Dose-Time Effect of Artificial Colors in Hyperactive Children

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Four previous studies from our laboratory have provided inconsistent data with respect to the role of artificial food colors on the behavior of hyperactive children. In the first study (Conners, Goyette, Southwick, Lees, & Andrulonis 1976), a significant improvement of behavior was found in children when on a food-additive-free diet compared with a control diet, but the effect was true for only one of the orders of treatment administration. A second study examined the effects of a challenge with artificial colors in a double-blind ABAB crossover (Goyette, Conners, Petti, & Curtis 1977). No effects were found for parental observations, but short-term acute effects were seen in a visual-motor tracking task, suggesting a rapidly acting pharmacologic activity that might have been obscured in parental ratings done twice weekly at the end of the day. A third study, therefore, repeated the double-blind crossover but with daily parental ratings made during the three-hour period immediately following ingestion of the chocolate cookies containing the challenge or placebo. That study found a significant worsening of behavior during the challenge period. Finally, a larger study of an exact replication of the previous study was recently completed, but the results were entirely negative: no differences were found between parental or teacher ratings during the blind challenge or placebo periods. These and other studies have been summarized recently (Conners 1980).

The present experiment was conducted to determine if those children apparently most reactive to the food dyes could show a pharmacologic dose-time effect by using more sensitive laboratory instruments and observations than the relatively uncontrolled global instruments previously utilized.

METHOD

Subjects

Nine children who had participated in the previous trials were selected for study: four girls and five boys ranging in age from 5 years to 10 years 6 months and all with normal or higher IQ. During the previous studies eight of these children showed a significant behavioral improvement during the nonblind dietary phase of the trials compared with baseline, as rated by both parents and teachers on the Abbreviated Parent and Teacher Scales. They also showed a differential behavioral response during the challenge and placebo phases of the double-blind trials. One child had not participated in the previous trials but was included because parents reported a marked sensitivity to artificial colors and the child had shown a marked improvement on the Feingold diet carried out by parents.

All of the subjects were following the Feingold (KP) diet during this study. They had all been screened by a child psychiatrist and found to satisfy DSM II criteria for hyperkinetic reaction of childhood (308) or DSM III criteria for attentional deficit of childhood.

Dependent Measures

First, activity level was measured by two methods. Actometers attached to the nondominant ankle and
wrist were read each 45 minutes of the study, providing scores in units per minute. The actometers were constructed so as to require six movements of hand or leg before registering one count (McPartland, Foster, Matthers, Coble, & Kupfer 1975). A chair used by the subject was wired with microswitches so that seat rotations, seat tilting, or foot movements activated counters. Scores were expressed as counts per minute.

Behavioral ratings of six 5-point scales were made during each hour by the experimenter (Newman). The scales covered gross motor activity, distractibility and concentration, frustration tolerance, mood, attention-seeking devices, and impulse control. Scores for the six scales were summed to provide an overall score with a theoretical range from 5 to 30 points.

Attention and learning were measured by a paired-associate learning task as designed by Swanson and Kinsbourne. The stimuli consisted of pictures of animals to be paired with a response number. List length varied from 3 to 24 items depending on the child’s ability as determined from a practice session. Each child began with a list of three to eight items; this was increased if a criterion of two errorless repetitions was reached in 10 trials. The list was lengthened until either the criterion could not be attained or a 24-item maximum was reached. The longest list for which the criterion was satisfied was defined as the capacity list. This list length was used for all subsequent testing sessions (Swanson, Kinsbourne, Roberts, & Zucker 1978). Ten seconds were allowed for a response. If the response was incorrect, the correct response was provided. Each trial was presented in a different randomized order to prevent serial position effects. Scores consisted of the number of trials to criterion and the total number of errors.

**Design and Procedure**

Two sessions were scheduled for the same time of day at one- to two-week intervals. Each session began with a baseline period during which the child completed the learning task and the activity measures were recorded. Two chocolate cookies were then distributed under double-blind conditions. At a given session each of the cookies contained either 15 mg of artificial colors or placebo. Further learning tests were then conducted at 45, 90, 135, and 180 minutes after cookie ingestion, with activity and rating measures obtained concurrently. Four of the subjects were randomly assigned to the active cookies followed by the placebo. (AP order), and five were assigned to the PA order. Data were analyzed by analysis of variance with tests of linear, cubic, and quadratic trends.

**RESULTS**

No significant treatment effects were found for any of the dependent measures. Examination of the activity and rating data shows a very consistent picture of behavior during the sessions: the children became more active during the first hour following the baseline measurement and then stabilized and returned to baseline in subsequent sessions (see Figures 1, 2, and 3). The same pattern was found for each of the two testing days.

The results for the learning task were somewhat different from the activity measures. Figure 4 shows that on the first day those subjects who received the active cookie showed a worsening of performance, which reached a peak at two hours and then declined. In contrast, the placebo subjects showed a strong improvement or practice effect, also reaching a peak at two hours followed by a fatigue effect. However, this effect was not repeated on the second testing day, which showed a substantial between-day practice effect, with both active and placebo groups showing a very similar pattern of initial further improvement followed by some fatigue effect in the later sessions. Analysis of variance failed to demonstrate a significant treatment or treatment-by-order interaction. There was a significant day-by-time cubic component, indicating that the S-shaped curve of performance over time was different between the two days.

**DISCUSSION**

This experiment failed to demonstrate a significant pharmacological dose-time effect between the active and placebo materials. The children’s activity level appears to increase following ingestion of both kinds of material—active and placebo—and then return gradually to baseline. This effect is highly consistent for all three measures of activity. The effects could represent a normal pattern of boredom and satiation, a hypoglycemia-induced overactivity that is reduced by the digestion of the cookies, or possibly a reactive effect to the chocolate or other materials in the cookies. In any case, it is clear that whatever cause underlies this pattern of behavioral change in these subjects, any possible effects of the challenge materials per se would be superimposed upon this pattern.
FIGURE 1. Observational ratings of behavior concentration and mood.

FIGURE 2. Counts per minute of feet and seat movements during testing.
FIGURE 3. Counts per minute of wrist and ankle actometer.

FIGURE 4. Paired-associate learning errors for active and placebo conditions.
Conceivably, this normal activity course could mask any specific effects due to the challenge colors.

The paired-associate learning task had been selected on the presumption that it would be relatively practice-free. It has been used in experiments by Swanson and Kinsbourne and has shown pharmacologic sensitivity in our earlier experiments. In their experiments Swanson and Kinsbourne are able apparently to repeat the task with relatively little practice effect once a capacity list has been achieved, but we did not find this to be the case in our study. The marked practice effect between days may have served to mask the treatment effect on the second day. The first day of treatment showed exactly the kind of curve one would expect from a pharmacologically active substance that impairs performance and then wears off. The placebo subjects on the first day, on the other hand, showed a strong apparent practice effect followed by a fatigue effect, thus maximizing the contrast between the two treatment groups. Despite this apparent contrast, the treatment effect was not consistent enough to reach statistical significance.

One could argue that the low power of the test with small numbers of subjects partially accounts for the lack of significance. This factor in combination with unknown dosage effects could explain the lack of effect in the present study and the variable effects across several studies previously carried out in our laboratory. Unfortunately, we accepted the recommendations of the interagency collaborative group of the National Institute of Mental Health to employ a double-blind challenge material supplied by the Nutrition Foundation. The figure of 15 mg of artificial colors recommended by that group as half the average daily intake of colors by adults may, in retrospect, be a considerable underestimation. One study (Wilson 1976) estimates that children consumed 2.5-fold previous estimates of color additives in foods and drugs when figures are adjusted to account for the food habits and preferences of children. This could amount to a maximum of 53 gm/child/year when only a few selected foods are considered.

It is now clear that further experiments to test the hypothesis of a relationship between ingestion of artificial food colors and behavior in children must include a pharmacologic dose-response analysis. Early efforts, guided by the initial presumption that very small amounts could "trigger" a behavioral reaction or possibly cause an allergic type of response, may have been in error. Our own data have suggested previously a transient acute effect of dye ingestion on sensitive laboratory measures but equivocally on cruder global measures. These inconsistent effects may well represent the borderline effects that would occur with a low-dose but pharmacologically active substance. Smaller subjects or those who are especially sensitive would then show an effect, but group studies would possibly miss such effects, depending upon factors such as age, body mass, time of measurement, stomach contents, etc.

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REFERENCES


