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Pathophysiologic Findings in Nonretarded Autism and Receptive Developmental Language Disorder[1]

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In nonretarded autistic, receptive developmental language disordered, and normal subject groups, we recorded in auditory and visual target detection tasks two neurophysiological components of the event-related brain potential, Nc and P3b. Existent research shows that, in normals, Nc and P3b appear early in development, are associated with attention and memory processes, and are endogenous which means that they are triggered by internal, consciously initiated attentional and cognitive mechanisms and that they can be triggered even by the omission *of sensory stimulation so long as it has meaning or importance for the subject. In this report, Nc and P3b were recorded in response to auditory and visual stimulation and to the omission of auditory and visual stimulation. Consistent with the hypothesis that nonretarded autism involves abnormal attentional and cognitive responses to important information, P3b was found to be smaller than normal and Nc was small and often absent in the nonretarded autistic group even under the condition when no auditory language or sensory processing was required. Receptive developmental language disorder has been linked with difficulties in processing sequences of auditory stimuli, and in this study P3b was found to be somewhat enlarged in this group even under the conditions when P3b*

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was elicited by stimuli separated by 1 sec and also when P3b was elicited by the omission of stimulation.

INTRODUCTION

Infantile autism and receptive developmental language disorder (or "receptive developmental dysphasia") are disorders present early in development. Autism is a pervasive developmental disorder whose core symptom is social maldevelopment and whose associated clinical symptoms include delayed and impaired language and cognitive development (Cohen, Caparulo, & Shaywitz, 1976; DeMyer, Hintgen, & Jackson, 1981; Kanner, 1943; Lincoln, Courchesne, Kilman, Elmasian, & Allen, 1988; Rutter, 1978a, 1978b). Receptive developmental language disorder (R-DLD) is a disorder of language development (Cohen et al., 1976; Rutter, 1978b; Tallal, 1985). The language disorder in autism is qualitatively different from that in R-DLD. In autism, the pragmatic foundations of language are impaired, but in R-DLD they are generally intact. Unlike those with R-DLD, autistic individuals demonstrate deficits in reciprocal interaction, imitation, the use of gesture for communicative intent, representational play, and prosody; they may also have pronominal confusion and atypical word usage.

The neurophysiological bases for infantile autism have been elusive, and no distinctive neurophysiological pattern characteristic of infantile autism has been identified. The same has been true of R-DLD. It is generally assumed that these two disorders result from distinct and different neural pathophysiologies since the cardinal symptom in autism is a severe impairment of social development, whereas the cardinal symptom in R-DLD is an impairment in the development of comprehension and expression of language (Cohen et al., 1976; Kanner, 1943; Rutter, 1978b; Tallal, 1985).

A remarkable range of neurophysiological and anatomical explanations for infantile autism have been proposed (e.g., Cohen et al., 1976; Courchesne, 1987; Damasio & Maurer, 1978; DeLong, 1978; Ornitz, 1985; Rimland, 1964). Some models have placed emphasis on disorder in brainstem systems affecting arousal, orienting, and attention and have implicated catecholamine pathways and the reticular activating system (RAS) (Cohen et al., 1976; Courchesne, 1987; Ornitz & Ritvo, 1968; Rimland, 1964). Other models and suggestions have placed emphasis on limbic structures, particularly those mediating memory such as the hippocampus (DeLong, 1978). Finally, models have placed special emphasis on dysfunction in portions of frontal cortex, limbic system, and basal ganglia consequent to abnormalities in dopaminergic pathways (e.g., Damasio and Maurer, 1978).

Recent theoretical considerations and experimental findings have raised the possibility of links between two neurophysiological responses and sever-

al of the systems that have been implicated in infantile autism. The Nc response in the event-related brain potential (ERP) has been suggested to reflect neural activity in frontal and central cortex that is triggered by input from the RAS (Courchesne, 1987; Courchesne, Elmasian, & Yeung-Courchesne, 1987). The auditory P3b response is abolished by lesions of the posterior portion of the superior temporal gyrus (Knight, Scabini, Woods, & Clayworth, submitted); such lesions can also produce Wernicke's aphasia (Benson, 1985).

Nc and P3b are endogenous responses in the ERP: they represent neurophysiological activities that are generated by purely internal, consciously initiated attentional and cognitive mechanisms, and can be triggered by events that are attention getting or important to the person being recorded, even if the event is the *omission* of an expected stimulus (Courchesne, Elmasian, et al., 1987; Pritchard, 1981; Sutton & Ruchkin, 1984; Sutton, Tueting, Zubin, & John, 1967). That is to say, a purely endogenous component does not require the presence of a stimulus to be elicited. Nc is the earliest endogenous component to appear during human brain development, and it is elicitable from humans of all ages from infancy through young adulthood (Courchesne, 1977, 1978, 1983; Courchesne, Ganz, & Norcia, 1981; Holcomb, Ackerman, & Dykman, 1985, 1986; Karrer & Ackles, 1987; Kok & Rooijakkers, 1985; review: Courchesne, Elmasian, et al., 1987). P3b emerges during the third and fourth years of life, and is found throughout the remainder of the human life-span (Courchesne, 1977, 1978; Friedman, Brown, Vaughan, & Erlenmeyer-Kimling, 1984; Mullis, Holcomb, Diner, & Dykman, 1985; review:Courchesne, in press). Nc is a negative electrical potential which achieves its highest amplitude over frontal scalp, and P3b is a positive electrical potential with its highest amplitude over parietal scalp (review: Courchesne, Elmasian, et al., 1987).

When a subject is required to pay special attention to a particular type of event—a target event—in a series of stimuli, then it evokes both an Nc and P3b response whether the target event is the occurrence of a particular stimulus or the omission of expected stimulation. Targets that are stimulus omissions do not, of course, evoke sensory physiological responses and so evoke only endogenous responses such as Nc and P3b. Thus, by recording Nc and P3b responses to the occurrence of a target stimulus (termed here *target-present* event) and to targets which are stimulus omissions (*target-omit* events), it is possible to evaluate these Nc and P3b attention-related physiological responses disentangled from sensory physiological responses.

If attentional dysfunction in infantile autism is not solely dependent upon or the direct consequence of abnormal sensory physiological activity, then Nc and P3b in autistic subjects should be similarly abnormal in response to target-present and target-omit events. A hint that this may be so comes from Novick, Kurtzberg, and Vaughan (1979) who recorded target-omit P3b

responses in three autistic subjects and found that P3b was small and often absent; Nc was not studied. The small sample and lack of a comparison of behavioral and P3b responses under target-present task conditions in their study encourage further and fuller studies.

The ERP responses in our contrast patient group, R-DLD, should be quite different from those in the autism group. Dysfunction in R-DLD has been attributed either to abnormalities in language mechanisms or to an impaired ability to perceive the temporal sequence of rapidly presented auditory stimuli (i.e., when interstimulus intervals are shorter than 0.5 sec) (review: Tallal, 1985). Based on either of these two alternative views of dysphasia, one would *not* predict Nc and P3b abnormalities in the following experiment because (a) interstimulus intervals are long (1 sec) and (b) simple, nonlinguistic target stimuli and target-omit events (which do not engage auditory sensory processing systems) are used to elicit Nc and P3b.

In the present study, Nc and P3b were elicited by target-present events and by target-omit events in nonretarded autistic and R-DLD subjects. In many ERP studies of autism, researchers have failed to controlled for nonspecific behavioral and state differences between autistic and control groups (e.g., Nakamura, Toshima, & Takemura, 1986), and, consequently, the ERP data on P3b are not interpretable (see review: Courchesne, 1987). In the present study, all subjects were required to respond with a button press as quickly and accurately as possible to each and every target event. All behavioral responses (correct and incorrect) were recorded, and all ERP responses were sorted according to response accuracy.

METHODS

Subjects

The nonretarded autistic subjects met the full criteria for Pervasive Developemental Disorder-Early Onset: Infantile Autism as defined by DSM III (American Psychiatric Association, 1980). These criteria include (a) onset < 30 months, (b) an extreme lack of social responsiveness, (c) delayed language development, (d) deviant language development, (e) atypical behaviors and responsiveness to the environment, and (f) a lack of hallucinations or delusions. Autism was the only diagnosis for these individuals. None had other forms of neurological or physical disorder. All of the parents of these autistic subjects reported that they were first concerned about their child's abnormal development by the time their child was 24 months. In addition, in each case the diagnosis of autism had been formally made by a physician, psychologist, or specialized child development center prior to the child's 6th year of life. For example, one subject was described as appearing "deaf, blind, and ignoring people" during his first 24 months of life. He was first diag-

nosed autistic at 30 months, and this diagnosis was confirmed by an experienced child psychiatrist and state agency serving developmentally disabled individuals. Another parent described their child as "bright," but "not communicating" at 24 months of age (see further description in Courchesne, Hesselink, Jernigan, & Yeung-Courchesne, 1987). This child was evaluated at 3 years of age at John Hopkins by a child psychiatrist who worked with Leo Kanner. Another parent described their child as "very placid" during the first and second year of life. This child was diagnosed by a national expert in autism at UCLA. A fourth subject in our study was not talking spontaneously at 24 months, but then suddenly began to read spontaneously at 25 months of age. This child was also evaluated and diagnosed by a distinguished team at UCLA prior to his 4th birthday.

The R-DLD subjects met the full criteria for Developmental Language Disorder, Receptive Type, as defined by DSM-III (APA, 1980). These criteria include (a) impairment in the ability to develop comprehension (decoding) and vocal expression (encoding) of language; and (b) not due to hearing impairment, trauma, mental retardation, or Childhood Onset Pervasive Developmental Disorder. In addition, each R-DLD subject in this study had (a) a *documented* history of an early onset of abnormal language development (little or no expressive speech by 4 years of age); (b) normal oral-motor functioning; (c) evidence of continuous language impairment up to the present time, including (i) current scores on tests of receptive language and receptive vocabulary (e.g., Peabody Picture Vocabulary Test-Revised) below normal, and (ii) consistent history of and current enrollment in special education classes for the learning and language impaired.

After being identified, an autistic individual was included if his or her Wechsler Performance IQ was 70 or greater. After being identified, an R-DLD person was included in this study if he or she had a Wechsler Performance IQ of 70 or greater *and* a Wechsler Verbal IQ 1 standard deviation or more below the Performance IQ. The mean Performance IQ minus Verbal IQ for the R-DLDs selected for this study was 27 IQ points (range 15 to 37 IQ points).

Autistic subjects and R-DLD subjects selected for these experiments were also administered language tests from which a "language quotient" was derived. Although the language tests given to each group differed, the derived language quotients provide a means of qualitatively comparing the two groups to each other. The autistic group was administered the Test of Adolescent Language Development; a language quotient for each autistic subject was directly calculated from the scores on this test. The R-DLD subjects were administered the Peabody Picture Vocabulary Test-R (PPVT-R), subtests from the Detroit Tests of Learning Aptitude, and the Clinical Evaluation of Language Functioning (CELF). "Language age" scores on each test was calculated. In order to derive an "average language age score," we took the

sum of the language age scores from the PPVT-R, Detroit, and CELF, and divided that sum by three. This average language age score was then divided by the individual's chronological age. This resulted in a ratio language quotient for each R-DLD subject.

In the following experiments, 11 nonretarded autistic subjects, 9 R-DLD subjects, and 16 normal subjects were studied.[3] All subjects were highly cooperative adolescents or young adults. Chronological ages were normal subjects = 16.9 ±1.9 years, R-DLD subjects = 15.3 ± 1.3 years, and autistic subjects = 19.7 ± 3.2 years.

IQs were based on Wechsler Intelligence Test scores. The mean Verbal and Performance IQ was 78 and 90 for the autistic group, 74 and 101 for the R-DLD group, and 108 and 110 for the normal group. Autistic subjects had a mean language quotient of 65. R-DLD subjects had a mean language quotient of 67 (see above description of the derivation of this quotient); the range of their overall language age minus chronological age was −4 to −7.3 years; and their mean PPVT-R score was 70 (range 45–79).

Procedures

The nature and possible consequences of the study were fully explained to all subjects and their parents or legal guardians, and informed consent was obtained.

ERPs were recorded from Oz, Pz, Cz, Fz, Fp2+ (an electrode placed midway between Fp2 and F8), and LoE (below the right eye); reference was the right mastoid. EEG band pass was 0.15 and 100 cycles/sec. Trials with eye blinks, eye movements, or excessive muscle artifact were detected and excluded by computer algorithms. ERP measurements were relative to a baseline defined as 200 msec of the average pre-event EEG. P3b peaks were designated as the maximum positive peak at Pz between 280 and 420 msec for auditory events and 360 and 550 for visual ones. Nc was measured at Fz, Fp2+, and LoE; the Nc measure was an area relative to the baseline between 250 msec and 650 msec for auditory conditions and between 300 and 700 msec for visual ones.

During ERP recording subjects attended to sequences of 50-msec stimuli presented every 1.05 sec. Within a given sequence, 90% of the events were identical nontarget stimuli and 10% were target events. ERPs elicited by every target and nontarget event were recorded. Subjects were instructed to press a button whenever they detected a target event. There were four types of experimental conditions (a) auditory/target-present, (b) auditory/target-omit,

[3]We do not report the data from an additional three autistic and three R-DLD subjects because their ERP data were contaminated by excessive muscle and eye blink artifact.

(c) visual/target-present, and (d) visual/target-omit. In the target-present conditions, a target event was a stimulus different from the ongoing nontarget stimuli in a stimulus sequence. For example, a target event would be a red square in sequences of blue nontarget squares. In the target-omit conditions, a target event was simply the omission of a stimulus so that the interstimulus interval between nontargets was 2.05 sec instead of 1 sec.

There were two stimuli used in the visual conditions: (a) blue squares and (b) red squares, each subtending 2° of visual angle. To control for stimulus- bound factors, we counterbalanced subjects and stimuli in the following manner: For some subjects, the blue square was the nontarget stimulus and the red square was used for the target-present event. For others, the nontarget and target colors were the reverse. Similarly, two stimuli were used in auditory conditions: (a) a 1 kHz and (b) a 2 kHz 70 dB SPL triangular-wave sound presented binaurally. For some subjects, the 1-kHz sound was the nontarget and the 2 kHz the target-present. For the others, the nontarget and target sounds were the reverse.[4]

RESULTS

All subjects were highly cooperative and quite able to perform the required task of pressing a button with each target detection. There were no statistically significant ($p < .05$) differences in reaction time (Table I) and in the percentage of correctly detected targets between autistic, R-DLD, and normal subjects. These results indicate that subjects understood the task requirements, were able to perceive the stimuli, and were able to select and rapidly execute simple motor actions appropriate for dealing with the information presented to them.

Although the three subject groups displayed similar overt behavior, their nervous systems functioned quite differently. The three groups generated Nc and P3b responses that were quite different from each other. Figures 1 and 2 contrast the ERP responses of autistic, R-DLD, and normal groups.

In normals, our procedure produced the endogenous components Nc and P3b in normals, as predicted by the literature (normal ERPs are dotted lines). Figures 1 and 2 also show that, in normal subjects, auditory Nc and P3b were similar to visual Nc and P3b. Nc was largest at electrode sites over frontal scalp, and P3b was largest over parietal and occipital scalp.

[4]Since the number of autistic and dysphasic subjects was not an exact multiple of four, it was not possible to precisely counterbalance the assignment of conditions and stimuli across subjects. However, to the extent possible with the available subjects, approximate counterbalancing was done, and there is no reason to beleive that the slight differences in assignments would affect the outcome of the data (e.g., that the auditory target-omit Nc or P3b would be affected by whether the nontargets were 1 kHz or 2 kHz).

Table I. Nc, P3b, and Reaction Time Means and Standard Deviations

Variable		Autistic	Normal	R-DLD
Nc area at Fp2+ (μV/msec)				
Target-omit	Auditory	+ 4.6 ± 4.4[a]	−10.9 ± 11.4	− 8.1 ± 15.3
	Visual	+ 2.1 ± 6.5[a]	− 6.3 ± 7.1	− 3.5 ± 13.3
Target-present	Auditory	+ 7.3 ± 9.9[a]	−13.3 ± 15.2	−10.8 ± 15.8
	Visual	+ 3.6 ± 6.5[a]	−11.6 ± 16.4	− 9.3 ± 19.5
P3b amplitude at Pz (μV)				
Target-omit	Auditory	+ 7.1 ± 4.0[a]	+11.2 ± 6.7	+17.7 ± 7.2[a]
	Visual	+ 9.0 ± 6.6	+11.6 ± 5.0	+15.2 ± 8.6
Target-present	Auditory	+11.2 ± 6.0[a]	+19.7 ± 7.5	+29.8 ± 9.0[a]
	Visual	+16.4 ± 7.7	+20.8 ± 9.0	+25.3 ± 7.2
Reaction time (msec)				
Target-omit	Auditory	477 ± 116	489 ± 93	502 ± 97
	Visual	525 ± 108	545 ± 70	571 ± 82
Target-present	Auditory	360 ± 55	393 ± 78	392 ± 79
	Visual	434 ± 67	441 ± 58	484 ± 81

[a] $p < .02$.

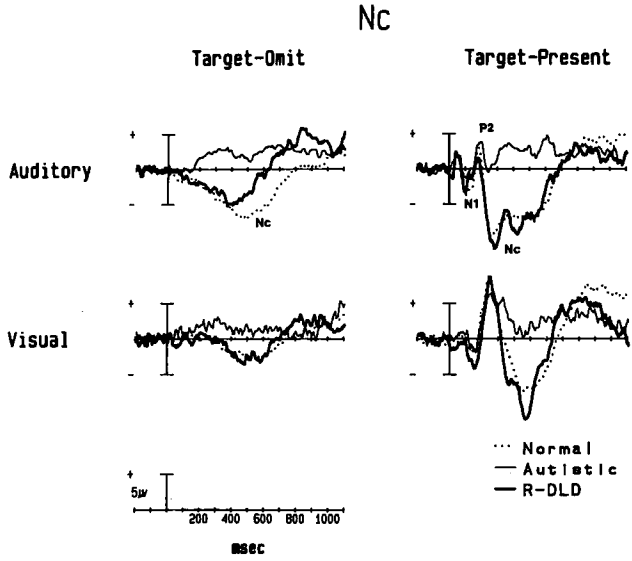

Fig. 1. Aberrant Nc in autistic subjects contrasted with normal Nc in R-DLD and normal subjects. Nc elicited by target/omit and target/present events in auditory and visual stimulus series. Nc responses are the average response of 8 autistic subjects, 9 R-DLD subjects, and 16 normal subjects. Scalp electrode site showing Nc is midway between Fp2 and F8, located over frontal scalp. In addition to Nc, target/present events elicited N1 and P2 components—they are "exogenous" components that must be elicited by a physical stimulus and cannot be elicited by an omitted event.

As shown in Figure 1, in the autistic group, there was actually a *positive* potential over frontal scalp where the negative Nc potential normally resides. This positive potential was elicited whenever target events, be they auditory, visual, omit, or present, were presented (Figure 1; Table I). This stands in direct contrast to the normal response mentioned above, which is a *negative* Nc potential elicited by all target events. Figure 1 also shows that the Nc responses of the R-DLD subjects were within normal limits (Table I).

So, under these conditions, nonretarded *autistic* subjects appear to produce, over frontal scalp, neurophysiological activity that behaves in a fashion opposite to that of normal and R-DLD subjects [Nc area at Fz, Fp2+, and LoE: normal vs. autistic subjects, $F(1, 22) = 32.2, p << .001$; R-DLD vs. autistic subjects, $F(1, 15) = 7.65, p = .014$; normal vs. R-DLD dysphasic subjects, $F(1, 16) = 0.79, p = .38$].

With respect to ERPs recorded over parietal cortex, the auditory P3b showed large differences from normal in both autistic and R-DLD groups (Figure 2). In the autistic group, the auditory P3b was very much smaller than normal, but in the R-DLD group it was larger than normal (Figure 2; Table I). [P3b to auditory target events at Pz: normal vs. autistic subjects,

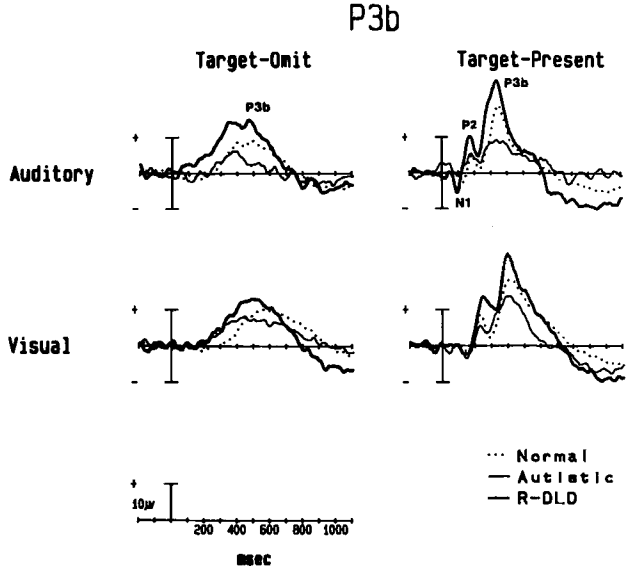

Fig. 2. Abnormally small P3b in autistic subjects and abnormally large P3b in R-DLD subjects. P3b elicited by target/omit and target/present events in auditory and visual stimulus series. P3b responses are the average response of 11 autistic subjects, 9 R-DLD subjects, and 16 normal subjects. Scalp electrode site showing P3b is Pz, located over parietal scalp. In addition to P3b, target/present events elicited N1 and P2 components—they are "exogenous" components that must be elicited by a physical stimulus and cannot be elicited by an omitted event.

$F(1, 25) = 7.31, p = .012$; R-DLD vs. autistic subjects, $F(1, 18) = 29.52$, $p << .001$; normal vs. R-DLD subjects, $F(1, 23) = 8.28, p = .0085$.]

The visual P3b was much less aberrant than the auditory P3b in both the autistic and R-DLD subject groups. Nonetheless, the visual P3b echoed the significant auditory P3b differences by showing tendency to be smaller than normal in the autistic group but larger than normal in the R-DLD group (Figure 2; Table I). [P3b to visual target events at Pz: normal vs. autistic subjects, $F(1, 18) = 6.29, p = .022$; normal vs. R-DLD subjects, $F(1, 23) = 2.14, p = .16$.]

No significant differences between groups were found in the latencies of Nc or P3b.

DISCUSSION

These Nc and P3b differences between our nonretarded autistic and R-DLD subject groups, and the differences between these two groups and the normal group, are not easily explained in terms of sensory or language dysfunction per se. Of course, this does not completely exclude the possibility that sensory or language dysfunction may also be present in these disorders. The abnormal endogenous Nc and P3b responses were elicited even in the absence of sensory and linguistic stimulation, and were of the same nature whether elicited by the presence or absence of sensory stimulation. Also, these aberrant ERP responses were evident even though our tasks did not require complex verbal understanding; demanded no complex task performance; involved no processing of complex sensory stimuli or making of subtle sensory distinctions; and did not call for language or linguistic processing.

In other words, pathological neural mechanisms in autism may be triggered even in the simplest information-processing situations, and whether or not auditory sensory processing or modulation is required. This latter conclusion is consistent with our previous reports (Courchesne, Courchesne, Hicks, & Lincoln, 1985; Grillon, Courchesne, & Akshoomoff-Haist, submitted) in which we found normal auditory brainstem and middle latency sensory ERPs in the same nonretarded autistic subjects who participated in the present study. Moreover, the abnormal P3b and Nc responses in the target-present and target-omit conditions in the autistic group are consistent with the hypothesis that attentional dysfunction in nonretarded autism is not necessarily a direct consequence of or dependent upon sensory physiological activity. Recent MRI evidence (Courchesne, Hesselink, et al., 1987; Courchesne, Yeung-Courchesne, Press, Hesselink, & Jernigan, 1988) and theoretical considerations (Courchesne, 1987) raise the possibility that

neuroanatomical abnormalities in specific regions of the cerebellum may contribute to the attentional dysfunction in autism as well as sensory modulation disturbances which have also been reported in autism.

Paradigms analogous to the auditory and visual target-present conditions have been conducted in other subjects with developmental disorders: dyslexia, attention deficit disorder (ADD), and Down syndrome (Holcomb et al., 1985, 1986; Lincoln, Courchesne, Kilman, & Galambos, 1985; Loiselle, Stamm, Maitinsky, & Whipple, 1980; Lovrich & Stamm, 1983). The pattern of abnormal ERP responses in our nonretarded autistic and R-DLD groups differ not only from each other and normals but also from each of these other developmental disorders. For instance, in nonretarded autism, (a) Nc is very much smaller than normal under these conditions, but is similar to normal in these other disorders; and (b) the amplitude of only the auditory P3b is statistically smaller than normal, but (i) in dyslexia and ADD, both auditory and visual P3b tend to be somewhat smaller, (ii) in Down syndrome, P3b amplitude is similar to normal, and (iii) in R-DLD, auditory P3b is larger than normal (see review: Courchesne & Yeung-Courchesne, 1987, for further details).

Discussion of P3b Findings

The finding that Nc and auditory P3b responses of autistic and R-DLD subjects differed strikingly from each other also agrees with previous conclusions (e.g., Cohen et al., 1976) that the pathophysiology involving auditory procesisng in one disorder must be of a quite different nature from that in the other.

Nonretarded Autistic Subjects

The abnormally small auditory P3b in autism is a robust effect. Our present results replicate and extend previous evidence in the literature (Courchesne, Kilman, Galambos, & Lincoln, 1984; Courchesne, Lincoln, Kilman, & Galambos, 1985; Dawson, Finely, Phillips, Galpert, & Lewy, 1988; Novick et al., 1979; Novick, Vaughan, Kurtzberg, & Simson, 1980). Adding our findings to that literature, abnormally small auditory P3b responses in autism have now been elicited by verbal, phonemic, nonverbal, and nonsensory (i.e., omit) target events in the auditory modality. By contrast, in analogous paradigms, visual P3b responses in autism differ little (present study) or not at all (Courchesne et al., 1985) from normal.

In clinical studies, reduced P3b amplitudes in response to targets in paradigms analogous to the present ones are typically associated with poor-

er or slower task performance. However, the nonretarded autistic subjects in the present study performed the auditory target detection tasks as accurately and rapidly as normals. Such an unexpected combination of reduced P3b amplitude in association with high performance in such auditory paradigms is found in normal adults with perfect pitch (Klein, Coles, & Donchin, 1984). Apparently, such adults do not engage and deploy attentional resources in the same fashion as normals with average pitch discrimination ability, but instead may use some automatic, pre-attention processes to successfully perform simple pitch discrimination tasks. The point here is not about perfect pitch and autism but, rather, that the autistic subjects may have been using some unusual or alternate physiological processes, as compared to the normal subjects, to detect the target events. These possibilities as well as that of limited attentional resources in autism, constitute the topic of current ERP research in autism.

Since P3b is traditionally thought to be modality nonspecific, this striking modality effect in autism is a surprise. However, this evidence that there is a dissociation between auditory P3b and visual P3b in autism can be added to other recent evidence of a dissociation which comes from studies of P3b development and intrasubject correlational evaluations of P3b. Taken together, the evidence from autism, developmental, and correlational studies calls into serious question the old notion that P3b is a unitary, modality nonspecific physiological response, and raises the possibility that auditory P3b and visual P3b may have separate neural generators (e.g., Woods & Courchesne, 1988; see discussion: Courchesne, in press). In addition to this basic ERP information, the present evidence also provides evidence that these P3b responses are distinct and independent neurophysiological phenomena from Nc, since they can occur in the absence of Nc in autistic subjects (also see Lincoln, Courchesne, & Elmasian, 1987).

Receptive Developmental Language-Disordered Subjects

This study presents the first ERP evidence regarding endogenous components in this developmental disorder. The larger than normal auditory P3b in these R-DLD subjects has not been found in any other developmental disorder (review: Courchesne & Yeung-Courchesne, 1987). The fact that this enlargement is greater for auditory than for visual is compatible with behavioral studies of R-DLD which show that although auditory and visual processing may be impaired, auditory processing is much more so than visual in older dysphasics (Tallal, Stark, Kallman, & Mellitis, 1981).

Nonetheless, at present there does not appear to be a clear means of interpreting the abnormal auditory P3b responses in our R-DLD subjects in the context of the notion that developmental language disorder involves

deficits in the perception of the temporal sequence of rapidly presented auditory stimuli. First, behavioral indices of processing difficulties in R-DLD have been suggested to be most prominent when auditory stimuli are presented rapidly (review: Tallal, 1985). In the present ERP study, however, abnormal auditory P3b responses in the R-DLD subjects occurred even though information was presented slowly (i.e., at 1-sec intervals). Second, the abnormal auditory P3b response occurred whether or not sounds were presented (i.e., auditory target-present and target-omit P3b responses). The information-processing requirements in the present ERP paradigm may invoke neurophysiological processes that differ from those invoked by the behavioral paradigms that demand the extraction of the temporal sequence of rapidly presented auditory stimuli.

The ERP data in the present study are the first evidence that autism and receptive developmental language disorder have distinct and different pathophysiologies. Replications and extension of this beginning require studying individuals who have unequivocal histories of early identification of receptive language impairment not directly explicable by medical history (e.g., tumors, neurosurgical procedures) and who have extreme language impairments side-by-side with normal nonverbal IQ. Whether our subjects represent a subgroup within the realm of receptive developmental language disorder is important to determine. Certainly, it may expected that the pathophysiology of these subjects will differ from that of those R-DLD individuals who have less impairment in receptive language ability.

Discussion of Nc Findings

In nonretarded autistic subjects, we found evidence of much reduced and often absent Nc responses to auditory and visual target events that should be attention getting. Such aberrant Nc responses to targets were not present in the R-DLD subjects, and are not present in dyslexic children, attention deficit disorder (with and without hyperactivity) children, and Down syndrome children (review: Courchesne & Yeung-Courchesne, 1987; Holcomb et al., 1985, 1986; Lincoln et al., 1985).

Nc and Nc-like components have been elicited in normal infants, children, adolescents, and adults under circumstances similar to those that trigger the reticular–thalamic–cortical activating system (RAS) (see review and discussions: Courchesne, 1987, in press). Several researchers have shown that in normal newborns, infants, children, and adults, large Nc-like negative potentials are elicited by surprising, interesting, or important pictures and sounds (Courchesne, 1977, 1978, 1983; Courchesne et al., 1981; Gullickson, 1973; Karrer & Ackles, 1987; Kurtzberg, 1985; Symmes & Eisengart, 1971). Such important, surprising, or biologically significant stimuli are also thought

to trigger the RAS. In cats, a depolarizing potential in the superficial layers of cortex begins at 100–200 msec after electrical stimulation of reticular formation, and reaches peak amplitude at about 360 msec (Inubushi, Kobayashi, Oshima, & Torii, 1978a, 1978b); such surface depolarizations might produce surface negative potentials. These onset and peak latency parameters show a noteworthy coincidence with the parameters of Nc; for example, Figure 1 shows Nc onset of about 100–200 msec and peak of about 350–450 msec in response to target/omits. Thus the question is raised as to whether Nc is associated in some way with the initial cortical depolarization triggered by the RAS, a system crucial to the activation, adjustment, and maintenance of attention and consciousness (Castaigne, Bige, Escourolle, & Masson, 1962; Facon, Steriade, & Wertheim, 1958; Hobson & Steriade, 1985; Moruzzi & Magoun, 1949; Steriade & Glenn, 1982).

The answer to this question could significantly impact our understanding of autism. Rimland (1964) was the first to propose that autism resulted from abnormality in the brainstem and thalamus. Specifically, his model implicated RAS in autism; this was one of the earliest postulations on the neurobiological substrate of autism. Since then others have also espoused the idea that autism involves disordered functioning in brainstem and thalamic systems which mediate arousal, orienting, and attention, including the reticular activating system and catecholamine pathways (Cohen et al., 1976; Courchesne, 1987; Ornitz, 1985; Ornitz & Ritvo, 1968). For instance, based on behavioral, physiological, and neuroanatomical data (Courchesne, 1987; Courchesne et al., 1987, 1988), we have recently conjectured that aberrant activity in deep cerebellar nuclei due to neuronal loss in cerebellar cortex might interfere with the normal functioning of the reticular activating system and catecholamine pathways. Since Nc is present in normal newborns, an understanding of its neural generator and the physiological systems that may interfere with its genration in autism may be a clue to the developmental origin of this devastating neural disorder.

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