

Children with seizures exhibit preferences for foods compatible with the ketogenic diet

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Abstract

Although highly effective for the treatment of intractable epilepsy, the ketogenic diet is not always included in the treatment option hierarchy presented to families, in part due to perceptions that children will find the high-fat/low-carbohydrate regimen unpalatable. This study assessed if children with seizures exhibit food preferences compatible with the diet, as well as if caregivers were accurate in predicting preferences. Children aged 2–17, with ($n = 29$) and without ($n = 30$) a history of seizures, participated in a paired choice food preference assessment while parents estimated child preferences verbally. Children with seizures exhibited significantly higher preferences for fat versus carbohydrate foods compared with controls, and parents demonstrated low accuracy. Future studies could use similar assessment methods to prospectively track whether such preferences predict diet compliance and/or efficacy. Research into the underlying metabolic basis for this preference and possible related neurophysiological mechanisms in seizure etiology and treatment is warranted.

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1. Introduction

The ketogenic diet is a high-fat, low-carbohydrate and protein diet used to treat children with intractable seizure disorders. Even though side effects are low, and efficacy is well established in retrospective and prospective studies [1,2], the diet remains low on most neurologists' treatment algorithms [3,4]. One major reason may involve perceived diet unpalatability and consequent assumptions by caregivers

that children will be noncompliant with diet items and restrictions [5,6].

No study has previously attempted to evaluate food preferences in children with seizures as a group. In one case study [7], a choice procedure was used to assess relative preferences for food items available on the ketogenic diet in an adolescent with severe epilepsy. In this case, many of the high-fat items included in the diet were found to be highly preferred, and these preferences were underestimated in caregiver predictions [7].

Atypical food preferences have been documented in clinical populations. Research on conditioned food or taste aversions suggests that animals and humans learn to avoid foods associated with negative postingestive consequences [8]. Conversely, it has been proposed that humans and

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animals may prefer or choose certain items to compensate for physiological, metabolic imbalances [9]. For instance, significantly increased sodium-seeking behavior and hedonic preference for salty foods were found among adolescents with congenital adrenal hyperplasia [10]. Research has also demonstrated that carbohydrates are selectively craved by certain clinical population subgroups, particularly those experiencing depressed mood [11–13]. We hypothesized that patients with seizures may prefer ketogenic (high-fat) as opposed to “anti-ketogenic” (high-carbohydrate) food items, and also that parents of children with epilepsy would demonstrate low accuracy in predicting these preferences.

2. Methods

2.1. Study population

A group of 31 children and adolescents with a history of seizures were recruited from outpatient clinics at The Kennedy Krieger Institute and Johns Hopkins Hospital in Baltimore, MD, USA. Of the 29 subjects who participated in the study, 19 were classified with partial and 10 with generalized epilepsy. Etiologies included idiopathic (12), childhood absence epilepsy (4), benign rolandic epilepsy (2), B-6 dependency (2), juvenile myoclonic epilepsy (2), stroke (1), myoclonic-astatic epilepsy (1), Sturge–Weber syndrome (1), cortical dysplasia (1), juvenile absence epilepsy (1), anoxic-epileptic seizures (1), and Lennox–Gastaut syndrome (1). Seizure frequency for the children in this group was reported by parents as daily (7), monthly (4), annually (13), and less than annually (5).

Thirty-one matched controls were recruited from the children, relatives, and acquaintances of institute and hospital employees, as well as from among institute outpatients and their siblings. Subjects were matched using a subgroup matching process within three age-stratified groups, with efforts to distribute across ages within each group. Subjects were matched on gender, socioeconomic status level as determined by the Hollingshead Index score [14], and cognitive developmental delay level (none or mild/moderate) as reported in the medical chart or by parent response on a demographic questionnaire. Efforts were also made to match on race and ethnicity.

During recruitment for both groups, children with a history of significant feeding problems (e.g., gastrostomy tube dependence), food allergies, adherence to special diets (e.g., vegetarian or kosher), use of the ketogenic or any other therapeutic diets, or clinical depression were excluded. Children in the control group were excluded if they had a diagnosed metabolic disorder. After recruitment, one child in the seizure group, presenting with profound mental retardation and visual and motor deficits, was disqualified from the study due to an inability to exhibit consistent observable choice behavior during the assessment process. A second child in this group (3-year-old with mild delays) was disqualified due to noncompliance with study procedures. One adolescent in the control group was excluded after recruitment due to revelation of a recently acquired traumatic brain injury, with subsequent administration of an anticonvulsant.

Results of parametric and nonparametric independent sample tests conducted on matching variables revealed no significant differences between the final groups. Demographic information for subjects is provided in Table 1.

2.2. Apparatus

A standard group of 14 food items was used (Table 2). Food items were reviewed by a licensed dietitian and were chosen on the basis of their nutritional composition [15,16]. The seven ketogenic items were chosen for high fat and low carbohydrate content, whereas the seven anti-ketogenic foods were chosen for high-carbohydrate and low-fat content. Within the anti-ketogenic group, items were distributed between salty, sweet, and blander flavors, a distribution not possible within the ketogenic group

without the addition of artificial sweeteners, a potential confound in macronutrient identification. However, for both groups, attempts were made to distribute between higher- and lower-intensity flavors, and to avoid brand-name and heavily advertised foods to control for the effects of media exposure on children’s food preferences [17]. Foods that required it were prepared according to the manufacturer’s directions and were served at the appropriate temperature.

2.3. Child preference and caregiver prediction assessments

This study employed applied behavior analysis methods refined for use with populations with varying degrees of cognitive disability and found to be quite accurate in identifying preferences in the clinical population. Specifically, a paired choice procedure was conducted as described by Fisher et al. [18]. Based on a concurrent operant, or forced-choice, paradigm [19], this method of presentation results in greater differentiation between stimuli than single-item presentation and rating [18]. The method is supported by the basic operant research on schedules of reinforcement [20], taste preference research with humans and animals [7,21,22], and identification of reinforcers for children and adults with cognitive delays [23].

The child preference assessment for this study consisted of paired presentations of food items, such that every food item was paired with every other food item. Items were presented simultaneously, and the child was asked to choose one item from the pair. The percentage of trials in which the child exhibited a positive choice response for each item was calculated by dividing the number of trials in which the item was chosen by the number of trials in which it was presented, and a rank order was derived. Aggregate scores for each food group were also calculated by summing the percentages for all items in each category.

An additional measure was derived based on the conventional behavioral definition of high preference for each food type. Specifically, items chosen 80% of the time or more frequently in paired choice assessments are considered high preference [18]. For this study, frequency of high-preference choices for ketogenic and anti-ketogenic foods was measured by counting the number of items for each macronutrient that were chosen for $\geq 80\%$ of trials.

Caregiver predictions of child food preferences were obtained using a modification of the child assessment described above. Item pairs were represented by words on index cards, rather than use of actual food item samples, and parents were asked to pick which item they predicted their child would prefer. As with the child assessment, percentages were calculated for the number of trials in which each food item was selected, and two separate rank orderings, for ketogenic diet and anti-ketogenic diet food items, were obtained for each parent. Congruence scores for ketogenic and anti-ketogenic items for each parent–child pair were obtained using the Spearman rank-order correlation.

Because differences in previous exposure to specific food items might have confounded preference ratings for a few of the very youngest participants [24], a brief food experience inventory was administered to the caregiver for potential screening purposes. Parent estimate of child past exposure was assessed on a continuous “0” to “20+” frequency scale for each study item.

Types and dosages of anticonvulsant medications were obtained from answers on a demographic questionnaire. Children were categorized as receiving anticonvulsants that may be associated with appetite suppression/weight loss (zonisamide, topiramate, felbamate) or those that may potentially induce weight gain (gabapentin, valproic acid) [25].

Participants were recruited via institutional review board-approved study flyers and recruitment letters. After parental consent and child assent were obtained, the child and parent assessments were conducted by trained research assistants. When possible, the parent assessment was completed first, so that predictions would not be affected by child results (e.g., via observation).

Prior to the assessment procedure, a small sample taste of each food item was offered to each child to control for item presentation novelty (e.g., butter served alone instead of as a condiment) and to partially control for the effects of differential exposure. Children were then administered the choice assessment. Each of the 14 items was presented once

Table 1
Demographics of participants

Group ^a	Age at study	Male gender (%)	Socio-economic status	Cognitively delayed ^b (%)	Race/ethnicity (%)
Seizure					
Younger (<i>n</i> = 8)	3.3	63		13	
Middle (<i>n</i> = 11)	7.4	55		18	
Older (<i>n</i> = 10)	14.3	40		40	
Overall (<i>n</i> = 29)	8.6	52	4.07	24	Caucasian = 76; Black or mixed = 21; Hispanic/latino = 3
Control					
Younger (<i>n</i> = 11)	3.6	45		10	
Middle (<i>n</i> = 9)	7.7	56		13	
Older (<i>n</i> = 10)	13.6	40		40	
Overall (<i>n</i> = 30)	8.1	47	4.33	20	Caucasian = 70; Black or mixed = 23; Hispanic/latino = 3; Asian/caucasian mixed = 3

^a Groups stratified by age: younger (2–5), middle (6–10), older (11–17).

^b With mild/moderate cognitive delay versus no delay.

Table 2
Food list

Food item	Amount (g)	Fat (g)	Carbohydrate (g)	Protein (g)
Ketogenic				
Butter	100	82	0	0
Mayonnaise	100	80	.7	1.4
Cream cheese	100	33.9	2.5	8.2
Hot dog	100	29.2	1.7	8.2
American cheese	100	31.8	1.8	22.5
Bacon	100	49.5	.53	30.5
Bologna	100	28.6	3.2	10.7
Anti-ketogenic				
Candy corn	100	0	95	0
Jelly bean	100	0	92.5	0
Pretzel	100	2.9	80	.43
Tortilla chip	100	1.8	85.7	10.7
Noodles	100	1.8	75	12.5
Potato (baked)	100	.1	25.3	2.3
Bread (white)	100	3.1	50	8.3

with every other item, resulting in a total of 91 trials. Items were presented in randomly selected pairs to control for order and satiation effects on preferences for either category of foods. The child was able to taste or consume a very small, “taste-sized” amount (approximately one-eighth of a teaspoon) of the selected item. Each single-item presentation weighed ≤ 1 g, and the maximum amount any child could consume in total (all food trials combined) during the assessment equaled approximately 62.7 g, or 2.2 oz. Assessment duration ranged from 15 to 30 (for the youngest children) minutes.

Parent prediction data were not collected for nine participants (*n* = 5 for the seizure group, *n* = 4 for controls) due to prior parent observation of child choice responding. For both groups, these were parents of the children in the youngest group and one parent of a child with moderate mental retardation in the seizure group. Choice assessments with these children were conducted immediately on obtaining informed consent, with parent present, due to child behavior (tantrums, stranger anxiety) and/or parent concern about child behavior/fatigue. These cases were excluded from the related analyses (parent predictions of child preferences).

This study employed an independent cross-sectional group design. Separate univariate analyses of variance were conducted for ketogenic and anti-ketogenic aggregate scores. Multinomial logistic regression was used to examine group \times food type interaction on items chosen as high preference. Correlations between parent–child dyads in the seizure group and controls were compared using independent sample tests (*t* test) and the Wilcoxon rank sum test.

3. Results

3.1. Preliminary analysis

The groups did not appear to differ on either exposure ratings or effects. Several of the children in both groups (seizure group *n* = 15, control *n* = 14) were rated as having had no exposure to more than one food item (seizure group *M* = 2.7, control *M* = 3.1). This lack of exposure did not appear to affect overall food selection. Specifically, many previously unexposed food items were chosen by children at a frequency that indicates moderate to high preference (e.g., in 16 cases, unexposed items were selected between 6 and 12 times each; in 5 cases, unexposed items were consumed for all 13 trials). During the choice assessments, only one child was observed to avoid all of multiple (3) items rated as having zero previous exposures, but this child also avoided items to which previously exposed (both fat and carbohydrate) and had overall scores comparable to those for the rest of the group (control).

For the seizure group, the impact of type of medication on aggregate preference scores was examined. Because of the variability of scores and the small number of children in each group (appetite suppressant group *n* = 4, appetite stimulant/weight gain group *n* = 6), formal analyses were not conducted. The distribution of scores for children in these two groups, as well as differences in scores for the two food types for each child, was inspected. Within the appetite suppressant group, inspection of scores for individual children did not reveal an identifiable pattern.

Two of the four children had higher ketogenic than anti-ketogenic scores, whereas two displayed the opposite. Two of the children had very slight differences between scores for both food groups, whereas two children had more distinct differences in scores but with opposite preferences from each other. Within the appetite stimulant/weight gain group, scores appeared normally distributed for both food groups, and a pattern was more clearly identified. Four of the six children displayed distinctly higher scores for ketogenic versus anti-ketogenic items.

For the seizure group, correlations among the dependent variables for child preference and seizure frequency were calculated; these correlations were not significant (all values of $P \geq 0.62$). The impact of seizure disorder type on preferences was not examined due to group heterogeneity.

Pearson product-moment correlations among the dependent variables for child food preference and the potential covariate, age, were calculated. Age was positively correlated with child anti-ketogenic scores, reaching significance in the total group and control group, and approaching significance in the seizure group.

3.2. Child preferences

A one-way analysis of variance (ANOVA) demonstrated that the mean aggregate ketogenic food item score of the seizure group (316.79, $SD = 82.55$) was significantly higher than that in the control group (265.03, $SD = 77.16$), $F(1, 57) = 6.20$, $P = 0.016$. A one-way analysis of covariance (ANCOVA) comparing mean aggregate anti-ketogenic food item scores of the seizure and control groups, while controlling for age, also was significant. Controls had significantly higher mean aggregate anti-ketogenic food item scores (368.27, $SD = 65.98$) than did children in the seizure group (311.28, $SD = 95.89$), $F(1, 57) = 8.95$, $P = 0.004$.

Multinomial logistic regression was used to examine children's high-preference items by food category and group (seizure/control). The odds ratio of having high-preference ketogenic versus anti-ketogenic items was higher in the seizure group (one ketogenic item, $P < 0.0001$; two ketogenic items, $P < 0.001$). This interaction is represented in Fig. 1.

The top choice item (chosen above all other foods) for each seizure group and control child was examined. Table 3 displays the frequency with which each specific item in the assessment was chosen as the top item by children in each group. The most popular item among children with seizures was bacon, and among the control group, noodles.

3.3. Caregiver predictions

Mean and median parent-child congruence scores were low for both groups. The mean correlation value for parent prediction of anti-ketogenic food preferences in the seizure

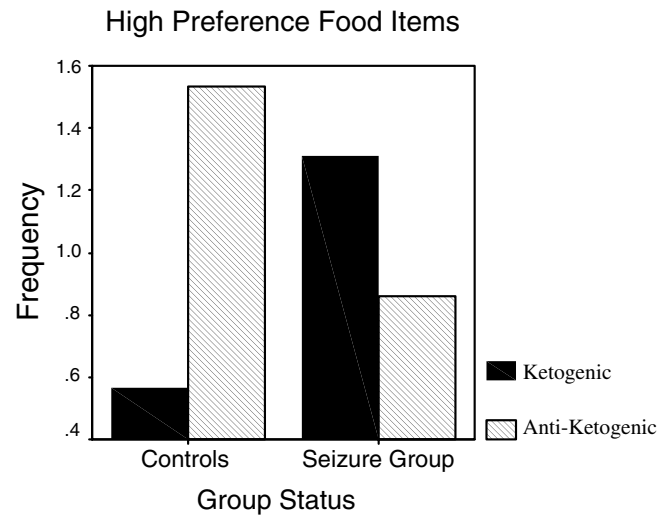


Fig. 1. Number of high-preference items by food type (ketogenic/anti-ketogenic) and group (seizure/control).

Table 3

Top items: individual ketogenic and anti-ketogenic foods

Food item	Seizure group	Controls
Ketogenic		
Bacon	7	1
Cream cheese	5	0
Mayonnaise	4	0
American cheese	3	0
Hot dog	2	2
Butter	1	0
Bologna	1	2
Total	23	5
Anti-ketogenic		
Noodle	1	8
Candy corn	0	4
Tortilla chip	0	4
Jelly bean	1	3
Baked potato	1	3
Pretzel	2	2
White bread	1	1
Total	6	25

group (0.30, $SD = 0.46$) was not significantly different from the mean correlation value for controls (0.35, $SD = 0.44$), $t(48) = -0.381$, $P = 0.71$. There were no significant differences in the median correlations between groups for prediction of ketogenic diet item preference, $P = 0.46$ (median correlation for seizure group = 0.45, $SD = 0.42$; median correlation for controls = 0.64, $SD = 0.36$).

4. Discussion

The purpose of this study was to examine caregiver predictions and actual child food preferences among children with a history of seizures. More specifically, this study investigated preferences for food items that are both compatible and incompatible with the ketogenic diet. The data

supported the prediction that children with seizures would exhibit higher preferences for high-fat than high-carbohydrate foods compared with controls. This is a novel finding, without precedent in the literature.

Identification of the mechanisms underlying the efficacy of the ketogenic diet is a topic of some renewed interest [26,27]. To date, however, the mechanisms are still unknown. What is known is that the consumption of fat versus carbohydrate as the primary source of energy is highly effective in controlling seizures in individuals on the diet, as well as improving behavior, alertness, and mood. Thus, in the context of the application of this dietary regimen for the control of seizures in this clinical population, it can be conceptualized that consumption of fat versus carbohydrate has positive consequences (e.g., reduced abnormal electrical discharge activity, increased alertness, or improved mood). As such, it is possible that some individuals with seizures develop a preference for high-fat foods versus carbohydrates via taste–post-ingestive consequence learning. In striking illustration of this, one young child with seizures in this study was observed to scoop out and consume the samples of butter, cream cheese, and mayonnaise, commenting to her mother on two occasions “this one makes me *feel* better.”

Higher aggregate scores for carbohydrate foods were noted for older children in both groups, with this trend reaching significance in the control but not the seizure group. Age was not significantly correlated with differences in aggregate score fat preferences for either group or in differences in items chosen as high preference. Research with typically developing children indicates that there are many environmental variables that affect food preferences, such as exposure, media, adult and peer modeling, and social-affective context [28,29]. As such, it might be expected that some children exhibiting preferences that are unusual or atypical (i.e., as a result of an underlying medical condition) would modify preferences over time. It is possible that some of the older, nondelayed adolescents with seizures would display different food choices (i.e., more similar to those of their peers) when in a more naturalistic setting (e.g., in a high school cafeteria) versus an experimental paired choice paradigm [30]. However, atypical preferences and consumption (e.g., for salt) have been observed among teenagers and adults in other clinical populations [10–13].

Parents of children in both groups displayed low accuracy in predictions. This finding is consistent with the limited literature on the accuracy of parent predictions of child food preferences [31,32]. This level of accuracy has a different implication for the clinical population, in that parents may reject potentially beneficial treatment options (e.g., a therapeutic diet) based on erroneous assumptions about child preferences and/or compliance. Our findings suggest that any parental claims that their child will not enjoy typical ketogenic diet foods may need to be challenged.

These low correlations may seem surprising, given that caregivers are primarily responsible for the purchase and preparation of food items and are also present for many,

if not most, child meals, during which they can observe child consumption patterns. However, parents may select and serve items based on factors other than child preferences [33]. Caregivers may also perceive that what his or her child *accepts* is equal to what he or she *prefers*. In this study, for instance, the parent of twins (one with seizures, one control) completed the paired choice for one child, and then indicated that the research assistant could copy the identical ratings for the sibling, stating “they both eat what I give them . . . they like the same things.” In the actual assessments, one twin chose two carbohydrate and zero fat items as highly preferred, whereas the other chose two fat and one carbohydrate, with no shared items. In addition, direct observation of the assessment procedure modified the perceptions of preferences for some parents. Several of these parents then reassessed prior opinions about the tolerability of the ketogenic diet.

This study has several limitations. The use of a paired choice methodology with specific food items chosen to represent macronutrient content was both a strength and limitation of this study. Many previous food preference studies with children have used methods that rely on verbal mediation and the ability to categorize [34,35]. Given the prevalence of cognitive delay in this clinical population, a method was chosen that has been widely used with individuals with developmental delays and which has demonstrated good predictive validity. However, the paired choice assessment requires a child’s attention and compliance for approximately 20–30 minutes of continuous trials. Also, the use of specific items in the paired methodology may have resulted in the possible reduction of the aggregate scores for a particular group of foods for some children (i.e., if several of the items in a preferred *category* were nonetheless nonpreferred specific *items*). Analysis of the macronutrient category of the most preferred items (vs aggregate scores of all items in each group) resulted in perhaps a clearer representation of both within- and between-group differences in actual preferences for fats and carbohydrates. It is also impossible to determine if the appearance, taste, or texture of the foods played a role in selection, as opposed to the fat or carbohydrate content. To dissociate these factors, future studies could potentially incorporate methods such as assessing preferences using similarly flavored yogurts or drinks with differing fat and carbohydrate content [36,37]. Finally, the paired methodology used in this study does not make it possible to infer whether children with seizures are preferentially choosing high-fat items or actually avoiding carbohydrates, an important distinction in future research about possible mechanisms underlying the efficacy of the ketogenic diet [26].

Because of the heterogeneity of diagnoses in this relatively small sample, the relationship between seizure type and food preferences could not be examined. It is also possible that more apparent within-group differences in preferences by seizure frequency or medication regimen would have been detected in a larger sample. Lastly, interpretation

of between-group differences would be strengthened if body mass index (BMI) data had been systematically obtained for participants, as BMI has been associated with fat preferences in some studies [38].

This study has many implications for future research. This detection of unique preferences compatible with the high-fat/low-carbohydrate diet in the clinical population may warrant further research on underlying metabolic and neurophysiological differences as they are related to both seizure etiology and treatment. Perhaps most importantly, future studies could use the results of systematic food preference assessments conducted with children who are being started on the ketogenic diet to prospectively track whether strong preferences compatible with the diet can predict not only behavioral compliance but also diet efficacy. If true, then this food preference assessment would have predictive value prior to using the ketogenic diet. Some clinicians and researchers have proposed that the ketogenic diet be considered earlier in the treatment hierarchy, rather than as a “last resort,” and have advocated for and begun more systematic research to identify variables that might predict the best responders to the ketogenic diet [3,39,40]. A positive food preference assessment performed early in the course of epilepsy in an individual child might identify these responders. It would be useful to investigate whether the assessment procedure could be modified (e.g., shortened in length via elimination of some items) to be as clinically efficient as possible while maintaining good predictive validity.

In conclusion, results of the study indicate that children with seizures prefer high-fat items compatible with the ketogenic diet, and that parents may not always be aware of such preferences without systematic assessment. These findings may have important implications for the clinical treatment of seizures, and for future research into understanding why these preferences exist and if they are related to optimal benefits from the ketogenic diet.

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