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Visual Augmenting/Reducing and P300 in Autistic Children[1]

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Visual event-related potentials were recorded from five male autistics and five matched controls. Sensory effects were investigated by having subjects passively view flashes of three different but equiprobable intensities (augmenting/reducing paradigm). Cognitive effects were examined by having subjects count infrequent, target, flashes of one intensity embedded within a series of frequent, nontarget, flashes of a different intensity (oddball paradigm). In the augmenting/reducing paradigm, the sensory N100 wave of autistic but not controls showed a significant increase in amplitude (augmenting) as flash intensity increased. The cognitive P300 wave of autistics did not differ from controls in the oddball paradigm. Unlike controls, autistics had an equally large P300 in the no-task augmenting/reducing paradigm. It is concluded that autistics may experience a degree of stimulus overload in the visual modality.

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INTRODUCTION

Infantile autism is a developmental disorder with symptoms suggestive of organic brain pathology. Although individual cases of autism may vary widely in the extent to which cognitive functioning is impaired, a core set of symptoms is present in all cases. From this, a common neurological substrate has been inferred (Damasio & Maurer, 1978; Ornitz, 1983). Evidence indicates that autistics display abnormalities in several indices of CNS functioning, including a lack of left hemisphere electroencephalogram (EEG) activation during linguistic tasks (Small, 1975), and reduced blood flow to the cerebral cortex (Sherman, Nass, & Shapiro, 1984). The primary etiology of autism remains unknown, although it has been linked to a heterogeneous set of CNS insults (see Ornitz, 1983, for a review).

Event-related brain voltage potentials (ERPs) have recently been employed in an effort to study dynamic brain functioning in autistic children. Most of these studies have focused on the cognitive P300 (P3b) component of the ERP. P300 is a positive voltage wave that peaks somewhere after 300 ms poststimulus and reaches maximum amplitude over the parietal area of the scalp (see Pritchard, 1981, for a review). The amplitude of P300 appears to index the degree to which a given stimulus engages a finite set of attentional resources of a perceptual nature (Printchard, 1981). P300 can reliably be produced in subjects by employing a version of the so-called oddball paradigm (Duncan-Johnson & Donchin, 1977). In this paradigm, the subject must differentially process (e.g., count) intermittent target stimuli that are embedded in a background sequence of more frequent nontargets. The infrequent targets usually elicit a larger P300 wave than do the frequent nontargets.

To date, several studies have employed auditory versions of the oddball paradigm to study autistics versus matched controls. Most have found that target P300 is significantly smaller in autistics than in controls (Courchesne, Kilman, Galambos, & Lincoln, 1984; Courchesne, Lincoln, Kilman, & Galambos, 1985; Niwa, Ohta, & Yamazaki, 1983; Novick, Kurtzberg, & Vaughan, 1979; Novick, Vaughan, Kurtzberg, & Simson, 1980), while one had reported no differences (August et al., 1984; it should be noted that in this latter study, six of the eight controls were biological siblings of the patient group). The general interpretation given to these results is that attentive auditory information processing is abnormal in autistic subjects.

Studies employing visual versions of the oddball paradigm have been fewer in number (Courchesne et al., 1985; Novick et al., 1979). They have found that the target P300 of autistic children does not appear to be significantly attenuated relative to controls. This suggests that autistic children may be less deficient in processing visual information than they are in processing auditory information (see Courchesne et al., 1985). The present in-

vestigation collected visual oddball P300 data from autistic children in an attempt to replicate and extend these findings.

In addition to employing a visual version of the addball paradigm to investigate the P300 component, the present study also investigated visual augmenting/reducing of the earlier N100 component. Visual augmenting/reducing has been proposed to index the "tuning" properties of a cortical gating mechanism regulating sensory input in the visual modality (see Buchsbaum, 1976, 1978). In visual augmenting, the amplitudes of the early sensory ERP components increase as photic intensity increases. In visual reducing, component amplitude either remains constant or actually decreases as photic intensity increases. In normal individuals, augmenting is held to be associated with a visual system tuned to "seek out" increases in stimulus intensity, while reducing is held to be associated with a "protectively tuned" visual system that attempts to shut out increased stimulation. The authors are aware of no previous study that has investigated augmeting/reducing in autistic children.

METHOD

The present study was conducted in conjunction with the multicenter collaborative project investigating the effects of fenfluramine on autism. The ERP procedure reported in the present study was one aspect of a more extended study protocol and was unique to investigators at the University of Texas Medical Branch. The autistic ERP data reported in this paper were collected during the placebo phase of the fenfluramine study. Effects of fenfluramine on the ERPs of autistics is reported elsewhere (Pritchard, Raz, & August, in press).

Subjects

Five male autistic children (range 6–14 years, mean 10) participated in the study. A sixth child, age 4, was dropped from the study owing to excessive ERP artifact. Each child received an extensive evaluation prior to the study, which included a review of developmental history, psychological evaluation, behavioral observations, and a neuropsychiatric interview. These data were rated by four diagnosticians who were blind to the subject's identities and clinical diagnoses. The diagnosis of autism was based on the criteria of the Definition of Autism of the National Society for Autistic Children (Ritvo & Freeman, 1977) and the DSM-III (American Psychiatric Association, 1980). Complete agreement among the four diagnosticians was required. None of the patients had a history of seizures or gross neurological deficit, and none had received psychotropic or other related medications for 6 months. The mean nonverbal IQ for the autistic subjects was 70 (range

40–102) and the mean verbal IQ was 65 (range 30–88). The parents of each subject were provided with a thorough description of the research protocol, including any potential risks to the child. Informed consent was received in each case. While ERPs were being recorded from the autistic subjects, at least one parent was present throughout the procedure to encourage compliance.

Five control subjects (1 normal and 4 with a DSM-III diagnosis of conduct disorder) were recruited for comparison purposes. These controls were matched for sex and chronological age. Previous research has indicated that conduct-disordered boys do not differ from normals for a variety of ERP measures (see Satterfield & Schell, 1984).

Recordings

Control of the experiment was effected by a Masscomp MC500 computer. Recordings of the EEG were made from the midline frontal (Fz), midline central, or vertex (Cz), and midline parietal (Pz) electrode loci of the international 10-20 system. These active electrodes were referred to the right mastoid, a common reference for recording ERPs (Vaughan, 1974). Subjects were grounded via the forehead, and the electrooculogram (EOG) was monitored from electrodes placed above and to the outside of the left eye. All electrode impedances were less than 5 kohms. On each trial, the EEG and EOG were amplified by a Model EEG-4221 Nihon Kohden polygraph having a 5-second time constant and a high-frequency cutoff of 35 Hz (30% attenuation). The EEG and EOG were digitized once every 4 ms for a 1.1-sec period that began 100msec prior to stimulus presentation.

Trials manifesting either EEG or EOG deflections exceeding 100 μu were excluded from further analysis. For the remaining trials, positive correlations with evoked EOG activity was statistically removed prior to off-line averaging. This was done on a trial-by-trial basis by first computing the correlation between the 275 digitized amplitude measures (1 every 4 msec) of evoked EEG activity available for a given trial and the 275 digitized amplitude measures of that EEG segment's corresponding evoked EOG segment. If this correlation was positive, a regression line was plotted through that trial's EEG/EOG amplitude scatter plot. The regression line, along with the amplitude scatter plot around it, was then rotated so that the regression line had a slope of zero, thereby reducing the EEG/EOG correlation for that trial to zero.

Stimulus and Task Parameters

All stimuli employed in the experiment were 10-microsecond light flashes generated by a Grass Model PS2 photostimulator. Each subject was seated in a reclining chair in a darkened room and wore a pair of headphones that allowed the masking of extraneous sounds by continuous white noise. Flashes were presented to each subject in a white Ganzfeld consisting of a 40.5-cm-diameter sphere having a circular 24-cm hole in one side. The interior of the sphere was painted flat white, and the viewing hole was positioned approximately 4 cm from the subject's face. At the apex of the sphere was the Grass photostimulator bulb.

The experiment was divided into three runs of trials, with a 2-minute rest between runs. Each run consisted of a series of 81 flashes, with a 7-sec interflash interval to allow full recovery from the previous flash. A constant interflash interval was employed for technical reasons related to the amount of computer random memory available for control of the experiment. Subjects were instructed to keep their eyes closed in a relaxed manner while flashes were being presented. This was done to minimize EOG artifact, a ubiquitous problem in visual augmenting/reducing research (see Iacono, Gabbay, & Lykken, 1982). All flashes, regardless of intensity, were clearly perceivable with the eyes closed.

Augmenting/reducing data were collected during the first run. Subjects were presented with flashes of three different intensities occurring in a random order, 27 flashes per intensity. The intensities corresponded to settings 1, 4, and 8 on the Grass photostimulator.[3] Subjects were instructed to focus their attention on the flashes, but otherwise viewing during this run was passive.

Oddball paradigm P300 data were collected during the second and third runs. On one of these runs, bright flashes (intensity setting 8) were designated as targets, and dim flashes (intensity setting 1) were designated as nontargets. On the other run, the intensity–target relationship was reversed. The order of the intensity–target pairings was counterbalanced across subjects. For each oddball run, 21 of the 81 flashes were targets, and subjects were told to keep a running count of the target flashes in their heads. All control subjects attempted to count the flashes. All autistic subjects verbally indicated that they

[3]For intensity setting 8, the central axis of the light beam produced by the PS2 bulb is about 750,000 candlepower (Instruction Manual for Model PS2 and PS3 Photostimulators; Grass Instruments, Quincy, Massachusetts, 1970); the intensities of settings 4 and 1 are 375,000 and 93,750 candlepower, respectively.

understood the count instructions, but only three of them consistently attempted to comply.

RESULTS

Behavior

For the three autistic subjects that attempted to comply with the "count" instructions of the oddball paradigm, performance did not differ significantly from controls.

N100 Augmenting/Reducing

As is customary (Buchsbaum, 1978), the augmenting/reducing data were analyzed at the Cz electrode site. Separate averages were obtained for each subject for each of the three intensity levels. Measurements of N100 amplitudes were made peak to peak; that is, N100 amplitude was taken as the distance in μv separating the peak of the N100 wave and the peak of the preceding P100 wave. This represents a common method of measuring N100 (Buchsbaum, 1978). N100 was defined as the largest negative deflection in the record between 100 and 200 msec. P100 was defined as the most prominent positive deflection between 50 and 150 msec preceding N100. N100 amplitude measurements for a given subject were made blindly with respect to that subject's clinical status.

Overall N100 amplitude did not differ significantly between autistics and controls. Autistic subjects did tend to be N100 augmenters to a significantly greater degree than controls. A one-way within-subject analysis of variance (ANOVA) performed on the N100 data of the autistic subjects (drug condition $\times$ stimulus intensity) revealed a significant effect of stimulus intensity, with N100 amplitude getting larger as stimulus intensity increased ($F(2, 8) = 5.42, p < .05$). In contrast, stimulus intensity did not significantly affect N100 amplitude in control subjects.

Oddball Paradigm P300

P300 data were analyzed at all three electrode sites. Separate averages were obtained for each intensity by probability by scalp locus combination. Measurements of P300 amplitude were made baseline to peak, with baseline defined as the average of the 100-msec epoch immediately preceding flash onset. P300 was defined as the largest positive deflection in the record past 280 msec that was positive-going at all three electrode sites. A clear P300

peak was visible in all the oddball records. P300 amplitude measurements for a given subject were made blindly with repsect to that subject's clinical status.

The P300 of both autistics and controls was similar in form, manifesting the "classic" pattern of being parietally maximal and frontally minimal (see Figures 1, 2, and 3). Adult subjects run in the same setting had shown a significantly larger P300 to the low probability target flashes than to the high probability nontarget flashes (Pritchard et al., 1985). However, stimulus probability did not have a significant effect on P300 amplitude for either the

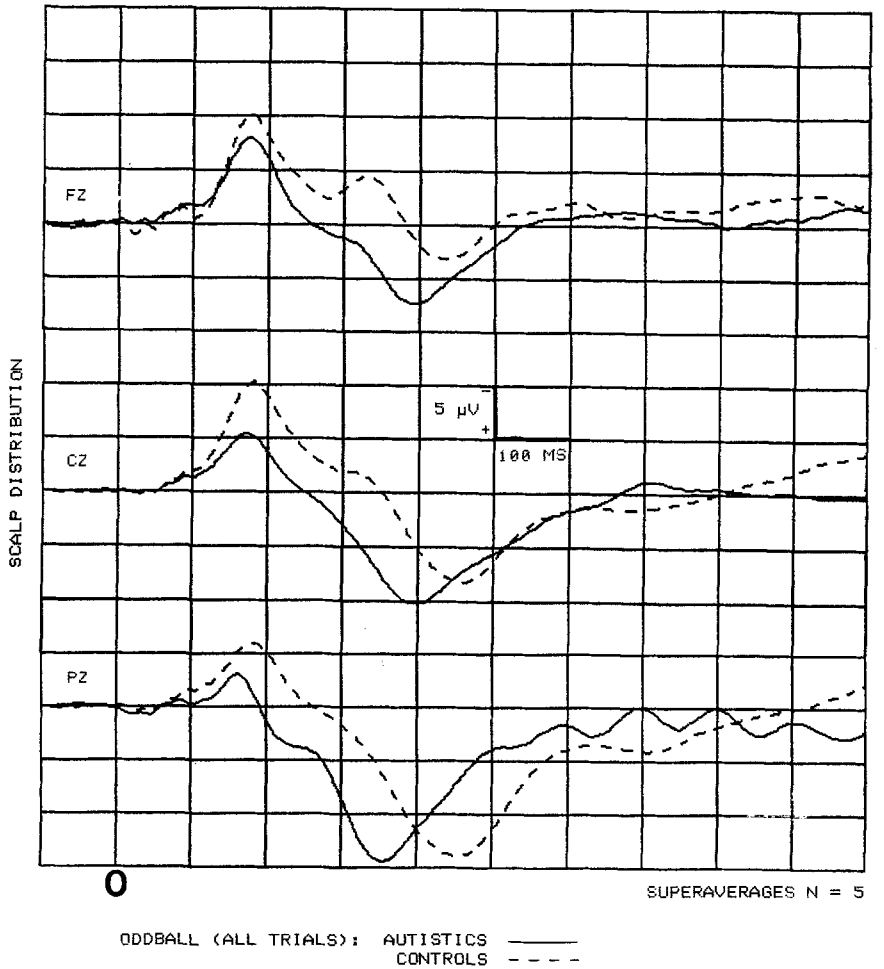

Fig. 1. Oddball paradigm P300 waves (averaged across levels of probability) at all three electrode sites, autistics versus controls. Apparent differences in amplitude (autistic P300 > control P300) did not reach statistical significance (0 indicates flash onset).

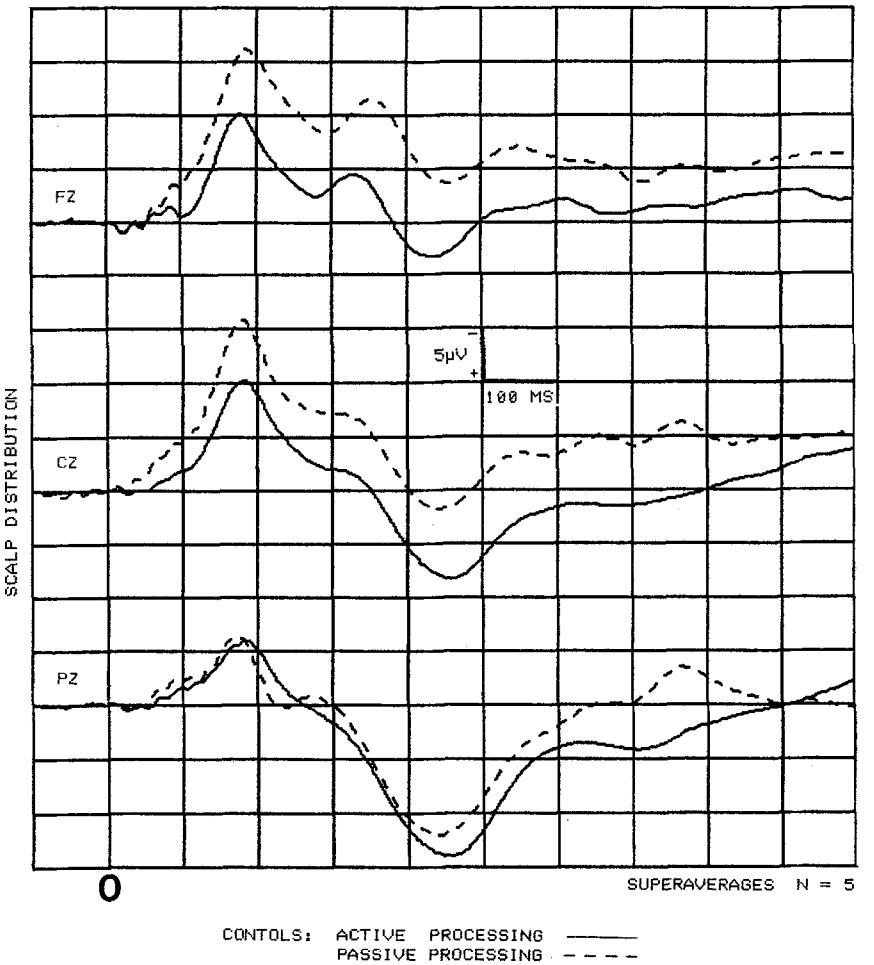

Fig. 2. Active processing (oddball paradigm having a task) versus passive processing (augmenting/reducing paradigm having no task) P300 waves for control subjects (0 indicates flash onset). P300 was significantly smaller in the passive (no-task) condition.

autistic or the control subjects. This unexpected result may have been a function of the long interstimulus interval employed (see below). Further, the overall amplitude of the oddball paradigm P300 did not differ significantly between autistics and controls (see Figure 1). This result is in harmony with the results discussed earlier indicating that target P300 tends to be smaller in autistics relative to controls in the auditory but not the visual modality.

One interesting P300 difference that did emerge between autistics and controls related to the difference between the P300 wave evoked during active processing (counting the infrequent targets) in the oddball paradigm ver-

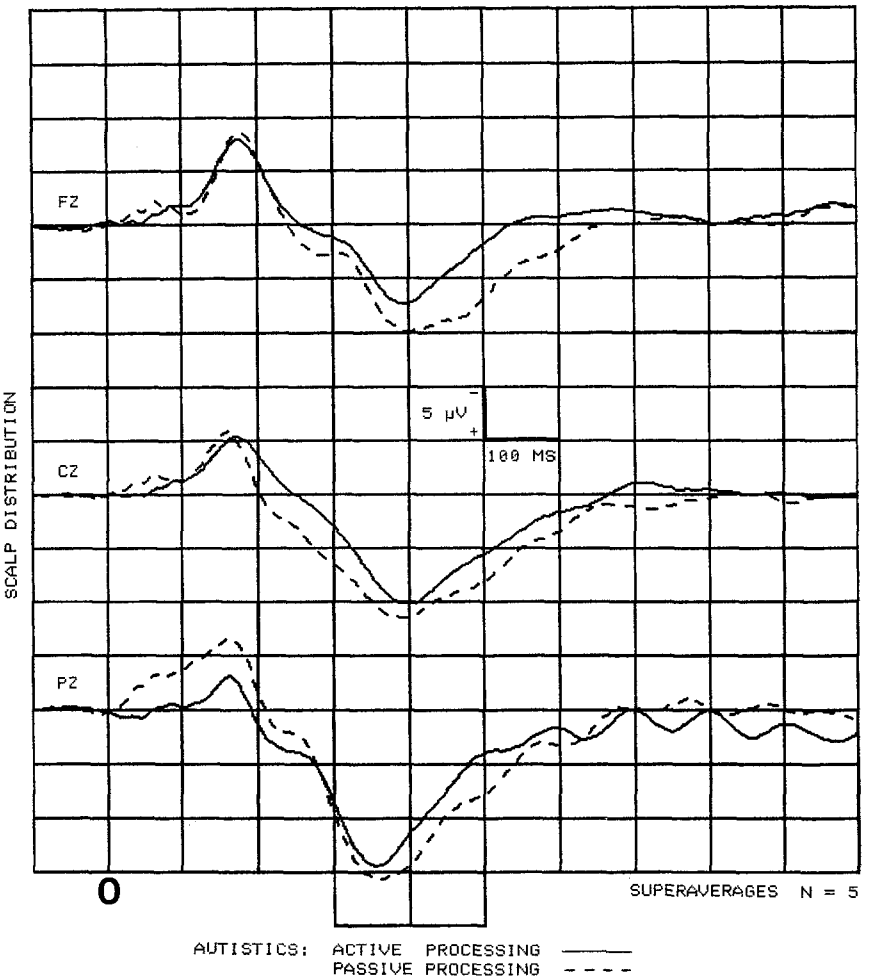

Fig. 3. Active processing (oddball paradigm having a task) versus passive processing (augmenting/reducing paradigm having no task) P300 waves for autistic subjects (0 indicates flash onset). P300 did not differ significantly as a function of active (task) versus passive (no-task) conditions.

sus passive viewing in the no-task augmenting/reducing paradigm. For the control children, the expected pattern of a significantly smaller P300 under no-task conditions can be seen in Figure 2. In contrast, P300 amplitude did not differ significantly as a function of task versus no-task conditions, as illustrated in Figure 3. Separate two-way within-subjects ANOVAs (scalp locus $\times$ task/no-task averaged across levels of stimulus probability) were performed on the P300 amplitude data of both controls and autistics. A significant main effect of scalp locus was obtained for both groups (controls: $F(2, 8) = 8.44, p < .025$; autistics: $F(2, 8) = 4.06, p = .06$), verifying

the parietally maximum scalp distribution pattern evident in the figures. The ANOVA on the control subjects' P300 data also revealed a significant task versus no-task main effect ($F(1, 4) = 12.21$, $p = .025$), verifying the difference between the task and no-task conditions evident in Figure 2. In contrast, the P300 of the autistic subjects did not differ significantly as a function of task versus no-task (see Figure 3). In essence, all stimuli presented in the visual modality seemed to evoke a uniformly large P300 in autistic children.

DISCUSSION

The results of the present study must be interpreted with caution because of the small number of subjects involved, as well as the rather broad range of the subjects' ages. Moreover, the control group employed might more properly be labeled a "comparison" group because of its mixed nature (although, as mentioned above, others have reported no significant ERP differences between conduct-disordered children and normals).

Taken as a whole, however, the results of the present investigation are consistent with the notion that autistic children may experience a degree of overload from stimulation in the visual modality. The response of the visual system of autistic children to increases in stimulus intensity was greater than controls, as evidenced by significant N100 augmenting. In normal subjects, augmeting is associated with a behavioral pattern of extroversion, impulsiveness, and sensation seeking (see Barratt, Pritchard, Faulk, & Brandt, 1985; Pritchard, 1986). The augmenting pattern found in autistics thus suggests a conflict between their behavioral pattern of extreme introversion and a sensory system that fails to gate out increases in stimulus intensity. Further, all visual stimuli, regardless of the appropriate cognitive context in which they are presented (i.e., task versus no-task), appeared to engage an equally large P300 wave in autistics, indicating a uniformly large investment of attentional resources of a perceptual nature (see Pritchard, 1981).

This finding of no difference in P300 amplitude between task and no-task conditions in autistic subjects contrasts with that obtained by Courchesne et al. (1985). Courchesne et al. found that visual P300 increased in amplitude for both autistics and controls in going from a no-task to a reaction time version of the oddball paradigm. It should be noted, however, that controls in the Courchesne et al. study showed nearly a fourfold increase, versus only a twofold increase for autistics. This difference between the present results and those of Courchesne et al. may be due to factors such as differences in the age of the subjects (the mean age of the Courchesne et al. subjects was 16.7 versus 10.0 for the present investigation), the ISIs employed (1.7 versus 7 sec), or the tasks (count versus reaction time button press, the latter being an easier task that is perhaps more appropriate for autistic subjects,

as evidenced by the inability of two of the five autistic subjects in the present investigation to comply with the count instructions).

The lack of a significant effect of stimulus probability on P300 amplitude in both the autistic and control groups is not necessarily surprising, given the relatively long interstimulus interval (ISI) employed (7 sec). Recent evidence (Heffley, unpublished, cited by Donchin & Bashore, in press) indicates that at long ISIs, all stimuli tend to invoke a uniformly large P300. In effect, all stimuli at such long ISIs may be treated as targets "by default." Younger subjects may be particularly sensitive to this effect.

The P300 data of the present study, along with those of previous studies employing visual versions of the oddball paradigm (Courchesne et al., 1985; Novick et al., 1979), clearly indicate that the P300 of autistic subjects is not *necessarily* attenuated relative to controls. Again, previous studies reporting significantly attenuated P300s in autistics have all employed auditory stimuli. This raises the possibility that autistics show a distinctive difference in the way attentional resources are engaged by visual versus auditory stimulation. In autistic children, the system of limited-capacity perceptual information-processing resources indexed by P300 may thus be engaged fairly normally by visual stimuli, or even inappropriately overengaged in no-task situations if the rate of stimulus information delivery is relatively slow (as was the case in the present study). Auditory information, on the other hand, appears to underengage this system of limited-capacity perceptual resources.

This autistic pattern of modality differences contrasts not only with normal children but with schizophrenic children as well. Although the overall amplitude of P300 in schizophrenic children is attenuated relative to normal controls, the two groups appear to show comparable P300 responses across the visual and auditory modalities (Saitoh et al., 1984; Strandburg, Marsh, Brown, Asarnow, & Guthrie, 1984; see Pritchard, 1986, for a review). The apparent modality difference in P300 response found in autistic children has potential implications for areas such as education. For example, visual methods of instruction may prove to be more efficacious than auditory methods of instruction, and vice versa, depending on the circumstances involved.

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