One-year follow-up of treatment outcomes and patient opinions of Retraining and Control Therapy (ReACT) for pediatric functional seizures

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ABSTRACT

Retraining and Control Therapy (ReACT), a short-term treatment for pediatric functional seizures (FS), has been demonstrated to improve FS in children compared to supportive therapy. However, long-term maintenance of FS-reduction after ReACT is unclear. This study aims to assess seizure frequency 1 year after ReACT and determine patient and parents' opinions of ReACT. Children with functional seizures who previously completed ReACT and their parents were asked to report 30-day FS frequency 1 year after completing ReACT. They also reported if ReACT was helpful. Paired samples *t*-tests were used to compare FS frequency before ReACT to 1 year after and to compare FS frequency in 30 days after ReACT to 1 year after. Fourteen children (Mean$_{age}$ = 15.43) and their parents participated. Seven-day FS frequency for patients at 1-year follow-up (Mean = 0.15) was significantly lower than 7-day FS frequency pre-ReACT (Mean = 5.62; *p* = 0.005). No differences were found when comparing FS frequency during 30 days post-ReACT (Mean = 0.29) and in 30 days before 1-year follow-up (Mean = 0.71). This study confirms long-term maintenance of FS-reduction after ReACT and supports the efficacy of targeting FS directly as opposed to mood or stress for reducing FS. Additionally, children and parents believe ReACT is beneficial.

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Background

Functional seizures (FS; also known as psychogenic nonepileptic seizures or PNES) are a type of functional neurological disorder (FND) in which patients experience seizure-like symptoms that are not associated with epileptiform activity [1]. About one in five patients in seizure clinics are diagnosed with FS [2], and in children under 16, the incidence of FND in pediatric neurological services is at least 6 per 100,000x [3].

FS significantly impact physical, social and academic functioning for children and their families [4–7]. Children with FS have increased physician visits and trips to the emergency room and miss around a month and a half of school. Their parents also miss work to take them to appointments and take care of them at home [4,5]. Therefore, FS present a significant burden to families and the healthcare system. Further, long-term prognosis is related to the duration of FS symptoms [8,9], making early diagnosis and prompt referral for treatment critical.

Although FS typically begin in adolescence or young adulthood [10], there is no gold standard, evidence-based treatment for pediatric FS. The current standard of care for adults and children recommends targeting mood or trauma to improve FS [11,12]. However, as psychiatric comorbidities have been found in less than 50% of children and adolescents with FS [13], other treatment targets may be more effective for pediatric FS [14]. Given the heterogeneity in the development of FS, novel treatment targets may be identified in the various biopsychosocial etiological models proposed for FND [10,15,16]. The recently published Integrated Etiological Summary Model for FND proposes classical conditioning and symptom expectations as the primary etiological mechanisms for FS in children and adults [16]. This model suggests that previous experiences, such as personal illness or injury history or exposure to illness or injury in one's family members and friends or via media, can result in classical conditioning or symptom expectations that produce reflexive, involuntary symptoms. Onset may occur after a single classical conditioning event, consistent with sudden onset of FS after an injury or trauma [17,18], or through shaping, which occurs through repeated pairing, consistent with the common gradual onset of FS [19]. Additionally, symptoms may be the result of preconscious symptom expectations, which

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have been found to produce the expected symptom [16]. After onset, FS can be triggered by other neutral situations that were paired with symptoms, such as locations (i.e., school or work) or strong emotions (e.g., fear) [16]. Predisposing factors such as comorbid anxiety and depression, illness exposure, and/or adverse experiences may contribute to the development of FND but are not required for onset of symptoms [16]. Given its lack of reliance on psychiatric symptoms in the development of FND, this model includes several potential treatment targets for the development of a novel FS intervention.

Retraining and Control Therapy (ReACT) is a manualized intervention for pediatric FS based on the Integrated Etiological Summary Model (16) that uses cognitive behavioral principles to retrain involuntary FS symptoms by targeting sense of control over symptoms and catastrophic symptom expectations [20], as compared with treatments that target mood. The only randomized controlled trial (RCT) assessing treatment outcomes of an intervention for pediatric FS compared the efficacy of ReACT in treating pediatric FS versus supportive therapy [20]. In this RCT, ReACT resulted in greater FS reduction than supportive therapy, with 100% of patients having no FS in the 7 days after ReACT, and 82% of patients remaining FS-free for at least 60 days after ReACT. Notably these improvements in FS occurred without significant improvements in anxiety or depression, suggesting pediatric FS may be effectively treated without targeting mood [20]. This finding is critical, as the use of a brief, targeted treatment for pediatric FS may increase treatment access for patients and fits well within the increasingly interdisciplinary nature of modern medical settings in which psychologists are not always able to provide long-term treatment.

Although ReACT appears to be a promising treatment for pediatric FS with an excellent short-term response, additional research is needed to confirm the benefits of ReACT are maintained for at least a year (similar to other treatment studies) [21] given the previous RCT only reported outcomes for 60-days after treatment [20]. Further, given the profound stigma experienced by patients with FND and the potential negative impact of their experiences with stigma on patient outcomes such as treatment efficacy and adherence [22,23], it is necessary to evaluate children and parents' opinions of ReACT to assess acceptability and continue to refine the intervention. Thus, the aim of the present study is to provide a longitudinal follow-up assessment of children's FS frequency one year after initial completion of ReACT and evaluate children and parents' perceptions of their experience in ReACT to determine treatment efficacy and acceptability. Based on initial treatment outcomes, researchers hypothesized that patients who underwent ReACT would have continued symptom reduction at 1-year post-treatment.

Methods

Design overview

This is a longitudinal follow-up study to a previously published RCT assessing treatment outcomes of ReACT compared to supportive therapy [20]. In that study, children with FS completed ReACT and prospectively reported FS frequency during the 7 days before and the 60 days after ReACT [20]. This study reports FS frequency one year after ReACT and assesses children and parents' opinions of ReACT. For the previously published study, all participants provided informed consent at a baseline visit, and both children with FS and their parents tracked daily episode frequency via FS diaries for at least 7 days before beginning 8 sessions of ReACT (Supplementary Table 1). For the initial post-treatment assessment, participants continued tracking FS frequency for 30 days after finishing ReACT (see prior paper for details) [20]. For this study, children

Table 1
Patient demographics.

Characteristics		%
Sex	Female	92.9
Race	White	64.3
	Black	28.6
	Other	7.1
Income	Below $20,000	21.4
	$20,000–$39,999	14.3
	$40,000–$59,999	0.0
	$60,000–$79,999	21.4
	$80,000–$99,999	14.3
	Above $100,000	28.6
		Mean ± SD
Age (yrs)		15.43 ± 1.79

and their parents completed 1-year post treatment phone interviews assessing FS symptom frequency and their opinions regarding the ReACT treatment. Data were entered twice and inconsistencies were corrected.

Participants

As described in the original publication [20], 17 participants completed the ReACT intervention (Mean$_{age}$ = 15.1 years, SD$_{age}$ = 2.5; 72.2% female; 57.1% white, 28.6% black). Participant enrollment for the original study occurred from November 2016 to March 2020 at The University of Alabama at Birmingham. This study is registered on ClinicalTrials.gov (#NCT02801136). Eligibility criteria for the current study included children who previously completed ReACT as part of the RCT that compared ReACT and supportive therapy [20]. Participants who completed supportive therapy were not included because they were removed from the study and offered the ReACT treatment due to continued FS after the 7-day follow-up. The 1-year follow-up visits were not part of the initial study design, and all participants provided updated verbal informed consent prior to their 1-year follow-up phone interviews. Institutional approval for this addition to the study protocol was obtained from the University of Alabama at Birmingham.

ReACT

ReACT aims to retrain physical symptoms by developing opposing responses to FS symptoms and challenging catastrophic symptom expectations. Detailed description of the ReACT treatment for this sample is outlined in a previous study [20]. All participants in this study completed 8 sessions of ReACT.

Measures

Demographics. Each participant's parent completed a demographics survey used to assess age, gender, race, and income (Table 1).

FS Frequency. During the previous study, participants and their parents both prospectively recorded the number of FS that occurred in the 7 days before treatment using a daily FS diary. After the 8th ReACT session, participants and their parents continued to record FS frequency for 30 days [20]. Inconsistencies in reported FS frequency between parent and child were discussed and clarified to find a consensus. At the 1-year follow-up, parents and children were asked to independently report FS frequency over the last 7 days, 30 days, and 1 year. Parents and children agreed 100% in FS frequency reporting at the 1-year follow-up. Given the consensus between parent and child report of FS, participant report of FS is used throughout the rest of the paper.

Perceived Treatment Efficacy. At the 1-year follow-up, parents and children were also asked "Did you find our treatment helpful?" For this open-ended question, both parents and children provided individual responses, and data for each individual were dichotomized as 0 = no and 1 = yes based on the response. Data coded as 1 = yes included responses of "yes" or "definitely." One participant who responded "somewhat" was also included in the "yes" group, as this was the only participant who did not respond with either yes or no but acknowledged at least some benefit.

Most Helpful Parts of Treatment. At the 1-year follow-up, parents and children who endorsed that the treatment was helpful were also asked "What was the most helpful part of treatment?" Participants provided open-ended responses that were analyzed qualitatively via thematic induction [24].

Data analysis

Because participants only prospectively reported 7-day FS frequency pre-ReACT and there was a floor effect of 7-day FS frequency in the 7 days post-ReACT (Mean = 0), which restricted the variability of this factor, we completed two paired samples *t*-tests. The first compared FS frequency for patients during the 7 days pre-ReACT to 7-day FS frequency at their 1-year follow-up. The second one assessed differences in 30-day FS frequency between the initial post-treatment assessment and the 1-year follow-up. Using 30-day FS instead of 7-day FS for the second analysis also provided a longer and more accurate assessment of current FS frequency. Finally, inductive thematic analysis [24] was used to identify common themes in participant responses regarding the most helpful aspect of treatment.

Results

Fourteen of the original 17 ReACT participants completed 1-year follow-up assessments to evaluate long-term treatment outcomes (Mean$_{age}$ = 15.43 years, SD$_{age}$ = 1.79; 92.9% female; 64.3% white, 28.6% black; Table 1).

A paired samples *t*-test revealed significantly reduced 7-day FS frequency for patients at their 1-year follow-up (Mean = 0.15) as compared with 7-day FS frequency pre-ReACT (Mean = 5.62; *t* (12) = −3.389, *p* = 0.005; Table 2). No significant differences were found when comparing FS frequency during 30 days post-ReACT (Mean = 0.29) and the 1-year follow-up (Mean = 0.71; *t* (13) = −1.10, *p* = 0.29; Table 3).

In sum, 12 of the 14 individuals (86%) reported having no FS in the 30 days immediately following treatment. One year later, parents and children reported that 8 of the 14 (57%) had no FS in the 30-days prior to their 1-year follow-up (Table 4).

Overall, 13 parents provided data at their 1-year follow-up regarding perceived treatment efficacy. Of these participants, 100% reported believing that ReACT was helpful in treating their child's FS (Table 4). In assessing which parts of treatment were most helpful, the following themes arose: having a plan to control/manage FS symptoms in the moment (38.46%), increased understanding of episodes (23.08%), and parent involvement in the treatment (15.38%; Table 5). For one parent, when asked to describe what was most helpful, they responded, "*All of it. The*

one-on-one, parent involvement." Other parents provided responses focused on singular aspects of treatment such as "*working with parents to provide tools and coping mechanisms for episodes*" and "*learning how to handle situations when she felt an episode coming on.*"

Thirteen children also provided 1-year follow-up data regarding perceived treatment efficacy of ReACT. Overall, 12 of the 13 children reported that they believed ReACT was helpful in treating their FS (Table 4). Common themes that arose regarding the most effective aspects of treatment included: having a plan to address episode symptoms and learning to control episodes (46.2%) and having someone to talk to (38.5%; Table 5). For one patient, they concisely summarized these themes, noting that the most helpful part of treatment was "*being able to talk to someone and learn to take control.*" Another participant expanded on how they felt the treatment increased their control over symptoms, reporting that the treatment was effective in "*helping me to be more confident in myself, to fight off the episodes and teaching me that I CAN fight them off. [ReACT] helped me learn what was happening and how to fight them off.*" The one child who did not think ReACT was helpful did not provide further explanation.

Discussion

This follow-up study of ReACT demonstrates maintenance of FS treatment outcomes for at least one year and acceptability of ReACT by children with FS and their parents. ReACT significantly reduces FS frequency, requiring less than 5 sessions on average until participants have no FS for at least 7 days, and 82% were FS-free in the 60 days after treatment in a previous study [20]. The results of this study indicate that a majority of patients continue to experience sustained treatment benefit throughout the following year, with an average of less than 1 FS in the 30-days prior to the 1-year follow-up and 57% of children having no FS during that time. It is noteworthy that this sustained improvement in FS occurs after treatment directly targeting FS symptoms instead of mood. In the initial study, there were no significant improvements in anxiety or depression [20]. Given the continued reduction in FS one-year after ReACT, this indicates treatment of mood is unnecessary to treat or prevent relapse of pediatric FS [14]. However, it is important to highlight that this does not suggest all patients with FS do not need treatment for comorbid mood disorders. Given the greater than normal rates of anxiety and depression in children with FS [13], thorough assessment of psychiatric comorbidities and, if warranted, referral for treatment is recommended for children with FS. However, FS can be successfully treated independently of psychiatric comorbidities.

Research suggests children with FND have a 77% rate of remission in adulthood [3]. However, duration of symptoms is associated with prognosis [8,9], and prolonged symptoms of FS during childhood likely have negative long-term psychosocial effects [25], making prompt resolution of FS critical to children's long-term wellbeing. Therefore, the significant reduction in FS within the short-term, 8-week ReACT treatment suggests implementing ReACT immediately after FS diagnosis could minimize the psychosocial effects of FS and increase the chance for long-term remission.

The short-term design of ReACT also fits well into pediatric behavioral health treatment models in which pediatric psychologists are integrated into specialty services (e.g. neurology) to provide targeted treatment for diagnoses related to physical symptoms. This model would allow for increased access to evidence-based treatment for FS and has been found to be preferable for patients and providers in other areas of healthcare. In a study assessing the feasibility and acceptability of integrated psychological treatment for chronic pain (e.g., migraines) within

Table 2
7-Day FS frequency and test statistics for paired samples *t*-tests comparing FS pre-ReACT and at 1-year follow-up.

FS pre-ReACT M (SE)	FS at 1-year Follow-up M (SE)	d*f*	*t*	*p*
5.62 (1.58)	0.15 (0.10)	12	3.39	0.005

Table 3

30-Day FS frequency and test statistics for paired samples *t*-tests comparing FS at the initial post-ReACT assessment and at 1-year follow-up.

Initial Post-ReACT FS M (SE)	FS at 1-year Follow-up M (SE)	d*f*	*t*	*p*
0.29 (0.22)	0.71 (0.27)	13	−1.10	0.29

Table 4

Patient outcomes and treatment opinions 1-year post treatment (*N* = 13).

Characteristics	*N* (%)
Patients with no FS in the 30-days immediately following treatment	12 (85.71)
Patients with no FS in the 30-days prior to their 1-year follow-up	8 (57.14)
Parents who believed ReACT was helpful	13 (100.0)
Patients who believed ReACT was helpful	12 (92.31)

Table 5

Themes endorsed 1-year post treatment by parents and patients regarding the most helpful aspects of treatment.

Parents	*N* (%)
Having a plan to control/manage episode symptoms in the moment	5 (38.46)
Increased understanding of episodes	3 (23.08)
Parent involvement in the treatment	2 (15.38)
Patients	*N* (%)
Having a plan to address episode symptoms and learning to control episodes	6 (46.2)
Having someone to talk to	5 (38.5)

a primary care setting, researchers found that 100% of care providers preferred this model as opposed to outpatient referrals for long-term care, and 100% of patients expressed interest in and willingness to engage with this treatment model [26]. Further, this model is effective within other specialty clinic settings in producing significant improvements in overall health, with many patients not needing long-term psychological care [27]. In a study of integrated behavioral health for pediatric gastroenterology in which psychologists treated diagnoses of encopresis, abdominal pain and irritable bowel syndrome, one-third of patients required treatment for less than one month, and another third required treatment for between 1–4 months [27]. Integrating ReACT into a similar treatment model could significantly improve outcomes for children with FS and provide epileptologists with an effective treatment recommendation for their patients. Further, as the majority of mental health care providers feel uncomfortable treating FND [28], an effective short-term treatment for FS will provide increased access to evidence-based treatment.

This study also confirms that both children and their parents find ReACT acceptable and agree that ReACT is effective. The acceptability of ReACT is significant, as the explanation used in ReACT to describe FS as a reflexive response that can be retrained is inconsistent with the common explanation of FS as the result of stressors [12,29,30], and the treatment targets FS directly instead of aiming to improve mood. Notably, 100% of parents and 92% of children approved of ReACT. Although this may be an overestimation since this does not include participants who did not finish the treatment, the overwhelming positive impression one-year after completing the treatment suggests this etiological explanation and treatment focused on retraining FS instead of treating mood is widely acceptable to children and their families.

Although ReACT aims to target sense of control and catastrophic symptom expectations to improve FS [20], the relationship between the change in these targets and the change in FS has not been confirmed. However, children and parents' opinions of the most effective part of ReACT are consistent with the proposed targets. Specifically, both parents and children reported that they like that ReACT helps them control the FS symptoms.

The strengths of this study include the use of both parent and child report of FS and the mixed methods assessment of qualitative patient opinions in combination with quantitative FS frequency. Limitations of the study include small sample size, the absence of a control group, no assessment of other secondary outcomes (e.g., mood, health-related quality of life, etc.) at 1-year follow-up and that the 1-year assessment was not originally planned at the beginning of the study. The study is also limited by sample demographics, as the majority of participants identified as white and female. While this is consistent with the expected demographic make-up of FND patient samples in the US [31], additional research is needed to assess how treatment acceptability and efficacy may vary among different geographic, demographic and cultural groups. For example, parent involvement and parent–child interactions may vary by culture, which could impact treatment outcomes and acceptability [32,33]. Additional research is needed to confirm engagement of ReACT's treatment targets. Other areas for research include assessing the efficacy of a planned booster session to improve long-term symptom remission after ReACT and assessing other predictors and mediators related to treatment outcomes to further assist in adapting ReACT to the needs of individual patients. Possible mediators for treatment outcomes include acceptance of the FS diagnosis by the patient and family, duration of symptoms prior to treatment, and family support and participation in treatment. A larger RCT assessing these factors and the long-term efficacy of ReACT compared to a control is needed.

Overall, this study confirms the long-term maintenance of FS-reduction after ReACT and supports the efficacy of a short-term treatment targeting FS directly as opposed to treatment of mood or stress for reducing FS. Additionally, this study confirms the acceptability of ReACT to children and parents.

Ethical Statement

This work has not been published previously. It is not under consideration for publication elsewhere, and it has been reviewed and approved by all authors. If it is accepted, it will not be published elsewhere in the same form without the written consent of the copyright-holder.

Conflicts of Interest

Editorial Work: Editorial board member for Epilepsy & Behavior, Journal of Epileptology (associate editor), Epilepsy & Behavior Reports (associate editor), Journal of Medical Science, Epilepsy Currents (contributing editor), and Folia Medica Copernicana.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ebr.2021.100503.

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