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Presurgical language lateralization assessment by fMRI and dichotic listening of pediatric patients with intractable epilepsy

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ABSTRACT

Objective: The aim of this study was to evaluate the clinical use of a method to assess hemispheric language dominance in pediatric candidates for epilepsy surgery. The method is designed for patients but has previously been evaluated with healthy children.

Methods: Nineteen patients, 8–18 years old, with intractable epilepsy and candidates for epilepsy surgery were assessed. The assessment consisted of two functional MRI protocols (fMRI) intended to target frontal and posterior language networks respectively, and a behavioral dichotic listening task (DL). Regional left/right indices for each fMRI task from the frontal, temporal and parietal lobe were calculated, and left/right indices of the DL task were calculated from responses of consonants and vowels, separately. A quantitative analysis of each patient's data set was done in two steps based on clearly specified criteria. First, fMRI data and DL data were analyzed separately to determine whether the result from each of these assessments were conclusive or not. Thereafter, the results from the individual assessments were combined to reach a final conclusion regarding hemispheric language dominance.

Results: For 14 of the 19 subjects (74%) a conclusion was reached about their hemispheric language dominance. Nine subjects had a left-sided and five subjects had a right-sided hemispheric dominance. In three cases (16%) DL provided critical data to reach a conclusive result.

Conclusions: The success rate of conclusive language lateralization assessments in this study is comparable to reported rates on similar challenged pediatric populations. The results are promising but data from more patients than in the present study will be required to conclude on the clinical applicability of the method.

1. Introduction

Today, mapping of brain networks related to language using fMRI methodology is commonly performed as a part of the planning procedure for the neurosurgical treatment of epilepsy in adults and, increasingly so, in pediatric populations (Medina et al., 2004; Swanson et al., 2007). In a study of language fMRI in 209 healthy children between 5 to 18 years of age, the reported rate of successful assessments was approximately 80%, with age being an important factor (Byars et al., 2002). Other researchers have reported that with thorough preparation and training of children one can expect to obtain reliable and useful data in 95% of typically developing children aged 8 and older and in 80% of typically developing children 4–5 years old (O'Shaughnessy et al., 2008). O'Shaughnessy and colleagues report relatively high success rates with older children and early teenagers with neurodevelopmental disorders as well, which is an important aspect since such disorders are common in children with epilepsy (Davies et al., 2003; O'Shaughnessy et al., 2008; Pellock, 2004).

A comparative analysis of the outcome from the usage of language fMRI and of the intracarotid amobarbital, or Wada test, has shown high concordance (Abou-Khalil, 2007; Adcock et al., 2003; Arora et al., 2009; Woermann et al., 2003) but in patients with atypical language lateralization results tend to have lower concordance (Adcock et al., 2003; Bauer et al., 2014; Gaillard et al., 2002). In a recent review (Spritzer et al., 2012), the authors concluded that the amount of data to support a recommendation of the routine usage of language fMRI in pre-surgical examinations is still insufficient. However, there is a fairly broad consensus that language fMRI in general is superior in reliability and validity (Arora et al., 2009; Binder, 2011; Spanaki et al., 2001), and that WADA usually has disputable added value, unless fMRI is inconclusive. Because of the associated risk factors WADA might be avoided on most patients being evaluated for epilepsy surgery (Sharan et al., 2011).

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There are several methodological factors of importance to conduct successful language fMRI examinations of pediatric patients to ensure that the collected data are of high quality. The validity and reliability of language fMRI data profoundly depends on the language task used as well as on the control/baseline condition employed. Ideally, an fMRI paradigm should employ a control condition that contains the same subcomponents as the task condition but exclude the cognitive process to be examined (Swanson et al., 2007). Other basic requirements of language fMRI assessments are that the patient has a good understanding of the tasks in the MR-scanner, sufficient motivation to perform the tasks and a good compliance — since fMRI is sensitive to motion. These requirements can largely be dealt with by careful preparation of the patients prior to the scanning procedure (Byars et al., 2002; O'Shaughnessy et al., 2008). Neurodevelopmental disorders are common in patients with epilepsy, such as Attention Deficit Hyperactivity Disorder (ADHD), Autism Spectrum Disorders (ASD), and different forms of learning disabilities. Therefore the language test material should be designed to take into account such potential difficulties for pediatric patients with epilepsy and it should also be possible to adapt the material in accordance with the patient's language proficiency.

A potential limitation of analyses of language fMRI data that previously has been mentioned in the literature is that visual inspection of fMRI brain activation patterns has often been used in previous studies (Adcock et al., 2003; Berl et al., 2014; Spritzer et al., 2012). Relying only on visual inspection of the results may weaken the reproducibility of the results and also make it more difficult to compare different studies and instead it is suggested to rely on quantitative analyzes.

In a previous study of language lateralization in 17 healthy 10–11 year old children we evaluated newly developed materials and methods designed to minimize the influence of the aspects mentioned above that potentially could decrease the validity and reliability of language fMRI data (Norrelgen et al., 2012). While planning that study we took into consideration that some uncertainty has been reported regarding the interpretation of language fMRI data for patients with intractable epilepsy (Spritzer et al., 2012; Wellmer et al., 2009). For that reason we decided to add an independent measure of language lateralization in order to get a broader basis of data to build a conclusion of language lateralization on, particularly for those cases when fMRI data are limited or inconclusive. The measure that we considered implementing was Dichotic Listening (DL), which is a behavioral assessment of language lateralization. There are several different versions of DL but they are all based on the principle that contralateral auditory cortical projections are stronger than ipsilateral projections (Rosenweig, 1951). Thus when two competing speech stimuli are presented to each ear simultaneously, many times, the average of responses to the stimuli presented to the contralateral ear of the language dominant hemisphere will show an advantage over stimuli presented to the ipsilateral ear. In individuals with typical left-sided language dominance there is thus a Right Ear Advantage (REA). One version of DL is the Fused Dichotic Words Test (FDWT: Wexler and Halwes, 1983). In two studies the FDWT was compared with fMRI (Fernandes et al., 2006) and with WADA (Fernandes and Smith, 2000) for children with intractable epilepsy, and it was concluded that DL provide valid data of language lateralization in a high proportion of cases and that the concordance with fMRI and WADA is high. A German version of the FDWT (Hattig and Beier, 2000) has been compared with language fMRI in two studies of typical subjects. Hund-Georgiadis et al. (2002) found excellent concordance between fMRI and DL but another study concluded that FDWT was not applicable to determine language laterality and that the concordance with fMRI was poor (Bethmann et al., 2007). No clear explanation to the very different outcomes between these studies was given but Bethmann suggest that different scoring criteria between studies may have caused the discrepancy. However, the version of DL that we decided to implement is based on consonant-vowel stimuli (Hugdahl and Asbjørnsen, 1994). This test is easy to administer also with children and does not involve reading (which the original version of FDWT do). In a number of studies this version of DL has been found to have good concordance with WADA (Hugdahl et al., 1997), PET (Hugdahl et al., 1999), fMRI (e.g. van den Noort et al., 2008) and electro-physiological measures of language (Brancucci et al., 2004, 2005).

In our previous study of healthy children, a conclusion regarding language lateralization of each individual was reached based on a well-defined quantitative analysis of the compiled lateralization indices from the frontal-, temporal- and parietal lobes in the two fMRI paradigms and from the two indices from DL (Norrelgen et al., 2012). A conclusive overall result regarding language dominant hemisphere was obtained for 88% of the subjects. We found no contradictory results between DL and fMRI data and in 12% of the cases DL provided critical information for reaching an overall conclusion about hemispheric language dominance. Our conclusion was that the quantitative analysis method, combining data from fMRI and DL, was useful and that the risk of obtaining incorrect results may have been reduced by this approach.

In the present study our aim was to evaluate the use of the method on a group of pediatric epilepsy patients who were candidates for epilepsy surgery. Specifically we wanted to assess the overall success rate and possible influences on success rate of age and neurodevelopmental problems.

2. Materials and methods

2.1. Ethics statement

All examinations were carried out according to the ethical guidelines and declarations of the Declaration of Helsinki (1975) and the current study was approved by the regional ethics committee at the Stockholm County (2008/1826-31). All participants in the study were potential candidates for epilepsy surgery. The neurologist at the hospital informed the parents and the child/adolescent about the study and asked if they were willing to participate in the study. Oral consent to participate in the study was required for participation.

2.2. Patients

In this study, the criteria for the selection of the pediatric patients in this study were that they had intractable focal epilepsy, were potential candidates for epilepsy surgery, and that the pediatric neurologist deemed it likely that they would be able to collaborate in the presurgical language lateralization assessment. The overall functioning of the patient was taken into account for this selection and an IQ < 70, for example, did not necessarily disqualify a patient for participation. Nineteen patients were contacted about participation in the study by their neurologist at the hospital and all conceded to participate. In a second step a research speech language pathologist met with each of the nineteen patients one to two weeks prior to the planned fMRI assessment in order to further evaluate their ability to participate (for details about the evaluation see "Preparation and pre-training for fMRI session" section). If the patient was deemed likely to be able to participate in the language fMRI assessment, detailed information was given to the patient and the parent about the fMRI procedure. Patient data are displayed in Table 1.

2.3. Cognitive and language comprehension assessment

The cognitive assessment was carried out by a psychologist according to the WISC-IV (Wechsler, 2005) and language comprehension was assessed by a speech language pathologist with the Test for Reception of Grammar (TROG-II: Bishop, 2003). In two cases the cognitive assessment data were based on Ravens Progressive Matrices (Raven et al., 2003). These two results were not converted to IQ scores, instead percentile scores were used (see Table 1).