Grid structure of brain pathways – Validation and the character of turns

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TARGET AUDIENCE

Researchers in dMRI of the brain, tractography, brain structure and connectivity.

BACKGROUND

Evidence has been presented based on dMRI that brain fiber pathways have geometric structure - that they follow the axes of a 3D curvilinear coordinate system or grid, similar or identical to the axes of development. Here two questions are addressed (i) Can the grid structure of dMRI pathways be defined objectively? and (ii) If brain fiber pathways follow 3 axes, how do they turn?

METHOD: GRID STRUCTURE DEFINED OBJECTIVELY

To quantify objectively the grid structure of pathways in dMRI, for distinct fields *u* and *v* of fiber directions in a volume, we measure their Lie bracket [1, supplement S2]. To implement this, at each voxel two ODF max vectors are chosen, *u* and *v*, and paths extended from each by deterministic tractography. These serve as "seed" axes of a 2D grid - on each axis is seeded a regular array of paths, near parallel to the other axis. Then the gap between the fiber at position *a* on the *u*-axis and that at position *b* along the *v*-axis represents the commutator *[au,bv]*. Their adherence of the *{u,v}*-field to the grid model is measured by the normalized commutator *[au,bv]/|axb|*, representing the numerical obstruction to integrability of *{u,v}* as a foliation of co-dimension 1. Graphic representation of grid structure is accomplished by retaining the subsets of the paths where *[au,bv] < const*.

RESULTS. In DSI and QBI of primate brains including human, inetgrability of grid structure measured by fiber commutators tends to be highest in large central white matter areas such as *callosum* and *centrum semiovale*, decreasing into the gyri and cortex. Graphic representation indicates continuous grid structure throughout cerebral white matter, but with gaps complex areas, including extreme capsule, crux of the Sylvian fissure, and mesial temporal lobe (Fig. 1). Thus, grid structure can be defined objectively and applies to extensive sections of cerebral white matter.

METHOD: ANALYSIS OF A PATH TURN – THE CORTICOSPINAL TRACT – WITH TRACER INJECTION

The corticospinal tract is an eloquent pathway of biomedical interest, and its transverse-to-axial turn has been discussed as a potential counterexample to grid structure [2,3]. To study this, tracer injection was performed in rhesus monkey to the motor cortex hand area and imaged with optical microscopy.

RESULTS. Tracer uptake was present in axons of two principal orientations - transverse and axial. Axonal turns are abundant throughout the tracer region (Fig. 2). These turns are transverse-to-axial, and of microscopic radius, including simple *L*-turns of axon curvatures ≤50μm radius and interstitial *T*-branches with curvatures <10μm. The locations of these turns lack obvious topographic organization. Axons of other orientations are fewer in number, and thinner than the axial and transverse axons. Thus, the turn of the corticospinal tract emerges from axons that follow the grid structure *via* innumerable subcellular turns.

DISCUSSION

Grid structure can be defined objectively and makes valid predictions of cerebral fiber architecture from macro- to micro-scopic scales. In a known pathway, dMRI accurately represents axonal orientations. However, the turn of the tract, though a major feature of connectivity, does not correspond to a visible turn in dMRI orientations. If the corticospinal case is typical, then present dMRI underestimates connectivity.

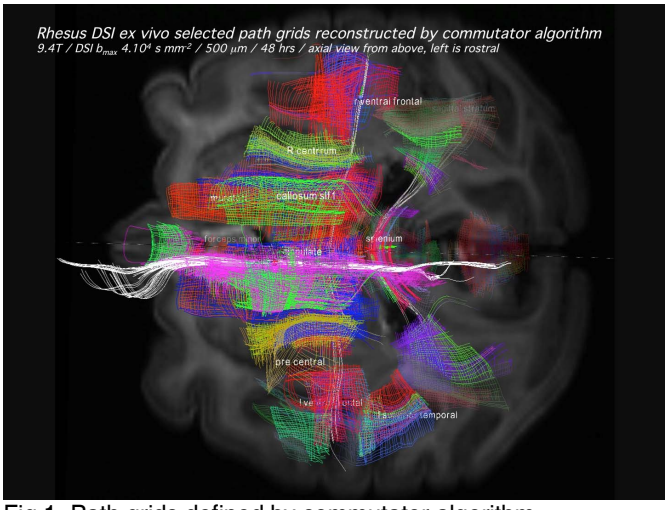

Fig 1. Path grids defined by commutator algorithm.

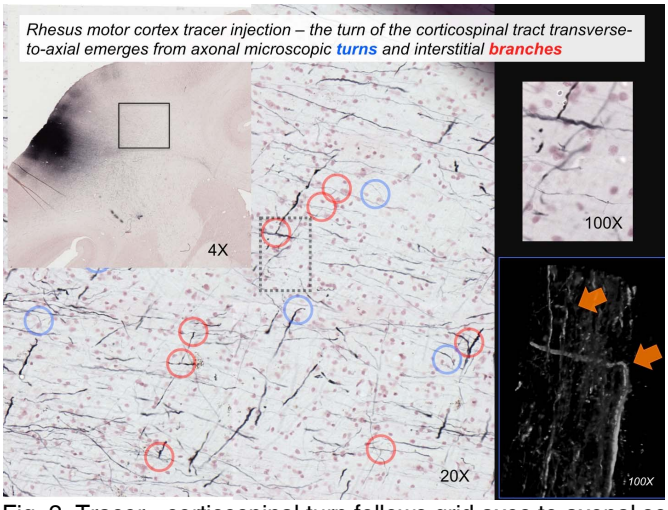

Fig. 2. Tracer - corticospinal turn follows grid axes to axonal scale.

References [1] Wedeen VJ, *et al.* Science. 2012 Mar 30;335:1628-34. [2]. Catani M, Bodi I, Dell'Acqua F. Science. 2012 Sep 28;337:1605. [3] Wedeen VJ, *et al.* Science. 2012 Sep 28;337:1605.

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