Introduction
Probabilistic tractography of diffusion weighted images allows to study in vivo the connectivity of the human cortex, and to parcellate the cortex based on the similarity of the obtained tractograms. Existing methods, however, are typically restricted to finding a predefined number of clusters (Anwander et al. 2007) in small brain areas. Hierarchical clustering may be the key to whole-brain analysis, where the correct number of clusters is unknown and depends on the desired granularity. Agglomerative clustering of previously obtained information-based partitions of cortical areas were applied by Gorbach et al. 2010 and Sujazow et al. 2010. We introduce a fast, fully hierarchical connectivity-based parcellation of the whole-brain and compare two different agglomerative methods.

Methods
High resolution diffusion MR images (dMRI) were acquired on a Siemens TimTrio scanner (1.5 mm isotrop, 60 directions, b = 1000 s/mm², GRAPPA/3, AV=3) in one young healthy participant. The data was corrected for subject motion and registered to the T1 anatomy (1 mm resolution). All voxels at the cortex/white matter boundary (FA >= 0.15) were selected as individual seed points for probabilistic tractography (implemented in parallel on the GPU; comp. time < 1 day for 130 000 tractograms). The similarity among the tractograms was computed as their normalized inner product and a bottom-up agglomerative hierarchical tree of clusters was generated for each hemisphere using the average linkage method. Alternatively, a new faster and low-memory consuming algorithm was implemented by using neighborhood restrictions on the centroid method applied to tractogram space. The trees for both methods were interactively explored while displaying the result on the brain surface using the OpenWalnut software.

Results
As examples of different granularity both trees have been cut at fixed levels resulting in 15, 50 and 100 clusters (Figure 1). The clustering results show a high degree of similarity in the boundaries of the partitions between the methods, while the centroid-neighborhood algorithm takes only 20 hours of computational time against a week in the case of the average linkage. The subdivisions follow anatomical landmarks for a wide spectrum of granularities. The clustering shows variations in granularity between the different lobes of the brain, tending to bigger regions in the anterior temporal lobe and finer subdivisions in the temporal lobe for a given level in the tree structure (Figure 2). Single clusters may be selected at any granularity level and then further partitioned for additional exploration (Figures 3 and 4).

Conclusions
We used full-brain connectivity-based clustering in one subject in order to explore the functional-anatomical organization of the brain. Previous clustering methods have relied on prior information on the number of clusters or desired granularity. This might not fully account for the reality of the brain, as there might be numerous hierarchical levels of functional-anatomical organization. Hierarchical clustering is an elegant means for fully representing the similarity structure of cortical connectivity. We have shown that by incorporating neighborhood information into the algorithm, one can reduce dramatically the complexity of the problem. The most important challenge for the future will be to extract the most relevant partitions from such a tree. This might include: validity measures based on intra-cluster density and inter-cluster similarity; branch length (distance to closest cluster) and graph-cut algorithms, among others.

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References