Title: Domain-specific role of the dorsal cingulum bundle in conflict monitoring

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Introduction

Activity in the anterior cingulate cortex (ACC) has been associated with cognitive control processes such as error detection and conflict monitoring (*1*). Much less attention has been paid though to white matter (WM) tracts associated with the ACC. The dorsal area of the cingulum bundle (DCB) is connected to the dorsal ACC, and, therefore, it may influence cognitive functions subserved by the ACC (*2*). Integrity of the DCB, commonly assessed with fractional anisotropy (FA) measures computed from diffusion tensor images, has been related to conflict monitoring performance in pathological samples (e.g., schizophrenia), but not in healthy subjects (*3*, *2*). Possible reasons for this lack of correlation are small sample sizes and the lack of a complete set of tasks tapping verbal, spatial and numerical contents concurrently. Here we analyzed the relationship between WM integrity in the DCB and several conflict monitoring measures including verbal, spatial, and numerical contents using a large sample.

Methods

81 healthy subjects (53 females, 28 males; mean age= 19.7, SD= 1.7) took part in this study. Verbal and numerical versions of the Eriksen flanker task (Eriksen and Eriksen, 1974) and a version of the Simon task (Simon, 1969) were administered (Figure 1). Mean Reaction time (RT) for congruent and incongruent conditions were computed for each subject, along with compatibility effects (CE=RTi-RTc) and coefficients of variation (CV=mean(RT)/SD(RT)) for each task and condition.

DTI was acquired for each subject in a 3T scanner. The pulse sequence was single-shot, diffusion-weighted, echo planar acquisition (TR=8200ms;

TE=minimum; NEX=2; matrix=256mm x 256mm; FOV=240mm x 240mm; slice thickness=2.4mm; interslice gap=0.3mm; in-plane resolution=1mm^2; b value= 1000 s/mm^2; diffusion gradient directions=15). The volumes were eddy current and motion corrected using FMRIB's Diffusion Toolbox (FDT, http://www.fmrib.ox.ac.uk/fsl/) (*4*) prior to further processing. Nonbrain tissue was extracted by applying a mask drawn manually over each subject's T2-weighted image, and then the FDT was used to fit a diffusion tensor model at each voxel. Fractional anisotropy (FA) and mean diffusivity (MD) values were calculated at each voxel.

FA images were linearly registered to the ICBM-DTI81 FA template (*3*) using FLIRT (part of FSL) with a 9-df transformation, followed by a non-linear inverse consistent elastic intensity-based registration (*2*). Cingulum ROIs were obtained from the white matter parcellation map associated with the ICBM-DTI81 FA template, manually edited to exclude those non-dorsal areas. The registration process was inverted to register the DCB ROIs back to each subject's native space (Figure 2). Average FA and MD were computed for each subject, separately for the left and right DCB.

Results

No sex differences were found in EC, mean RT and CV for the three tasks. Men showed higher mean FA in the right DCB than women (F=8.901, p=.004). Both males and females showed higher MD in the left DCB than in the right DCB (females t=7.577, p<.001; males t=5.024, p<.001). No differences in FA were found between left and right DCBs.

For females, bilateral negative correlations, controlling for age and handedness, were found between FA and RT in the congruent and incongruent conditions of the numerical flanker task only (Table 1), whereas males showed a lateralized negative correlation between FA in the right DCB and both congruent and incongruent RT in the numerical flanker task. However, the incongruent RTs were no longer significantly related to FA when the contribution of the congruent RT was partialled out (for females: left DCB r=-.235, p=.101; right DCB r=-.146, p=.310. For males: left DCB r=-.334, p=.103; right DCB r=-.032, p=.879). Spatial and verbal RTs did not correlate significantly with FA. Mean diffusivity did not correlate with any RT measure either.

The pattern of correlations between CVs and FA-MD was consistent with that observed between mean RTs and FA-MD: a negative correlation between FA in the right DCB and numerical CV was found for the incompatible trials only, in both sexes (Table 2), and for the compatible trials in males.

Regarding the compatibility effects, FA correlated negatively in the right DCB in females, but not in males, with the CE in the spatial task (Table 1). MD correlated positively in the left DCB in females, but again not in males, with the CE in the numerical task.

Conclusions

The lack of a detectable correlation between FA/MD in the DCB and verbal or spatial controlled attention tasks in healthy subjects has been reported elsewhere (*5,6*). However, we found significant correlations with numerical RTs. Further, this latter relationship was lateralized in males only.

For females, the spatial CE correlated negatively with FA in the right cingulum, whereas the numerical CE correlated positively with MD in the left cingulum. This could mean that the DCB is germane for both RT and conflict monitoring. Both characteristics appear to be independent, since FA correlated with CE but not with RT in the spatial task, and with RT but not with CE in the numerical task.

It remains to be answered why we did not find significant correlations with EC in the male subsample. Do men and women differ in their respective conflict monitoring brain networks?

References

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Table 1. **Correlations between Fractional Anisotropy, Mean Diffusivity, Reaction Times and Compatibility Effects separately for men and women.** Effects of age and handedness were partialed out. *p<.05; **p<.01; L = Left Dorsal Cingulum Bundle; R = Right Dorsal Cingulum Bundle; FA = Fractional Anisotropy; MD = Mean Diffusivity; RT = Reaction Time.

		RT Incompatible			RT Compatible			Compatibility Effect		
		Verbal	Num.	Spatial	Verbal	Num.	Spatial	Verbal	Num.	Spatial
	FA L	-.169	**-.387****	-.147	-.188	**-.322***	-.100	.109	-.129	-.171
Women	FA R	-.142	**-.331***	-.179	-.185	**-.301***	-.086	.160	-.056	**-.310***
(N=53)	MD L	.058	.024	.087	-.032	-.147	.072	.208	**.374****	.065
	MD R	-.029	-.077	-.020	-.079	-.184	-.060	.138	.237	.110
	FA L	-.047	-.282	-.076	-.185	-.173	.052	.248	-.327	-.201
Men	FA R	.012	**-.410***	-.087	-.156	**-.430***	-.068	.335	-.025	-.082
(N=28)	MD L	.260	.142	.141	.227	.122	.004	.188	.077	.232
	MD R	.015	.172	.142	.002	.207	-.052	.034	-.056	.315

Table 2. Correlations between Fractional Anisotropy, Mean Diffusivity, and Coefficients of Variation separately for men and women. Effects of age and handedness were partialed out. *p<.05; L = Left Dorsal Cingulum Bundle; R = Right Dorsal Cingulum Bundle; FA = Fractional Anisotropy; MD = Mean Diffusivity; CV = Coefficient of Variation (SD/mean).

		CV Incompatible			CV Compatible		
		Verbal	Num.	Spatial	Verbal	Num.	Spatial
Women (N=53)	FA L	.145	-.200	-.185	.096	-.144	.271
	FA R	.113	**-.297***	-.101	-.011	-.110	.185
	MD L	.101	.135	.234	.052	.042	.085
	MD R	.108	.131	.149	.093	.047	.105
Men (N=28)	FA L	-.035	-.276	-.076	.018	-.215	.041
	FA R	.114	**-.425***	-.070	.015	**-.399***	-.043
	MD L	.239	-.061	-.065	.270	.111	.109
	MD R	-.091	.025	-.105	.024	.138	.147

Figure 1. Example of compatible and incompatible trials for the Verbal and Numerical Flanker tasks, and for the Simon task.

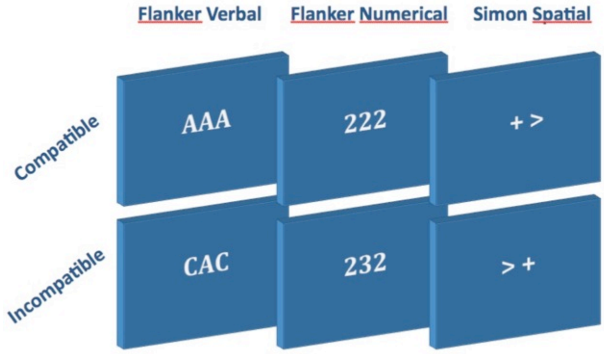

Figure 2. Example of regions of interest for left and right dorsal cingulum bundles in native space.