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CEREBRAL CORTEX FUNCTION FOLLOWING PERIPHERAL DEAFFERENTATION

by

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INTRODUCTION

A number of visual deficits have been observed in animals reared in darkness or diffuse light. Dark-reared rats show deficits in depth perception and the discrimination of letters and geometric forms, which in many instances may be overcome with experience in a lighted environment (Michels, Bevan and Strasel 1958, Tees 1968a,b, Walk and Bond 1968). Visually restricted primates and carnivores also reveal severe retardation in the discrimination of depth, movement or geometric pattern, which following extended restriction from infancy might prove irreversible (Riesen and Aarons 1959, Riesen 1965a, Ganz and Fitch 1968, Dews and Wiesel 1970). These visual deficits show many similarities to those observed in animals deprived of visual cortex (e.g. as reported by Lashley 1931, Kluver 1941, Meyer 1963, Wetzel, Thompson, Horel and Meyer 1965, Schneider 1967).

Recently, characteristic morphological changes in visual cortex, such as alterations in dendrites and dendritic spines, as well as, cellular hypotrophy have been described as a result of light restriction in a number of mammalian species (Globus and Scheibel 1967a,b, Valverde 1967,1968, Coleman and Riesen 1968, Fifkova 1968). Furthermore, the same restriction procedures induced such neurophysiological changes in visual cortex as; a decrement in the primary negative wave of the direct cortical response, a decrement in the later negative wave of the evoked potential and the number of cortical units responding to light stimuli, increased fatiguability and unpredictability of cortical units, as well as a loss of precise receptive field definition (Wiesel and Hubel 1963b,1965a, Ganz et al., 1968, Hubel and Wiesel 1970, Zislina and Arkhipova 1970).

While anatomical and biochemical changes in the peripheral receptor and subcortical visual stations have also been found to be consequences of visual restriction in a variety of species (Brattgard 1952, Riesen 1960, Gyllensten and Malmfors 1963,1965, Rasch, Swift, Riesen and Chow 1961, Fifkova and Hassler 1969, Maletta and Timiras 1967, Wiesel and Hubel 1963a), electrophysiological changes in these structures (e.g. as reported by Zetterstrom 1956, Ganz, Fitch and Satterberg 1968, Cornwell, Sharpless and Kanor 1962, Riesen 1965, Wiesel and Hubel 1963b, Burke and Hayhow 1960, Wickelgren and Sterling 1969a,b) have been less than anticipated, and seem insufficient, to account for the severe behavioral alterations observed.

The cortical anomalies following restriction, coupled with the similarity of behavioral dysfunction following visual restriction and ablation of visual cortex (and the limited electrophysiological dysfunctions at the receptor and subcortex) suggest the behavioral deficits following restriction may reflect the altered functional capacity of the visual cortex.

The method of intracranial electrical stimulation (ICS) introduced by Loucks (1938) seems well suited to further explore the cortical dysfunctions produced by visual restriction. Mogenson (1962) reported retarded acquisition of a conditioned emotional response to ICS presented to the visual cortex of orbitally enucleated rats. Rats enucleated at infancy or maturity showed equal retardation in this task situation. However, the effects of such surgical deafferentation may differ from those of light restriction (Goodman 1932, Riesen 1966) and Mogenson's findings may have reflected the direct atrophic effects of enucleation rather than the effects of visual restriction *per se*. Furthermore, Mogenson's (1962) data failed to reveal whether these effects were limited to the primary cortical projection area, as only the visual cortex was tested. In light of changes in "extravisual" cortical areas coincident with visual restriction (Krech et al., 1963, Gyllensten et al., 1966) one might expect altered responsiveness to intracranial electrical stimulation in these areas as well. In addition, it has recently been noted that auditory deficits are induced by auditory restriction (Batkin and Ansberry 1964, Tees 1967a,b, Batkin, Groth, Watson and Ansberry 1970) which, in many respects, are similar to those resulting from ablation of auditory cortex (e.g. as reported by Diamond and Neff 1957). Assuming a fundamental similarity of sensory systems, one might expect functional changes in auditory cortex resulting from auditory restriction to approximate those in the visual cortex as a result of visual restriction.

The present study employed ICS in an attempt to explore these possibilities in animals who retained their peripheral receptors. Specifically the questions of interest were:

1. Will visual or auditory restriction affect the ability to utilize intracranial electrical stimulation of cortex as a discriminative stimulus? If so,
2. Will such influences be limited to the primary cortical projection area? And
3. Will the age at which restriction is initiated or the duration of restriction differentially affect such utilization?

LITERATURE REVIEW

Many investigators have employed sensory restriction in an attempt to determine the contributions made by early sensory experience to later sensory function. The bulk of the data is in the area of visual function; therefore, the visual modality will be stressed here. Since a variety of species (e.g. mouse, rat, rabbit, dog, cat, monkey, chimpanzee) as well as different methods (e.g. dark-rearing, diffuse-light rearing, rearing with contact occluders, lid-suturing, orbital enucleation) have been employed in the study of visual restriction, the following review will draw from a number of different species and procedures in an attempt to describe how early sensory experience affects later sensory function in the visual and auditory modalities.

Behavioral Consequences of Sensory Restriction

Many early studies attempting to compare the visual capacities of dark- and light-reared animals were conducted to resolve issues concerning the genesis of sensory capacities.

Using a jumping-stand apparatus, Lashley and Russell (1934) compared the ability of dark-reared rats with that of normally reared rats to graduate the force of their jumps to a distant stand. They concluded that the ability to judge distance developed independently of antecedent visual experience. The evidence assembled later on visual cliff performance supported this conclusion (Walk, Gibson and Tighe 1957, Nealey and Edwards 1960). While all these investigators demonstrated that the capacity for the perception of distance is present in visually naive animals, no graded tests of this capacity were administered to determine whether experience served to refine the existing mechanism. More recently such graded tests have revealed a persistent deficit in depth perception in dark-reared rats, thereby suggesting the importance of visual experience for the development of fine discriminative performance (Walk and Bond 1968). The importance of this contribution is more readily observed in visually naive cats (Walk and Gibson 1961, Ganz and Fitch 1968) and monkeys (Riesen, Ramsey and Wilson 1964) than in rats. These data taken together suggest that experience is of increasing import in the visual behavior of more advanced species.

While these investigations indicated that a perceptual deficit was present in visually restricted animals, it might appear that such factors as oculomotor maladjustment, emotional disturbances and intellectual impairments may have confounded the data. Few systematic studies have been conducted for the express purpose of eliminating these possibilities. However, investigations have shown that visually naive rats can: a) orient to a source of light b) discriminate lights of differing intensities c) discriminate between horizontal and vertical striations and d) discriminate fine differences in the orientation of rectangles (Turner 1935, Hebb 1937, Woodruff and Wickens 1951, Woodruff and Slovak 1965, Tees 1968a,b). While discriminations such as those listed above are readily acquired, form discriminations (e.g. geometric figures, letters) present great difficulties for such animals (Michels, Bevan and Strasel 1958, Tees 1968a, b). These findings make it improbable that oculomotor disturbances can explain the defects in animals restricted of vision. Furthermore, it seems that the perceptual deficits are task specific rather than based upon difficulty *per se*. This is best illustrated by two studies conducted by Tees in 1968.

In these investigations, light- and dark-reared rats were compared with respect to their ability to learn orientation-, intensity- and pattern- (N versus X) discriminations using a shock-avoidance paradigm. In the first of these investigations, no superiority of **light** over dark-reared subjects was demonstrated on the intensity discrimination (luminous flux), in contrast to an earlier study by McAllister (1955)(however McAllister may have required a luminance rather than a luminous flux discrimination). The intensity discriminations were of two levels of difficulty; "easy" (1.5 versus .01 mL.) and "hard" (1.0 versus .5 mL.). The second study revealed no differences in the ability of dark- or light-reared rats to learn a vertical-oblique orientation discrimination. However, in both of these studies light-reared animals were clearly superior to dark-reared subjects on an "N" versus "X" discrimination, despite the fact that such a discrimination was found to be easier for these animals than either the "hard" intensity discrimination or the vertical-oblique orientation discrimination. These data indicate that the visual deficits exhibited by dark-reared rats were related to specific stimulus characteristics rather than task difficulty per se. Therefore, any hypothesis which would predict poorer performance of visually naive subjects on the basis of intellectual and/or emotional impairments fails to receive any support from these studies.

It is evident that visual experience in the rat is not crucial for the discrimination of fine differences in light intensity, nor is such experience necessary for the discrimination of lines (striations) or the orientation of such lines. However, once these latter stimuli are arranged to form a figure, and configuration becomes the discriminative stimulus, an obvious performance deficit may be observed in visually restricted subjects. These findings indicate that patterned-light experience may be a necessary precondition for discriminations based upon the organizational properties of visual stimuli.

We have used the term "pattern" in this review several times and must point out that it has long been recognized that specifying just what a "pattern" or a "pattern discrimination" is, is a difficult task (Weiskrantz 1963). Although few investigators have dealt with this problem directly, Dodwell and Freedman (1968, pp 559-560) stated that,

> "...one can define a pattern discrimination largely by exclusion; it must be a visual discrimination not based on differences in brightness, brightness gradient, or position. In addition it is desirable to choose patterns that are drawn in outline, so that contour becomes the primary cue, and that are symmetrical about horizontal and vertical bisectors of the shape so that general orientation is not available as a cue... To establish that the discrimination is based on differences in pattern per se it is necessary to run some transfer tests, to show whether or not part-figure discrimination occurs, and to find out whether other stimulus parameters affect the discrimination."

Despite the difficulties encountered with this term its usefulness in expressing the idea apparent in the paragraph above, remains. Therefore, investigators will continue to use the term and we will do so here with its difficulties in mind.

Investigations with dark- or diffuse-light-reared primates have yielded findings similar to those already noted in rats. Lack of patterned-light stimulation from birth does not preclude head orientation to light passed across the retina nor does it interfere with the acquisition of light intensity discrimination, whereas pattern discrimination is significantly retarded (Riesen 1947,1958,1961,1965a, Riesen, Chow, Semmes and Nissen 1951). Riesen (1950) reported that dark-reared chimpanzees will react to changes in illumination and to slowly moving light but show no initial reactions to complex patterns of light. Senden (1932) described the arduous process involved in learning to discriminate geometric figures, following the removal of congenital cataracts in human subjects. Visual acuity and thumb-finger opposition also appear to be dependent upon patterned light stimulation in primates, although less so than visual placing and visual cliff performance (Riesen, Ramsey and Wilson 1964, Wilson and Riesen 1966, Riesen 1965a). Wilson and Riesen (1966) also reported that visual acuity was very poor in restricted monkeys early in testing, but showed a developmental course similar to that which has been reported for the normal infant monkey (Lashley and Watson 1913, Foley 1934, Mowbray and Cadell 1962).

Data derived from visually restricted cats supports the findings obtained with restricted rats and primates. While an intensity discrimination is readily learned by dark- or diffuse-light-reared cats (Riesen and Aarons 1959, Aarons, Kitsui and Riesen 1960) a pattern or movement discrimination is impaired (Riesen and Aarons 1959, Riesen 1965a, Ganz and Fitch 1968). Recently it has been shown that these disturbances are absent if such restriction is begun at maturity, and it is now apparent that there is a definite developmental period during which kittens are sensitive to the effects of visual restriction. This period begins at approximately the second month of life and declines thereafter until termination at approximately the fourth month of life (Dews and Wiesel 1970). As will be seen later in this paper, a corresponding period of sensitivity to visual restriction exists for electrophysiological changes.

Sensory restriction in infancy may have long-lasting consequences. Thus, Wolf (1943) and Gauron and Becker (1959) reported that rats undergoing short periods of visual or auditory restriction in infancy were less efficient in their responses to signals presented in the previously deprived modality. As Hunt (1961) stated "... it appears ... that a relatively brief period of receptor deprivation in infancy leaves the lowly rat with a lessened readiness to utilize information from the deprived receptor modality." Permanent behavioral deficits following early visual restriction have also been reported in cats (Wiesel and Hubel 1965b, Dews and Wiesel 1970).

Following monocular training, normal animals will readily show appropriate responses when the training stimulus is presented to the untrained eye (interocular transfer). This capacity for interocular transfer demands that the visual system process altered sensory inflow in such a manner as to allow for the same response. Some evidence has been offered which indicates that monocular rearing can limit visual defects to the deprived eye with a resulting impairment in interocular transfer.

Riesen, Kurke and Mellinger (1953) reported that patterned-light restricted cats failed to show interocular transfer when brightness (luminance) was the discriminative stimulus. The possibility that transfer was impaired due to the asymmetry of the visual environment during rearing rather than to patterned-light restriction per se seems implausible, as Riesen and Mellinger (1956) showed that stimulating both eyes simultaneously is not a necessary precondition for later interocular transfer. However, visually restricted cats will show immediate interocular transfer of intensity (luminous flux) discriminations (Riesen and Aarons 1959). It may be noted that the learning of, or interocular transfer of, an intensity discrimination does not require the presence of visual cortex (Aarons, Kitsui and Riesen 1960, Aarons, Halasz and Riesen 1963). Thus, even the extensive cortical changes (to be described later in this paper) produced by visual restriction might not be expected to affect the interocular transfer of such a discrimination. Chow and Nissen (1955) have also demonstrated that visually restricted chimpanzees will fail to transfer color, orientation or form from the trained to the untrained eye.

A recent study by Meyers and McCleary (1964) did show immediate transfer of a pattern discrimination (circle versus cross) in dark-reared cats. They suggested that earlier studies failed to show transfer due to the presence of visuo-motor deficits which were minimized by the use of a leg-flexion response in their study. However, this suggestion fails to explain why intensity discriminations may be transferred while brightness discriminations are not (in form deprived cats) when the responses involved require an integration of motor elements (as in the studies of Riesen, Kurke and Mellinger 1953 and Riesen and Aarons 1959). In addition, the findings of Dews and Wiesel (1970) are at odds with the suggestion of Meyers and McCleary (1964) as they revealed an absence of persistent visuo-motor deficits following monocular visual restriction in cats. Furthermore, Meyers and McCleary have not demonstrated convincingly that transfer was on the basis of a pattern discrimination rather than on the basis of the spatial distribution of light.

Since sensory restriction has been shown to result in retarded discrimination, one might expect sensory enrichment to facilitate such discrimination. A number of studies have indicated that animals reared with complex visual stimuli may later show enhanced discriminative performance to complex visual stimuli (Forgus 1956, 1958a,b, Gibson and Walk 1956, Gibson, Walk, Pick and Tighe 1958, Gibson, Walk and Tighe 1959, Walk, Gibson, Pick and Tighe 1958, 1959, Cool and Hake 1965, McCall and Lester (1969). It is interesting to note that multimodal experience with stimulus complexes may be most effective in facilitating pattern discriminations within the visual modality (Meir and McGee 1959, Held and Hein 1963).

Investigations have also indicated that specific visual restriction during development may produce specific visual deficits at maturity. Thus, the discrimination of hue may be dependent upon experience with this stimulus dimension under some developmental conditions (e.g. as reported by Ganz and Riesen 1962, Peterson 1962, Malott 1968).

Thus far we have been dealing almost exclusively with the visual modality. Assuming a fundamental similarity of sensory systems we might expect the development of auditory sensitivity to be dependent upon experience with auditory cues. Such an expectation receives some support from a preliminary report by Batkin and Ansberry (1964) which indicated that decreased auditory activity in rats resulted in insensitivity to sound, as well as lack of pinna-reflex development. On the basis of findings in the visual system it might be expected that the greatest deficits would occur when the animals who have been sound restricted early in life are called upon to utilize complex auditory signals. Two studies by Tees in 1967 have confirmed this expectation. In the first of these investigations it was demonstrated that rats reared under conditions of auditory restriction readily learned a frequency discrimination (4,000 cps, versus 2,000 cps) but were significantly inferior to normal animals when a pattern discrimination was required. Two pattern discrimination problems were employed: high-low-high versus low-high-low and high-high-high and low-low-low versus high-low-high (high = 4,000 cps, low = 2,000 cps). In the second study rats were raised either in an environment impoverished with respect to auditory cues, or with the addition of two hours of white noise per day. While intensity discriminations did not did not appear to be any more difficult for these two groups of animals than for normal controls, both groups were inferior to controls on a duration discrimination problem. Thus, patterned-auditory stimulation appears to play a role somewhat similar to that played by patterned-light stimulation as both make later pattern discrimination possible within their respective modalities.

Restriction-Produced Changes at Retina and Subcortex

The exclusion of vision in infancy has been shown to result in reduced retinal cholinesterase, retinal enzymes, protein and nuclear protein fractions in rodent, carnivore and primate (Brattgard 1952, Shimke 1959, Rasch, Swift, Riesen and Chow 1961, Riesen 1960, Liberman 1962). On the other hand, intense stimulation has similar effects upon some of these measures possibly due to a transient depletion of metabolic stores (e.g. as shown by Carlson 1902/3, Gomirato and Baggio 1962). Anatomical changes at the retina such as ganglion cell degeneratin collapse of the inner plexiform layer, and changes inoptic disc and nerve have also been shown to accompany visual restriction in a number of species (Chow, Riesen and Newell 1957, Weiskrantz 1958, Gyllensten and Malmfors 1963) and it has been suggested that primates, as compared to other species, are most susceptible to these effects (Riesen 1965b).

The fact that the integrity of the retina is dependent upon visual experience indicates that the perceptual deficits already described may reflect a functionally inadequate neural system. Modification of centrally located visual centers has also been found to follow visual restriction.

The earliest studies of visual restriction-produced changes in subcortical visual stations involved enucleation of the eye. These reports revealed transneuronal degeneration in the lateral geniculate body following monocular damage to, or enucleation of the eye in monkey (Minkowski 1913,1920, Le Gros Clark 1932, Le Gros Clark and Penman 1933-4, Glees and Le Gros Clark 1941, Mathews, Cowan and Powell 1960). Transneuronal changes following enucleation or damage to the eye have also been noted in mice, rabbits, rats, guinea pigs and cats (Goodman 1932, Tsang 1937, Cook, Walker and Barr 1951, McClure 1958, Hess 1957,1958,1960, Terry, Roland and Race 1962, Maraini, Carta, Frangaellis and Santori 1963, Altman and Das 1964, Gyllensten and Lindberg 1964, Miller, Heller and Moore 1969).

The choice of restriction procedure depends upon the interest of the investigator and the tasks required of the subject. Enucleation of the eye is employed only when later visual behavior is not observed. Aside from eliminating activity initiated by visual stimuli, this procedure eliminates the influence of spontaneous retinal activity upon centrally located structures, and may also produce direct degenerative changes in the next order nerve cell. Therefore, it might be expected that the effects, upon centrally located visual centers, of this procedure are not equivalent to those produced by ocular occlusion or dark-rearing. An early study by Goodman (1932) specifically investigated whether or not different restrictive methods produced different effects on optic centers in the rabbit. In this study, the methods of monocular enucleation, lid-suturing and dark-rearing were compared. After three months of such sensory restriction he found no effect of the latter two methods on the structure of the eyes, optic nerves, superior colliculi, lateral geniculate bodies or pulvinar, whereas enucleation resulted in degenerative changes in the optic tract and these primary optic centers. At this time the prevailing view of the nervous system was one excluding functional contributions to its development (Tsang 1937, Weiss 1950) and the Goodman findings were taken as further support for this position. Investigations since 1932, however, using more refined histological and microscopic techniques, as well as a number of different species, have pointed to anatomical, biochemical and electrophysiological changes (as have already been noted in retina) resulting from ocular occlusion, lid-suturing and dark-rearing which are similar although not equivalent to those produced by enucleation (Riesen 1966). Consistent with the view that similarities do exist between the effects of light-restriction and enucleation is the finding that atrophy in the lateral geniculate body is a consequence of either lid-closure or enucleation in kittens (Kupfer and Palmer 1964) and the finding that dendritic spines are sensitive to light-restriction and enucleation (Globus and Scheibel 1967a,b, Valverde 1967,1968).

In recent years an increasing number of investigators have been employing light-restriction methods in the study of modifications in subcortical visual structures. Examination of the lateral geniculate nuclei of visually restricted cats, rats and mice have revealed atrophic changes, volumetric decreases, decreases in internuclear material and reductions in acetylcholinesterase, as well as a decrease in the number of axon terminals (Wiesel and Hubel 1963a, Gyllensten et al., 1965, Maletta and Timiras 1967, Cragg 1969, Fifkova and Hassler 1969). In agreement with the behavioral findings, changes in the LGB of mature animals restricted for equivalent periods are conspicuously absent (Wiesel and Hubel 1963a, Maletta and Timiras 1967, Hubel and Wiesel 1970).

On the basis of restriction-induced changes in the peripheral and subcortical visual system electrophysiological anomalies might also be expected. Recent evidence has been offered to show that these changes are less than those anticipated. For example, while the "b" wave of the ERG is the component most sensitive to light-restriction, its development is retarded but not blocked by dark-rearing or lid-suturing in cat (Zetterstrom 1956, Ganz et al., 1968, Baxter and Riesen 1961, Cornwell, Sharpless and Kanor 1962) or monkeys (Riesen 1965a), and no changes in receptive field organization or cellular responsivity have been noted in the lateral geniculate body or its radiations in cat (Wiesel and Hubel 1963b, Burke and Hayhow 1960, Ganz et al., 1968) despite findings of obvious atrophy (Wiesel and Hubel 1963b). The alterations in retina and subcortex following visual restriction, thus, seem less than anticipated to account for the severe visual deficits that have already been described. When the consequences of visual restriction are viewed at the cortical level, however, the hypothesis that neural changes in the visual system underlie the behavioral changes noted becomes more plausible.

Restriction-Produced Changes at Cortex

Ablation Studies

Despite the fact that removal of visual cortex may disrupt a preoperatively established light-dark habit under some conditions (Lashley 1935, Thompson 1960) and that some permanent loss of intensity discrimination may occur (Gunin 1960), such discriminations may be relearned. If spatial cues are minimized when the initial intensity discrimination is being established, no postoperative loss may be encountered - indicating that earlier studies failed to take into account the use of different cues by normal and posterior neodecorticate animals (Bauer and Cooper 1964, Bland and Cooper 1970). It is generally agreed that the visual cortex is essential for the perception of patterns and that subcortical structures may support visual localization, following and intensity discriminations (Kluver 1941, Pasik and Pasik 1965,1968,1969, Schneider 1967). Thus, Lashley (1931) found that the visual cortex was essential for pattern vision in the rat, and Schneider (1967) reported that although visual localization could be accomplished in the hamster in the absence of visual cortex, its presence was required for pattern vision. Primates have also been shown to fail on tasks involving patterned light discriminations, but may still acquire intensity discriminations following destruction of visual cortex (Kluver 1941, Orbach 1959). It appears, however, that a rudimentary "contour" discrimination, based upon total retinal activity (length, flicker, movement and total luminous flux) is still possible in such animals (Weiskrantz 1963, Humphrey and Weiskrantz 1967) and may explain the isolated report of "pattern perception" in the rat following visual cortex removal (Lewellyn 1969).

Investigations of the effects of ablation of the visual cortex of cats have yielded results somewhat similar to those described above for rodent and monkey. Adult cats deprived of visual cortex are severely retarded in the acquisition of a pattern discrimination (Meyer 1963, Wetzel, Thompson, Horel and Meyer 1965). Although, Winans (1967) reported that adult cats could discriminate an erect from an inverted triangle in the absence of visual cortex, this may have been a discrimination of the spatial distribution of luminous flux (Winans 1967, Dodwell and Freedman 1968, Buchtel 1969). Striatectomy in cats has also been shown to impair photic frequency and brightness discriminations (Tucker, Kling and Scharlock 1968). As in rats and monkeys, intensity discriminations are easily mastered following visual cortex resection in cats (Smith 1937, Meyer 1963).

While some investigators have reported that infant cats undergoing posterior neodecortication may show indications of pattern vision as adults (Doty 1961, Wetzel et al., 1965) similar studies in rat have shown no greater recovery of pattern vision following early as compared to late lesions (Bland and Cooper 1969).

Taken as a group, these studies indicate that the neocortex is intimately involved in the perception of form, and unless flux or "contour" cues are available, visual pattern perception does not occur in the absence of the geniculo-striate system. In view of these findings, neocortical alterations resulting from visual restriction may exert a significant effect upon the capacity to react to patterned light. The fact that visual cortex removal does not preclude the formation of intensity discriminations is also in accord with the restriction studies which have indicated that visual experience is not necessary for the performance of intensity discriminations.

Auditory cortex has also been removed in an effort to describe the tasks not requiring its presence and the deficits in audition following its removal. These investigations have revealed that the cat can learn to respond to the onset of sound (Kryter and Ades 1943), make frequency discriminations (Goldberg Diamond and Neff 1958) and intensity discriiminations (Neff 1961) in the absence of auditory cortex. However, Diamond and Neff (1957) reported that such animals could not discriminate changes in the temporal pattern of tones (i.e. different frequencies presented in sequences such as low-high-low versus high-low-high). In addition, such neocortical lesions destroy the ability to discriminate changes in the duration of pure tones (Scharlock and Neff 1959). Similar findings have been reported for the monkey (Jerison and Neff 1953). As in the visual system of cat, lesions in the auditory cortex of infant kittens have a less deleterious effect upon later auditory discrimination than when comparable lesions are performed at maturity (Scharlock, Tucker and Strominger 1963). The above ablation studies in the cat led to the behavioral investigations following auditory restriction in the rat (Tees 1967a,b). His findings (described earlier) can be viewed as consistent with damage to the primary cortical projection area. The fact that intensity discriminations are possible following either cortical ablation or sensory restriction may reflect the capacity of subcortical areas to support such behavior in spite of restriction-produced structural modifications in the neocortex.

Biochemical and Anatomical Effects at Cortex

Many studies concerned with the effects of "enriched" or "impoverished" environmental conditions on the development of young animals, have noted that the biochemical and neural constituents of cortex are sensitive to manipulations of this environment (Krech, Rosenzweig and Bennett 1962,1965, Rosenzweig, Krech, Bennett and Diamond 1962, Diamond, Law, Rhodes, Lindner, Rosenzweig, Krech and Bennett 1966, Diamond 1967). Hence one might expect specific manipulations of the visual environment to be reflected in a similar manner. It has been reported that mice raised in the dark until 60 days of age had decreased levels of cortical RNA, while animals raised in thelight to 60 days of age had intermediate levels of RNA but, highest RNA levels were found in a group dark-reared to 60 days of age and then brought into light for one hour prior to sacrifice (Riesen 1967). Just why this latter group showed such dynamic changes is, at present, unknown. However, similar findings have been reported by DeBold, Firsheim, Carrier and Leaf 1967).

Although cholinesterase levels may be increased in visual cortex (rodents) by enriched visual experience (Singh, Johnston and Klosterman 1967), blinding or dark-rearing does not lower cholinesterase or acetylcholinesterase levels (Krech, Rosenzweig and Bennett 1963, Maletta and Timiras 1967). These findings together with findings of increased cholinesterase activity in the visual cortex of enucleated animals reared under "enriched" environmental conditions (Krech et al., 1963) indicates that the visual cortex may serve nonvisual as well as visual functions.

Initial attempts to determine if changes in cortex would resul from visual restriction were rather crude, and early investigation reported negative findings (Goodman 1932, Tsang 1937, Hess 1957). As investigator and instrument sophistication increased, however, it became evident that the cerebral cortex was quite sensitive to manipulations of the organism's visual history. One of the first descriptions of cortical changes following visual restrictio directed at cell bodies was reported by Gyllensten (1959). He raised mice in darkness from birth to 20 or 30 days of age. After 20 days cell nuclei and internuclear material were reduced in laminae II/III and IV of striate cortex, resulting in increased packing density and relative vascularity of that area. After 30 days, however, no such differences were apparent, suggesting a normalization of neural processes. This suggestion was supported by Gyllensten, Malmfors and Norrlin (1965) who also noted that similar hypotrophic changes in subcortical structures showed no such normalization. Adults placed in darkness for equivalent periods showed no changes in nuclear diameter although a reduction in internuclear material was evident. Cortical thickness was also found to be reduced in mice reared from birth in darkness but not in adults. These findings are in agreement with behavioral, anatomical and electrophysiological findings indicating the importance of the interaction of the age of the nervous system and the effects of sensory restriction.

The fact that extensive cellular normalization in dark-reared mice was reported by Gyllensten et al., in 1965 (although a conspicuous and unexplained absence of normalization follows enucleation - Gyllensten, Malmfors and Norrlin-Grettve 1967), suggested compensation by means of the activity of nonvisual afferents. The possibility that increased activity of other sesory systems may result from visual restriction leads directly to the hypothesis of compensatory functioning of these systems to aid in behavioral adaptability. While no substantial behavioral verification of such a suggestion has been forthcoming Gyllensten et al., (1966) have reported hypertrophic changes in the auditory cortex of visually restricted mice. Other researchers have also postulated the operation of compensatory mechanisms following sensory restriction. Krech et al., (1963) have described a greater development of somesthetic cortex following ocular enucleation, and in addition, increased cholinesterase activity has been reported in the cortex of one hemisphere following lesioning of the other (Krech, Rosenzweig and Bennett 1960). Enhancement of the evoked potential (extr-primary) to photic stimuli in nonvisual cortical areas following visual restriction has also been described (Scherrer and Fourment 1964). To account for the increased activity and development in these areas Gyllensten et al., (1966) have also offered the suggestion that the underdeveloped visual cortex removes an inhibitory influence on neighboring cortical areas (morphogenetic inhibition).

In recent years a number of specific and quantitative evaluations of restriction-produced cortical changes have been reported. Coleman and Riesen (1968) reared cats in darkness from birth to six months of age, whereupon dendritic branchings were measured in visual cortex and posterior cingulate gyrus (because of possible involvement in visual function - Harman and Berry 1956, Hughes 1959, Ingvar and Hunter 1955, Cuenod, Casey and MacLean 1965, MacLean 1966). Dark-reared animals were found to have significantly fewer numbers of dendritic branches on stellate cells (layer IV striate cortex). The basal dendritic processes of the pyramidal cells in the posterior cingulate gyrus showed similar changes. Stellate cell changes following blinding have also been reported by other investigators in rabbit and cat (Gomirato and Baggio 1962, Dzidzishvili 1963). The probability of dendritic branching has also been related to environmental enrichment or impoverishment (Holloway 1966). Since the stellate cells in layer IV of striate cortex are generally recognized as receiving direct visual afferents, reductions of cell size and/or changes in dendritic ramifications may reduce the capacity to react to visual stimuli. On this basis, increases in cellular size and/or integration might prove to be behaviorally advantageous. Interested in this possibility

Clendennin and Eayrs (1961) induced cellular hypertrophy, as well as greater numbers and lengths of cortical dendrites in rats by the administration of growth hormone during gestation and found these rats to be superior to normal controls on spatial learning tasks. Similar findings of behavioral advantage following growth hormone administration have been reported by Block and Essman (1965).

A number of recent investigations have looked more closely at dendritic processes and have noted changes in dendritic spines, now recognized as postsynaptic sites (Gray 1959, Colonnier 1968, Scheibel and Scheibel 1968, Valverde and Ruiz-Marcos 1969). Globus and Scheibel (1967a) reported that unilateral enucleation or lesions of LGB significantly reduced the number of spines along the apical shaft of the pyramidal cell in striate cortex in rabbits. Spine loss on these dendrites has also been reported following enucleation of the eyes in the mouse (Valverde 1968). It is important to note that the receptor need not be removed for similar changes to occur. Thus, Globus and Scheibel (1967b) reported that spine-deformity was a consequence of dark-rearing in rabbits, Valverde (1967) found a decrease in spine density following dark-rearing in the mouse, and Fifkova (1968) noted a decrement in the population of spines in layer IV-V of the contralateral visual cortex of rats following monocular lid-suturing.

Valverde and Ruiz-Marcos (1969 p 280) stated "... that the specific afferents in the visual cortex synapse on the dendrites of short axon cells. The results of Colonnier (1966) support our contention that a great number of contacts over apical dendrites of layer V pyramidal cells might derive from cortical cells... The specific geniculo-cortical fibers would affect indirectly the apical dendritic spines through those cortical cells." It would, thus, appear that a decrement in spine population and stellate cell dendritic ramification would have far-reaching consequences with respect to intracortical organization.

It is interesting to note that the largest increase in spine numbers in the striate cortex of the mouse occurs at 10-19 days of age, the approximate time of eye opening when there is a marked increase in the intensity and quality of photic stimulation (Valverde and Ruiz-Marcos 1969). These data further indicate that spine formation along the apical dendrites of visual cortex is intimately related to the visual history of the organism. Such dendritic structures have also been shown to increase in numbers in the visuo-auditory area of cortex following increased multi-dimensional stimulation from birth (Schapiro and Vukovich 1969), and the size and number of synaptic sites in the visual cortex have been reported to depend upon photic stimulation (Cragg 1967).

On the basis of these reports it does not seem unreasonable to expect that these decreases in synapses, cell numbers, sizes and processes, following visual restriction alter the ability of the organism to respond to visual stimuli.

Electrophysiological Changes At Cortex

Electrophysiological investigations have revealed some of the functional consequences of early visual restriction. For example, Zislina and Arkhipova (1970) have reported decreases in the primary negative wave of the direct cortical response. Furthermore, while four fifths of the cells in the striate cortex of the normal cat can be driven by stimulation of either eye (Hubel and Wiesel 1962), only about seven per cent of these cells can be influenced through the restricted eye after 10-12 weeks of monocular visual restriction (binocular influences upon cortical units may also be reduced by strabismus or alternating monocular experience, - Hubel and Wiesel 1965). These cortical units are readily fatigued, unpredictable and lack precise receptive fields (Wiesel and Hubel 1963b,1965a, Ganz et al., 1968, Hubel and Wiesel 1970). In view of the finding that the infant kitten does not differ markedly from the adult cat with respect to these measures (Wiesel and Hubel 1963b) a disruption of function rather than a developmental failure appears to have been produced by visual restriction. The variability or unpredictability of the cortical units of visually restricted organisms must be viewed in conjunction with the variability of evoked potentials (Fox, Inman and Glisson 1968) and dendritic processes (Globus and Scheibel 1967b, Coleman and Riesen 1968), perhaps indicating that neuronal maturation is in some way directed by visual experience so as to maximize behavioral adaptability. A recent report by Hirsch and Spinelli (1970) suggested that predictable changes in the orientation of receptive fields of cells in the visual cortex of kittens may be produced by environmental stimuli, thus, lending support to the above suggestion.

The behavioral literature has indicated a paucity of effects when sensory restriction is begun at maturity. Generally, studies involving anatomical, or electrophysiological measures following sensory restriction are in good agreement with the behavioral literature. In addition to age, duration and severity of the restrictive conditions (amount of light restricted) have been found to be relevant variables, with greater effects obtaine with young animals severely restricted for relatively long period (e.g. as reported by Wiesel and Hubel 1963b,1965a, Fox et al., 1968). Hubel and Wiesel (1970) have recently indicated that ther is a sensitive period to the effects of visual restriction in cats beginning at about the fourth week of life and ending before the fourth month of age. During this period only several days of visual restriction will severely reduce the effectiveness of photic stimuli upon cortical neurons. Furthermore, longer restrictive periods encompassing greater portions of this sensiti period result in virtually irreversible effects, while shorter restrictive periods allow some electrophysiological recovery. These neurophysiological changes have been related to behavioral changes in kittens with similar histories (Dews and Wiesel 1970).

On the basis of neurophysiological findings with monocular visual restriction it was expected that binocular restriction would result in a cortex almost totally unresponsive to photic stimuli. However, contrary to expectation, 41% of the cortical cells responded normally in binocularly restricted cats even after several months of visual restriction (Wiesel and Hubel 1965a). The greatest changes appeared to be in the presence of a large number of unresponsive cells (27%) and a number of cells showing unpredictability, lack of orientation specificity, poor receptive field definition and response sluggishness (32%). The authors concluded that "... the functional integrity of the visual pathway may depend not only on the amount of afferent impulse activity, but also on the interrelationships between the various sets of afferents" (Wiesel and Hubel 1965a, p 1038).

Evoked potential changes following visual restriction have also been recorded in monkeys (Lindsley, Wendt, Lindsley, Fox, Howell and Adey 1964) and rats (Rhodes and Fleming 1969). However, no gross abnormalities in the spontaneous EEG have been observed in visually restricted kittens, although repetitive photic stimulation may induce atypical EEG responses (Baxter 1966, Satterberg and Ganz 1967).

Recently, Scherrer and Fourment (1964) demonstrated that the latency of the primary responses of the evoked potential in the occipital area is longer for dark-reared than for normally reared rabbits and that the amplitude of this response was diminished in the visual cortex. Large amplitude responses with shorter latencies were recorded in somesthetic and motor areas to light stimulation. In addition, dark-rearing appeared to have increased the amplitude of the evoked responses to auditory and somesthetic stimuli in the occipital area of these animals. Whether or not this indicates the action of more sensitive nonvisual sensory systems through some sort of compensatory mechanism remains to be determined.

Unfortunately, very little is known about the electrophysiological consequences of auditory restriction. The one reported study indicated a loss of responsiveness as measured by threshold determination for auditory evoked potentials in the rat (Batkin, Groth, Watson and Ansberry 1970).

Intracranial Stimulation

Since Loucks (1938) demonstrated that electrical stimulation of the visual cortex could serve as a conditioned stimulus for leg-flexion or salivary responses in dogs, numerous studies using similar methods have been conducted. These investigations have failed to reveal any unconditionable cortical loci in the cerebral cortex of the cat or monkey (e.g. as reported by Doty, Rutledge and Larsen 1956, Doty and Rutledge 1959, Doty 1965a, 1967, 1969). Such cortical stimulation appears to be discriminable with respect to stimulus frequency and to whether it is applied centrally or peripherally (Schuckman 1966, Schuckman and Battersby 1966). In addition, cortical locus has been shown to be discriminable in the monkey (Doty 1963,1965b,1967, Fantl and Schuckman in preparation). In rats, electrical stimulation of the cortex has also been shown to serve as a conditioned stimulus and stimulus parameters, as well as cortical loci may be discriminated (Mogenson 1959,1962, Grosser and Harrison 1960, Weinberg 1968).

Generalization from peripherally to centrally applied stimuli has generally been found to be absent thus suggesting a lack of stimulus equivalence (Doty 1969, Doty and Rutledge 1959, Schuckman 1966,Schuckman and Battersby 1966). Although Kitai (1965, 1966) did report generalization in rats from a steady light to a test cortical or optic chiasm stimulus, Doty (1969, p 308) criticized these findings by pointing out that "... random intertrial pressing, especially in response to onset of extinction procedures, may have influenced the outcome..."

Thus, a method for stimulating the cortex without first involving the various peripheral and subcortical structures has been developed. Such a method appears admirably suited for an evaluation of the status of the cortex following sensory restriction. Only one such study has been reported. Mogenson (1962) found retarded acquisition of a conditioned response to an electrical stimulus delivered to the visual cortex of orbitally enucleated rats. However, as noted earlier, the effects of surgical deafferentation may differ from those of light-restriction, and these findings may have been due to the direct atrophic effects of enucleation rather than to the effects of light-restriction per se. Furthermore, these data failed to reveal whether the effects were restricted to the primary cortical projection area, as only the visual cortex was stimulated. On the basis of reports indicating possible compensatory mechanisms in restricted animals we might expect visual restriction to facilitate acquisition of a conditioned response to electrical stimulation of auditory cortex.

METHOD

Subjects

The subjects were 43 laboratory raised Long Evans hooded rats. Each animal was assigned to one of seven groups as listed in Table I. Group I contained seven rats while the other groups contained six.

Sensory Restriction

Visual restriction was accomplished by means of eyelid suturing. Animals in group I had their eyelids surgically separated and then sutured together at 13 days of age. At 22 days of age these animals were fitted with tape hoods to prevent them from removing the sutures and to restrict still further the passage of light to the eyes. Groups II and III underwent lid-suturing and were fitted with hoods at 40 days of age (see Table I).

Auditory restriction was accomplished by placing cotton into the external meatus of each ear and covering the cotton liberally with collodion so as to form a hard fibrous plug. It was necessary to change these plugs periodically since the animals would loosen or remove them on occasion. Animals in group IV were fitted with these plugs at 13 days of age, while animals in groups V and VI received the plugs at 40 days of age.

All animals were removed from the mother and housed individually at 22 days of age. Electrode implantations were

Table I

Experimental Groups and Treatments

Group	N	Modality Restricted	Age at Restriction (Days)	Age at Training (Days)
I	7	Visual	13	45
II	6	Visual	40	45
III	6	Visual	40	85
IV	6	Auditory	13	45
V	6	Auditory	40	45
VI	6	Auditory	40	85
VII	6	Unrestricted	--	45

conducted at 40 days of age and restrictive conditions were maintained throughout training.

Surgery

For impantation, animals were anesthetized with sodium pentobarbital (35 mg per kg diluted with 1/2 cc of saline, administered intraperitoneally) and also received atropine at the time of surgery to dry mucous passages (.01 cc).

Operations were conducted under asceptic conditions. A midline incision was made in the scalp extending from approximately 4 mm in front of the bregma to approximately 4 mm behind the lambdoid suture. Following the insertion of 5-7 anchoring screws a craniectomy was performed. The dura was incised and reflected and the electrode assembly was set in place with the visual cortex electrodes approximately 5 mm posterior to and 1 1/2-2 1/2 mm lateral to the bregma. These placements were determined on the basis of the anatomical studies of Waller (1934), Lashley (1941) and Krieg (1946), which designated the "visual" and "auditory" areas of the rat neocortex. The exposed area was packed with gelfoam and covered with dental acrylic in order to hold the assembly in place by securing it to the skull and the anchoring screws.

Electrodes were constructed of .001 inch tungsten wire insulated with vinyl enamel and presoldered to a subminiature connector. The connector was designed especially for this purpose by Mi-Kro Connector Corp. The complete connector assembly consisted of four monopolar electrodes, two for auditory cortex and two for visual cortex. Electrode tips were bent at an angle of 65-75 degrees, were approximately 1 mm apart, 3/4-1 mm in length and were imbedded in the cortex.

Apparatus

Behavioral training was accomplished using a Lehigh Valley Testing Chamber. The chamber contained two steel levers (only one of which was operative) and a dipper located between the levers which would deliver water. A blower circulated air and masked extraneous sounds.

The output from a Grass stimulator (Model S-4) to a Stimulus Isolation Unit (Model SIU 4678) and a Constant Current Unit (Model CCU 1A) delivered intracranial electrical stimulation. Current was monitored by two Lafayette milliameters connected in series with the stimulating circuit. Stimulation and reinforcement were controlled by means of a BRS Electronics prgramming unit. The stimulus consisted of a 3 second train of rectangular pulses at 60 pulses per second (pulse duration was .3 msec).

Procedure

Following a five day post-operative recovery period the animals were deprived of water for 23 hours and then shaped to press a lever to obtain water. Daily records were kept of the number of responses emitted during a 15 minute free-responding period until stabilized responding was noted (the total number of responses per period differing by less than 10% on three consecutive sessions). Threshold for overt movement resulting from stimulation delivered to each cortical area was then determined. Overt movement consisted of a neck-flexion response in all subjects.

Following response stabilization and overt threshold determination, training was begun. During training, lever-press responses during intracranial stimulation of either the visual or the auditory cortex were followed by water delivery. The intertrial interval varied between 16 and 20 seconds, and responses in the absence of stimulation resulted in a recycling of the intertrial interval, delaying stimulation for at least 16 seconds. Animals received 25 stimulations of each area per day and were trained six days per week. The Gellermann order was employed to program the order in which the two cortical areas were stimulated. Initial training current was set at 80% of the current intensity necessary to evoke threshold responses. A correct response was defined as a depression of the lever during cortical stimulation. When correct responding reached a level of 80% or more, for five consecutive days, the animal was considered to have reached criterion for that area. Stimulation was continued in either area until criterion was reached for both areas. Unless the criterion was reached at the same time for both areas, a period of reestablishment was instituted such that both areas were again stimulated until 80% correct responses to stimulation of both areas was attained. Number of correct responses to stimulation of visual and auditory cortex was plotted as a percentage of blocks of 25 training trials in all figures presenting individual data. Group data was replotted on the basis of the mean number of blocks of trials required to reach and maintain or surpass four successive levels of training (20,40,60 and 80% correct responses). Following criterion performance at a current intensity of 80% of behavioral threshold current was reduced to 65% until the same criterion was reached and then again to 50% until criterion was reached. The number of correct responses and incorrect responses at each current intensity level were noted.

Following termination of all training and testing, 28 of the subjects were sacrificed and their brains were perfused with saline followed by 10% formalin. The brains and eyes were removed and placed in formalin. Electrode locations were confirmed by visual observation and the eyes of visually restricted and control animals were sectioned and stained (haemotoxylin and eosin) for histological examination of the retinae.

RESULTS

Behavioral Threshold

Table II presents the mean current intensities necessary to evoke threshold (behavioral responses) neck-flexion in all groups. Current intensities ranged from a low of 2.5 ua to a high of 100 ua (see Table XI in Appendix). This range of currents was somewhat wider than that reported by Mogenson (1962). He indicated a range of from 30 to 80 µa, but was unclear as to whether this range represented the current values for threshold behavioral response or the stimulating currents employed. (65% of threshold). It was also unclear as to whether this was a within- or between-subjects range. However, the mean threshold current obtained here (24.8 µa) fell just below the range he reported.

Although thresholds were somewhat higher in the visual cortex of 68% of the subjects, within-group t tests failed to reveal significant differences between the current values obtained in the visual and auditory cortex of any of the seven groups. Furthermore, no significant experimental-control group differences in the threshold currents obtained in either cortical area were found. These data are summarized in Tables II and III.

Cortical Conditioning In Unrestricted Control Animals

The individual acquisition data for unrestricted control animals (group VII) to stimulation of visual and auditory

Table II

Within-Group Comparisons Of The Current Magnitudes Required To Evoke Threshold Behavioral Responses

Group	Mean Current Magnitude (μa) Visual Cortex	 Auditory Cortex	t
I	36.28	29.00	0.39
II	28.80	14.50	1.34
III	22.00	28.80	0.46
IV	31.25	26.08	0.33
V	12.08	23.66	0.95
VI	29.67	19.83	0.60
VII	26.92	18.58	0.80

* $p \angle .05$
**$p \angle .01$

Table III

Experimental-Control Group Comparisons Of The Current Magnitudes Required To Evoked Threshold Behavioral Responses

Control (VII) versus Group...	Visual Cortex t	Auditory Cortex t
I	.52	.27
II	.15	.54
III	.38	.81
IV	.45	.46
V	1.68	.37
VI	.16	.16

* $p < .05$
** $p < .01$

cortex are shown in Fig 1. In the figure the percent correct responses made by each group VII animal (unrestricted controls) to stimulation of visual and auditory cortex are plotted as a function of successive blocks of training trials. It is evident from these figures that there were no differences in the acquisition of intracranial stimulation as a discriminative stimulus in either cortical area of these animals.

Fig 2 presents the pooled data for the entire group of unrestricted control animals replotted on the basis of the mean number of blocks of trials required to reach (and maintain or surpass) acquisition levels of 20, 40, 60 and 80% correct responses. This figure shows a good deal of similarity in the two functions. A treatments x treatments x subjects statistical analysis (Winer pp. 289-290) showed no significant differences between these two functions ($F=>1.00$, $df=1,5$). The variability of these functions was also found to be highly similar ($F=1.03$, $df=6,6$ - Snedecor 1937).

The results obtained here are also relevant to data other than those dealing specifically with changes in the central nervous system of sensory restricted animals. Thus, the findings that equal ICS current magnitudes may evoke movement when presented to the visual or auditory cortex of the rat, and that electrical stimulation of either cortical area is an equally effective CS, are in agreement with previous findings in other species (Hughes 1956, Doty et al. 1956, Lilly 1958, Doty and Rutledge 1959, Doty 1965a, 1967).

Fig 1A-D. Discriminative stimulus acquisition for group VII - individual data. Percent correct responses made by each group VII animal (unrestricted controls) to stimulation of visual and auditory cortex as a function of successive blocks of training trials. The horizontal line at 80 per cent correct represents the criterion level employed. The number in the upper left corner of each graph indicates the individual animal represented.

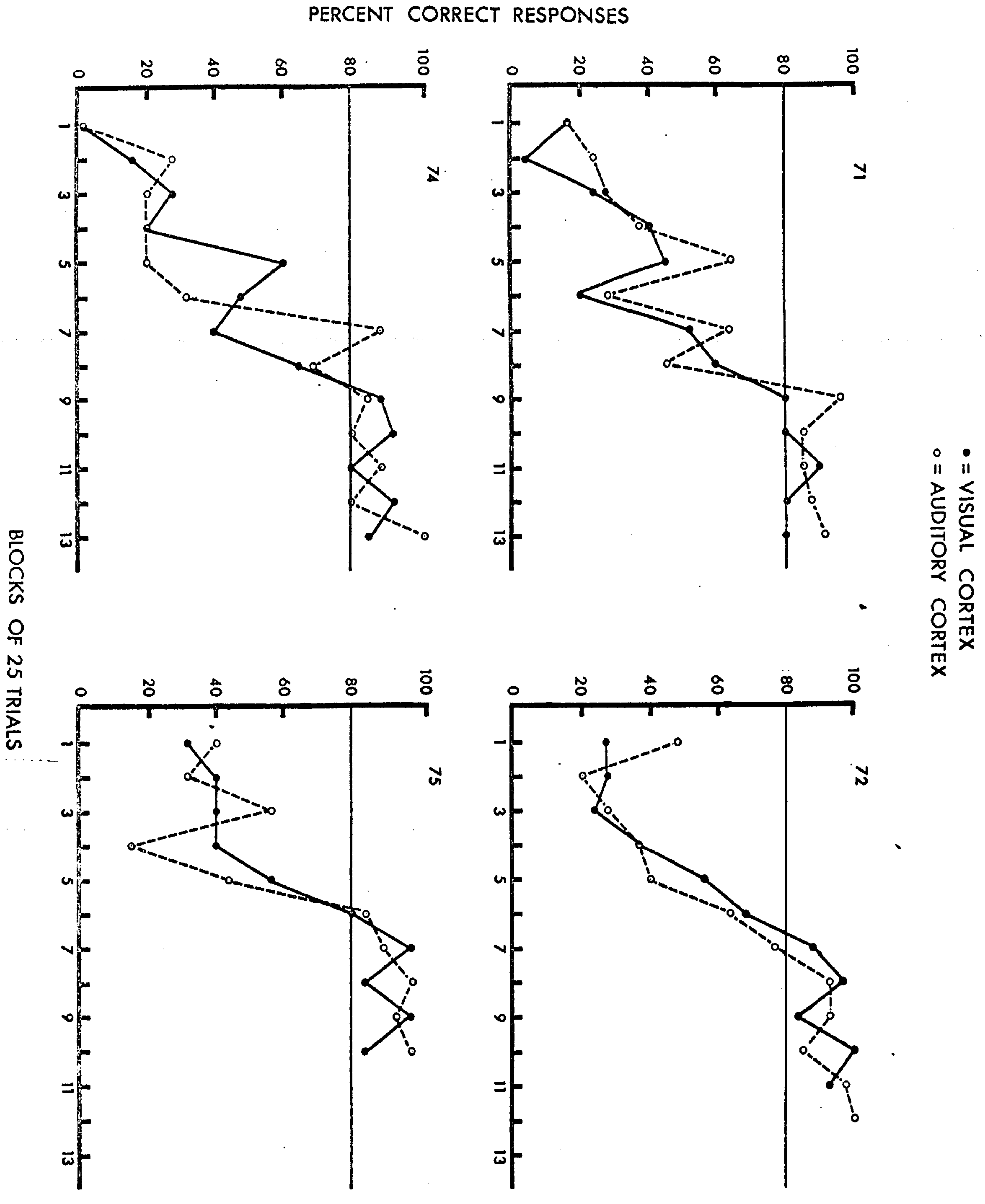

● = VISUAL CORTEX
○ = AUDITORY CORTEX
PERCENT CORRECT RESPONSES
BLOCKS OF 25 TRIALS
71
72
74
75
0
20
40
60
80
100
1
3
5
7
9
11
13

Fig 1E-F. Discriminative stimulus acquisition for group VII - individual data. For explanation of the figures see Fig 1A-D.

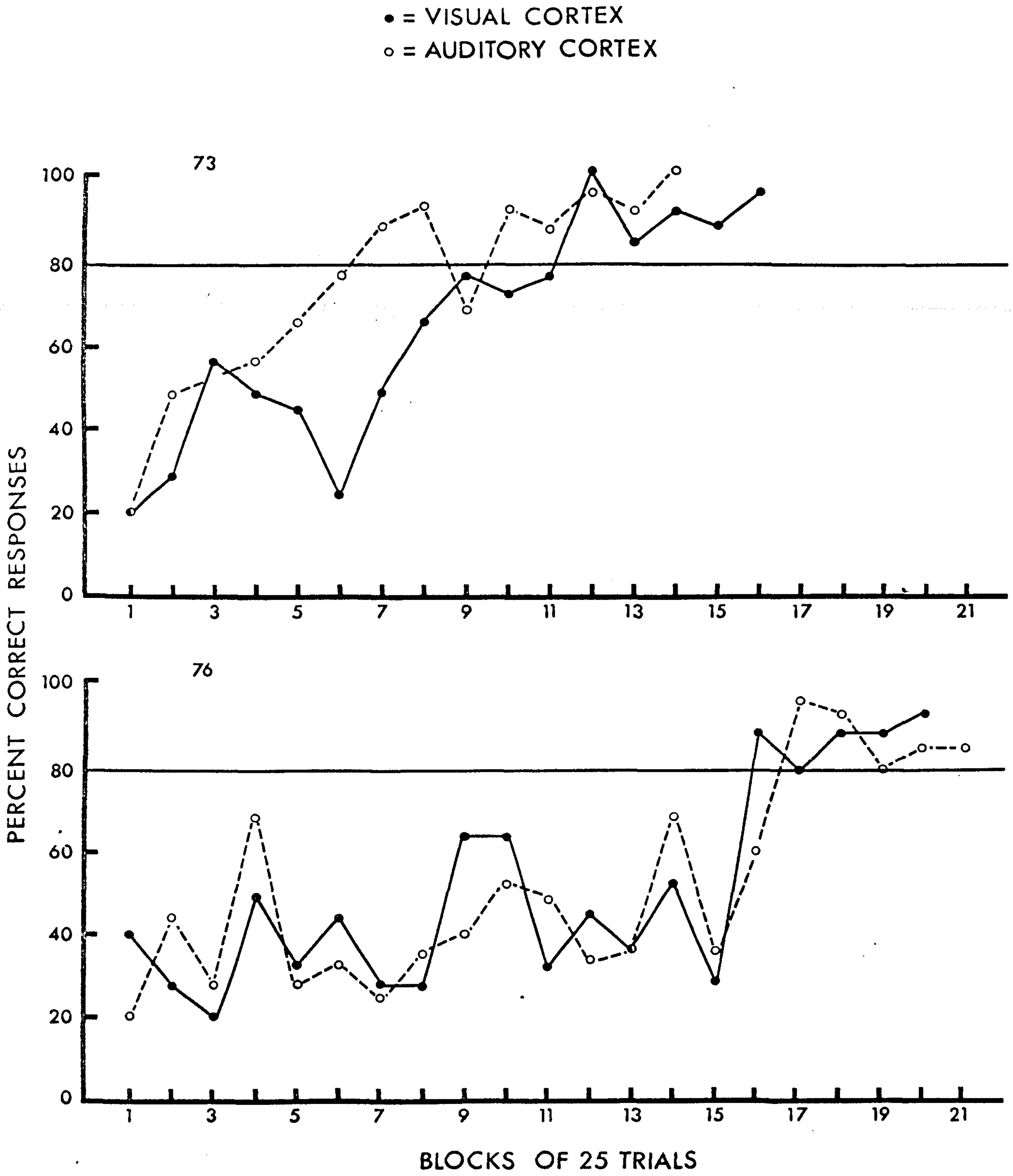
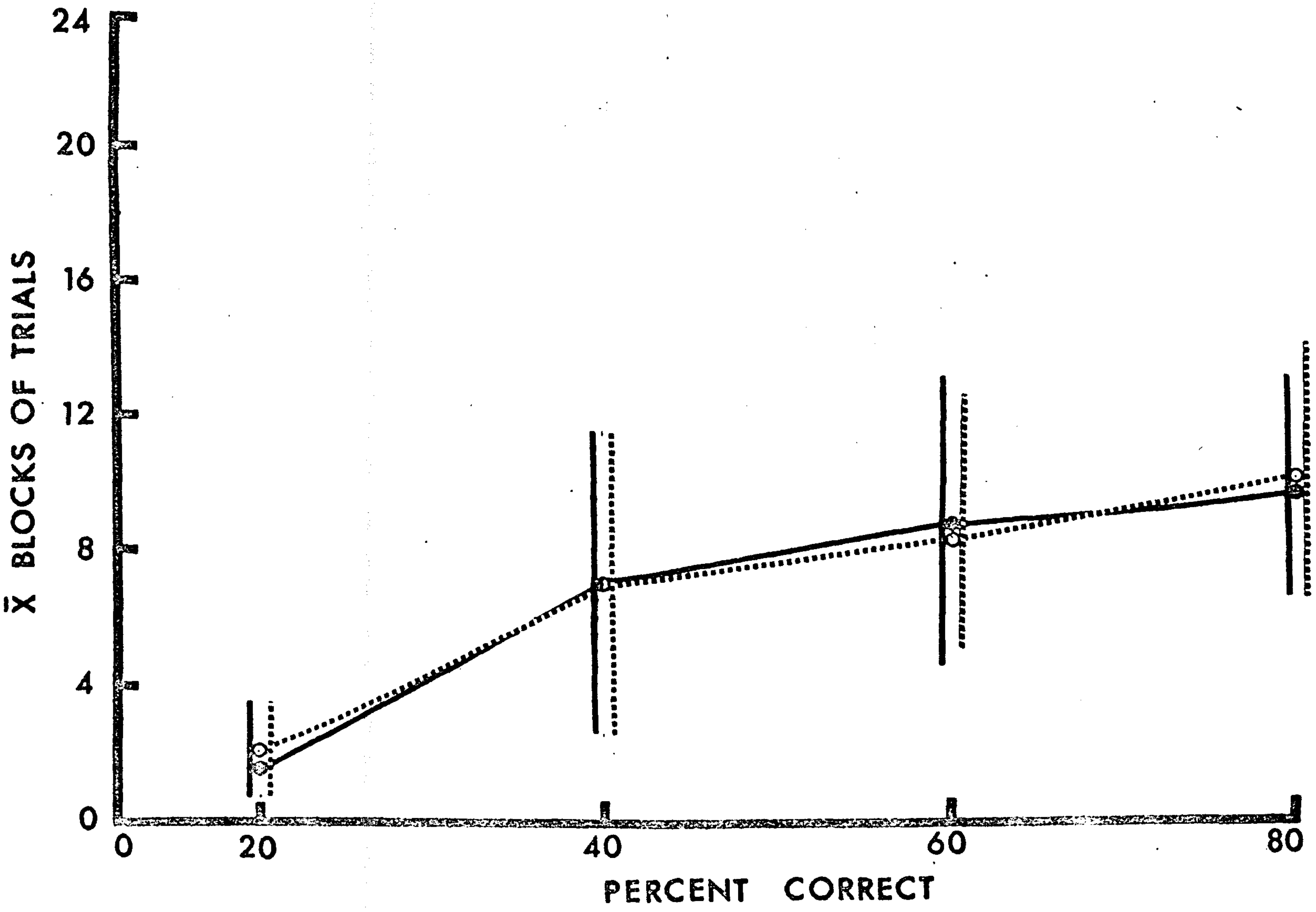

● = VISUAL CORTEX
○ = AUDITORY CORTEX
73
76
PERCENT CORRECT RESPONSES
0
20
40
60
80
100
1
3
5
7
9
11
13
15
17
19
21
BLOCKS OF 25 TRIALS

Fig 2. Discriminative stimulus acquisition for group VII - group data. Percent correct responses made by group VII (unrestricted controls) to stimulation of visual and auditory cortex during training. The figure is based on the mean number of blocks of trials required to reach and maintain or surpass four successive levels of training (20, 40, 60 and 80% correct responses). Standard deviations for each point are represented by dotted vertical lines to the right (auditory cortex) and solid vertical lines to the left (visual cortex) of plotted mean values.

UNRESTRICTED



Effects Of Visual Restriction Upon Cortical Conditioning

Early Visual Restriction - Early Run

Fig 3A-G present the individual data obtained from animals paranatally restricted of vision (eyelid suturing was conducted at 13 days of age) and trained at 45 days of age (group I). These figures reveal consistent differences in the responsiveness of the visual and auditory cortices. Per cent correct responses to stimulation of the auditory cortex were usually greater, while trials required to reach criterion were usually fewer. This difference between visual and auditory cortex in group I animals was not apparent during initial training, but emerged coincident with experience in the training situation.

Although all group I animals showed differences in the ease with which stimulation of visual and auditory cortex could serve as discriminative stimuli, these differences were not uniform. Thus, two animals (14 and 15) performed better in response to stimulation of the auditory than to stimulation of the visual cortex in the latter half of training, while four animals (12, 18,19 and 11) showed consistent performance differences throughout training. One animal (17), on the other hand, showed a performance reversal from initially superior performance in response to stimulation of auditory cortex to a somewhat better performance record in response to stimulation of visual cortex. Although this variability between animals was present, it appears that early visual restriction consistently rendered these animals more efficient in the development of appropriate responses when stimulation was delivered to the auditory cortex than when presented to the visual cortex.

Fig 4 presents the pooled data for group I plotted in the same fashion as was Fig 2. This figure reveals that greater numbers of blocks of trials were required to reach the successive performance levels of 20, 40, 60 and 80% correct responses when stimulation of visual cortex served as the discriminative stimulus. This acquisition difference showed a progressive increment across these levels and statistical analysis revealed this difference to be significant (F=13.05, df=1,6, $p = < .05$), while no variability differences between the functions attained statistical significance (F=1.50, df=6,6).

These figures and analyses revealed that early visual restriction somehow modified the capacity of these animals to acquire a discriminative stimulus based upon electrical stimulation of the cortex.

Late Visual Restriction - Early Run

To test the possibility that restricting photic stimulation during training would modify the acquisition of intracranial stimulation as a discriminative stimulus, animals in group II were visually restricted at 40 days of age and trained at 45 days of age. Fig 5A-F present the individual data obtained from these animals. It is apparent from these figures that while two animals (23 and 25) showed somewhat better

Fig 3A-C Discriminative stimulus acquisition for group I - individual data. For explanation of the figures see Fig 1A-D.

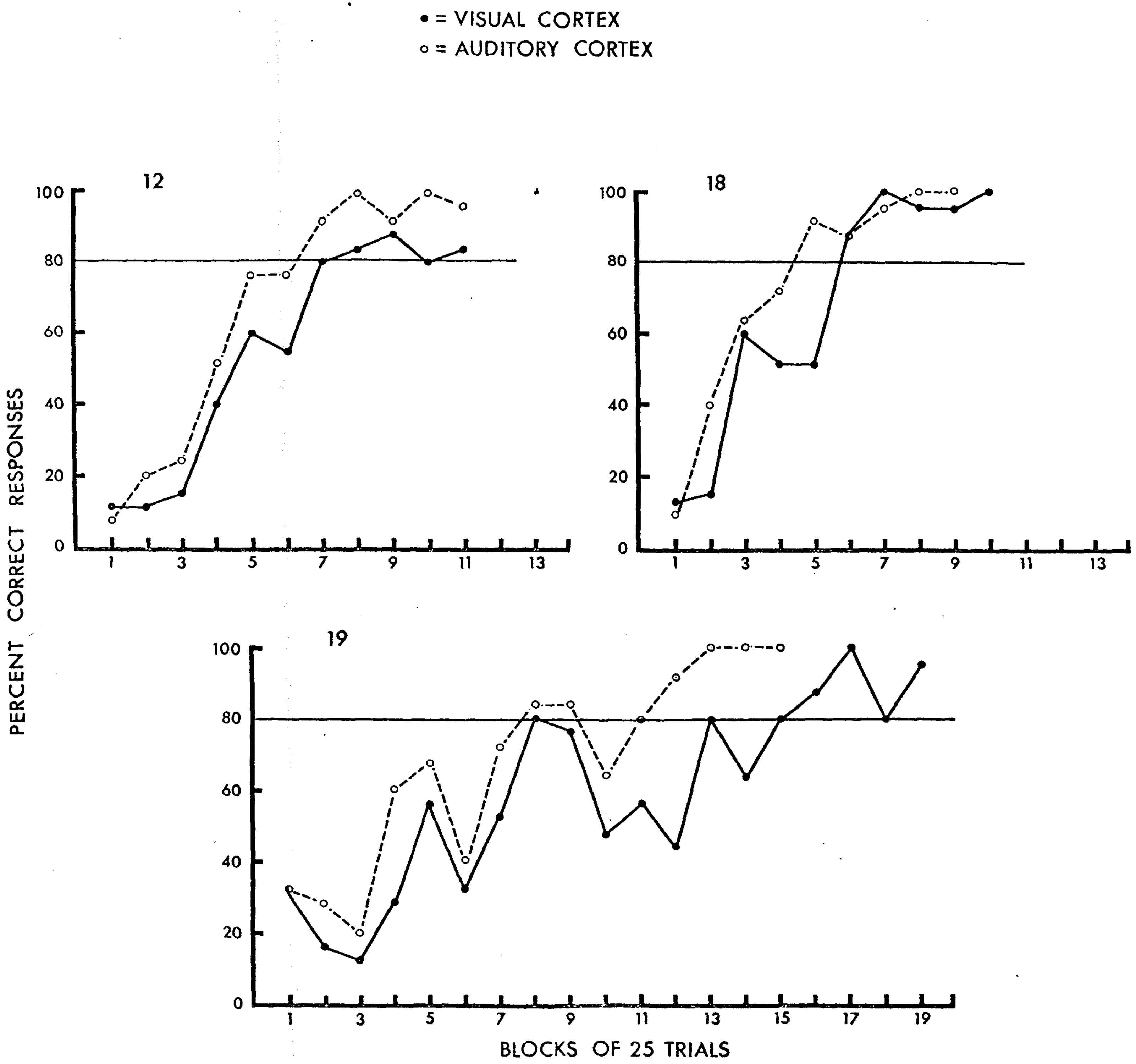
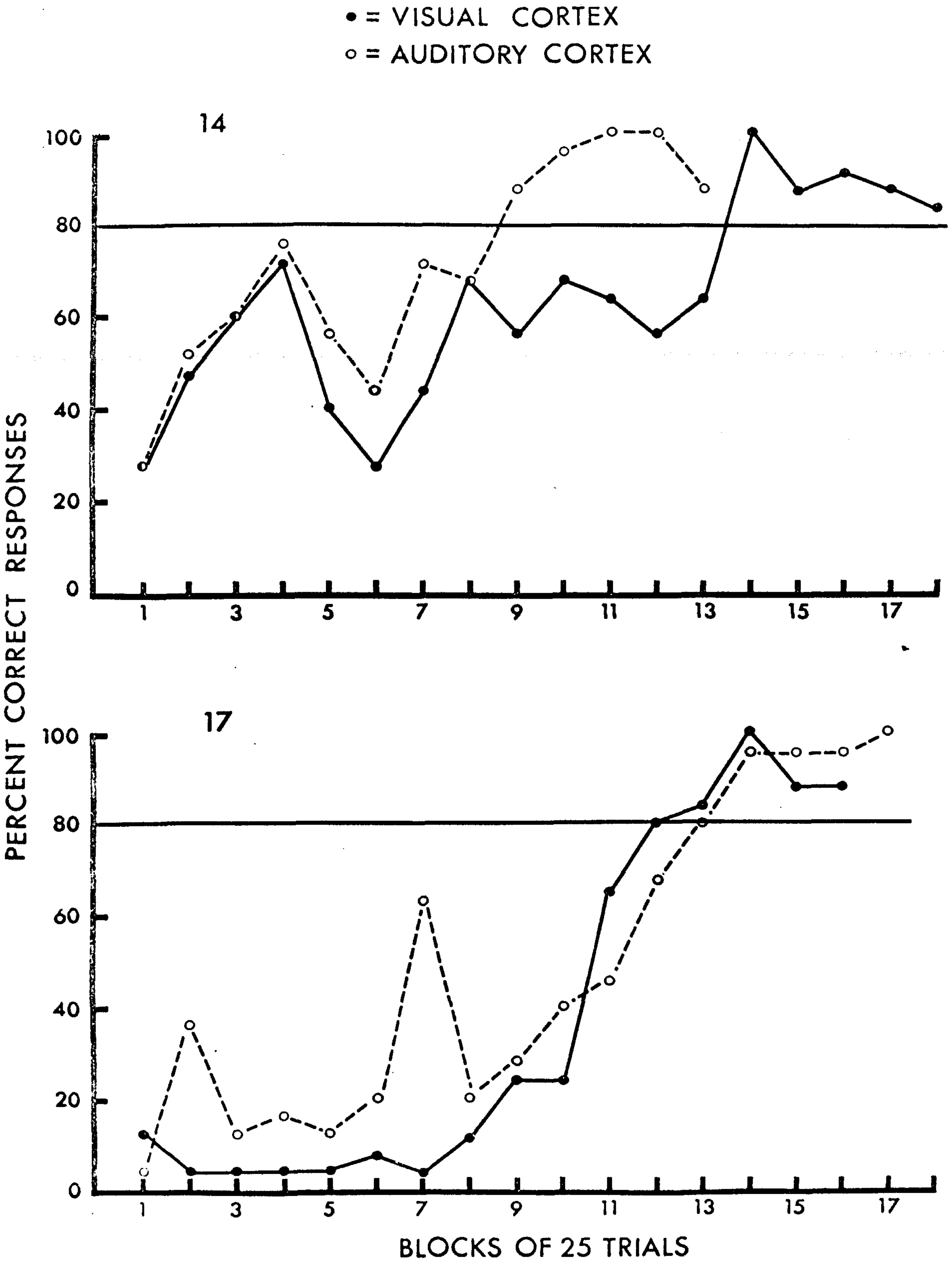

● = VISUAL CORTEX
○ = AUDITORY CORTEX
12
18
19
PERCENT CORRECT RESPONSES
0
20
40
60
80
100
1
3
5
7
9
11
13
15
17
19
BLOCKS OF 25 TRIALS

Fig 3D-E Discriminative stimulus acquisition for group I - individual data. For explanation of the figures see Fig 1A-D.



● = VISUAL CORTEX
○ = AUDITORY CORTEX
14
17
PERCENT CORRECT RESPONSES
0
20
40
60
80
100
1
3
5
7
9
11
13
15
17
BLOCKS OF 25 TRIALS

Fig 3F-G. Discriminative stimulus acquisition for group I - individual data. For explanation of the figures see Fig 1A-D.

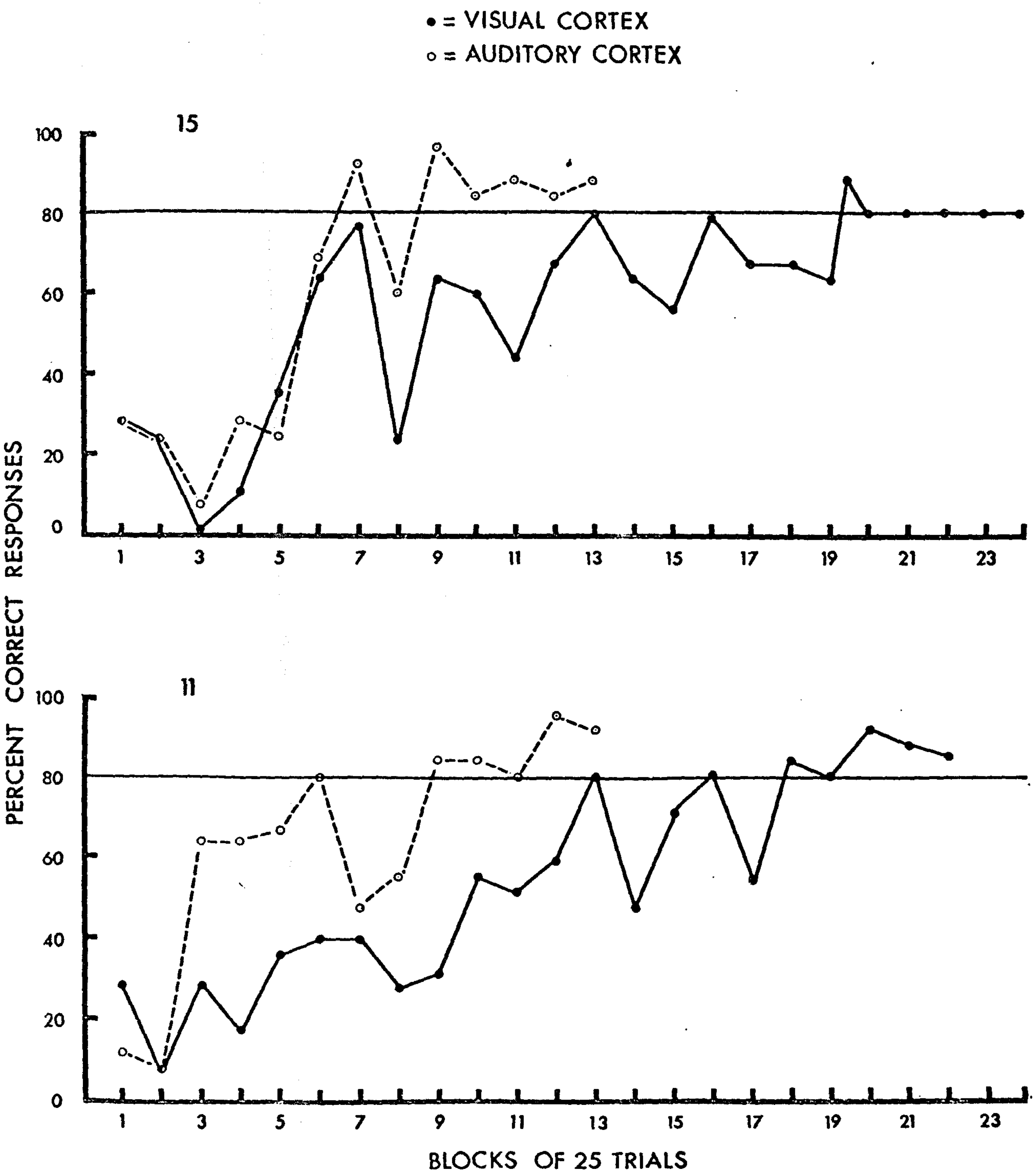
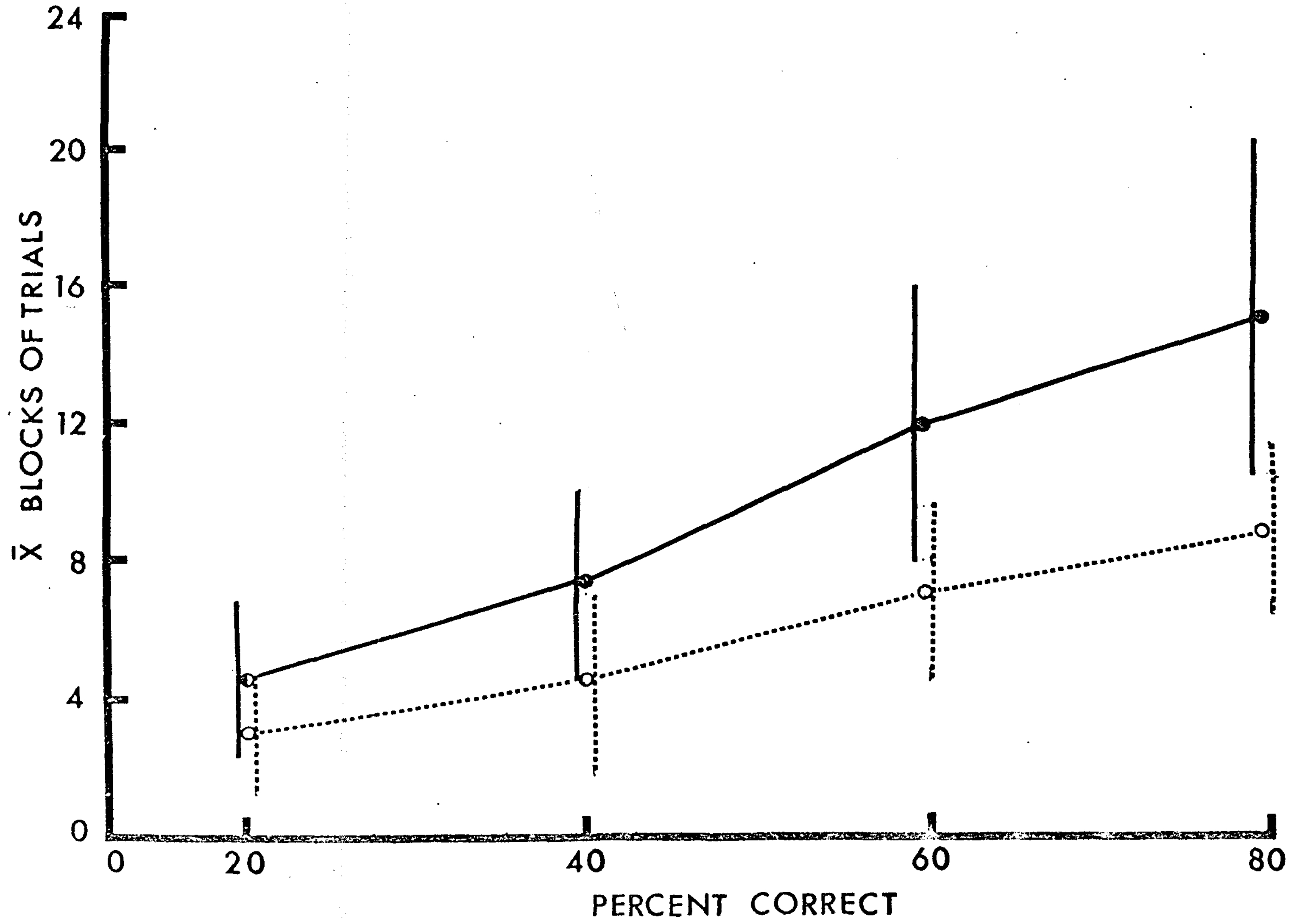

● = VISUAL CORTEX
○ = AUDITORY CORTEX
15
11
PERCENT CORRECT RESPONSES
0
20
40
60
80
100
1
3
5
7
9
11
13
15
17
19
21
23
BLOCKS OF 25 TRIALS

Fig 4. Discriminative stimulus acquisition for group I - group data. For explanation of the figure see Fig 2.

EARLY VISUAL RESTRICTION – EARLY RUN



performance in response to stimulation of auditory cortex, no consistent performance difference between areas was reflected in the performance of the rest of the group.

Fig 6 presents the pooled data for group II plotted in the same fashion as was Fig 2. Although a small difference between functions generated for the visual and auditory cortex appeared to indicate superior performance in response to stimulation of the auditory cortex, such differences failed to attain significance (F=>1.00, df=1,5). These functions were also tested for possible variability differences which might be a consequence of experimental conditions but no such differences were obtained (F=1.13, df=6,6).

On the basis of these data it may be stated that the restriction-produced modifications in the acquisition of intracranial cortical stimulation as a discriminative stimulus revealed by group I reflected more than the absence of adequate stimulation during conditioning, and that a relatively short period of visual restriction failed to distinguish between experimental and control animals.

Late Visual Restriction - Late Run

In order to investigate the possibility that the duration of visual restriction might be the critical factor in modifying cortical responsiveness rather than the age at which such restriction was initiated, animals in group III were visually restricted at 40 days of age and trained at 85 days of age.

Fig 7A-F present the individual data obtained from these

Fig 5A-D. Discriminative stimulus acquisition for group II - individual data. For explanation of the figures see Fig 1A-D.

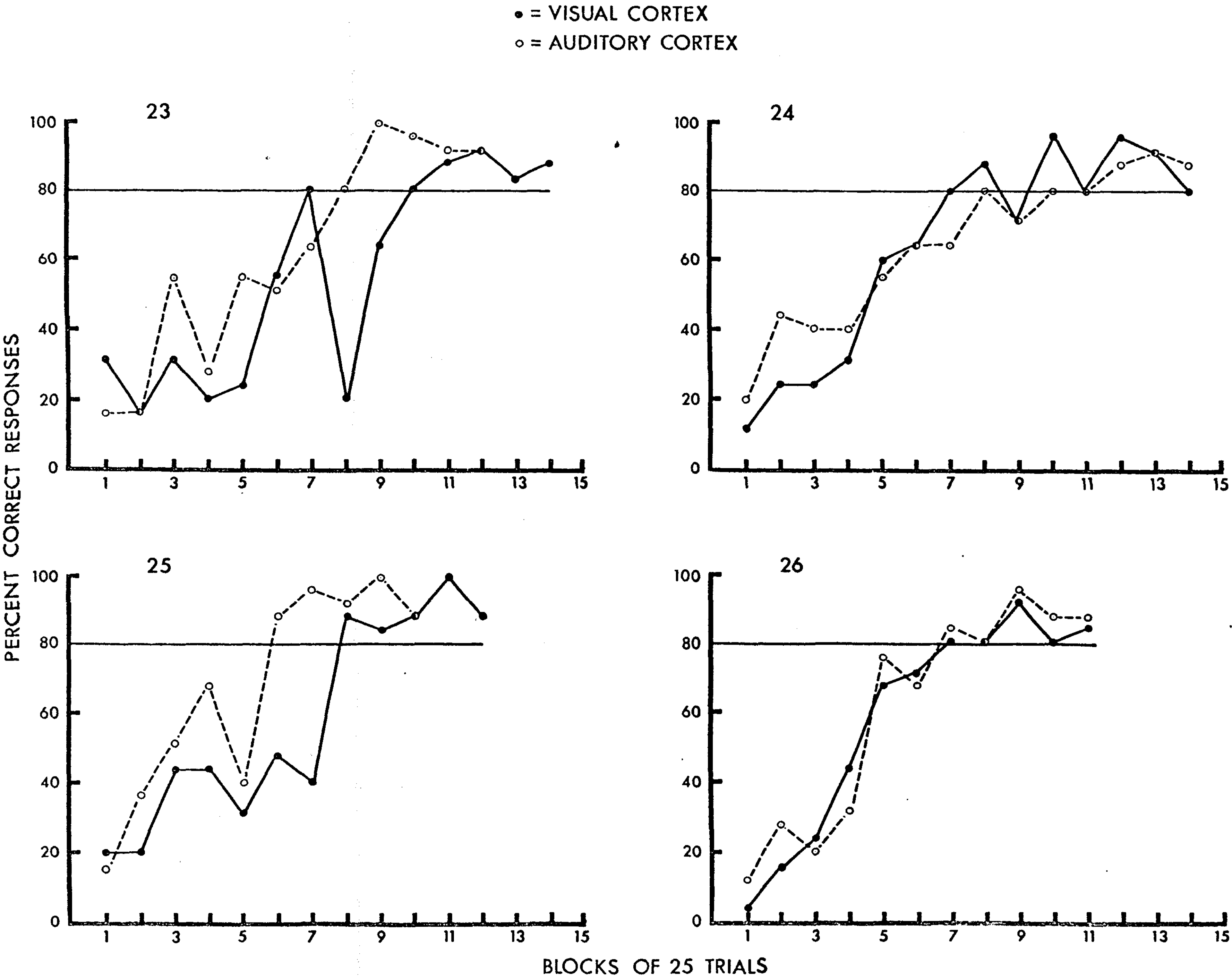
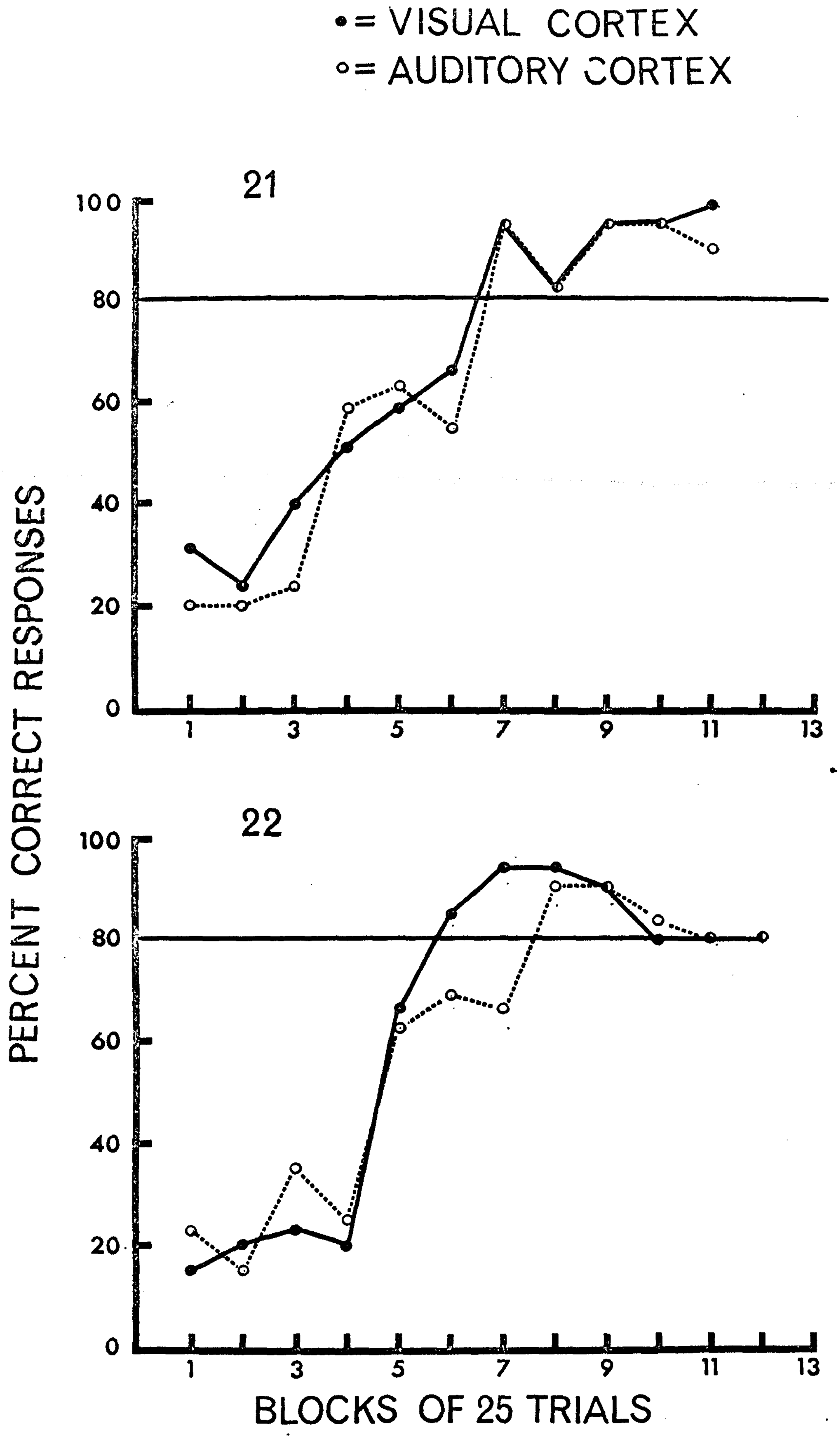

● = VISUAL CORTEX
○ = AUDITORY CORTEX
23
24
25
26
PERCENT CORRECT RESPONSES
0
20
40
60
80
100
1
3
5
7
9
11
13
15
BLOCKS OF 25 TRIALS

Fig 5E-F. Discriminative stimulus acquisition for group II - individual data. For explanation of the figures see Fig 1A-D.


● = VISUAL CORTEX
○ = AUDITORY CORTEX
21
22
PERCENT CORRECT RESPONSES
100
80
60
40
20
0
1
3
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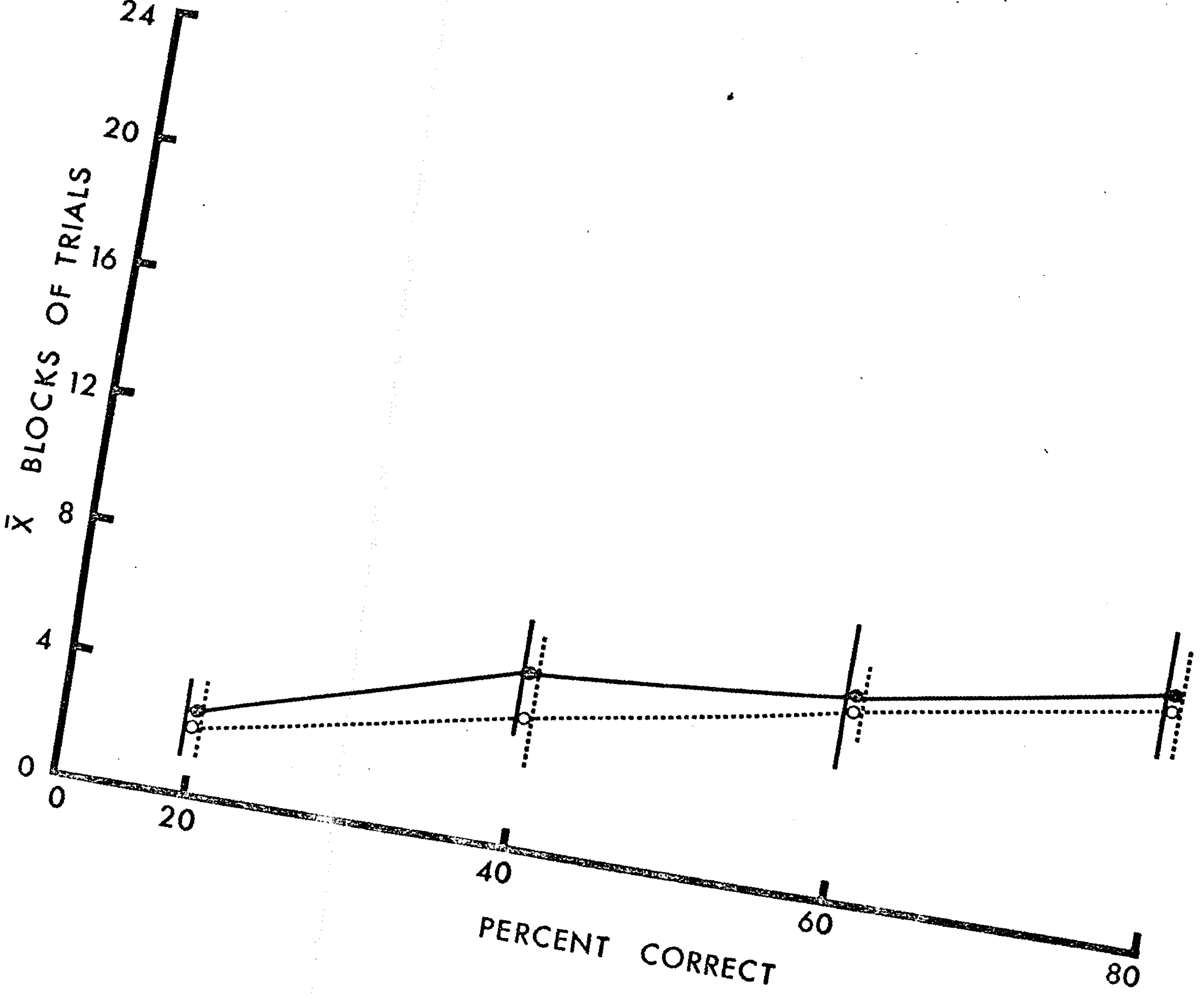
7
9
11
13
BLOCKS OF 25 TRIALS

Fig 6. Discriminative stimulus acquisition for group II - group data. For explanation of the figure see Fig 2.

LATE VISUAL RESTRICTION - EARLY RUN



animals and reveals no group trend. Thus, two animals (31 and 32) showed better performance (greater percentages of correct responses and fewer trials to criterion) in response to stimulation of auditory cortex, two animals (34 and 35) had better performance records in response to stimulation of visual cortex and two animals (33 and 36) revealed no performance differences in response to stimulation of these areas.

When these data were pooled across animals as in Fig 8 and replotted as in Fig 2, it was apparent that as a group the ease of acquiring electrical stimulation as a discriminative stimulus did not differ between the cortical loci tested. This observation was supported by the lack of statistical difference between these functions (F=≥1.00, df=1,5). Furthermore, no difference between the variability of the two functions was obtained (F=1.38, df=6,6).

The data presented thus far reveals that visual restriction can affect the acquisition of a discriminative stimulus based upon electrical stimulation of the cortex, rendering acquisition easier in the auditory cortex. These effects, however, are dependent upon the age at which restriction is begun.

One of the purposes of this investigation was to test the possibility that sensory restriction in the auditory modality might have similar effects upon the responsiveness of its primary cortical projection area. Therefore, three groups of animals restricted of audition at ages, and for durations, corresponding to those of groups I-III were employed to investigate this

Fig 7A-D. Discriminative stimulus acquisition for group III - individual data. For explanation of the figures see Fig 1A-D.

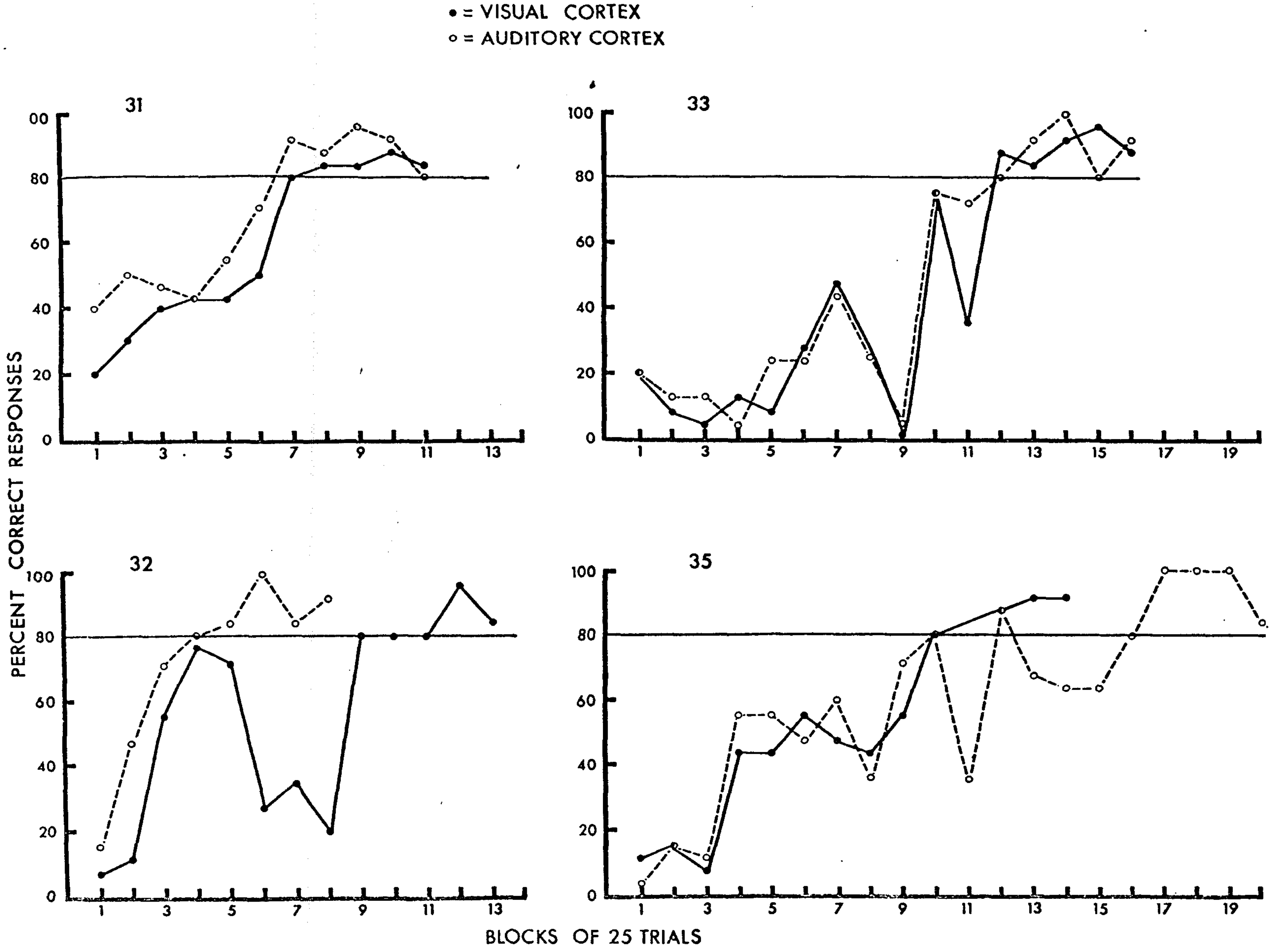

● = VISUAL CORTEX
○ = AUDITORY CORTEX
31
33
32
35
PERCENT CORRECT RESPONSES
BLOCKS OF 25 TRIALS
00
100
80
60
40
20
0
1
3
5
7
9
11
13
15
17
19

Fig 7E-F. Discriminative stimulus acquisition for group III - individual data. For explanation of the figures see Fig 1A-D.

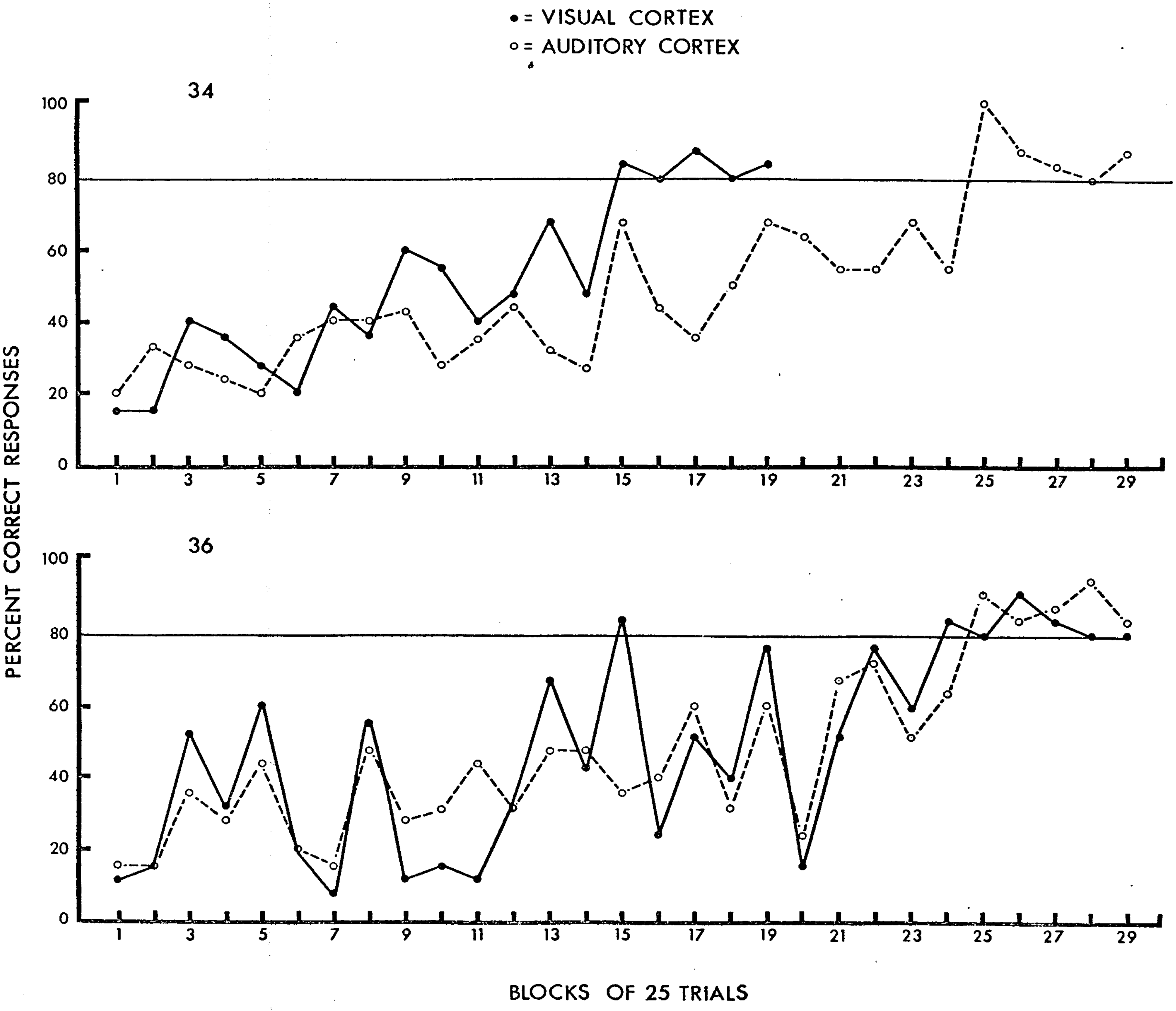
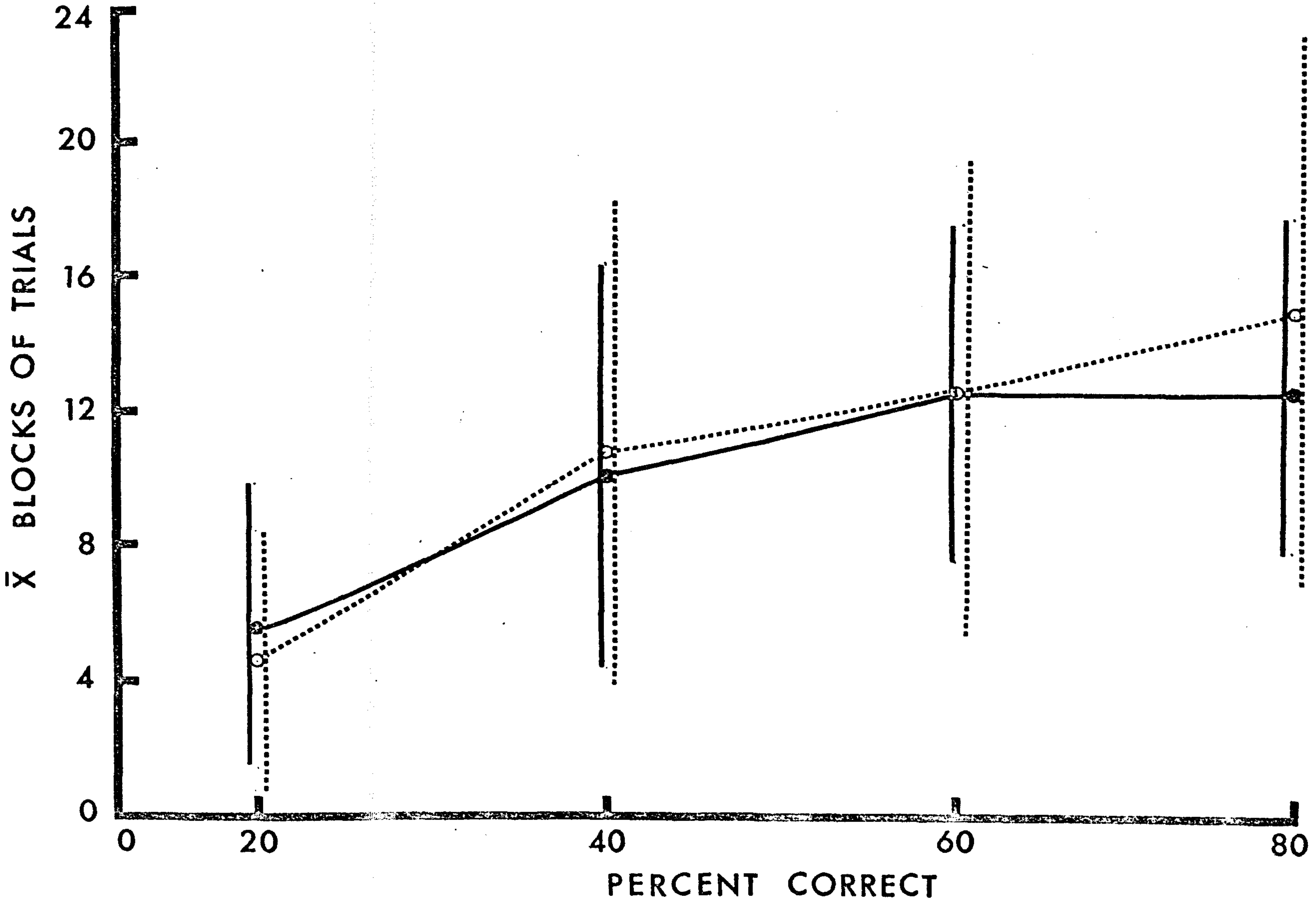

● = VISUAL CORTEX
○ = AUDITORY CORTEX
34
36
PERCENT CORRECT RESPONSES
0
20
40
60
80
100
1
3
5
7
9
11
13
15
17
19
21
23
25
27
29
BLOCKS OF 25 TRIALS

Fig 8. Discriminative stimulus acquisition for group III - group data. For explanation of the figure see Fig 2.

LATE VISUAL RESTRICTION – LATE RUN



possibility.

Effects Of Auditory Restriction Upon Cortical Conditioning

Early Auditory Restriction - Early Run

Fig 9A-F present the individual data obtained from animals whose hearing was restricted beginning at 13 days of age and who were trained at 45 days of age. As was true of the comparable visually restricted group, these animals revealed consistently superior performance when the nonrestricted cortical area was stimulated, so that greater numbers of correct responses per block of trials, as well as fewer blocks of trials required to reach criterion, were found in response to stimulation of visual cortex. This difference was negligible during initial training, but grew coincident with experience in the training situation.

The difference between discriminative stimulus acquisition in visual and auditory cortex is more clearly apparent in Fig 10, which presents the group data obtained from these animals (replotted as in Fig 2). Superior performance in terms of fewer blocks of trials required to reach these successive performance levels was evidenced in response to stimulation of the visual cortex. This disparate performance is more pronounced at the 40 and 60 per cent levels, than at the 20 and 80 per cent levels. These acquisition differences were found to be statistically significant ($F=13.18$, $df=1,5$ $p= <.05$) and no variability differences between functions were statistically significant ($F=1.35$, $df=6,6$).

Fig 9A-D. Discriminative stimulus acquisition for group IV - individual data. For explanation of the figures see Fig 1A-D.

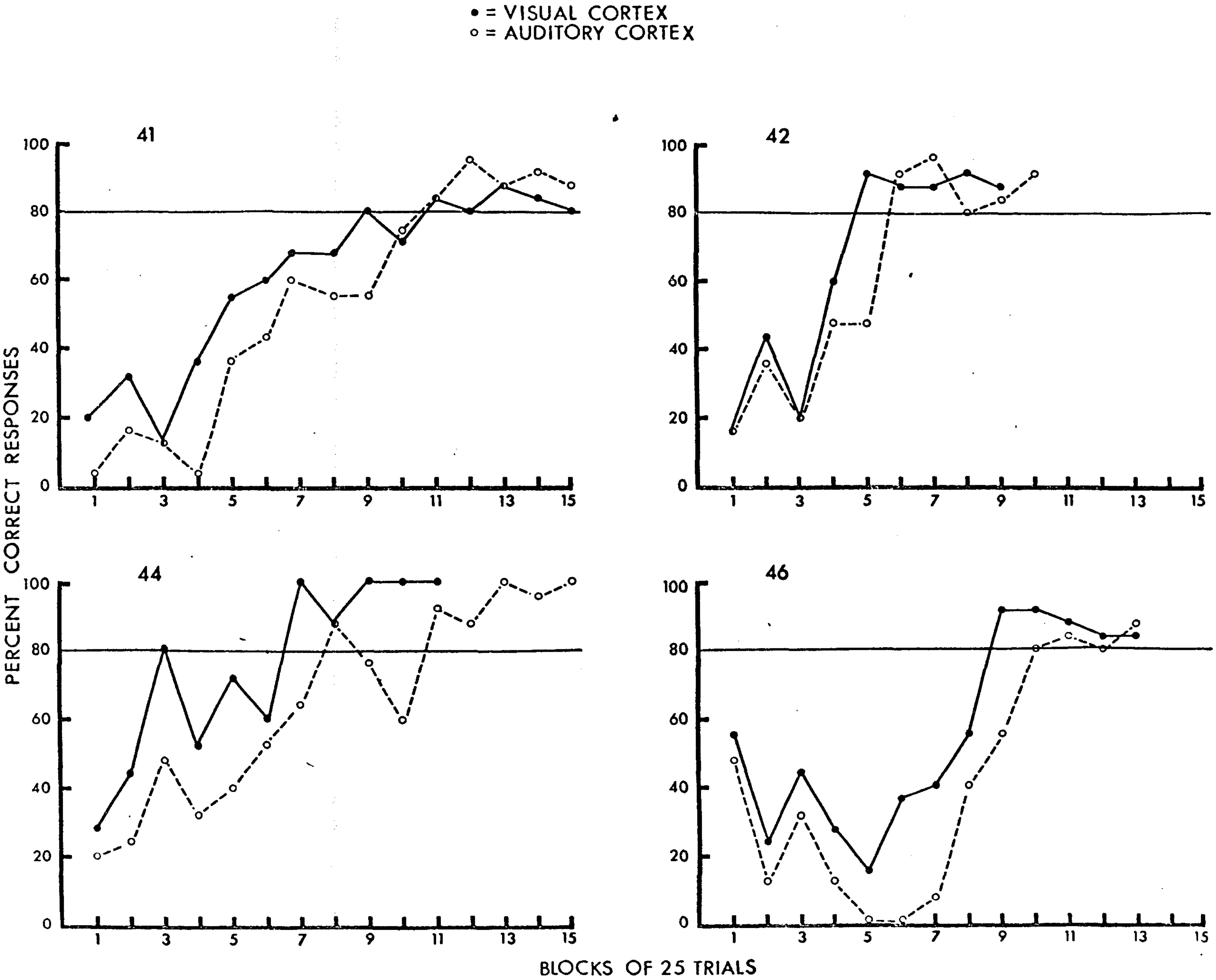

● = VISUAL CORTEX
○ = AUDITORY CORTEX
41
42
44
46
PERCENT CORRECT RESPONSES
0
20
40
60
80
100
1
3
5
7
9
11
13
15
BLOCKS OF 25 TRIALS

Fig 9E-F. Discriminative stimulus acquisition for group IV - individual data. For explanation of the figures see Fig 1A-D.

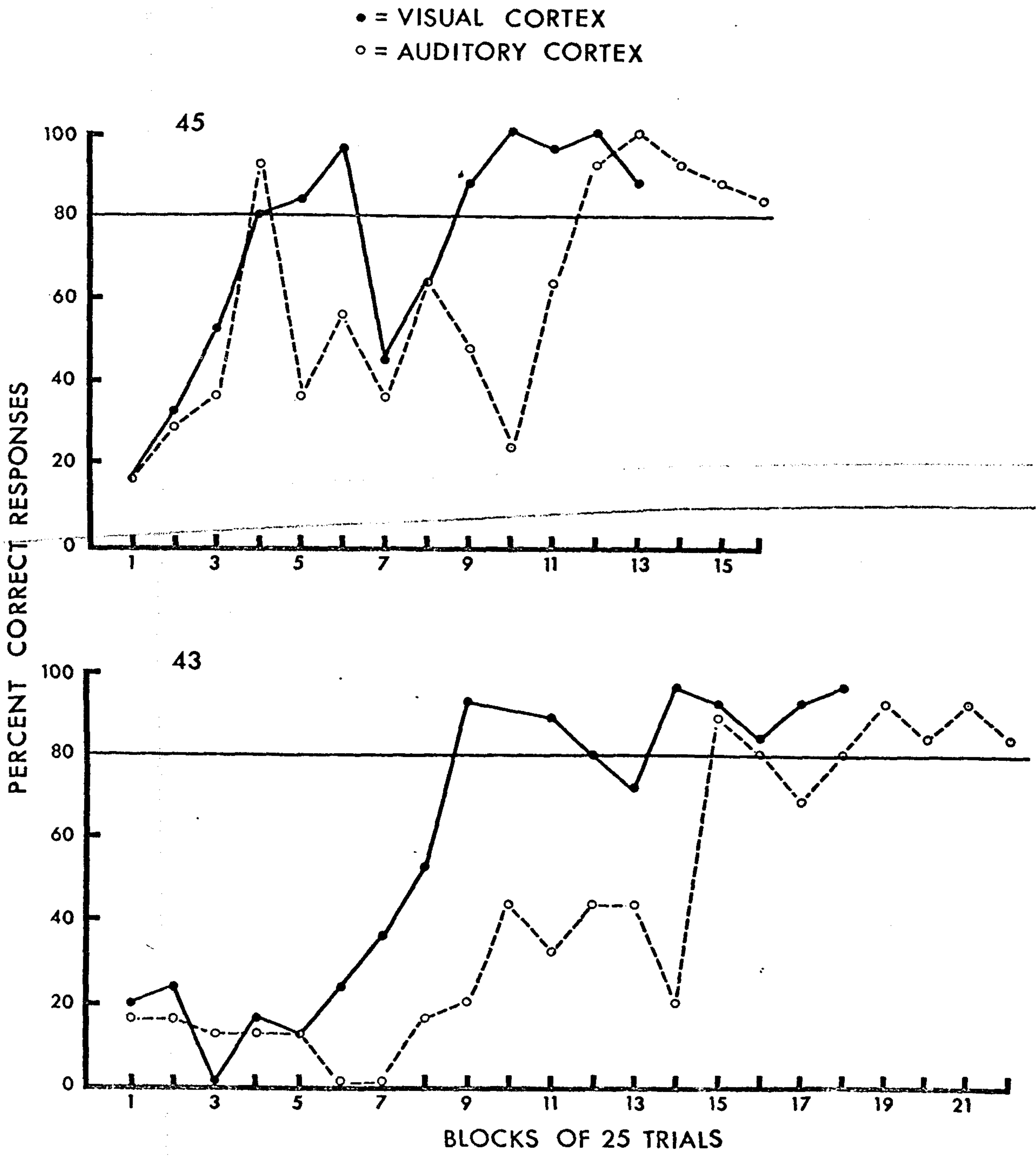
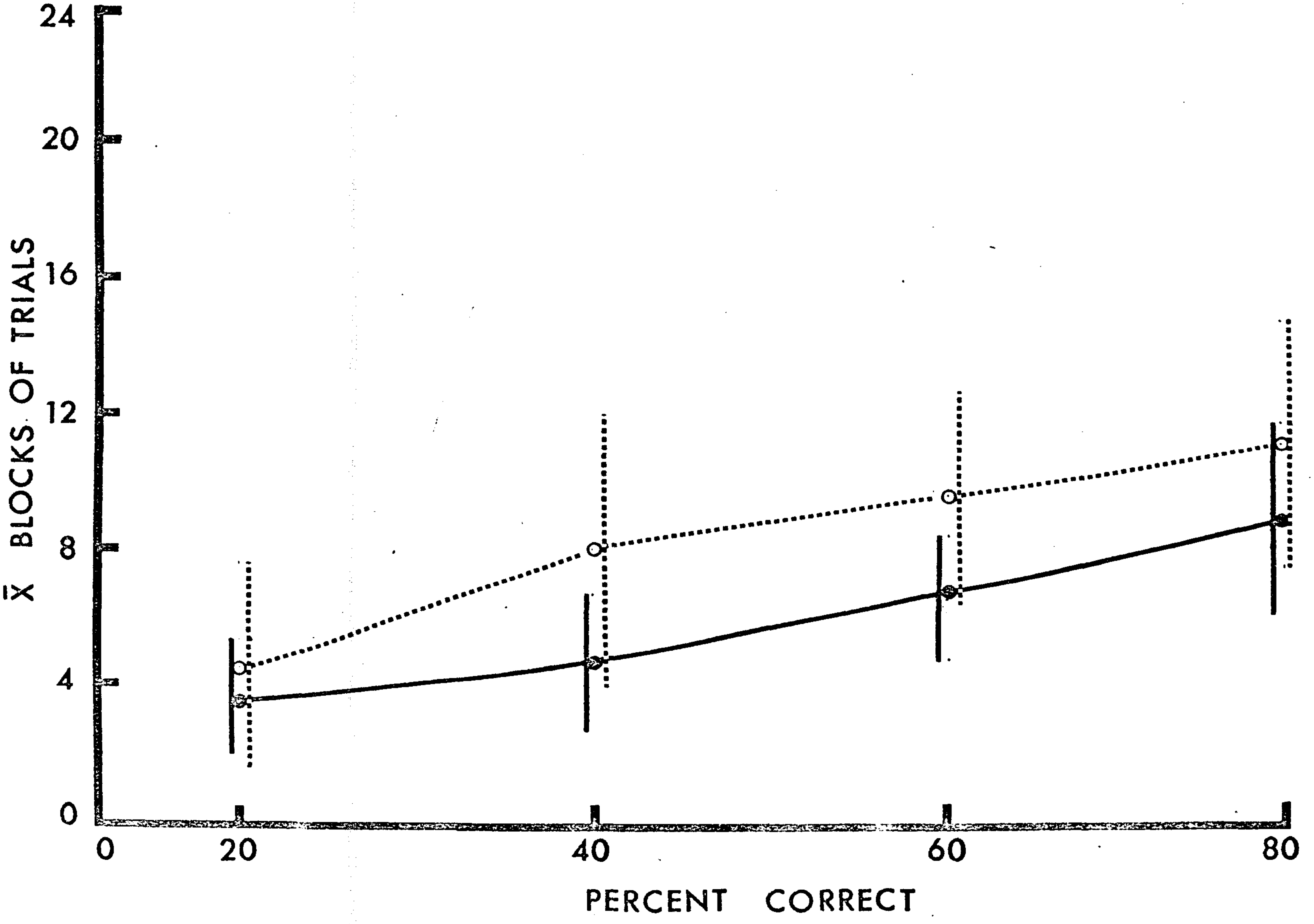

● = VISUAL CORTEX
○ = AUDITORY CORTEX
45
43
PERCENT CORRECT RESPONSES
0
20
40
60
80
100
1
3
5
7
9
11
13
15
17
19
21
BLOCKS OF 25 TRIALS

Fig 10. Discriminative stimulus acquisition for group IV - group data. For explanation of the figure see Fig 2.

EARLY AUDITORY RESTRICTION - EARLY RUN



Both early visual and early auditory restriction have the capacity to modify the ability of the organism to utilize stimulation as a cue for a lever-press response so that acquisition is facilitated in the nonrestricted as compared to the restricted cortical projection area.

Late Auditory Restriction - Early Run

Group V animals were employed for the same purpose as were group II animals - to test the possibility that a withdrawal of adequate stimulation during training was a significant contributor to the performance differences in response to stimulation of visual and auditory cortex observed in group IV. Therefore, animals in group V were restricted of hearing at 40 days of age and trained at 45 days of age. Fig 11A-F present the individual data for these animals and shows that no consistent differences between responses to stimulation of visual and auditory cortex were obtained.

Fig 12 presents the group data for these animals (replotted as in Fig 2). Although there appears to be a small difference between the functions in the number of blocks of trials required to reach the successive performance levels designated, statistical analysis reveals this difference to be nonsignificant (F=5.29, df=1,5). Similarly, no significant differences between the variability of these functions was obtained (F=1.06, df=6,6).

Apparently, auditory restriction at maturity for a comparatively short period of time has no greater effect upon the

Fig 11A-D. Discriminative stimulus acquisition for group V - individual data. For explanation of the figures see Fig 1A-D.

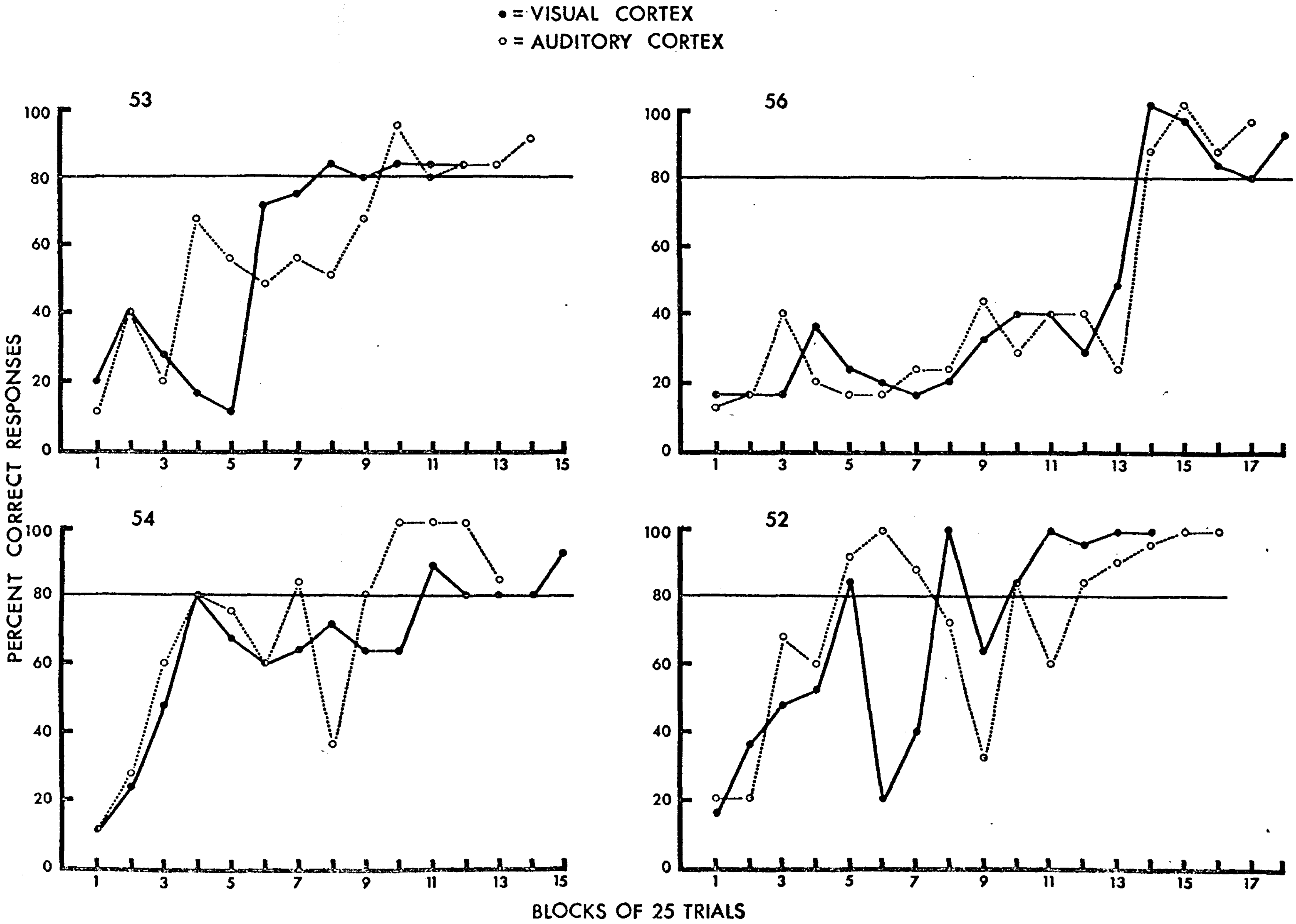

• = VISUAL CORTEX
○ = AUDITORY CORTEX
53
56
54
52
PERCENT CORRECT RESPONSES
0
20
40
60
80
100
1
3
5
7
9
11
13
15
17
BLOCKS OF 25 TRIALS

Fig 11E-F. Discriminative stimulus acquisition for group V - individual data. For explanation of the figures see Fig 1A-D.

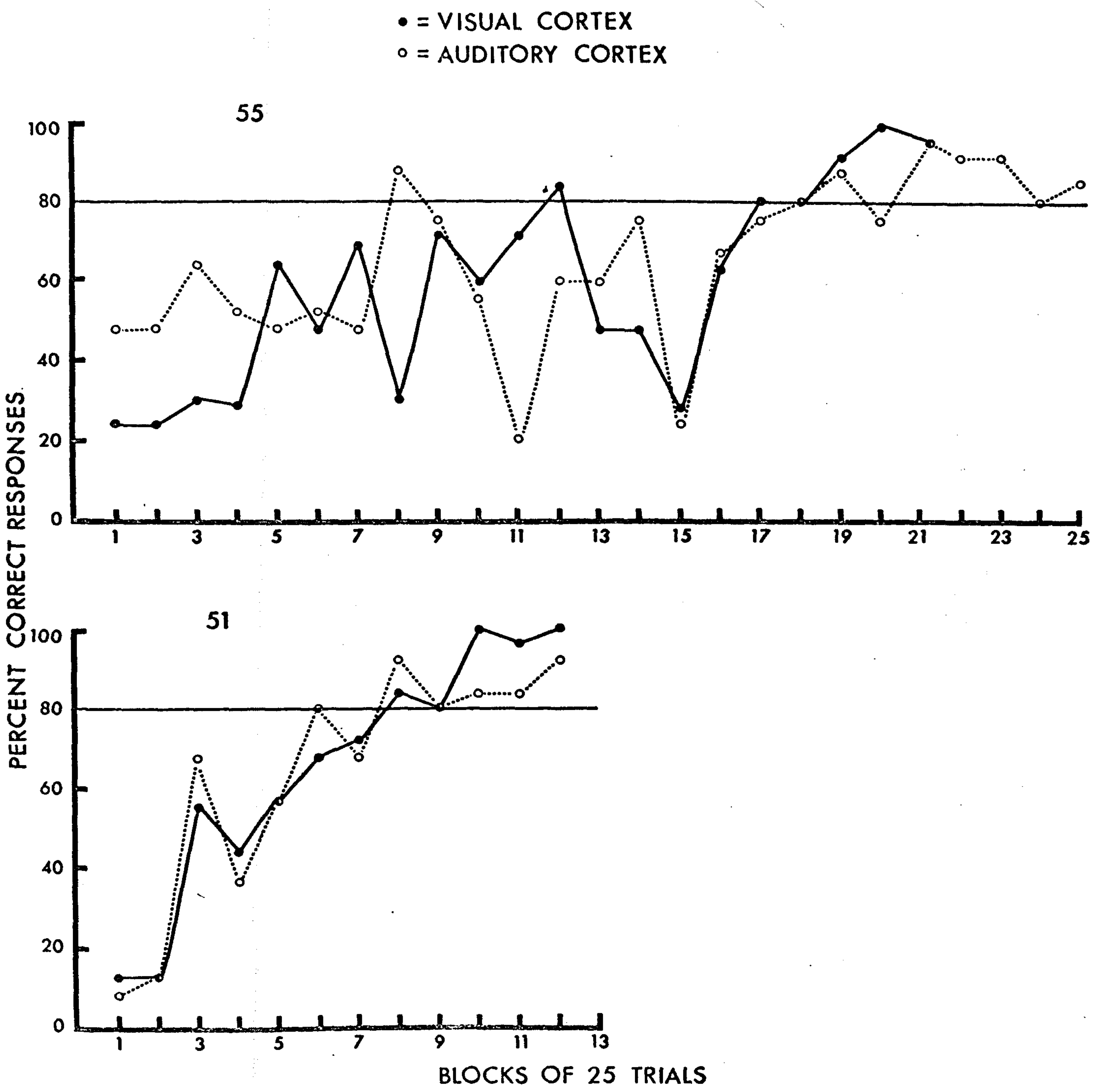
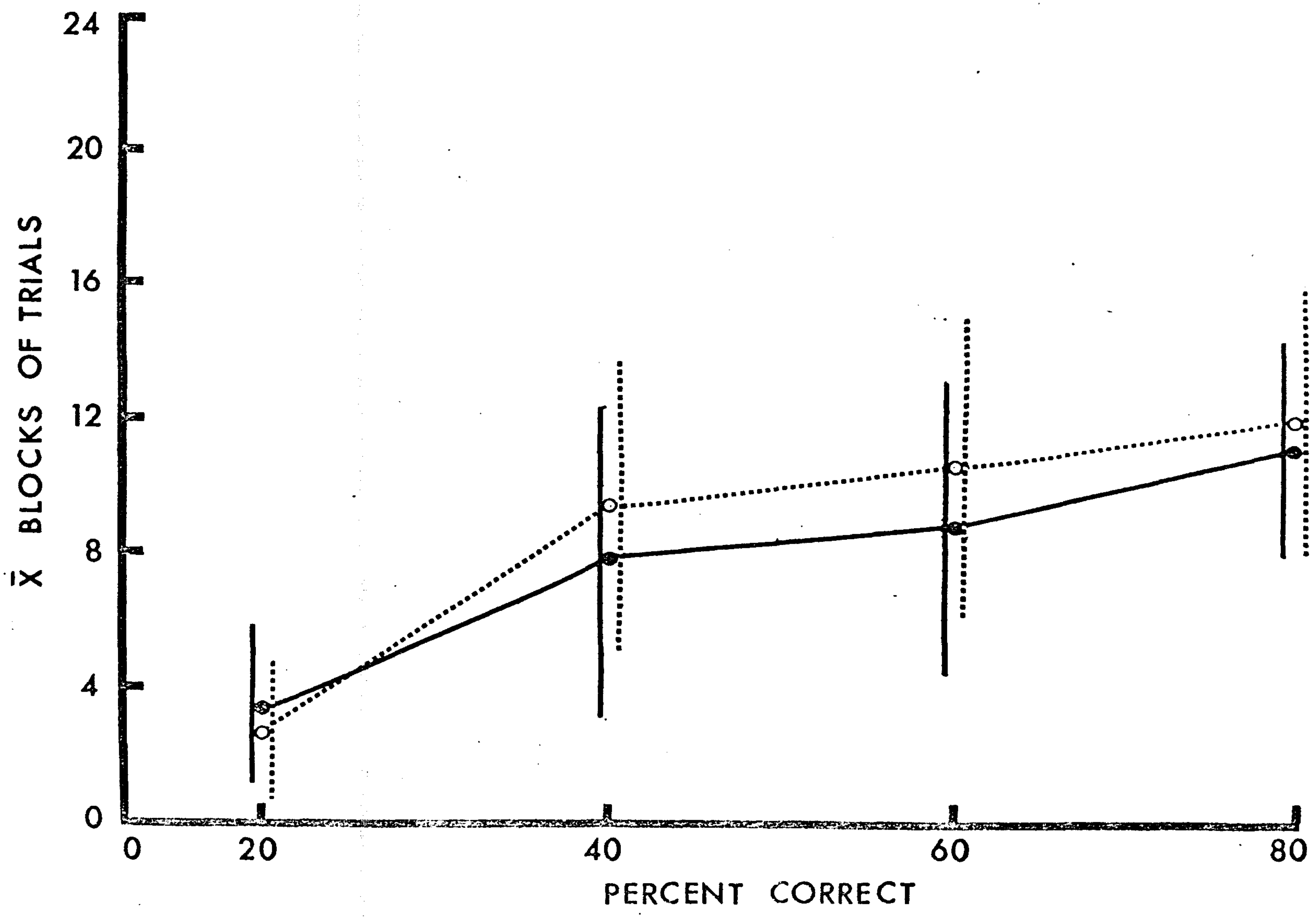

● = VISUAL CORTEX
○ = AUDITORY CORTEX
55
51
PERCENT CORRECT RESPONSES
BLOCKS OF 25 TRIALS
0
20
40
60
80
100
1
3
5
7
9
11
13
15
17
19
21
23
25

Fig 12. Discriminative stimulus acquisition for group V - group data. For explanation of the figure see Fig 2.

LATE AUDITORY RESTRICTION - EARLY RUN



acquisition of a discriminative stimulus based upon cortical stimulation than does a similar period of visual restriction at maturity.

Late Auditory Restriction - Late Run

Animals within this group (VI) were included in the present study to test the possibility that auditory restriction for a prolonged period at any age may induce changes in the effectiveness of cortical stimulation. Therefore, these animals were deprived of hearing at 40 days of age and trained at 85 days of age.

Fig 13A-F present the individual data obtained from group VI. As was true of group III, group VI appeared to have a rather nonuniform composition. While three animals (65,66 and 62) showed markedly better performance in response to stimulation of auditory cortex, one animal (63) performed better in response to stimulation of visual cortex, while two animals (61 and 64) responded equally to stimulation of either cortival area. The performance of animals 65,66 and 62 which showed considerably better performance in response to stimulation of the restricted cortical projection area was similar to the performance of animals 34 and 35. This lack of group consistency shown in groups III and VI may be a function of age rather than of restriction.

While the group differences represented in Fig 14 (replotted as in Fig 2) indicates superior performance of these animals in response to stimulation of auditory cortex, this performance difference failed to achieve statistical significance

Fig 13A-D. Discriminative stimulus acquisition for group VI - individual data. For explanation of the figures see Fig 1A-D.

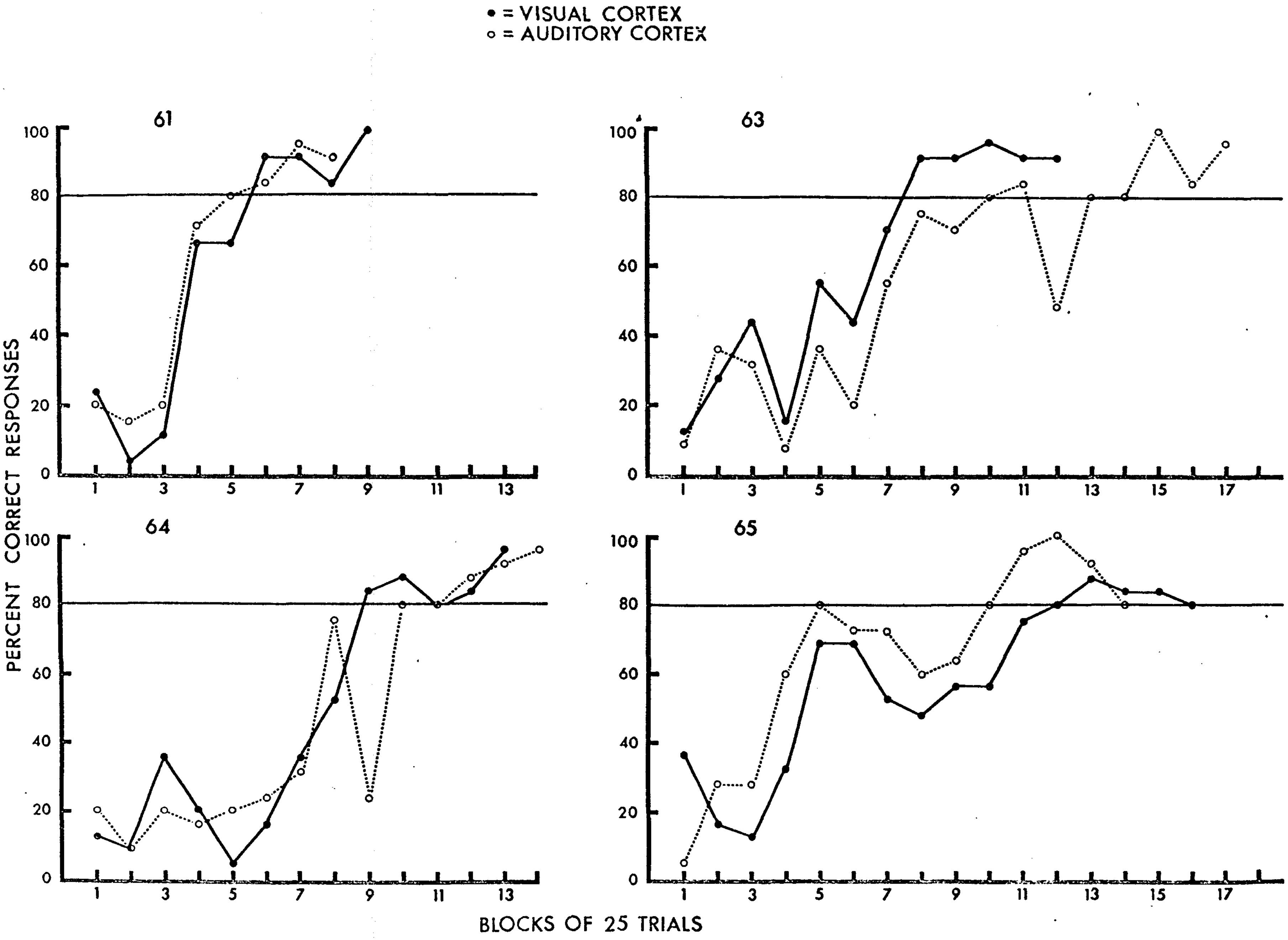

● = VISUAL CORTEX
○ = AUDITORY CORTEX
61
63
64
65
PERCENT CORRECT RESPONSES
0
20
40
60
80
100
1
3
5
7
9
11
13
15
17
BLOCKS OF 25 TRIALS

Fig 13E-F. Discriminative stimulus acquisition for group VI - individual data. For explanation of the figures see Fig 1A-D.

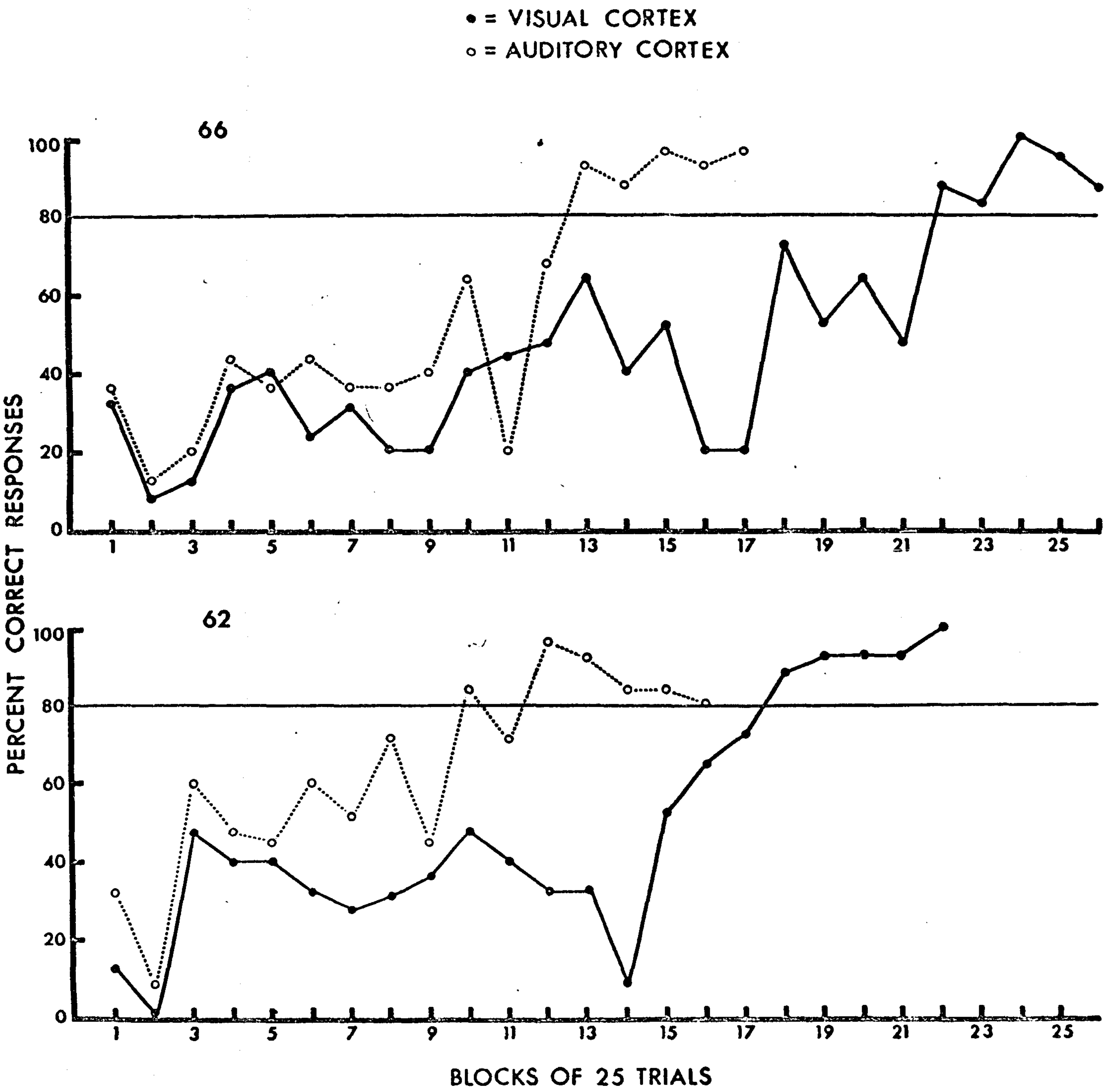
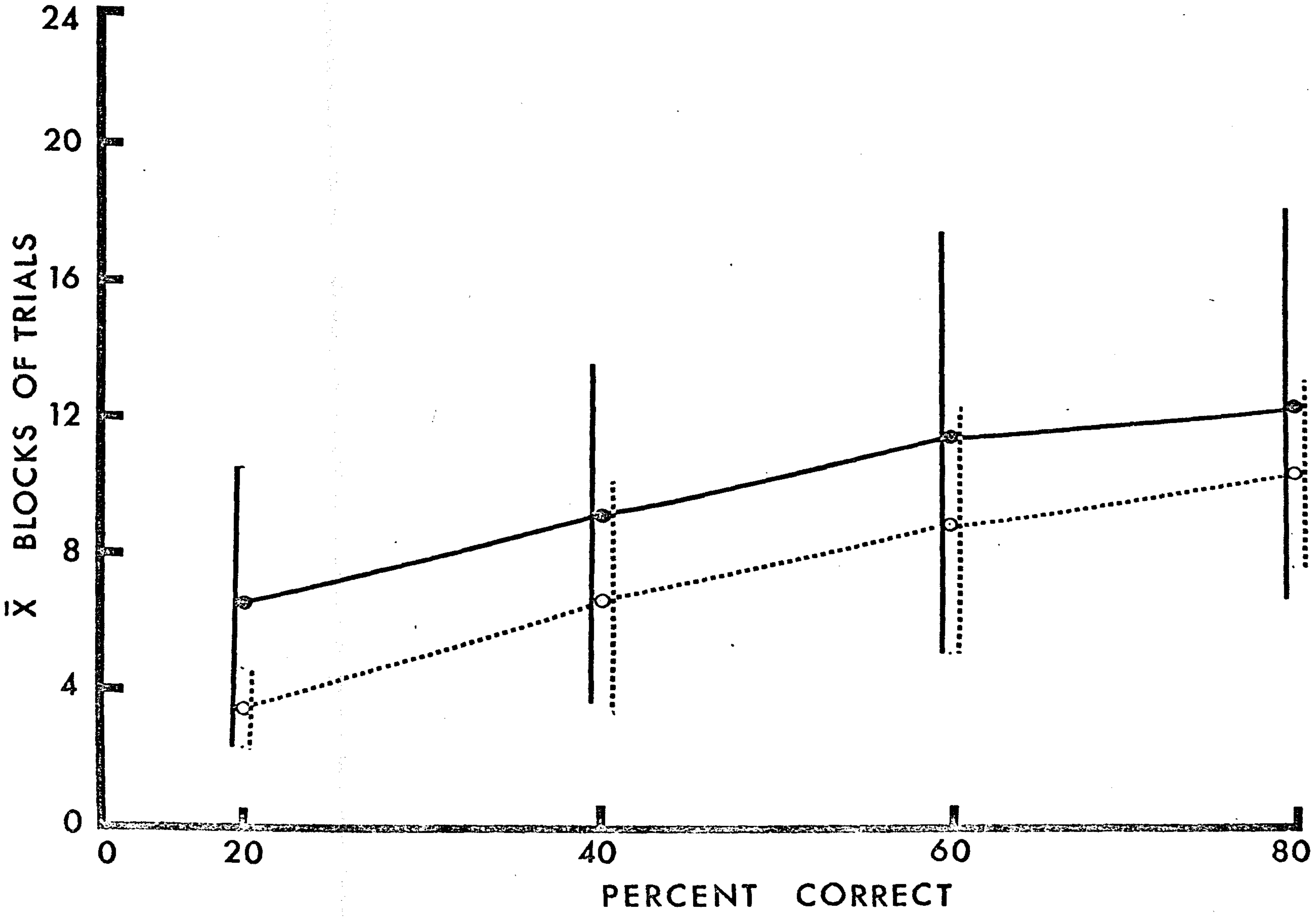

● = VISUAL CORTEX
○ = AUDITORY CORTEX
66
62
PERCENT CORRECT RESPONSES
100
80
60
40
20
0
1
3
5
7
9
11
13
15
17
19
21
23
25
BLOCKS OF 25 TRIALS

Fig 14. Discriminative stimulus acquisition for group VI - group data. For explanation of the figure see Fig 2.

LATE AUDITORY RESTRICTION - LATE RUN



(F=1.79, df=1,5). Variability between the functions also failed to show a significant difference (F=1.49, df=6,6).

These data indicate that paranatal sensory restriction modified cortical responsiveness so that acquisition of an intracranial electrical stimulus as a discriminative stimulus was easier in response to stimulation of the nonrestricted as compared to the restricted primary cortical projection area. Clearly these effects are dependent upon the age at which restriction was initiated and animals with histories of adequate sensory stimulation during infancy are resistant to these effects even when the restriction period, during adulthood, is extensive. These within-group comparisons of discriminative stimulus acquisition are summarized in Table IV.

Experimental-Control Group Comparisons

On the basis of the analysis presented thus far, it is not possible to determine whether the observed modifications in performance of groups I and IV were due to a decrement in the ease of discriminative stimulus acquisition in the restricted cortical area, or due to an increase in acquisition ease in the nonrestricted cortical area. Furthermore, the performance of groups II, III, V and VI may have differed from that of unrestricted controls in both cortical areas despite failure to obtain within-group differences when these areas were compared. Therefore, comparisons between experimental and control groups were carried out by means of a two-factor mixed design with repeated

Table IV

Within-Groups Comparisons Of Discriminative Stimulus Acquisition In Response To Stimulation Of Visual And Auditory Cortex

Group	F
I	13.05*
II	>1.00
III	>1.00
IV	13.18*
V	5.29
VI	1.79
VII	>1.00

* $p < .05$
** $p < .01$

Table V

Experimental-Control Group Comparisons Of Discriminative Stimulus Acquisition In Response To Stimulation Of Visual Cortex

Control (VII) versus Group...	F
I	1.97
II	1.15
III	1.82
IV	$<$ 1.00
V	$<$ 1.00
VI	1.69

* $p < .05$
** $p < .01$

Table VI

Experimental-Control Group Comparisons Of Discriminative Stimulus Acquisition In Response To Stimulation Of Auditory Cortex

Control (VII) versus Group...	F
I	> 1.00
II	2.44
III	1.72
IV	> 1.00
V	1.27
VI	> 1.00

* $p < .05$
** $p < .01$

Table VII

Experimental-Control Group F Tests For Restriction-Produced Variability

Control (VII) versus Group...	Visual Cortex F	Auditory Cortex F
I	1.09	1.42
II	1.69	1.98
III	1.32	1.77
IV	1.45	1.11
V	1.06	1.08
VI	1.28	1.19

* $p < .05$
** $p < .01$

measures on one factor (Winer 302-312). These data are summarized in Tables V and VI. The performance of each group in response to stimulation of a particular cortical locus was compared with the performance of unrestricted controls in response to stimulation of that same area. Despite the significant within-group differences obtained in groups I and IV, there were no significant differences between the performance of any experimenta group when compared to unrestricted controls. However, Fig 15 and Fig 16 suggest that unimodal sensory restriction influenced the acquisition of cortical stimulation as a cue when that stimulation was presented to, or outside of, the primary cortical projection area. In the case of group I this took the form of retarded learning (greater numbers of trials to successive performance levels) in response to stimulation of visual cortex, and somewhat facilitated learning in response to stimulation of auditory cortex. In group IV this took just the opposite form, with learning in response to stimulation of visual cortex showing enhancement while responses to stimulation of auditory cortex were retarded. These data suggest the possibility of compensatory mechanisms, or facilitated learning in nonrestricted sensory modalities.

On the other hand, groups II, III, V and VI showed neither within-groups differences, nor differences in comparison to unrestricted controls in discriminative stimulus acquisition (see Tables V and VI). Variability analyses were also conducted and revealed no significant differences between experimental and

Fig 15. Mean number of blocks of trials required by animals in groups I and VII to reach and maintain or surpass levels of 20,40,60 and 80 per cent correct responses. The abbreviation E.V.R. - E.R. denotes Early Visual Restriction - Early Run (group I) while UNRESTR. denotes unrestricted controls (group VII).

EARLY VISUAL RESTRICTION – EARLY RUN AND UNRESTRICTED

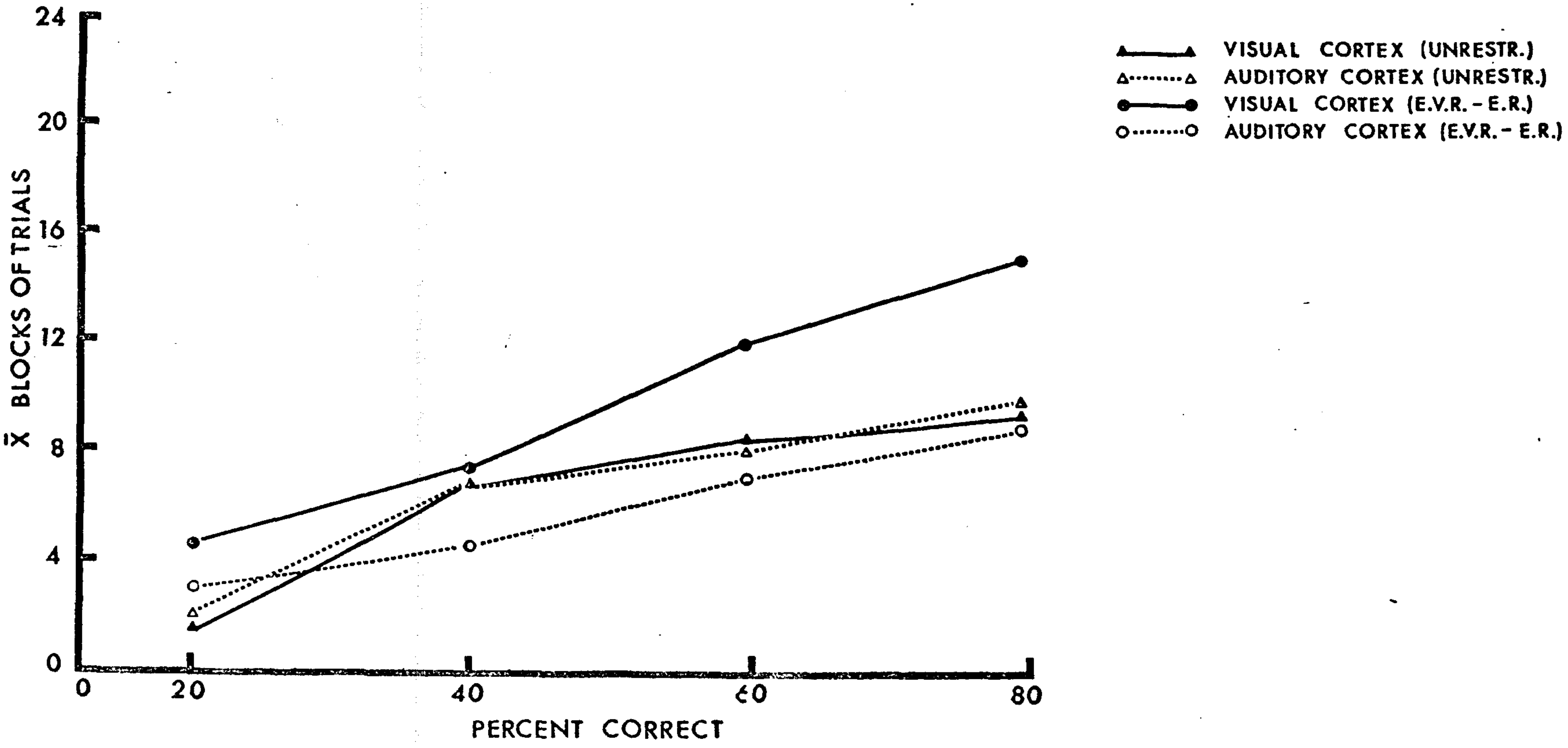
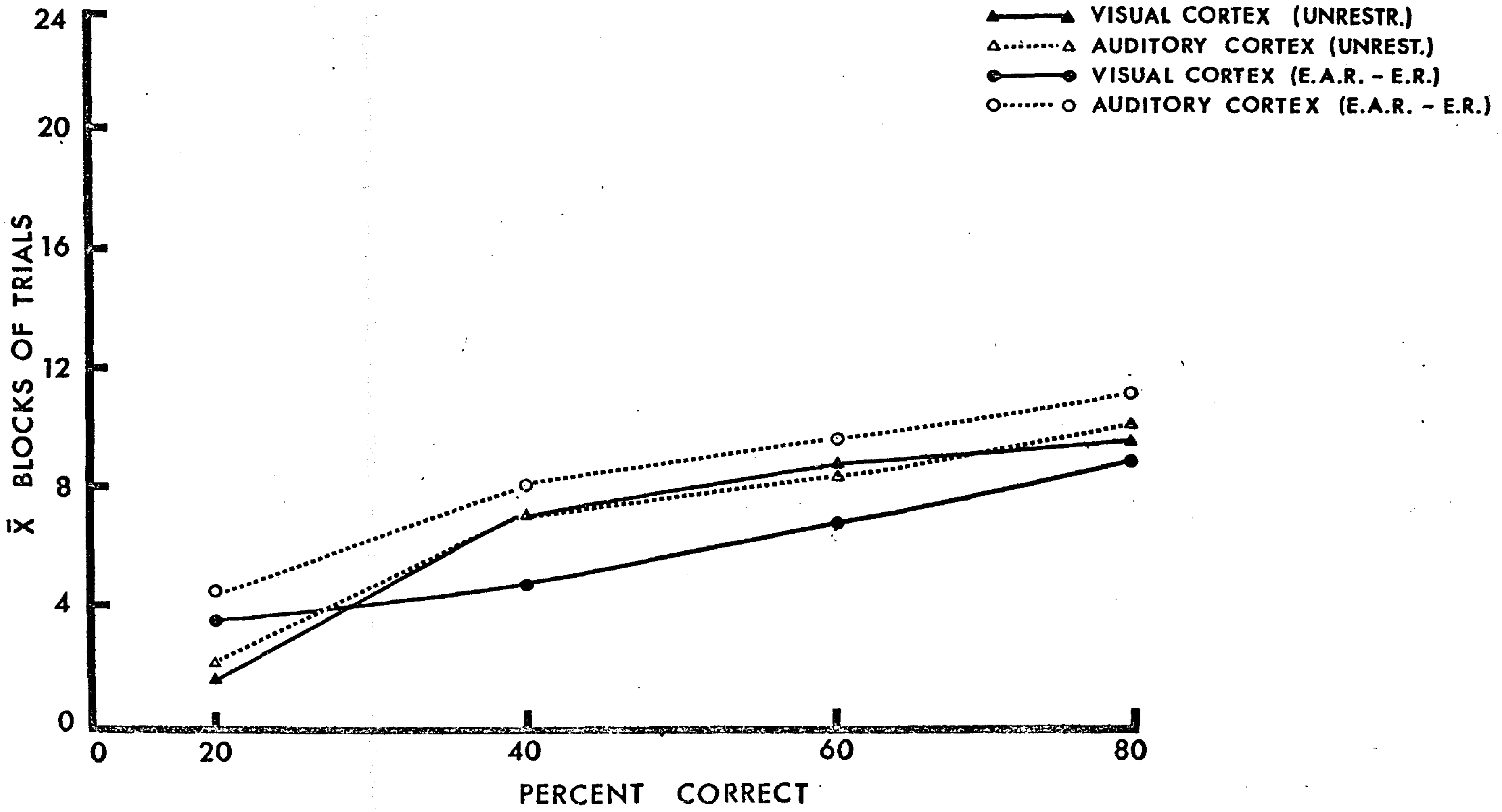


Fig 16. Mean number of blocks of trials required by animals in groups IV and VII to reach and maintain or surpass levels of 20,40,60 and 80 per cent correct responses. The abbreviation E.A.R.- E.R. denotes Early Auditory Restriction - Early Run (group IV) while UNRESTR. denotes Unrestricted controls (group VII).

EARLY AUDITORY RESTRICTION - EARLY RUN AND UNRESTRICTED



control groups (see Table VII). It was also noted that within-groups analysies failed to reflect significant variability differences in any of the groups employed in the present study.

It may now be firmly stated that treatment effects were reflected only in the experimental groups experiencing sensory restriction in infancy, with better performance being shown in response to stimulation of the nonrestricted as compared with the restricted primary cortical projection area.

Effects Of Decreasing Stimulus Intensity Upon Cortical Conditionir

Following criterion performance in response to stimulation of both visual and auditory cortex with a current intensity of 80% of behavioral threshold, current intensity was reduced to 65%. This was done first to test the possibility that a decrement in stimulus intensity would reveal treatment effects not observable at higher current intensities, and secondly, to tes the possibility that transfer of training or stimulus generalization would be less efficient in groups I and IV.

Only 14 of the 30 animals surviving to be tested at a current magnitude of 65% of behavioral threshold failed to reach criterion performance immediately (80% correct responses per block of trials for the first 5 blocks of trials). Table VIII presents the data for these animals. Of these 14 subjects, two (25 and 34) failed to reach criterion within the 15 blocks of trials limit set for such performance. Of the remaining 11 animals failing to reach criterion immediately, 9 showed below

Table VIII

Number Of Blocks Of Trials On Which Performance Was Below Criterion At A Current Intensity Of 65% Of Behavioral Threshold

Animal	Visual Cortex	Auditory Cortex	No. Of Animals Tested
Group I			5
15	1	4	
Group II			5
22	3	5	
24	1	1	
25	15	15	
26	1	1	
Group III			5
33	3	3	
34	12	15	
35	0	1	

Table VIII (Con't)

Animal	Visual Cortex	Auditory Cortex	No. Of Animals Tested
Group IV			3
41	1	1	
44	0	1	
Group V			3
53	0	2	
Group VI			5
63	1	1	
64	1	0	
65	2	0	
Group VII			4

Table IX

Number Of Blocks Of Trials On Which Performance Was Below Criterion At A Current Intensity Of 50% Of Behavioral Threshold

Animal	Visual Cortex	Auditory Cortex	No. Of Animals Tested
Group I			4
14	0	2	
17	0	1	
Group II			4
21	0	6	
26	1	15	
Group III			3
33	13	13	
Group IV			3
42	0	1	
44	0	2	

Table IX (Con't)

Animal	Visual Cortex	Auditory Cortex	No. Of Animals Tested
Group V			3
52	0	1	
Group VI			4
64	6	0	
Group VII			3
72	2	0	

criterion performance on only two occasions in either cortical area. In short, these data failed to discriminate between groups on the basis of transfer of training or task difficulty.

Of the 24 animals surviving to be tested at a current magnitude of 50% of behavioral threshold, only 10 failed to reach criterion immediately. These data are presented in Table IX. Only two of these animals failed to reach criterion within the allotted 15 blocks of trials (animals 26 and 57). Six of the remaining eight animals failing to reach criterion immediately performed at criterion or better on all occasions but two. These data failed to discriminate between groups. Apparently once criterion performance is shown in response to current intensities 80% that of behavioral threshold a decrement in stimulus intensity to 65 and 50% has a negligible effect upon performance.

Histological Retinal Examination

The eyes of 15 animals were examined for possible pathologica changes produced by experimental conditions. These subjects included all group I animals, three group II and three group III animals, as well as one group V and one group VII animal. No evidence of gross pathological changes was obtained.

Other Observations

In order to investigate the possibility that a lowered lever-pressing tendency might be a consequence of the experimental conditions, and that this might contribute to later performance differences in the training situation, numbers of lever-presses to obtain water in a 15 minute free responding situation were obtained prior to training animals with intracranial stimulation. Table X presents the mean number of such responses at stabilization (three consecutive 15 minute periods not differing by more than 10% in the number of responses emitted) for each group of animals. A significantly lower lever-pressing tendency was noted in groups I and VI(by two-tailed t tests) in comparison to unrestricted controls. However, lever-pressing rates were relatively high in all groups and response rate could in no way have predicted the double dissociation phenomenon present in groups I and IV. Furthermore, while group VI animals had a significantly lower lever-pressing tendency than controls, no performance differences were obtained in the later training situation.

Table X

Two-Tailed t Tests For Mean Number Of Lever-Presses Per 15 Minute Interval

Group VII versus Group...	Mean Number Of Lever Presses	t
I	322.57	3.13**
II	391.17	.22
III	416.06	.95
IV	409.22	1.11
V	394.00	.20
VI	325.90	3.41**
VII	385.06	----

* $p < .05$
** $p < .01$

DISCUSSION

The present study revealed that normal rats utilized intracranial electrical stimulation as a discriminative stimulus equally well when stimulation was presented to either the visual or the auditory cortex. However, ability to utilize electrical stimulation of a primary cortical projection area as a discriminative stimulus was affected by early restriction of the corresponding peripheral receptor organ. Early visual restriction resulted in significant retardation in learning when visual cortex as compared to auditory cortex was stimulated; auditory restriction had the opposite effect.

Since restriction begun at day 13 resulted in significant modifications in cortical responsiveness, but restriction begun at day 40 for a minimum of 45 days had no effect, it may be concluded that sensitivity to the effects of restriction terminated between 13 and 40 days of age. It must be noted in this context that early visual and early auditory restriction was initiated just prior to (or in some cases coincident with) eye or ear-opening. Thus, we have no way of determining if the age at which restriction was begun or the failure to experience vision was the critical factor, as the effects of these variables could not be separately evaluated.

The results of the present study also suggest that peripheral sensory restriction does not produce a permanent deficit in the ability to use intracranial stimulation as a cue. This is supported by the fact that while the acquisition of a discriminative stimulus was retarded in the restricted cortical projection area of animals restricted of vision or audition in infancy, all animals within these groups reached a high level of performance (80% correct responses or better). Furthermore, changing the discriminative stimulus by lowering stimulus intensity revealed that restricted animals were indistinguishable from normals in their ability to make the appropriate responses to altered stimulus conditions.

It would seem, therefore, that extended experience with intracranial stimulation may override the effects of visual or auditory restriction, as may experience with visual or auditory cues in a variety of species and circumstances (e.g. as reported by Tees 1967a,b,1968a,b, Ganz and Fitch 1968, Riesen 1965a, Dews and Wiesel 1970).

The speed with which experimental and normally reared rats acquired visual cortex stimulation as a discriminative stimulus was also compared. Similarly experimental-control comparisons were carried out for auditory cortex. Despite statistically significant within-group differences obtained in groups I and IV, no experimental-control group differences attained significance. However, there appeared to be some facilitation in the nonrestricted and some retardation in the restricted primary cortical projection areas of these animals. While the facilitation and retardation alone were too small to attain significance when compared to controls, statistical significance was attained when compared to each other.

Other factors possibly accounting for failure to obtain experimental-control group differences may have been the small sample size or the choice of the task itself. With an N of six or seven and great variability large differences in acquisition between experimental and control groups were required to obtain statistical significance. Had sample size been greater, experimental-control group differences may have attained significance.

Perhaps a less obvious factor accounting for failure to obtain significant experimental-control group differences was the type of discrimination required of the animals. Essentially this task required the animals to respond to the presence of intracranial electrical stimulation. Earlier it was noted that sensory restriction produces rather task-specific deficits. Thus, while little difficulty is encountered in the discrimination of the presence, intensity or location of adequate stimuli by sensory restricted animals, a "pattern" discrimination, appropriate to the restricted modality, is exceedingly difficult for such animals to acquire (Senden 1932, Turner 1935, Hebb 1937, Michels, Bevan and Strasel 1958, Riesen 1958,1965a, Riesen and Aarons 1959, Tees 1967a,b, 1968a,b). It should be recalled that these behaviors are similar to those shown by animals deprived of the relevant primary cortical projection area (e.g. as reported by Lashley 1931, Kluver 1941, Wetzel, Thompson, Horel and Meyer 1965, Schneider 1967). Therefore, the difficulty in discriminatin

pattern, present in sensory restricted animals, may be intimately related to the characteristic morphological (Gyllensten 1959, Gyllensten et al., 1965,1967, Cragg 1967, Globus and Scheibel 1967a, b, Valverde 1967,1968, Valverde and Esteban 1968, Coleman and Riesen 1968, Ruiz-Marcos and Valverde 1970), and electrophysiological (Wiesel and Hubel 1963b,1965a,b, Scherrer and Fourment 1964, Ganz et al., 1968, Fox et al., 1968, Batkin et al., 1970, Hubel and Wiesel 1970, Zislina and Arkhipova 1970) restriction-produced changes in the primary cortical projection area. These changes may reduce the efficiency with which the cortex may deal with patterned stimuli. Although this is speculative, one means of testing such a deficit, without first passing through the receptor and the various subcortical sensory stations, is to require a pattern discrimination based upon intracranial stimulation of cortex. A "go", "no-go" paradigm could be employed using two different patterns of stimulation presented to the restricted and nonrestricted cortical areas.
On the basis of the present study and the above suggestion, a restriction-produced deficit on this test might be expected to be greater than on one requiring a discrimination of the presence or absence of stimulation. Such a go, no-go, test might reveal a statistically significant retardation in the restricted, and a statistically significant facilitation in the nonrestricted cortical area in comparison to normal controls.

The suggestions of facilitated discriminative stimulus acquisition in the nondeprived cortical area of groups I and IV support the possibility of cerebral compensation. The idea of cerebral compensation is derived from studies showing hypertrophic cellular changes in the auditory cortex of visually restricted mice (Gyllensten et al., 1966) and increases in the weight and cholinesterase activity of the somesthetic cortex of rats following orbital enucleation (Krech et al., 1963). In addition, enhanced evoked potentials to acoustic and somesthetic stimuli in the cortex of dark-reared rabbits have been reported (Scherrer and Fourment 1964). However, these studies were indirect as they failed to demonstrate behavioral advantages accruing from these cortical changes.

Some behavioral evidence has been offered by Gamboni (1964), who reported that dark-reared rats, when brought into the light, showed a strong preference for nonvisual rather than visual cues in the solution of maze problems. While it would certainly be to the advantage of dark-reared animals to develop a greater capacity to use spatial cues (and Gamboni points to possible neurological changes in somesthetic cortex as providing a basis for this modification of cue preference), these animals may simply have attended to familiar rather than unfamiliar cues (perceptual set). Spigelman and Bryden (1967) have also reported that enucleated rats may perform non-spatial auditory learning tasks better than normally reared animals. These performance differences were not clear cut, they not only failed to reach statistical significance, but results similar in magnitude and opposite in direction, were obtained when an auditory localization task was employed. Thus, compensatory cerebral mechanisms must remain an intriguing possibility without experimental confirmation.

The fact that deficits in acquisition were only revealed in animals whose restriction was initiated in infancy is in contrast to the findings of Mogenson (1962) who reported that both paranatal and mature blinded rats (enucleates) were equally retarded in the acquisition of a conditioned emotional response to intracranial electrical stimulation of visual cortex. The discrepancy between Mogenson's findings and those of the present study raises the question considered both by Goodman (1932) and by Riesen (1966): can enucleation be considered an appropriate method with which to study the effects of light restriction? These investigators cautioned against equating the effects of enucleation with those of light restriction as unlike restriction the degeneration initiated by enucleation may induce direct atrophic effects on the next order nerve cell. Therefore, the deficits obtained in Mogenson's mature blinded animals may be attributable to the direct atrophic effects of enucleation rather than to the exclusion of vision <u>per se</u>. This would be congruent with the results of studies indicating that light restriction at maturity has negligible behavioral and electrophysiological consequences (Wiesel and Hubel 1963b, Fox et al., 1968, Dews and Wiesel 1970, Hubel and Wiesel 1970). To test whether the conflict between the present findings and those of Mogenson were due to the task or the method of restriction employed, one might substitute enucleation for lid-suturing in the experimental paradigm employed here and compare the results of such an investigation with those obtained in the present study.

In the present context we cannot ignore the fact that cortical stimulation may have subcortical consequences by means of spread of current, and more probably by ortho- and antidromic impulses. Thus the results obtained here may have been mediated by subcortical rather than cortical mechanisms. Both the visual and the auditory cortex of the rat have numerous direct efferent projections to subcortical nuclei. Visual cortex has been shown to project to LGB, nucleus lateralis posterior thalami, pretectal region, superior colliculus, zona incerta and pons (Nauta and Bucher 1954, Lund 1964,1966) while auditory cortex sends projections to the inferior colliculus and MGB (Krieg 1947). It is likely that stimulation of visual or auditory cortex influences the activity of these subcortical structures. However, electrophysiological evidence indicates that visual restriction appears to have little functional impact upon the primary subcortical visual station, the lateral geniculate body (Burke and Hayhow 1960, Wiesel and Hubel 1963a), and while electrophysiological changes in the superior colliculus have been related to visual restriction, these changes are dependent upon the cortical anomalies produced by such restriction (Wickelgren and Sterling 1969a,b). Unfortunately, no such investigations have been conducted in the auditory modality.

While these findings support a conclusion that the effects obtained in this study were due to restriction-produced cortical changes (at least in the case of visually restricted animals) atrophic changes, volumetric decreases and biochemical alterations have been found to result from visual restriction in the lateral geniculate, superior colliculus and pulvinar in rodents and carnivores (Wiesel and Hubel 1963a, Gyllensten, Malmfors and Norrlin 1965, Maletta and Timiras 1967, Fox et al., 1968, Fifkova and Hassler 1969). In light of these changes we cannot conclude that subcortical structures maintain their functional integrity, despite failure to reveal electrophysiological anomalies therein. Furthermore, brain stem activation by means of spread of current from cortically applied stimulation may have also been involved in the learning situation. Therefore, while a conclusion that cortical dysfunction underlies the results obtained in the present study is most attractive, we must await experimental confirmation (including lesioning and recording from subcortical structures during cortical stimulation of restricted animals) before we can exclude the possibility that they contribute to the modifications in the acquisition of an intracranial electrical stimulus as a discriminative stimulus in sensory restricted rats.

SUMMARY

The present study was concerned with the effects of sensory restriction on the ability of rats to utilize intracranial electrical stimulation as a discriminative stimulus.

Forty three laboratory-reared hooded rats were assigned to one of the following seven groups: a) restricted of vision or audition at 13 days of age and trained at 45 days of age (groups I and IV), b) restricted of vision or audition at 40 days of age and trained at 45 days of age (groups II and V), c) restricted of vision or audition at 40 and trained at 85 days of age (groups III and VI), and d) unrestricted controls, trained at 45 days of age (group VII).

Prior to training with intracranial stimulation all animals learned a lever-press response to obtain water and were allowed to reach stabilized responding in a free responding situation. Stimulating current was then determined on the basis of 80% of the current intensity necessary to evoke a threshold behavioral response.

Animals were then trained to a criterion of 80% correct responses on 5 consecutive blocks of 25 trials. Following criterion performance at a current intensity of 80% of behavioral threshold, current was reduced to 65% until criterion performance was observed and then again reduced to 50% until criterion was reached at this level.

An analysis of discriminative stimulus acquisition in

response to stimulation of visual or auditory cortex revealed that paranatal sensory restriction had a deleterious effect upon such acquisition when stimulation was presented to the restricted, as compared to the nonrestricted, cortical projection area. There were suggestions of facilitation in the nonrestricted and retardation in the restricted cortical projection area in comparison to normal controls but these differences were too small to attain statistical significance.

Decreasing the stimulus intensity failed to discriminate between groups, indicating that experience in the training situation had rendered early sensory restricted animals indistinguishable from controls on this task.

These findings were discussed with respect to restriction-produced changes in the cortical projection area.

APPENDIX

Table XI

Current Intensities For Threshold Behavioral Response In Both Cortical Loci For All Subjects

Animal	Current Intensity For Threshold Response (ua)	
Group I	Visual Cortex	Auditory Cortex
11	35	24
12	95	22
14	3	80
15	6	3.5
17	20	7.5
18	5	6
19	90	60
Group II		
21	17	7
22	17	13
23	6	11
24	13	14
25	65	32
26	55	10

Table XI (Con't)

Animal	Current Intensity For Threshold Response (ua)	
Group III	Visual Cortex	Auditory Cortex
31	65	35
32	40	45
33	4	17
34	15	70
35	3	2.5
36	5	3.5
Group IV		
41	42	12
42	26	7
43	22	8
44	13.5	5.5
45	38	100
46	46	24

Table XI (Con't)

Animal	Current Intensity For Threshold Response (ua)	
Group V	Visual Cortex	Auditory Cortex
51	10	60
52	8	8
53	6	4.5
54	19.5	60
55	16	5.5
56	13	4
Group VI		
61	8	18
62	7.5	31
63	4	4
64	100	31
65	8.5	10
66	50	25

Table XI (Con't)

Animal	Current Intensity For Threshold Response (ua)	
Group VII	Visual Cortex	Auditory Cortex
71	25	13
72	4	9
73	53	50
74	12.5	9.5
75	15	8
76	52	22

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