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Response inhibition of face stimuli linked to inferior frontal gyrus microstructure in adolescents

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Introduction

The ability to inhibit inappropriate behavior is an essential cognitive and social skill. Response inhibition of pre-potent motor responses as measured with a stop-signal or a Go/Nogo task improves throughout adolescence[1,2]. Performance on these tasks can be modulated by the valence of task stimuli. Inhibition of negative faces has been shown to be more difficult than that of positive faces[1,3]. The brain network underlying response inhibition includes the right inferior frontal gyrus (IFG), right presupplementary motor area (preSMA), and superior longitudinal fasciculus (SLF) bilaterally [4–6]. The white matter underlying these regions continues to develop throughout childhood and adolescence, as indicated by in an increase in fractional anisotropy (FA), possibly reflecting ongoing myelination, and/or increase in axon diameter and density[7,8]. Here we used an emotional Go/Nogo task to test the hypothesis that better response inhibition (i.e. lower false alarm rate) of negative faces would be associated with higher FA in right IFG, right preSMA, and bilateral SLF in adolescents.

Methods

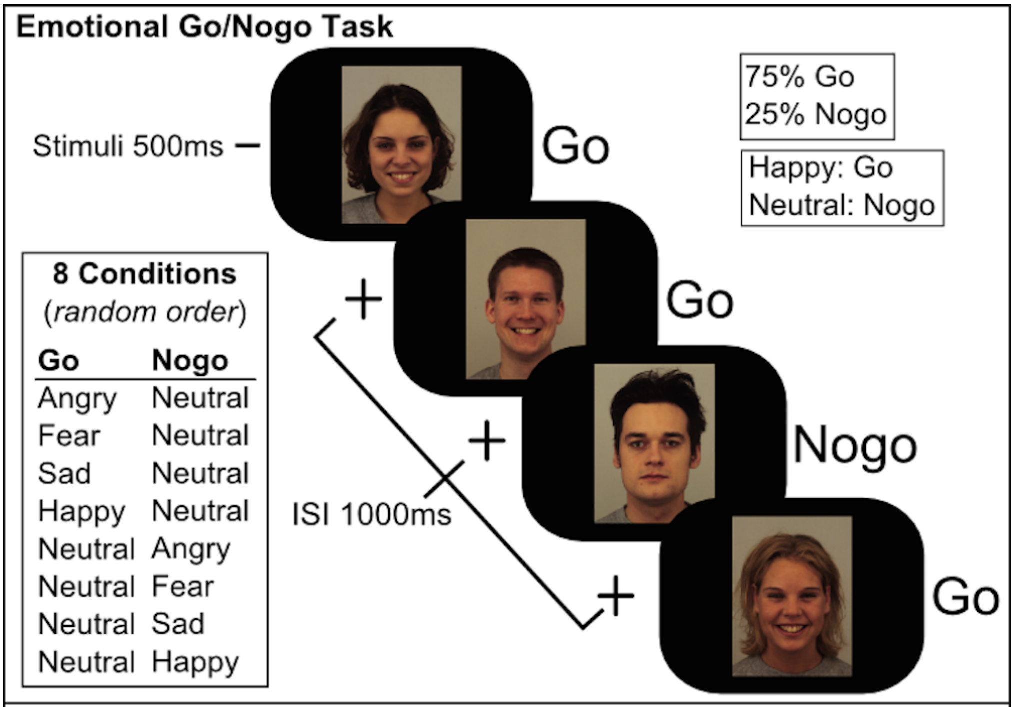
Sixty-three typically-developing adolescent (24M) aged 10–15 years were included. Participants completed an emotional Go/Nogo task (Fig. 1). False alarm rate was calculated (incorrect Nogo/(incorrect Nogo+correct Nogo)) for each condition, and mean false alarm rate for conditions with negative (angry, fearful, sad) Nogo's were calculated. Diffusion-weighted images were acquired using a 3T MR-scanner (61 directions, b=1200 s/mm2, 10 b=0 images). TBSS[9] was used for spatial normalization and to project the subjects FA data onto mean tract skeleton. Mean FA was extracted from regions-of-interest (ROIs) in the white matter underlying the right IFG, right preSMA, and bilateral SLF. Hierarchical linear regression models predicting mean false alarm rates for conditions with negative Nogo stimuli were used to test our a priori hypothesis.

Results

Plots of the mean false alarm rate of each condition, and mean false alarm rate for conditions with negative Nogo by age are presented in Fig. 2. Results for the a priori hypothesis predicting mean false alarms for negative faces are presented in Table 1. Model 1 included age, sex and the age by sex interaction term. No significant R^2-change was observed when adding the ROIs to the model (Model 2). However, a significant R^2-change was observed, when adding the ROI by sex interaction terms, which was mainly driven by the SLF by sex and right IFG by sex interactions. Follow-up analyses of boys and girls separately revealed a significant negative association between false alarms and right IGF FA in boys, while girls showed a weak positive association (Table 2). This association in boys was mainly driven by the conditions with angry and sad faces as Nogo stimuli (Fig. 3). All observed effects remained significant when additionally controlling for reaction time and d-prime of the emotional condition being tested, false alarm rate for conditions with the emotion being Go instead of Nogo, and whole skeleton FA. The latter indicates that observed effects were likely not due to differences in reaction time towards the Go stimuli, discrimination between the negative and neutral faces, the emotion being Go instead of Nogo, or overall white matter FA.

Conclusion

We found that the association between response inhibition and FA in the ROIs differed for boys and girls. Specifically, better response inhibition (fewer false alarms) for negative faces was associated with higher FA in the white matter underlying the right IFG in boys, but not in girls. This effect in boys was mainly driven by conditions with angry and sad Nogo stimuli. Observed effects persisted when controlling for reaction time, d-prime, and false alarm rate for neutral Nogo, or whole skeleton FA, suggesting that the effect is anatomical specific and might be directly linked to inhibition of angry and sad faces, and not inhibition of faces in general or speed accuracy trade off.



Go	**Nogo**
Angry	Neutral
Fear	Neutral
Sad	Neutral
Happy	Neutral
Neutral	Angry
Neutral	Fear
Neutral	Sad
Neutral	Happy

Figure 1. The task contains 8 conditions (presented in random order) pairing emotional with neutral face stimuli and vice versa. Stimuli are presented for 500 ms with a 1000 ms interstimuli interval (ISI) showing a fixation cross. A total of 56 stimuli are shown in each condition containing 75% Go and 25% Nogo stimuli. Participants were instructed to respond as fast as possible to Go stimuli, while withholding their responses to Nogo stimuli and to complete the task with as few errors as possible.

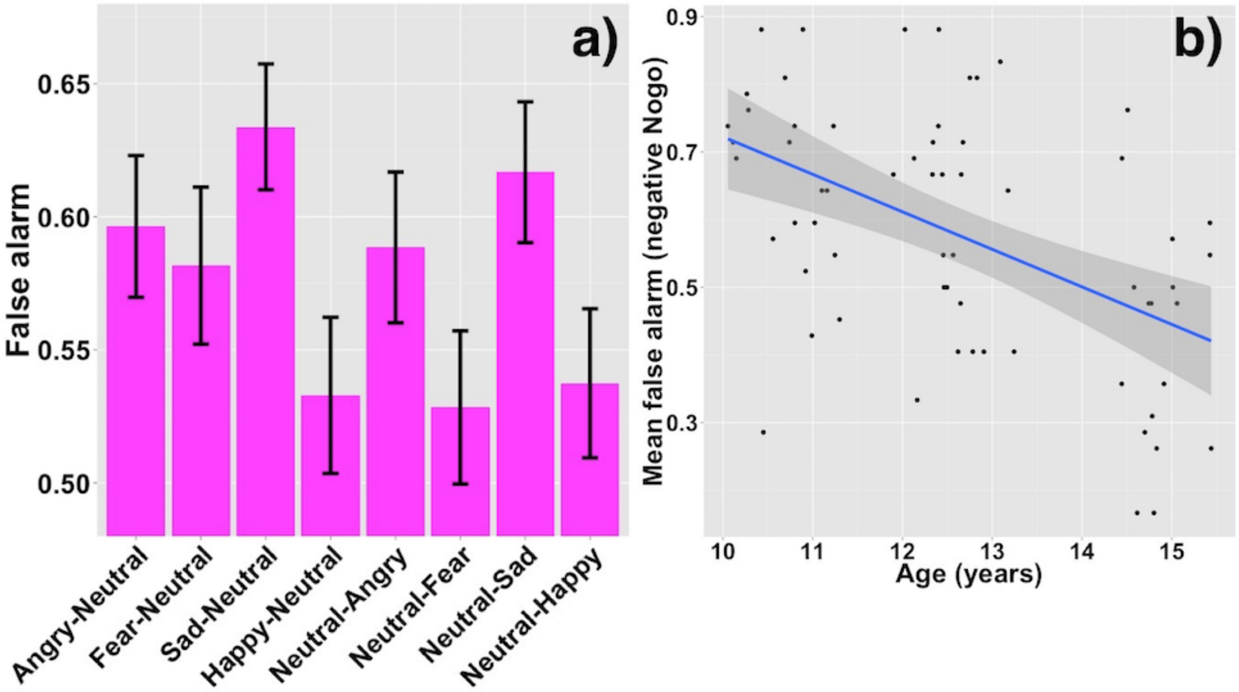


Figure 2. a) Bar chart showing false alarm rate for each condition. Bar names reflect Go followed by Nogo stimuli, e.g. Angry (Go) - Neutral (Nogo) on the first bar from the left. a) Scatter plot showing mean false alarm rate for conditions with negative (angry, fearful, and sad) Nogo conditions on the y-axis and age in years along the x-axis. The gray area around the line represents the 95% confidence interval.

Table 1. Hierarchical linear regression models predicting mean false alarm rate of conditions, where negative emotional faces were Nogo stimuli.

Mean false alarm for negative Nogo						
	Model 1		Model 2		Model 3	
Variables	*b*	*p*	*b*	*p*	*b*	*p*
Age	**-0.065**	**4.7E-05**	**-0.066**	**1.2E-04**	**-0.067**	**3.9E-05**
Sex:Boys	-0.179	0.576	-0.217	0.511	-0.696	0.424
Age*Sex	0.022	0.386	0.025	0.335	**0.048**	**0.046**
SLF FA			0.881	0.204	-0.763	0.391
Right IFG FA			-0.695	0.224	-0.093	0.893
Right preSMA FA			-0.013	0.986	-0.236	0.787
SLF FA*Sex					2.464	0.056
Right IFG FA*Sex					-1.776	0.096
Right preSMA FA*Sex					-0.536	0.697
R^2	0.324		0.356		0.467	
R^2 change	**0.324 *p*=3.5E-05**		0.032 *p*=0.343		**0.111 *p*=0.003**	
F-values	F(3.59)=9.408		F(6.56)=5.149		F(9,53)=5.161	

Mean false alarm rate of conditions, where negative emotional faces (angry, fearful, and sad) faces were Nogo stimuli, was used as dependent variable. Model 1 includes: Age, Sex (girls=0 and boys=1), and Age by Sex interaction. Model 2 added the FA values from the right IFG, right preSMA, and bilateral SLF. Model 3 added the ROI by Sex interaction terms.

Table 2. Linear regression models predicting mean false alarm rate of conditions, where negative emotional faces were Nogo stimuli.

Mean false alarm for negative Nogo				
	Boys		Girls	
Variables	*b*	*p*	*b*	*p*
Age	-0.037	0.082	**-0.073**	**3.8E-05**
SLF FA	0.956	0.347	0.308	0.735
Right IFG FA	**-2.515**	**0.010**	0.714	0.318
Right preSMA FA	0.557	0.638	0.639	0.478

Mean false alarm rate of conditions, where negative emotional faces (angry, fearful, and sad) faces were Nogo stimuli, was predicted by age, and FA values from bilateral SLF, and right IFG and right preSMA, in boys (n=24) and girls (n=39) separately.

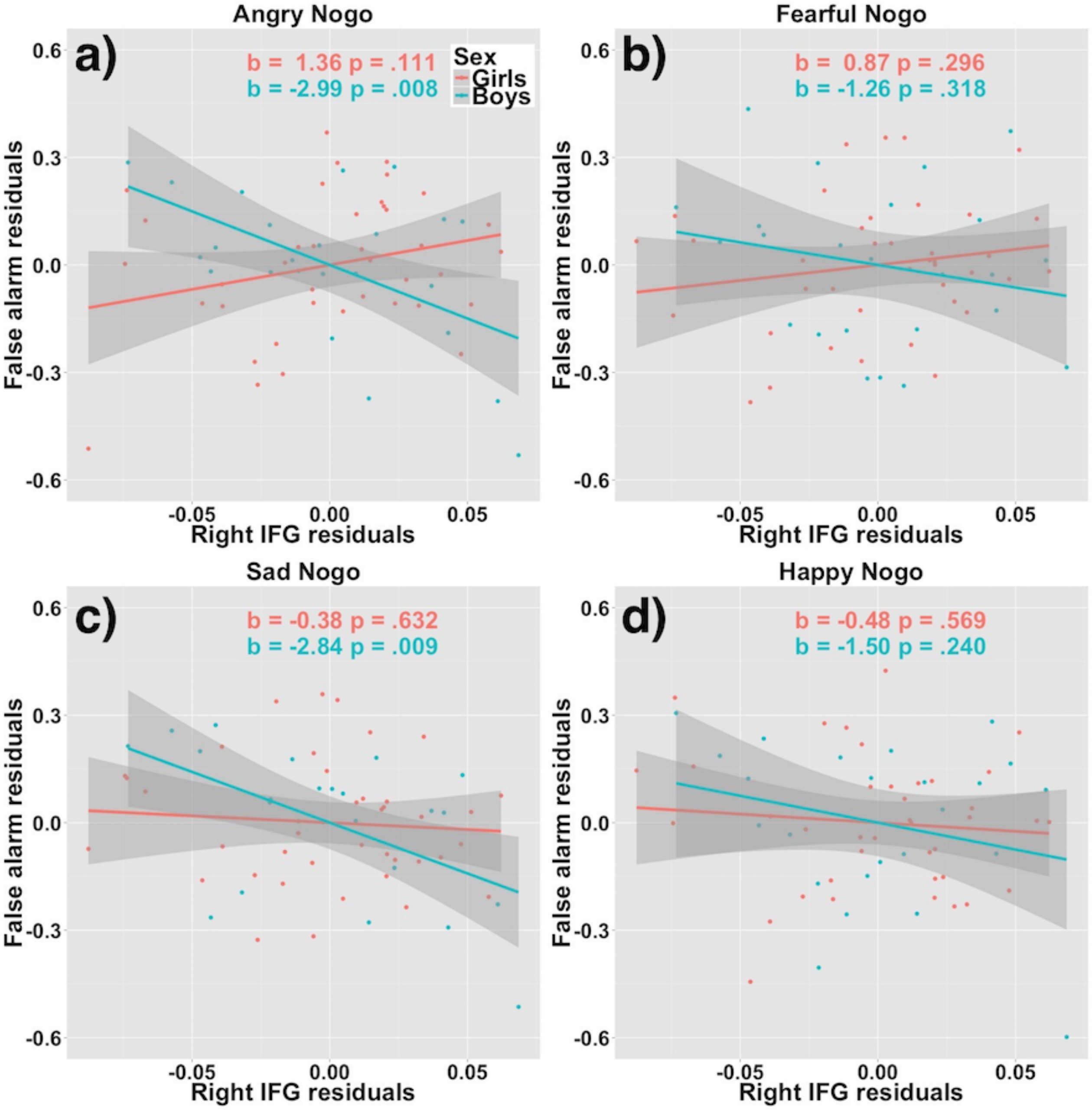


Figure 3. Partial regression plots showing the relations between false alarm rate and right IFG FA for boys (blue) and girls (red). The plots represent models predicting false alarm rate with the right IFG FA, controlling for age, in conditions, where a) angry, b) fearful, c) sad, or d) happy faces were used as Nogo stimuli. The gray area around the lines represents the 95% confidence interval.

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