

Development of interhemispheric visual integration: a DCM study

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INTRODUCTION and PURPOSE: In humans, visual spatial integration develops slowly, continuing through childhood into adolescence^[1,2]. In agreement with predictive coding theory, a more coherent (colinear) stimulus would cause activations in higher-order and deactivations in lower-order visual areas. Indeed this phenomenon has been observed in adults performing visual integration tasks^[3]. As recently shown with DCM, such dynamics in adults depends on top-down and lateral inhibition^[4,5] and is weakened with age but nothing is known about the development of top-down effects within the human visual cortices. We hypothesized that top-down inhibitory mechanisms continue to advance during the second decade of human life. On the assumption that this protracted course depends on the formation of networks with slowly developing top-down connections, we compared effective connectivity in the visual cortex between children and adults using a passive perceptual task.

METHODS: Thirteen children (4 girls, 9 boys, mean age 11.0 years, range 7 – 13 years) and fourteen normal adults (6 women and 8 men; mean age 29.8 years, range of 21 – 42 years) with normal vision and without known neurological or psychiatric illness participated in the study. Subjects viewed bilateral sinusoidal black-and-white gratings with a spatial frequency of 0.5 Hz, a contrast of 70%, a size of a lateral patch of 11° x 19°, and drifting with a temporal frequency of 2 Hz. The stimuli either obeyed Gestalt grouping rules (iso-oriented colinear gratings, *CG*) or violated them (non-colinear orthogonally-oriented, *NG*). The stimulus conditions were alternated with background (uniform gray screen of the same space-averaged luminance as the stimuli) in a balanced pseudo-randomized order. The subjects were imaged on a 3T Siemens Trio scanner with the same type of sequence and sequence (FA 90°, TE 30 ms, pixel size 3 x 3 mm², acquisition time 1.7 s, 32 slices, 3 mm thick, TR 2 s). Single subject and group analyses were performed with SPM8. The regions of interest for DCM were determined from activations in functional MRI contrasts *Stimuli > Background* and *CG > NG* (Fig. 1). They were symmetrically located in V1 and V3v areas of both hemispheres. We studied a common model, which contained reciprocal intrinsic and modulatory connections between these regions. For DCM analysis we constructed a model space comprising sixteen plausible four-area dynamic causal models of intrinsic connections and four models of modulatory connections. The selection of optimal model was based on the Bayesian model comparison in terms of model evidence.

RESULTS: Intrinsic connections and driving inputs do not change with age. Group-averaged estimates of the strength of intrinsic connections are shown in Fig. 2. All the parameters significantly differ from zero at $P < 0.05$ (two-tailed t -test, Bonferroni corrected). To explore the age-related changes in vertical effective connections between striate (V1) and extrastriate (V3) areas, including both intra- and interhemispheric connections, we applied a 3-way between-within ANOVA with factors of Age (children vs. adults), Direction (top-down vs. bottom-up), and Topography (4 levels: V1_L-V3_L, V1_L-V3_R, V1_R-V3_L, and V1_R-V3_R). Neither the main effect of Age, nor its interactions with the other two factors proved significant. We also failed to find age-related changes in horizontal interhemispheric connections at the striate and extrastriate levels, within the framework of a 3-way between-within ANOVA with factors of Age (children vs. adults), Hierarchy (V1 vs. V3), and Direction (V1(3)_L→V1(3)_R vs. V1(3)_L←V1(3)_R). Similarly, we found no differences in driving inputs between the groups or hemispheres as shown with a two-way between-within ANOVA with factors of Age (children vs. adults) and Hemisphere (left vs. right). **Modulatory connections strengthen with age.** All the modulatory connections turned out to be inhibitory (Fig. 3). Six out of 12 connections in children and all but one in adults significantly differ from zero at $P < 0.05$ (two-tailed t -test, Bonferroni corrected). Note that significant connections in children are mostly bottom-up. The vertical modulatory connections were analyzed with a 2-way between-within ANOVA, which includes the Age and Topography factors described for intrinsic connections. The main effect of Age was significant at $P = 0.037$ ($F = 4.88$, $df = 1$, $\eta^2 = 0.163$). The strength of inhibitory top-down connections builds up with age. A 3-way between-within ANOVA with the Age, Hierarchy, and Direction factors (described for horizontal intrinsic connections) revealed the main effect of Age ($P < 0.001$, $F = 18.289$, $df = 1$, $\eta^2 = 0.422$) for horizontal modulatory connections, which appeared to be stronger in adults. The planned between-group comparisons showed that only striate connections are significantly stronger in adults than in children ($P = 0.001$, V1_L→V1_R; $P = 0.013$, V1_L←V1_R).

DISCUSSION: Our DCM analysis has shown that intrinsic effective connections within the visual areas do not differ between children older than 7 years and young adults, suggesting that basic visual networks integrated via long-distance reciprocal excitatory pathways are established at this age. The intrinsic connections were modulated by the coherent CG stimulus both in children and in adults. All the descending and lateral modulatory connections turned out to be inhibitory. Therefore, here we have shown for the first time that inhibitory backward effective coupling recently reported in adults^[3,4] works in children as well. Our analysis of effective connectivity showed that top-down modulatory effects generated at an extrastriate level and interhemispheric modulatory effects between primary visual areas are significantly weaker in children than in adults, suggesting that the formation of feedback and interhemispheric effective connections continues into adolescence. Behavioral integration tasks need to be reconciled with DCM results in the future studies.

REFERENCES: [1] Atkinson (2000) Oxford University Press. [2] Fornari et al. (2007), Neuroimage [3] Knyazeva et al. (2006), Neuroimage [4] Cardin et al. (2011) Cereb Cortex [5] Rytzar et al. (2011), Neuroimage

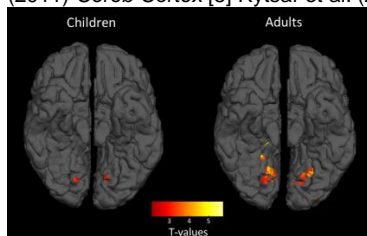


Figure 1. Interhemispheric integration effects shown by fMRI

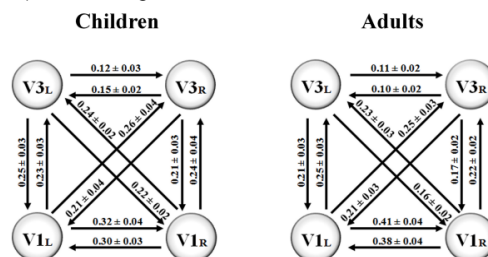


Figure 2. Intrinsic connections Gray-filled circles denote ROIs; arrows stand for intrinsic connections. The average strength of a connection in Hertz is shown next to the respective connection.

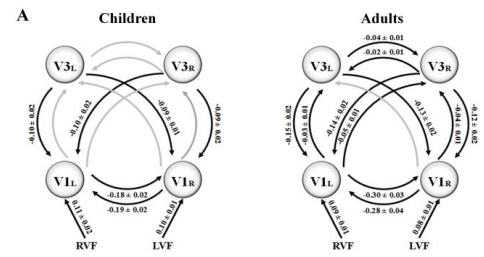


Figure 3. Modulatory connections The average estimates of modulatory parameters in Hertz with standard errors are shown alongside the respective connections.