Comparison of Cortical Folding Measures for Evaluation of Developing Cortex

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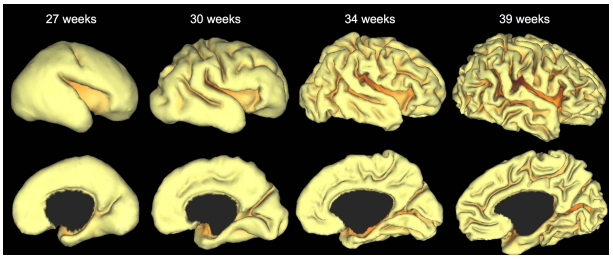
Introduction Studying cerebral cortical folding in normal development or in association with disease of injury requires assessing how folded cortex is. Recently, a series of surface-area independent measures of global curvature were proposed to study cortical folding in infants (1). We have systematically evaluated slightly modified versions of these measures using cortical surfaces derived from premature infants of differing postmenstrual age (PMA). Our analysis provides an indication of the sensitivity of different measures to the changes in cortical folding associated with development.

Materials and Methods

Patient population: *Infants* were recruited from the Neonatal Intensive Care Unit. If clinically stable underwent MRI studies as soon as practical after birth, at 30 wks PMA, 34 wks PMA, and term equivalent PMA. The MR studies included a T1-weighted, 3D MPRAGE acquisition of 1-mm isotropic spatial resolution, TI = 1100 ms, TR = 2100 ms, TE = 2.93 ms. Global folding measures were computed for 4 infants at each of the following PMAs: <27, 30-31, 34-35, and 38-39 wks.

Calculation of folding indices: Data were analyzed using mesh surfaces generated using Caret software (2). The measures of global curvature tested (1) fall into several broad categories according to the curvature values on which they are based. The intrinsic curvature index (ICI), negative intrinsic curvature index (NICI), Gaussian L2 norm (GLN), and absolute intrinsic curvature index (AICI) are based on the Gaussian curvature; the mean curvature index (MCI), negative mean curvature index (NMCI), mean L2 norm (MLN), and absolute mean curvature index (AMCI), are based on the mean curvature; the folding index (FI), curvedness index (CI), and shape index (SI), are based on a individual indices; the area area fraction of intrinsic curvature index (FICI), area fraction of negative intrinsic curvature index (FnICI), area fraction of mean curvature index (FMCI), and area fraction of negative mean curvature index (FNMCI) are calculate the proportion of total surface area where the Gaussian or mean curvature is either positive or negative; the last two measures (SH2SH and SK2SK) are ratios of other global curvature measures.



Results and Discussions The figure shows fiducial surface reconstructions in lateral (top) and medial (bottom) views at the indicated PMA's. Note the increase in cortical folding complexity with increasing PMA. The 17 measures tested can be organized into 5 groups that behave similarly on several evaluations of cortical folding (Table). In general, measures in groups 1 and 2 perform better (*i.e.,* increase monotonically with increased complexity of folding associated with development) than the other groups. These measures appropriately track the large complexity changes that occur with increasing PMA, maintain sensitivity to changes at several levels of cortical complexity. In contrast, the measures in groups 3 and 4 tend to become less sensitive to differences in cortical complexity as complexity increases. The measures in group 5 do not behave in a manner that is consistent with visual inspection.

Relative Global Curvature Values [Mean (SD), expressed as percent of average of 38-39 wk infant]

Group	Measure	< 27 wks PMA	30-31 wks PMA	34-35 wks PMA	38-39 wks PMA
1	ICI	31 (2)	45 (3)	70 (8)	100 (6)
	NICI	22 (2)	39 (4)	69 (9)	100 (6)
	AICI	27 (2)	42 (3)	69 (9)	100 (6)
	NMCI	21 (3)	49 (4)	77 (7)	100 (5)
	MLN	26 (2)	46 (4)	71 (8)	100 (7)
	FI	24 (3)	47 (4)	72 (7)	100 (8)
2	AMCI	48 (1)	66 (3)	83 (5)	100 (4)
	CI	44 (1)	64 (3)	83 (5)	100 (3)
	SH2SH	54 (3)	70 (4)	85 (4)	100 (4)
	FNMCI	36 (3)	64 (3)	86 (7)	100 (3)
3	MCI	66 (1)	77 (3)	88 (4)	100 (3)
	FnICI	72 (3)	89 (2)	97 (3)	100 (1)
4	SI	116 (3)	106 (1)	101 (2)	100 (0)
	FICI	129 (3)	112 (2)	103 (3)	100 (1)
	FMCI	136 (2)	120 (2)	108 (4)	100 (1)
5	GLN	23 (16)	25 (9)	87 (41)	100 (16)
	SK2SK	86 (56)	60 (23)	126 (62)	100 (12)

Conclusions There is a wide range of sensitivity of cortical folding measures to cortical development. We recommend using measures in groups 1 and 2 for evaluating the folding of developing brain. Further work is necessary to evaluate the relative sensitivity of these measures to anomalies in cortical folding associated with preterm birth.

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References **1**. Rodriguez-Carranza CE, *et al. Neuroimage* **41**, 462 (2008) **2.** Van Essen DC, *et al. J Am Med Inform Assoc* **8**, 443