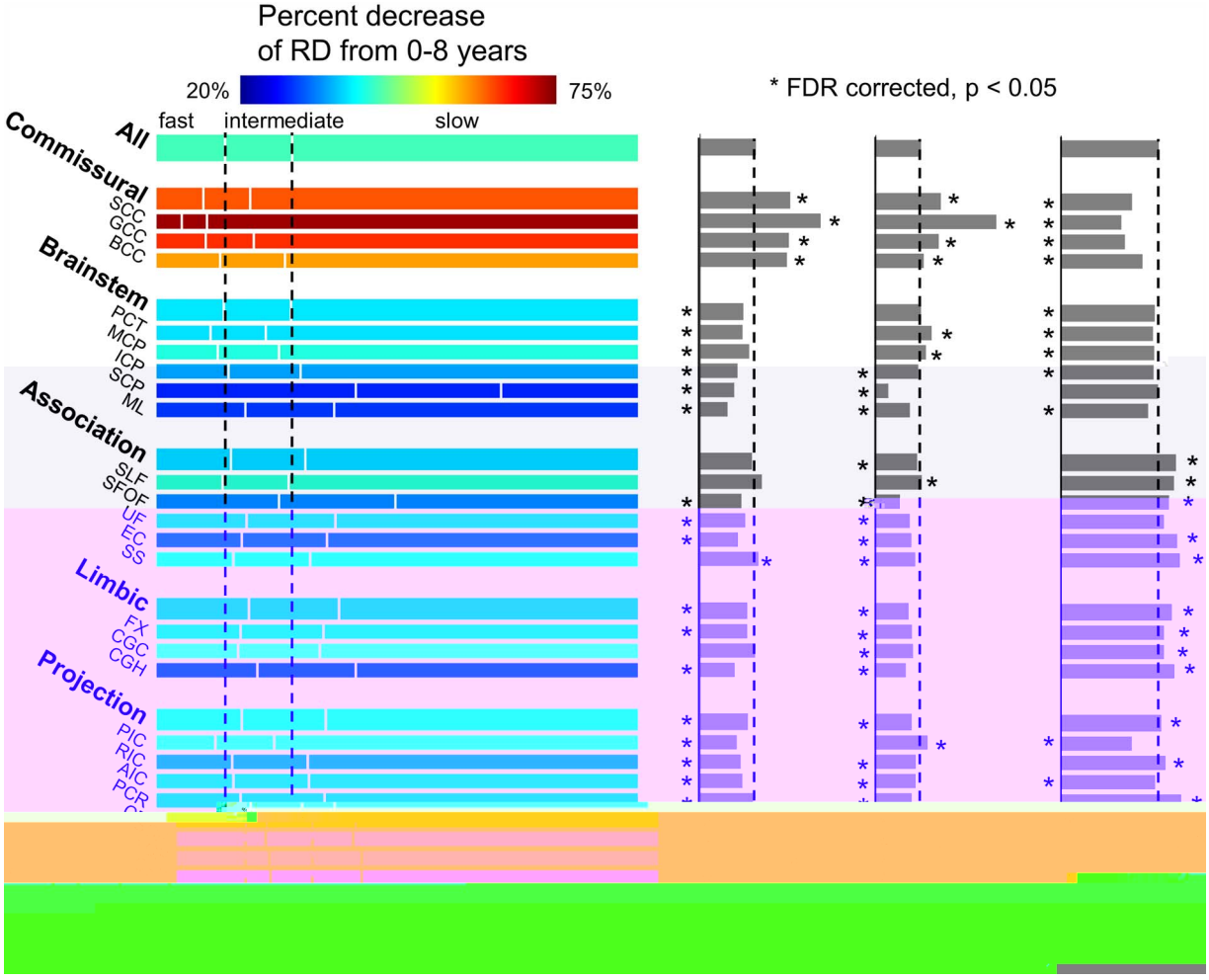

Figure 7. I RD 0 8 (1), (/ 4), a, b, c RD M . M M . O , M M (, ,), M a, b, c M,. RD 0 8 . * a, b, c M’, . P F 1 M .

0 8 . A , D. I D 0 8 , M F 2 M . I (. ., G) .

Conclusion

D M 0 8 . M , M A D. ,

Supplementary Material

Cerebral Cortex .

Funding

N I H D H (NIHMH092535, MH092535- 1 HD086984), C M D F (MO 2015CB351800), N N F C (N FC) D F (31421003 31671168) D P (81671651).

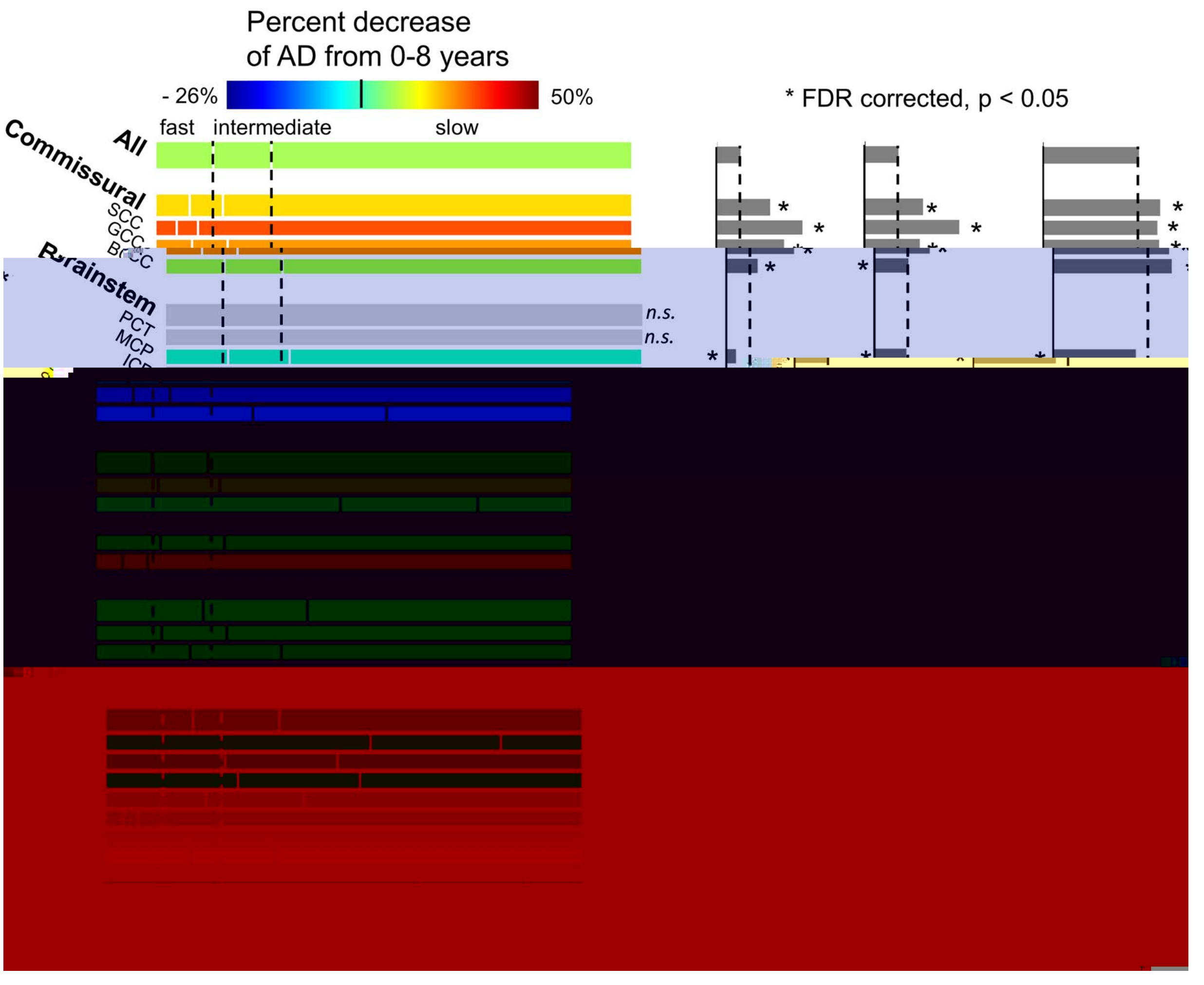

Figure 8. I AD 0 8 (1), (/ 5) , , AD M . M M . O , M M (, ,), M AD 0 8 . * , , M, . * ($R^2 < 0.223$) AD PC , ICP, F, CGH, C , , ( ) , , CP/ML M AD . P F 1 M .

Notes and Conflicts of Interest

L C '
H P . .

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