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Diffusion tensor tractography imaging in pediatric epilepsy – A systematic review

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ABSTRACT

Purpose: Recent years brought several experimental and clinical reports applying diffusion tensor tractography imaging (DTI) of the brain in epilepsy. This study was aimed to evaluate current evidence for adding the DTI sequence to the standard diagnostic magnetic resonance imaging (MRI) protocol in pediatric epilepsy.

Material and methods: Rapid and qualitative systematic review (RAE, Rapid Evidence Assessment), aggregating relevant studies from the recent 7 years. The PubMed database was hand searched for records containing terms ''tractography AND epilepsy.'' Only studies referring to children were included; studies were rated using ''final quality of evidence.''

Results: Out of 144 screened records, relevant 101 were aggregated and reviewed. The synthesis was based on 73 studies. Case-control clinical studies were the majority of the material and comprised 43.8% of the material. Low 'confirmability' and low 'applicability' referred to 18 and 17 articles (29.5% and 27.9%), respectively. The sufficient quality of evidence supported performing DTI in temporal lobe epilepsy, malformations of cortical development and prior to a neurosurgery of epilepsy.

Conclusions: The qualitative RAE provides an interim estimate of the clinical relevance of quickly developing diagnostic methods. Based on the critical appraisal of current knowledge, adding the DTI sequence to the standard MRI protocol may be clinically beneficial in selected patient groups with childhood temporal lobe epilepsy or as a part of planning for an epilepsy surgery.

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1. Introduction

Diffusion tensor imaging (DTI) is one of the magnetic resonance imaging (MRI) sequences that visualizes white matter bundles. Physiologically, the diffusion of water molecules in the brain is restricted to the long axis of the white matter. Parameters such as the direction of the diffusion of a single voxel can be defined thanks to the magnetic gradient set by the DTI sequence [1]. The obtained mathematical model is processed into maps of apparent diffusion coefficient (ADC), fractional anisotropy (FA) or mean diffusivity (MD). A three-dimensional model of individual white matter pathways is built by combining voxels aimed in a particular direction [1,2]. The analysis of all the connections between all areas of white matter produces a connectome (a whole brain connectivity map). It is noteworthy that DTI is a non-invasive method and does not generate additional costs. Many authors described white matter changes occurring in various epilepsy syndromes. However, there are neither guidelines nor any systematic reviews which objectively assess the clinical benefit of DTI in pediatric epilepsy. The existing literature presents scattered data limited to specific diagnoses, small patient samples and are often case-control studies with biased matching method [2–4].

The aim of this study is to qualitatively assess the existing evidence about the use of DTI in diagnosing pediatric epilepsy. The main research question: is it justified to add the DTI sequence to the standard MRI protocol to diagnose pediatric epilepsy?

2. Material and methods

After reaching consensus regarding the methodology, the authors designed the study protocol and divided the tasks. Rapid Evidence Assessment (RAE) and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [5,6] methods were chosen. Three authors identified, screened and included full-text articles as well as synthesized the data. The PubMed (Medline) database was searched using the phrase ''tractography'' AND ''epilepsy,'' restricted to the last 7 years. Included articles were cross-referenced and duplicates were removed using the Mendeley software (version 1.12.1, Mendeley, Inc., New York). Screening was based on titles and abstracts. Original articles, review articles, expert opinion and lab animal research reports were included. Only articles regarding the pediatric population and pediatric-type epilepsies were included (i.e. post-stroke or alcohol-induced epilepsy were excluded). The raw data were compiled; the quality of evidence of each study was assessed using the criteria set by Cesario [7] (Table 1).

Statistical analysis was performed using GraphPad Prism v.6.05 (GraphPad Company, La Jolla, CA).

Table 1 – Abbreviated instructions for qualitative assessment of scientific papers. In addition to the final mark (Q1–Q3), the papers were rated in terms of confirmability and applicability as key determinants of adding the tractography sequence to routine clinical practice. Adapted from Cesario and Santa-Donato [7].

Read the study and score each of the CATEGORIES.
Use the quality rating SCALE of 0–3.
Assess the FINAL QUALITY OF EVIDENCE.

CATEGORIES:
1. Descriptive vividness
2. Methodological congruence:
   a. Rigor in documentation
   b. Procedural rigor
   c. Ethical rigor
   d. Confirmability
3. Analytical precision
4. Theoretical connectedness
5. Heuristic relevance
   a. Intuitive recognition
   b. Relationship to existing body of knowledge
   c. Applicability

SCORING SCALE:
3 = ''good'' = 75–100% criteria met
2 = ''fair'' = 50–74% criteria met
1 = ''poor'' = 25–49% criteria met
0 = ''no evidence that the criteria is met'' = 0–24% criteria met

FINAL QUALITY OF EVIDENCE RATING:
Based on the total scores for each of the five categories described above (1–5).
Q1: total score of 23–30
Q2: total score of 15–22
Q3: total score of 0–15.

3. Results

The initial search yielded 126 records. Additional 39 records were found during the identification stage. After removing the duplicates, 144 articles were screened. At this stage 22 articles were excluded based on their titles and abstracts. In the eligibility stage, articles were assessed based on their full text. Finally, 101 articles were included in the synthesis (Fig. 1).

Of all the included articles, only 73 contained clinically useful information about pediatric epilepsy and were included in the analysis. A slight majority of the included studies were case-control studies ($n = 32$; 43.8%), followed by case series ($n = 23$, 31.5%), 11 review articles and 1 systematic review. There were no randomized clinical trials on this subject. Nearly half of the included articles were published in the US or UK ($n = 33$; 43.8%). The most frequent types of epilepsy noted in the analyzed literature were temporal lobe epilepsy (TLE) and mesial temporal lobe epilepsy (MTLE) ($n = 22$; 30.1%).

Of the 61 original articles assessed for quality, 21 (34.4%) were rated as Q1 and 20 (32.8%) each as Q2 and Q3. The mean and median quality scores in our sample were 60.7% (SD $\pm$ 20.6%) and 63%, respectively. The analysis of the individual Q ratings indicated that a relatively small number of articles were scored as having low confirmability (0 or 1 points; 18 articles (29.5%)) or low applicability (0 or 1 points; 17 articles (27.9%)). The quality of articles regarding TLE and MTLE was compared with the quality of articles about other types of epilepsy. The Q ratings and its individual components (e.g. confirmability and applicability) were similar. Specifically, the papers about TLE and MTLE had a non-significantly higher confirmability and applicability and a non-significantly lower final quality of evidence rating (Q) ($p = 0.15$–0.58) (Fig. 2B).