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Development and Evaluation of a Manual Segmentation Protocol of the Hippocampus for 3D Surface Mapping in Schizophrenia using High Resolution Structural MRI

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**Introduction:** The analysis of hippocampal volume has proven to be a valuable research method in psychiatric disorders including dementias, depression, and schizophrenia. Surface-based morphological methods, in addition, allow the analysis of further morphological characteristics of the hippocampus such as shape and radius, and allow investigating interactions with polymorphisms. The goal of the present project is to develop a reliable segmentation protocol for the hippocampus for high resolution MRI as a basis for surface-based hippocampal mapping in schizophrenia.

**Methods:** T1 weighted MRI sequences of 8 subjects were acquired using a resolution of 0.5 x 0.5 x 0.5 mm3 in a Gyroscan Intera 3.0 T (Philips, Best, NL). More than 30 different segmentation protocols for hippocampal segmentation were evaluated using the previously acquired T1 data, and an optimized segmentation protocol mainly based on protocols of K.L. Narr (UCLA) was developed. Three raters were then trained for four weeks to use the optimized protocol. MRI data were then segmented twice by all raters with a two weeks interval. For 3D surface modelling, methods of the Laboratory of Neuro Imaging (LONI, UCLA) were used.

**Results:** Existing segmentation protocols could be classified according to anatomic criteria. Suitability for high resolution MRI could be described. Our optimized protocol reached an inter- item- correlation higher than 0.9 (Cronbachs Alpha higher than 0.9) and proved high intra- and inter-rater-reliability.

**Discussion:** Previously published hippocampal segmentation protocols are heterogeneous and partly based on different anatomical definitions. Therefore, meta-analysis and comparisons of different studies are problematic and only meaningful if different methodologies are considered. The optimized protocol improves previously existing segmentation protocols and accounts for the particularities of high resolution structural MRI. The protocol proves reliable within and between trained raters. Hence the conditions for 3D analysis of hippocampal shape in schizophrenia are fulfilled. Genetic interactions of polymorphisms with hippocampal shape can be graphically displayed on 3D surface models.