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Prospective assessment of ictal behavior using the revised Responsiveness in Epilepsy Scale (RES-II)

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ABSTRACT

Impaired consciousness in epilepsy has a significant negative impact on patients' quality of life yet is difficult to study objectively. Here, we develop an improved prospective Responsiveness in Epilepsy Scale-II (RES-II) and report initial results compared with the earlier version of the scale (RES). The RES-II is simpler to administer and includes both verbal and non-verbal test items. We evaluated 75 seizures (24 patients) with RES and 34 seizures (11 patients) with RES-II based on video-EEG review. The error rate per seizure by test administrators improved markedly from a mean of 2.01 ± 0.04 with RES to 0.24 ± 0.11 with RES-II. Performance during focal seizures showed a bimodal distribution, corresponding to the traditional complex partial vs. simple partial seizure classification. We conclude that RES-II has improved accuracy and testing efficiency compared with the original RES. Prospective objective testing will ultimately lead to a better understanding of the mechanisms of impaired consciousness in epilepsy.

1. Introduction

Consciousness is a multidimensional construct, incorporating both subjective experience and objective external manifestations. One can also describe these dimensions in terms of the level and content of consciousness and the neuroanatomical and behavioral correlates of each of these [1–3]. Anesthesia, sleep, minimally conscious state, and epileptic seizures, among other states, all partially disrupt the "consciousness system" and impact the normal manifestations of consciousness yet preserve some elements of responsive behavior [4–8]. As different behaviors and abilities may be independently affected in each of these disorders, systematic behavioral testing can be highly informative.

Impaired consciousness in epilepsy is particularly difficult to study prospectively compared with other disorders of consciousness due to its unpredictable and transient nature [9]. We previously developed a standardized testing battery, the Responsiveness in Epilepsy Scale (RES), designed to rapidly assess behavior during seizures in an objective, prospective fashion [10]. The RES was based on the JFK Coma Scale, a comprehensive, validated tool for the assessment of impaired consciousness [11]. While RES was successful in its ability to obtain the behavioral data of interest, it was somewhat cumbersome to administer, prompting the current revision. In this study we describe the development and use of a revised version of the scale, "RES-II", and demonstrate its improved accuracy and efficiency compared with the previous version. In addition, we describe initial results of testing in a group of patients with the new instrument.

2. Methods

92 adult and pediatric patients were recruited into this study. Methods for the experimental setting, subject recruitment, tester training, test administration, and data acquisition for the first 68 patients were as described in detail in [10]. Briefly, epilepsy inpatients undergoing video-EEG monitoring were tested using the standard RES battery and results scored by concordance of two reviewers. Identical methods were used for the next group of 25 patients (one patient overlapped both groups), except that a revised version of the Responsiveness in Epilepsy Scale was employed during the period from September 2011 through April 2012 ("RES-II", see Supplemental Data S1, discussed below). All procedures were approved by the Yale University Human Investigations Committee.

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2.1. Development of the RES-II

We previously demonstrated that RES, a standardized behavioral testing battery, could be used to prospectively assess responsiveness during epileptic seizures. This aim was successful in spite of the inherent difficulty of performing rapid, interactive testing with a patient unpredictably experiencing an epileptic seizure. Based on this experience, we sought to improve both the reliability and efficiency of testing.

The original scale was adaptive in nature, such that the "level" of questioning depended on the success on previous questions. It was designed in this fashion to quickly shift to questions that would yield the most useful information during the limited timeframe of an epileptic event. However, doing so required an on-the-fly evaluation of responses, which often delayed rapid progression through the questions, limiting the amount of data collected for each event. This also was a source of error, as occasionally, the tester would jump to an incorrect level of questioning. Finally, data analysis was cumbersome because different questions were asked of each subject, requiring data to be reported in an abstracted, summary fashion ("consciousness score").

In designing the new scale, we sought to eliminate these issues by removing the stratification of question items, instead by reducing the scale to a sequence of ten items asked repeatedly during each seizure. The exception is an 11th item, (application of strong nailbed pressure to test response to a painful stimulus) which is only asked once in the case that a subject failed to give any response to any of the 10 primary items. Although the use of this item does require a dynamic assessment of prior responses, this is an easily discernible criteria and this approach restricts the administration of this potentially unpleasant test to rare instances when the patient is deeply unresponsive.

The ten primary testing items themselves consist of many of the same questions used in the original RES including tests of orientation, receptive and expressive language, visual processing, motor praxis, basic sensorimotor responses, and visual tracking (see RES-II protocol, Supplemental Data S1, online). However, two new items were added to meet another goal in designing RES-II: the greater use of non-verbal prompts and/or items eliciting non-verbal responses. For example, item 7 is the command "wave hello" wherein the action is demonstrated and a non-verbal wave back is sought. This is in contrast to item 5 in which the verbal command "touch your nose" is given, but the action is not demonstrated. This new sequence of items retains the diverse set of cognitive and sensorimotor functions we wish to test during seizures but greatly improves the accuracy and efficiency of the process. The new scale retains the testing performed after a patient returns to baseline; this involves memory recall for information presented at seizure onset, as well as postictal motor testing.

2.2. Data analysis

Within 24 h of any seizure tested with RES, each response was scored on a scale of 0 to 4 (see Supplemental Data S1, online) based on review of video recordings. Scores were determined by the agreement of two reviewers; one of whom was the person who performed the testing. We have previously established high inter-rater and intra-rater reliability on performance scores [10]. Timing of all test items and responses was determined relative to seizure onset and end, and separate analyses were performed for the ictal and postictal periods. All seizure onset times are reported as whichever occurred first between electrographic onset and behavioral onset and all offset times as whichever occurred last between electrographic offset and behavioral offset based on review of video-EEG data.

Testing errors were defined as the administrator asking a question out of sequence. For example, if a testing item was completely skipped or if the order of testing was incorrect, this was considered an error. We did not analyze more minor errors such as slight differences in the language used for questions or commands. Results were analyzed by Chi-squared test or Student's *t*-test. Bonferroni correction was used to adjust significance for multiple comparisons. Corrected significance threshold was $p<0.05$. All values are reported as mean ± standard error of the mean.

3. Results

3.1. Demographics and testing (RES cohort)

68 subjects were recruited into the first phase of the study utilizing the original RES scale; some patient data from this phase have been previously reported [10]. A total of 75 seizures were captured from 24 of the 68 subjects (10 M and 14 F; mean age 36.2; 20 right-handed) (see Supplemental Table S2, online). 15 of these subjects underwent scalp EEG alone, 3 underwent scalp EEG plus ictal single photon emission computed tomography (SPECT), and 6 patients underwent intracranial EEG. The mean seizure duration was 101 ± 17 s, and average duration of testing was 304 ± 58 s. The first question was asked an average of 46.0 ± 6.5 s after seizure onset.

3.2. Demographics and testing (RES-II cohort)

25 subjects were recruited into the recent phase of the study utilizing the RES-II scale. One subject had previously participated in testing with the original RES scale. A total of 34 seizures were captured from 11 of those subjects (7 M and 4 F; mean age 36.7; all right-handed) (see Supplemental Table S2, online). 5 of these subjects underwent scalp EEG alone, 5 underwent scalp EEG plus ictal single photon emission computed tomography (SPECT) study, and one patient underwent intracranial EEG. The mean seizure duration was 139 ± 24 s, and the average duration of testing was 225 ± 26 s. The first question was asked an average of 16.0 ± 2.0 s after seizure onset.

3.3. Comparison of RES vs. RES-II

We compared data from RES and RES-II (Table 1). A total of 1277 questions (36% ictal and 64% postictal) were asked with the revised scale vs. 2372 (23% ictal and 77% postictal) with the previous scale. Slightly more questions were asked per seizure (37.6 ± 4.0 with RES-II vs. 31.6 ± 3.0 with RES). With the use of the new RES-II scale, the average time required to ask one question during each seizure was 6.7 ± 0.6 s, similar to or slightly faster than the 8.5 ± 0.8 s per question with the original RES ($p=0.12$). In spite of this pace, there was a nearly ten-fold reduction in the average number of errors made per seizure during administration of the revised scale (0.24 ± 0.11 with RES-II vs. 2.01 ± 0.36 with RES; $p<0.01$). Errors involved the administrator asking either the wrong question or asking a question in the wrong order. We also compared the error rates in terms of complete seizures with or without any errors (Table 1). There was a significant decrease in seizures with errors from nearly 50% with RES to about 15% with RES-II ($\chi^2=11.8$, $p<0.001$).

We also observed a significant improvement between the two cohorts in other aspects of the data which were not related to the content of the testing scale. Approximately 2030 h of RES monitoring was

Table 1
Comparison of RES and RES-II.

	RES	RES-II	p Value
Time per question (s)	8.5 ± 0.8	6.7 ± 0.6	0.12
Time from sz onset until testing start (s)	46.0 ± 6.5	16.0 ± 2.0	<0.01
Errors per sz	2.01 ± 0.36	0.24 ± 0.11	<0.01
Szs with errors, % (szs with errors/total szs)	49.3% (37/75)	14.7% (5/34)	<0.01