Development of the ERN in adolescents and young adults: Associations with anterior cingulate white matter organization

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Introduction

- The anterior cingulum (AC) shares connections with the frontal lobe and is associated with cognitive and emotional processing [1]
- The AC plays a role in conflict monitoring and inhibitory control, in interaction with the lateral prefrontal cortex [2]
- Behavioral research has demonstrated age-related improvements in inhibitory control, as measured using go no-go tasks, during adolescence [3]
- ERP research has shown age-related increases in amplitude of the AC-generated error-related negativity (ERN) suggesting increased response conflict monitoring during adolescence [4]
- Increased response monitoring and inhibitory control may be related to AC white matter development during adolescence

Current Study

- This study is in its preliminary phase
- Three methods of studying AC development will be discussed
  - Electrophysiology: ERN
  - Diffusion tensor imaging (DTI): white matter organization
  - Behavioral assessment: Go no-go task performance
- The goals of this study are to
  1) study ERN development during adolescence
  2) use DTI to investigate AC white matter microstructure in adolescents versus adults
  3) examine associations between white matter organization and behavioral and ERP measures of inhibitory control

Hypotheses

- ERN amplitude will increase during adolescence, coincident with performance improvements on an inhibitory control task
- White matter organization in the AC will
  - be positively correlated with age-related task improvement
  - increase with age

Methods: ERN Pilot Sample

• Participants

Age	n	FSIQ
10-11	8	M = 111.4, SD = 8.1
15	4	M = 112.5, SD = 13.3
18-25	5	M = 112.0, SD = 11.2

• Procedure

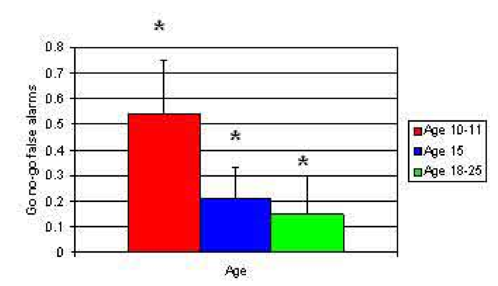
- **Go No-Go task [5]: Two trial blocks (140 trials per block)**
  - No-go block: omit response to "X"
  - Target detection block: respond to "X"
  - 20% Xs in both blocks
  - Stimuli presented for 100ms
  - 1500ms intertrial interval
- **Electroencephalogram**
  - EEG was sampled at 200 Hz, recorded from 32 channels referenced to Cz, rereferenced offline to averaged mastoids
  - Stimulus-locked and response-locked averages were derived for statistical analysis using 200ms and 100ms prestimulus and preresponse baselines, respectively

Results: ERN Pilot Sample

❖Behavioral

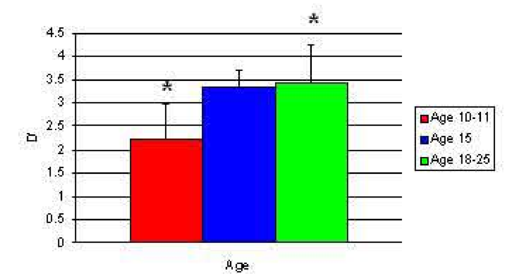
- A one-way ANOVA was conducted to determine if there were age-related differences in go no-go false alarm rate, hit rate, d′, and reaction time
- There were no significant hit rate or reaction time differences, but there were significant age-related differences in false alarm rate and d′

False alarm rate



$F(2,16) = 8.521, p < .01$

d′

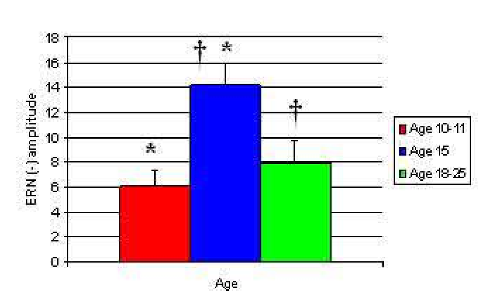


$F(2,16) = 4.83, p < .05$

❖Electrophysiological

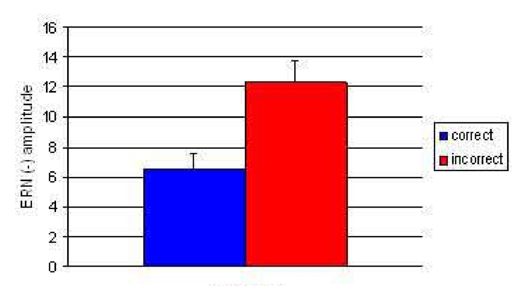
- A 2 response (correct, incorrect), 3 lead (Fz, Cz, Pz) repeated measures ANOVA was conducted on ERN amplitude with age as a between-subjects factor
- There were no significant differences in ERN latency

Main Effect of Age



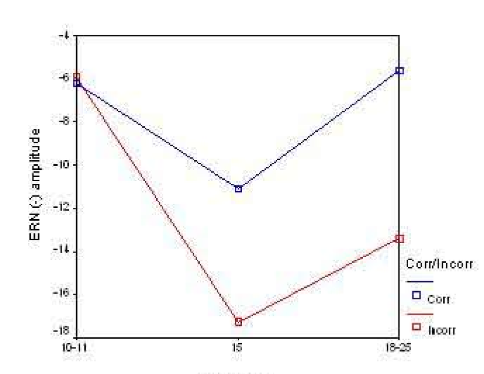
$F(2,13) = 7.11, p < .01$

Main Effect of Response



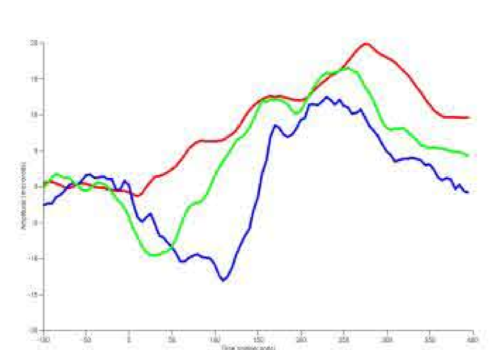
$F(1,13) = 9.02, p < .05$

Age X Response Interaction



$F(2,13) = 3.59, p = .057$

ERN at Cz



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References

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Methods: DTI Sample

•Participants

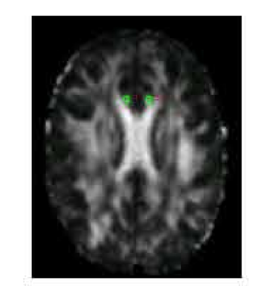
Age	n	FSIQ
9-11	15	M = 122.7, SD = 14.0
12-14	11	M = 113.4, SD = 1.9
15-17	16	M = 116.8, SD = 10.8
18-24	15	M = 118.6, SD = 7.9

•Procedure

- DTI scanning
  - Circular regions of interest (ROIs) of standard size (12 voxels) were placed bilaterally in the frontal white matter of axial slices, along a vertical (y) axis just inferior to the most caudal slice that contained the middle cingulum ("cognitive region")
  - ROIs were placed on axial slices corresponding to z = -10, -8, -6, -4, -2, and 0mm, in relation to the index slice (z = 0)

Index Slice (0mm)

ROIs at –6mm



  - Two DTI variables, mean diffusivity (MD) and fractional anisotropy (FA), were derived for each ROI; MD is an inverse index of how "densely packed" white matter is within a particular region, while FA reflects its degree of directional organization along fiber tracts
  - To simplify the presentation of results, values for left and right ROIs were averaged at each axial level
- **Go no-go task [5]: Three blocks of trials (160 trials per block)**
  - No-go: omit response to "X"
  - Target: respond to "X"
  - Shift: respond with right hand to non-"X", respond with left hand to "X"
  - 20% Xs
  - Stimuli presented for 250ms
  - 1000ms interstimulus interval

Results: DTI Sample

❖Behavioral

- Age was significantly correlated with go no-go false alarm rate, d′, and reaction time (RT) in the expected direction (behavioral variables were log transformed prior to analysis)

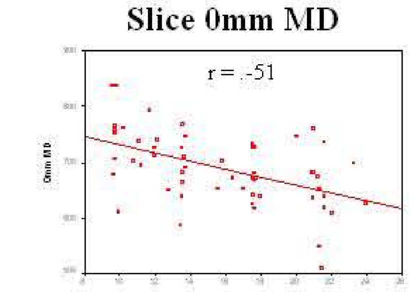
Task measure	r	Task measure	r	Task measure	r
No-go false alarm	-.54**	Shift false alarm	-.63**	Target false alarm rate	-.58**
No-go d′	.40**	Shift d′	.37**	Target d′	.41**
No-go RT	-.56**	Shift RT	-.58**	Target reaction time	-.56**

- False alarm rate and reaction time were significantly correlated in No-go ($r = .40, p < .01$) and Shift conditions ($r = .29, p < .05$), indicating the absence of a speed-accuracy trade-off
- Age was significantly correlated with white matter organization in the expected direction

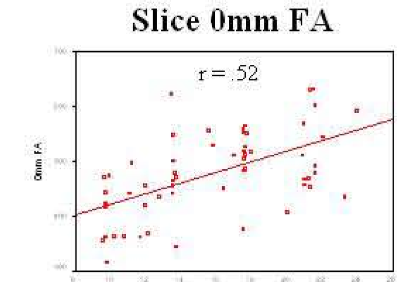
Slice	r	Slice	r
-8mm MD	-.54**	-6mm FA	.28*
-6mm MD	-.51**	-4mm FA	.35*
-4mm MD	-.54*	0mm FA	.52**
-2mm MD	-.47**		
0mmMD	-.51**		

*p < .05; ** p < .01

Slice 0mm MD



Slice 0mm FA



Results: DTI

❖Behavioral Performance – DTI Correlations

•White matter organization was significantly correlated with go no-go performance in the expected direction

No-go

Slice/value	False alarm	d′	RT
-10mm FA	ns	.31*	ns
-6mm FA	ns	.29*	-.30*
-4mm FA	ns	.28*	ns
-2mm FA	ns	.30*	-.36*
0mm FA	-.32*	.44**	-.44**

Slice/value	False alarm	d′	RT
-10mm MD	.50**	ns	.63**
-8mm MD	.37*	-.35*	.55**
-6mm MD	.34*	-.40**	.52**
-4mm MD	.34*	-.33*	.53**
-2mm MD	ns	-.43**	.50**
0mm MD	.31*	-.44**	.37**

Shift

Slice/value	False alarm	d′	RT
-6mm FA	ns	ns	-.35*
-4mm FA	ns	ns	-.31*
0mm FA	-.36**	.30*	-.47**

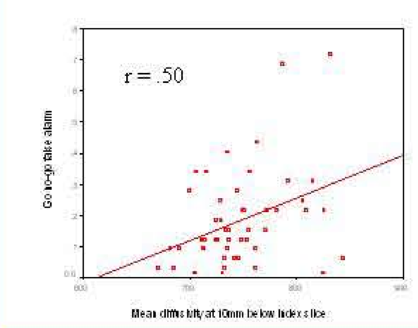
Slice/value	False alarm	d′	RT
-10mm MD	.39**	ns	.51**
-8mm MD	.35*	-.30*	.41**
-6mm MD	.34*	ns	.51**
-4mm MD	.40**	ns	.54**
-2mm MD	.33*	ns	.50**
0mm MD	.32*	ns	.38**

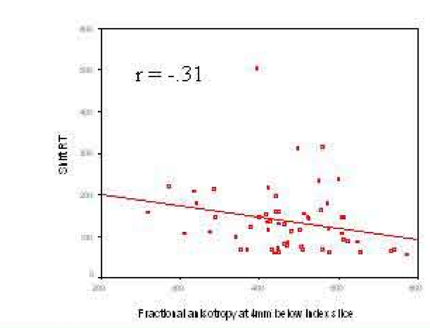
Target

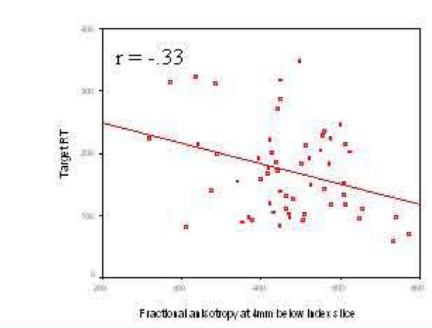
Slice/value	False alarm	d′	RT
-8mm FA	-.31*	.31*	ns
-6mm FA	-.42**	.35*	ns
-4mm FA	ns	ns	-.33*
-2mm FA	ns	ns	-.29*
0mm FA	-.44*	.29*	-.43**

Slice/value	False alarm	d′	RT
-10mm MD	.37*	ns	.51**
-8mm MD	.44**	ns	.35*
-6mm MD	.47**	ns	.43**
-4mm MD	.45**	ns	.51**
-2mm MD	.46**	-.30*	.43**
0mm MD	.38**	-.35*	.35*

* p < .05; ** p < .01







Conclusions

- Consistent with prior research[4], the ERN was greater in amplitude in older adolescents and adults compared to younger adolescents suggesting continued AC development during adolescence
- Older adolescents were significantly more accurate and had shorter reaction times on the go no-go task relative to younger adolescents suggesting improvements in inhibitory control and more efficient processing
- Significant age-related increases in AC white matter organization were found in addition to significant associations between behavioral performance and AC white matter organization
- The association between white matter organization in the AC and improvements in measures of inhibitory control was found independent of age effects, suggesting that behavioral improvements are related to increases in AC white matter organization
- The electrophysiological, behavioral, and structural imaging findings presented here provide preliminary evidence that the AC continues to develop during adolescence and that performance on AC-modulated tasks are related to increased white matter organization

Future Directions

- Directly examine associations between AC white matter and electrophysiological activity by obtaining DTI and ERP measures on the same participants
- Examine the associations of go-no go performance with white matter development in other prefrontal regions, such as the lateral prefrontal cortex
- Examine developmental brain-behavioral interactions longitudinally