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The Physiology and Psychology of Behavioral Inhibition in Children

Jerome Kagan, J. Steven Reznick, and Nancy Snidman

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KAGAN, JEROME; REZNICK, J. STEVEN; and SNIDMAN, NANCY. *The Physiology and Psychology of Behavioral Inhibition in Children*. CHILD DEVELOPMENT, 1987, 58, 1459–1473. Longitudinal study of 2 cohorts of children selected in the second or third year of life to be extremely cautious and shy (inhibited) or fearless and outgoing (uninhibited) to unfamiliar events revealed preservation of these 2 behavioral qualities through the sixth year of life. Additionally, more of the inhibited children showed signs of activation in 1 or more of the physiological circuits that usually respond to novelty and challenge, namely, the hypothalamic-pituitary-adrenal axis, the reticular activating system, and the sympathetic arm of the autonomic nervous system. It is suggested that the threshold of responsiveness in limbic and hypothalamic structures to unfamiliarity and challenge is tonically lower for inhibited than for uninhibited children.

There are three important advantages of gathering information on both physiological and psychological qualities in developmental investigations. First, such information permits deeper understanding. For example, through investigations of separation of infant primates from their mothers one gains a richer appreciation of the phenomenon by describing changes in both behavior and cortisol secretion because some infants show no change in behavior following separation but display elevated cortisol levels (Coe, Wiener, Rosenberg, & Levine, 1985). If investigators coded only the infants' behavior they might conclude that these monkeys were not distressed by the mother's absence. Most studies of separation from the caretaker in human infants, especially those that use the Strange Situation, record only behavior and do not gather any physiological evidence (Ainsworth, Blehar, Waters, & Wall, 1978).

Second, gathering both physiological and psychological information makes it possible to discover interactions between the inherent, biological characteristics of an organism and the nature of a class of incentive events with respect to some outcome variable of interest. Although most psychologists acknowledge the possibility of these interactions, and biologists continue to affirm them, most psychological investigations do not explicitly plan or search for such interactions. Third, when two very different sources of evidence

relevant to a phenomenon are gathered, as is the case with psychological and physiological data, investigators have a clearer recognition of the choice between use of qualitative or quantitative descriptions. For example, if only a proportion of phobic adults show relevant physiological signs, one can view that group as qualitatively different from the phobic subjects with no signs, or regard all the subjects as varying on a continuum of vulnerability to fear.

This article presents data indicating a correlation in young children between selected peripheral physiological characteristics and behavioral reactions to unfamiliar and cognitively challenging events. We believe that the individual differences in behavioral reactions to unfamiliarity, threat, or challenge are due, in part, to tonic differences in the threshold of reactivity of parts of the limbic lobe, especially the amygdala and the hypothalamus, which result in enhanced activity of the pituitary-adrenal axis, reticular activating system, and sympathetic nervous system—three circuits that are influenced directly by hypothalamic activity. The Discussion section contains a more detailed rationale for this hypothesis.

Activity in the hypothalamic-pituitary-adrenal axis, which is usually increased following exposure to a novel event that cannot be assimilated or a threat that cannot be removed, leads to the production of cortisol by

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the adrenal cortex. Both infant primates removed from their mothers (Levine, Coe, Smotherman, & Kaplan, 1978) and phobic adults exposed to relevant incentives react with elevated cortisol levels (Fredrikson, Sundin, & Frankenhaeuser, 1985). The hypothalamus also affects skeletal motor tracts through its projection to the reticular activating system. One such tract in the brain stem involves the nucleus ambiguus, which monitors tension in the skeletal muscles of the larynx and vocal folds. These muscles contract under stress, producing changes in both the average fundamental frequency and variability of the pitch periods of vocal output (Stevens & Hirano, 1981). The third circuit involves the sympathetic nervous system and its many target organs. Sympathetic activation, which usually follows encounter with unfamiliarity, threat, or challenge, is accompanied by increases in heart rate, blood pressure, and contractility of the heart, as well as dilation of the pupil and secretion of epinephrine from the adrenal medulla and norepinephrine from postganglionic synapses of the sympathetic nervous system (Ciarenello, 1983). The work to be reported reveals a correlation in children between signs of reactivity in one or more of these circuits and a tendency toward behavioral inhibition to unfamiliar events or situations that pose a psychological challenge that cannot be handled without effort.

Longitudinal Study

Our laboratory has been following two independent groups of Caucasian children, middle and working class, who were selected at 21 or 31 months of age from larger samples to be either behaviorally inhibited or uninhibited when exposed to unfamiliar rooms, people, and objects. The original classification into one of the two temperamental groups required a child to show consistent withdrawal or approach to a variety of incentives. We had to screen over 400 children, by telephone and/or observation, to find groups of 60 consistently inhibited and 60 consistently uninhibited children with equal numbers of boys and girls in each group (see Garcia-Coll, Kagan, & Reznick, 1984; Snidman, 1984, for details). It may not be a coincidence that when German kindergarten teachers in Munich were asked to select only those children who were extremely shy, 15% of the total school population of 1,100 were chosen—a proportion similar to the one we found in our screening (Cranach et al., 1978).

The index of inhibited or uninhibited be-

havior in Cohort 1, which was seen initially at 21 months, was based on the child's behavior with an unfamiliar female examiner, unfamiliar toys, a woman displaying a trio of acts that was difficult to recall and to imitate; a talking robot; and temporary separation from the mother. The signs of behavioral inhibition were long latencies to interact with, or immediate retreat from, the unfamiliar people or objects; proximity to the mother; and cessation of play or vocalization. The uninhibited children showed the opposite profile.

The index of inhibited behavior in Cohort 2 seen first at 31 months was based primarily on behavior with an unfamiliar peer of the same sex and age and, second, on behavior with an unfamiliar woman. The behavioral indexes of inhibition were similar to those used with Cohort 1—long latencies to interact with the child, adult, or toys; retreat from the unfamiliar events; and long periods of time proximal to the mother. Each of these samples was seen on two additional occasions after the original selection, the latest being at 5½ years of age, with about 10% attrition in the samples (see Garcia-Coll et al., 1984; Kagan, Reznick, Clarke, Snidman, & Garcia-Coll, 1984; Reznick et al., 1986; Snidman, 1984).

On the second visit, at 4 years of age for Cohort 1 and at 3½ years for Cohort 2, the primary index of inhibition was based on behavior with an unfamiliar child of the same sex and age. At 5½ years of age the index was based more broadly on behavior with an unfamiliar peer in a laboratory setting, with classmates in a school setting, with an examiner during a 90-min testing situation, and in a room that contained unfamiliar objects mildly suggestive of risk (a balance beam, a black box with a hole). An aggregate index of inhibition for Cohort 1 at 5½ years of age represented a mean standard score across the correlated variables from the separate situations noted above. (Analyses of the data for Cohort 2 are not yet complete.)

Preservation of behavior.—The behaviors that characterize inhibited and uninhibited children were preserved to a significant degree from the original assessment to the two later assessments at 4 and 5½ years of age. (The adjectives inhibited and uninhibited refer to the original classifications at 21 or 31 months, unless stated otherwise.) The correlation, for Cohort 1, between the index of inhibition at 21 months and the aggregate index at 5½ years was .52 ($p < .001$); the correlation between the indexes at age 4 and 5½ was .67 ($p < .001$). The correlation between

the behavioral indexes of inhibition at 31 and 43 months for Cohort 2 was .59 ($p < .001$).

The preservation of inhibited and uninhibited behavior also generalized to the school context. In her doctoral research, Gersten (1986) trained observers who did not know the child's prior classification to code the child's behavior in his or her kindergarten class during the first week of school in September, as well as during a day in the Spring of the same academic year. Each observer noted every 15 sec whether the target child was displaying one or more of a small number of responses, but especially whether the child was alone and isolated or in social interaction with the teacher or another peer. The children classified as inhibited at 21 months were more likely to be alone and less likely to be in social interaction on both the Fall and Spring visits ($r = .34$, $p < .05$, between the index of inhibition at 21 months and the index of inhibited behavior in the school setting across the two visits).

One of the most sensitive indexes of inhibition in a laboratory context at 5½ years was a reluctance to talk spontaneously to the female examiner during the 90-min testing battery. Videotapes of the testing session were scored by observers blind to the children's classification for the latency to the child's first two spontaneous comments to the examiner (a spontaneous comment was any remark that

was not a direct reply to an examiner's question), as well as the total number of spontaneous comments. Although the latencies to the first and second comments yielded similar results, the latter variable was more sensitive; hence, we used it in the analyses. Figure 1 illustrates a scatter plot of these two conversation variables for the children in Cohort 2 who had been classified as inhibited or uninhibited at 2½ years of age. Not one inhibited child, but 14 uninhibited children, issued their second spontaneous comment within 3 min of entering the room and, in addition, made 40 or more comments. By contrast, 13 inhibited but only two uninhibited children failed to make their second spontaneous comment until at least 10 min had passed, and they spoke less than 10 times ($p < .01$ by the Exact Test).

There was more obvious preservation of uninhibited than inhibited behavior in both cohorts, which we believe is a result of socialization experiences. This asymmetry in the stability of the two profiles seems reasonable because American parents, reflecting the values of their society, regard outgoing, sociable behavior as much more desirable and adaptive than shy, timid behavior (Singer, 1984). About 40% of the original groups of inhibited children became less inhibited at 5½ years, while less than 10% of the uninhibited children became more inhibited. There is, however, a gender asymmetry in the direction of change. More boys than girls changed from

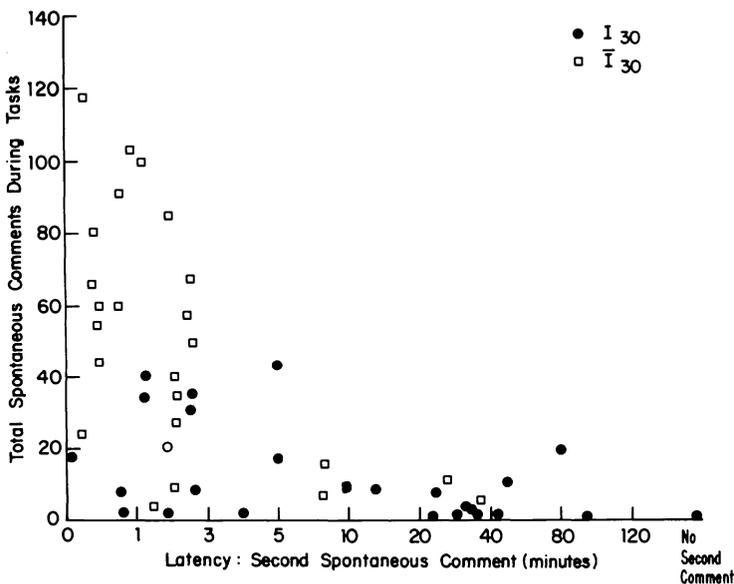


FIG. 1.—Scatter plot relating total spontaneous comments against latency to second spontaneous comment during testing session at 5½ years: Cohort 2.

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inhibited to uninhibited. Maternal interviews suggested that more of the mothers of children who had become less inhibited, compared with those who remained inhibited, had self-consciously helped their children to overcome their inhibition by introducing peers into the home and by encouraging the child to cope with stressful situations. A much smaller group of originally uninhibited children, about 10% and typically girls from working-class families, became more inhibited at later ages. The interviews with these mothers suggested they wanted a more cautious child and encouraged such a profile.

There are more inhibited children who are later- rather than firstborn—about two-thirds—and more uninhibited children who are firstborn—a result affirmed by Snow, Jacklin, and Maccoby (1981). Interpretation of this finding is unclear. It may be due to the fact that firstborn children are encouraged to be more independent of the mother when the next child arrives and, as a result, gradually learn to control behavioral signs of fear, while the youngest child may have fewer incentives promoting uninhibited behavior. A second interpretation, biological in nature, assumes that fetal stress is less likely during the first than during subsequent pregnancies. A third interpretation is that later-born status is associated with more stressful experiences for the small group of infants who are born with a biological disposition to become inhibited as a result of a lower threshold of reactivity in the limbic lobe. An infant with a low threshold of responsivity in limbic structures might react with psychological uncertainty to the mild, but unexpected, intrusions of an older 3- or 4-year-old sibling who seizes a toy, pinches an arm, or pushes the young infant off a chair. Although these aggressive and predatory acts might have minimal effects on most infants, they could generate limbic arousal and development of a habit of withdrawal to intrusion and unfamiliarity in those infants who possess the more excitable limbic structures.

Because any behavioral surface can be the result of different mediating processes, the reasonableness of the assumption that extremely inhibited children are born biologically different from uninhibited ones depends upon evidence showing that more inhibited than uninhibited children display some of the physiological signs to be expected from a lower threshold of limbic excitability to events that are unfamiliar or pose a potential threat. The following sections describe the physiological variables we quantified.

Heart period and heart period variability.—Because we measured the child's heart period and heart period variability to baseline and cognitive tasks on every assessment, we are able to make the firmest statements about these two autonomic parameters. Heart period variability was defined as the standard deviation of all the interbeat intervals during a particular episode. The mean heart period and variability for a multitrial episode was always the average of the values for the separate trials in that episode. Although we shall occasionally use the terms heart rate and heart rate variability in the text, the reader should understand that all statistical analyses were performed on the heart period values because that was the form of the original data. Average heart period and heart period variability in our data were always positively correlated under both relaxed conditions as well as under conditions of mild cognitive stress (correlations .6 and .7).

More inhibited than uninhibited children had high and stable (i.e., less variable) heart rates at every age of evaluation, with the magnitude of the correlation at 5½ years higher than the relation at 21 months. We suspect this is because of more effective sampling of heart rate under cognitive stress at the older age. At 21 months, heart rate was gathered while the child looked at slides or listened to auditory stimuli with no requirement for mental work. Individual differences in both heart rate and heart rate variability in Cohort 1 were preserved from 4 to 5½ years ($r = .58, p < .001$; $r = .64, p < .001$); differences in heart rate variability were preserved from 21 months to 5½ years ($r = .39, p < .01$). Further, the original index of inhibited behavior at 21 months predicted both a higher and a less variable heart rate at 5½ years ($r = .44, .39$) (see Table 1.)

More important, the inhibited children in Cohort 1 who had higher and more stable heart rates over the first two assessments were more likely to remain inhibited than the inhibited children who had lower and more variable heart rates. The former children were significantly more inhibited with the unfamiliar peer at 5½ years, had a larger number of unusual fears, and were more likely to have had symptoms suggestive of arousal of the sympathetic nervous system during the first year of life, especially chronic constipation, allergy, and sleeplessness (see Reznick et al., 1986).

Spectral analysis of heart rate.—Both heart rate and heart rate variability are under the joint influence of sympathetic and para-

TABLE 1

PRESERVATION OF BEHAVIOR AND HEART RATE VARIABLES IN COHORT 1 AND THEIR RELATION TO PHYSIOLOGICAL INDEXES

PREDICTOR VARIABLES	BEHAVIOR AND CARDIAC VARIABLES AT 5½ YEARS			MEAN PHYSIOLOGICAL INDEX
	Inhibited Behavior	Heart Period	Heart Period Variability	
21 months:				
Inhibited behavior52***	-.44**	-.39**	.70***
Heart period03	.15	.11	-.18
Heart period variability	-.06	.19	.39**	-.10
4 years:				
Inhibited behavior67***	-.46**	-.44**	.66***
Heart period	-.39**	.58***	.44**	-.44**
Heart period variability	-.39**	.54***	.64***	-.36*

* $p < .05$.** $p < .01$.*** $p < .005$.

sympathetic activity (Glick & Braunwald, 1965). Respiration exerts a major influence on heart rate variability, especially at rest, and this variability, called respiratory sinus arrhythmia, is mediated primarily by vagal activity (Chess, Tam, & Calaresu, 1975; Katona & Jih, 1975; Porges, McCabe, & Yongue, 1982). Other cyclical sources of variability in heart rate are much less obvious on a polygraph tracing; however, spectral analysis can express the complex beat-to-beat variation in a subject's heart rate as a power spectrum describing the separate rhythms, with peaks at characteristic frequencies. The total area under all of the peaks accounts for the total variability in the heart rate data, while the magnitude of each peak represents the contribution of that particular frequency to the total variation. Peaks at particular frequencies are associated with different physiological processes, especially respiration, blood pressure, and temperature regulations (Akselrod et al., 1981, 1985; Pomeranz et al., 1985). In human subjects, peak frequency between 0.2 and 0.5 Hz is due primarily to respiration and is associated with parasympathetic activity; peaks at lower frequencies are due primarily, but not exclusively, to sympathetic activity. But it is possible to assess the relative contribution of parasympathetic and sympathetic activity to the total heart rate spectrum, as well as to shifts in the balance of the two systems over time. Analysis of the changes in the heart rate power spectrum of the children in Cohort 2 at 43 months revealed that more inhibited than uninhibited children shifted to greater sympathetic activity from a baseline period prior to cognitive testing to a subsequent baseline period following the stress of a series of cognitive procedures ($p < .05$ by the Exact Test).

Pupillary dilation.—Additional support for the hypothesis that the temperamentally inhibited children have a lower threshold for sympathetic activation comes from data on pupillary dilation gathered while the children were administered a series of cognitive tasks that included recall memory for words and digits, a mental comparison of the relative size of objects, inferring an object from its features, and listening to a story. The inhibited children had significantly larger pupillary diameters than uninhibited children under both baseline and task conditions, even though the differences between the two groups were less striking for pupil size than for heart rate or heart rate variability. Additionally, more inhibited than uninhibited children in Cohort 1 maintained a larger pupil across a series of cognitive episodes (67% vs. 36% of each group). The combination of a tonically large pupil together with a high and stable heart rate across a series of cognitive episodes invites the inference that sympathetic activity is greater in inhibited children, presumably because of a lower threshold in the circuit that links the limbic lobe and hypothalamus to the sympathetic nervous system and its target organs.

Muscle tension.—The stress circuit involving the reticular activating system and skeletal motor tracts also seems to be at a lower threshold in inhibited children. The reticular activating system, which is influenced by hypothalamic activity, sends axons to nuclei in skeletal motor tracts, one of which is the nucleus ambiguus serving the muscles of the larynx and the vocal folds. Increased tension in these skeletal muscles is usually accompanied by a decrease in the variability of the pitch periods of vocal utterances (Lieber-

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man, 1961; Stevens & Hirano, 1981). The increased muscle tension can be due not only to discharge of the nucleus ambiguus but also, indirectly, to sympathetic activity that constricts arterioles serving the muscles of the larynx and vocal folds (Vallbo, Hagbarth, Torebjork, & Wallin, 1979).

In the production of human speech, the vocal cords of the larynx open and close at a rapid rate during the process of phonation to produce a sequence of puffs of air. The rate at which the vocal cords open and close defines the fundamental frequency of phonation (F_0). But the vocal cords do not maintain a steady rate as they open and close. The duration of each period of the successive phonatory cycles varies around a mean of 4 msec, even when a person is maintaining a steady average fundamental frequency. These perturbations in the rate at which the vocal cords open and close appear to be a consequence of the inherent interplay of aerostatic, aerodynamic, and tissue forces involved in phonation. The perturbations tend to decrease when the laryngeal muscles are under tension (Lieberman, 1961). If the expected increase in muscle tension in limbs and trunk that usually occurs under task demands also occurs in the vocal cords and laryngeal muscles, one consequence would be less variation in the duration of the successive cycles of the fundamental frequency of phonation (i.e., less variability in the duration of the pitch periods of a single utterance). The index of variability we used was the standard deviation of the normalized distribution of twice the difference between two successive periods divided by the sum of the periods (see Lieberman, 1961).

In her doctoral research, Coster (1986) has found that at 5½ years of age the inhibited, compared with the uninhibited, children in Cohort 1 showed less variability in the pitch periods of single word utterances spoken under psychological stress (the words were bed, cake, dog, goat, pipe, and tub). The child first spoke each of the six words singly (no stress) and then repeated the same words in a series of three to six words (mild stress due to requirement of recalling the words). Most children in both groups showed a marked decrease in variability of the pitch periods to this cognitive stress. In a second stressful condition, which followed immediately, the child was asked to guess which of the six words just repeated was the correct answer to a particular question (e.g., "Which

one chases squirrels?") "Which one is a bad pet?"). Under this last condition, inhibited children not only showed significantly lower average variability ($r = -.43$, $p < .01$, with the classification of inhibition at 21 months) but more often showed a decrease in variability across the six questions, reflecting increasing muscle tension. Figure 2 illustrates this decrease in variability for a single, but typical, inhibited child.

Note in Figure 2 that this child's variability is smallest to the first word spoken under the initial nonstressful condition. The variability decreases to the four words that had to be recalled but increases to recall of the six-word series. On the final test condition—elicited—variability decreased across the questions, reaching its lowest value on the fourth question ("Which one chases squirrels?").

In addition, the inhibited children showed a smaller standard deviation across all the variability values gathered under both stressful and nonstressful conditions ($r = -.39$, $p < .05$, with the classification of inhibition at 21 months). Further, the standard deviation of all of the fundamental frequency values (about 22 values), which was unrelated to the variability of the pitch periods, was also smaller (but not significant) for inhibited than for uninhibited children. Similar data from Cohort 2 seen at 43 months revealed that inhibited children showed a significantly greater decrease in variability than uninhibited children when data based on speaking single words (minimal stress) were compared with data gathered when the child had to recall the words as part of a series of four, five, or six words—identical with conditions 2 and 3 for Cohort 1.¹

Norepinephrine level.—Because norepinephrine is a primary neurotransmitter in the sympathetic nervous system, a urine sample collected from each child in Cohort 1 at the end of the test battery at 5½ years was assayed for norepinephrine and its derivatives using mass fragmentography (Karoum, 1983). The assays yielded values for norepinephrine, normetanephrine, 3-methoxy-4-hydroxyphenylglycol (MHPG), and vanillylmandelic acid (VMA). The concentrations of each compound were transformed into moles per gram of creatinine, and an index of total norepinephrine activity was computed by averaging the concentrations of the four products (in micromoles per gram of creatinine). This index

¹ This work is part of a collaboration with Philip Lieberman, Department of Linguistics, Brown University.

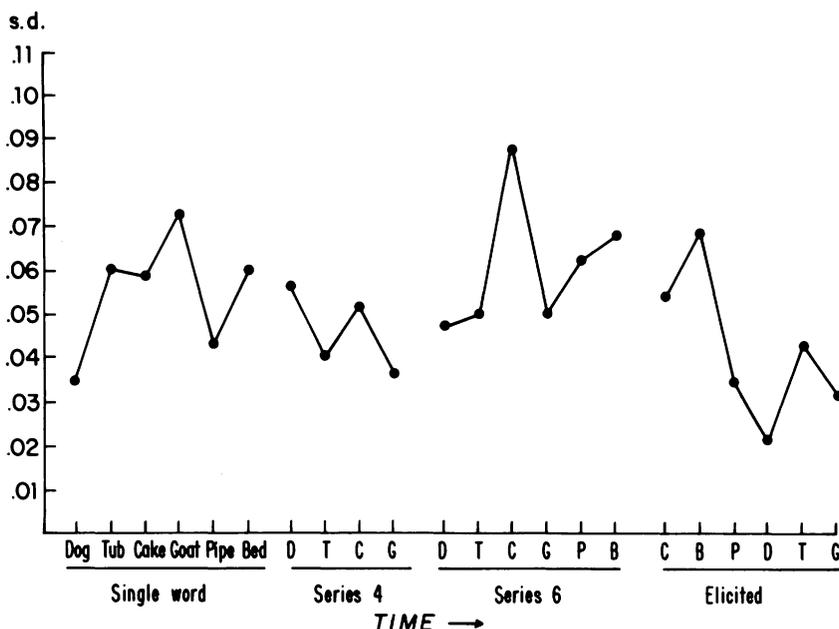


FIG. 2.—Sample of vocal perturbation index (ordinate) for an inhibited child at 5½ years: Cohort 1

reflected primarily peripheral norepinephrine activity, including the cardiac system. The relation between the index of norepinephrine activity and the original index of behavioral inhibition at 21 months was not significant ($r = .15$), but the correlations with the later indexes of inhibited behavior at age 4 and 5½ were significant ($r = .34$, $p < .05$, with the index at age 4 and $r = .31$, $p < .05$, with the index at age 5½). Although these correlations were modest, they imply greater sympathetic activity among the children who were behaviorally inhibited at 4 and 5½ years of age.²

Cortisol.—Samples of saliva were gathered on the children in Cohort 1 at 5½ years before and after the 90-min laboratory session, as well as at home on 3 days during the early morning hours before the stress of the day had begun. These saliva samples were analyzed for unbound cortisol level using a modification of a standard radioimmunoassay method (Walker, Riad-Fahmy, & Read, 1978). Levels of salivary cortisol correlate highly with levels obtained from plasma (Walker, 1984). The inhibited children had significantly higher cortisol levels than uninhibited children in both home and laboratory (see Fig. 3). The correlation between the

mean of the two laboratory values and the original index of behavioral inhibition at 21 months was .45 ($p < .01$); the correlation with the aggregate index of inhibition at 5½ years was .37 ($p < .05$). Further, the average cortisol level across the three morning samples at home was correlated with the index of inhibition at 5½ years ($r = .39$, $p < .05$).³ This last result suggests that the hypothalamic-pituitary-adrenal axis of inhibited children is at a tonically higher level of activity, even in minimally stressful contexts.

High levels of cortisol in the laboratory saliva sample were more discriminating of the two behavioral groups than any of the other physiological variables, for laboratory cortisol values correctly predicted the original 21-month behavioral classifications for 78% of the Cohort 1 children. Although very high levels of cortisol (roughly the top quartile and over 2,000 pmol/l) were more characteristic of inhibited children (nine inhibited vs. one uninhibited for the home value; 10 inhibited vs. two uninhibited for the laboratory value), about one-half of the inhibited children had relatively low cortisol levels. Recall that the correlation between cortisol level and contemporary behavior at 5½ years was 0.37.

² This work is part of a collaboration with Richard J. Wyatt and Farouk Karoum of St. Elizabeth's Hospital, Washington, DC.

³ This work is part of a collaboration with Peter Ellison, Terrence Deacon, and Pamela Lutz of the Department of Anthropology, Harvard University.

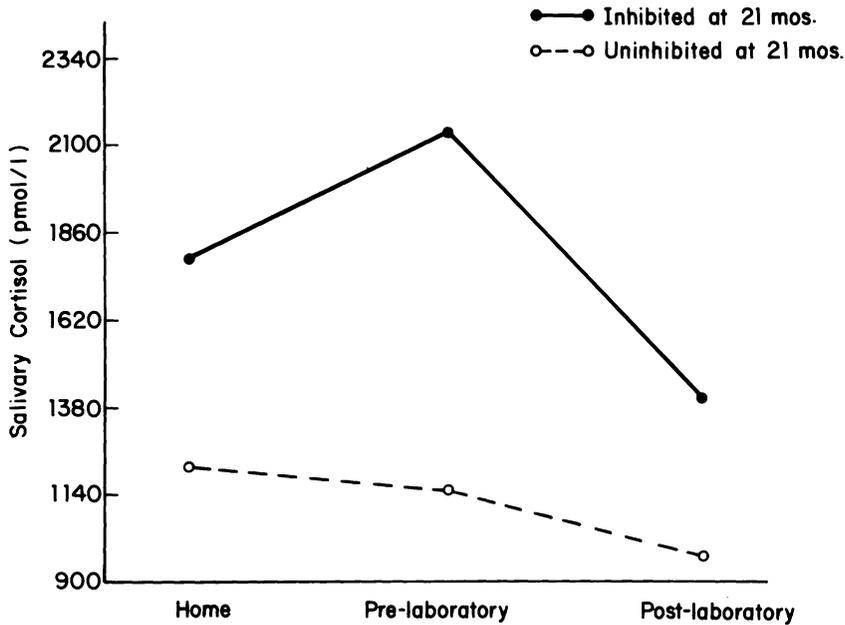


FIG. 3.—Mean cortisol levels at age 5½ in home and laboratory for children classified as inhibited or uninhibited at 21 months of age: Cohort 1.

However, nine inhibited children had high levels of cortisol (above the mean) for both the home and laboratory values. Most of these children differed in important ways from the remaining inhibited children, as well as all of the uninhibited children as described below.

One of the assessment situations at 5½ years was a 30-min play session with an unfamiliar child of the same sex and age but of the opposite behavioral style. Two- to 4-year-old inhibited children tend to remain proximal to the mother for the first few minutes. However, this particular behavioral sign is rare at 5½ years. Among the older, inhibited children, the usual signs of behavioral inhibition are more subtle; usually the children remain quiet, avoid the unfamiliar child, but stare at the unfamiliar peer frequently. Nonetheless, three of the nine children with cortisol levels above the mean for both home and laboratory assays remained proximal to their mother for the first 5–10 min of the session. This is atypical behavior for children at this age. One child sat passively in the middle of the room doing nothing, and one glanced at her mother frequently throughout the 30-min play session. Only two of the nine children showed no obvious signs of inhibited behavior in this context. In a similar peer play situation at 4 years of age every one of these nine children had scores above the mean index of inhibition, and two had the highest indexes at that age.

Interviews with all of the mothers revealed that six of the nine inhibited children with high cortisol for both home and laboratory showed other signs of high physiological arousal and either intense or unusual fears. For example, one child was constipated during infancy, retained urine during the first 3 years of life, and showed many contemporary fears, including a fear of loud voices. Another child was extremely irritable during the first year and at age 4 had a fear of blood, bugs, and defecating. A third child had allergies, chronic constipation, and colic during infancy and was afraid of playing alone during the second and third years. Currently, this child woke up frequently during the night with nightmares. A fourth child had a spastic colon as an infant and currently had nightmares, a fear of heights, and was afraid of being alone. A fifth subject displayed extreme separation fear during infancy and currently was asthmatic and had a fear of taking a bath. A sixth child was constipated as an infant, showed a long-lasting fear of going to nursery school, and currently was afraid of leaving her backyard. None of the uninhibited children, even those with high cortisol levels, showed these kinds of symptoms; these children tend to be more active and vigorous than the uninhibited children with low cortisol levels.

It is of interest that a group of French investigators studying preschool and kindergarten children found higher urinary levels of

a derivative of adrenocortical activity (17-hydroxycorticosteroids) in emotionally labile and fearful children than in less emotional children who were regarded as leaders by their peers (Montagner et al., 1978). Additionally, 1-year-old infants who were prone to extreme distress following maternal separation in the home also showed higher urinary cortisol levels than those who were minimally distressed (Tennes, Downey, & Vernadakis, 1977).

Physiological activity across the variables.—The inhibited, in contrast to the uninhibited, children in Cohort 1 were more likely to show the peripheral physiological consequences predicted from the hypothesis of lower thresholds of reactivity in limbic lobe. However, only about one-third of the inhibited children showed signs of higher activity in all three stress circuits, and most of the intercorrelations among the physiological variables described above were low and nonsignificant. With the exception of the correlation of .84 between heart period and heart period variability, the remaining 27 correlations ranged from $-.26$ to $+.33$, with a median coefficient of $+.10$. (See Nesse et al., 1985, for a similar finding.)

In order to assess the degree of concordance in responsivity across the indexes, we computed a mean standard score, and standard deviation, for eight physiological variables quantified on Cohort 1 at 5½ years of age. The eight variables were: (1) cortisol level in the morning at home, (2) cortisol level obtained in the laboratory, (3) heart period during cognitive tasks, (4) heart period variability during cognitive tasks, (5) pupillary dilation during cognitive tasks, (6) variability of pitch periods of the voice under the second cognitive stress, (7) standard deviation of all the fundamental frequency values, and (8) total norepinephrine level in the laboratory urine sample. We reversed the values for variables 3, 4, 6, and 7 so that a high standard score indicated greater limbic arousal. The correlations between the mean across all eight physiological variables and each of its component scores ranged from .36 to .56, with heart period, heart period variability, cortisol in the laboratory, and variability of the pitch periods having the highest correlations with the aggregate mean ($r = .56, .53, .51, \text{ and } .51$). The standard deviation of the eight physiological variables was unrelated to the individual measures and to the mean index ($r = -.17$).

We examined the relation between the aggregate mean of the eight physiological variables and the index of behavioral inhibi-

tion at each age for 22 inhibited and 21 uninhibited children (see Table 1). The correlation was highest with the original index of inhibition at 21 months ($r = .70, p < .001$) but statistically significant at the two later ages ($r = .66$ with the behavioral index at age 4; $r = .58$ with the aggregate behavioral index at 5½ years). Additionally, both heart period and heart period variability values obtained on these children at 4 years of age were positively related to the physiological index at 5½ years ($r = -.44, -.36, p < .05$).

Two of three formerly inhibited children with the lowest physiological indexes had become increasingly less inhibited across the period from 21 months to 5½ years. Two of the three formerly uninhibited children with the highest physiological indexes had become more inhibited at 5½ years. Thus the direction of change in behavior over the 4 years of study was accompanied by an expected level of physiological reactivity at 5½ years. But none of the uninhibited children was as physiologically reactive as the top quartile of inhibited children. A combination of both behavioral and biological variables led to a more accurate diagnosis of the children who remained inhibited or uninhibited over time than either variable alone. However, a multiple regression analysis that made inhibition at 21 months and the aggregate physiological index at 5½ years the two predictors, and the aggregate index of behavioral inhibition at 5½ years the criterion, was not significantly higher than the correlation with the index of inhibited behavior at 21 months (multiple $R = .62$ for both predictors vs. a correlation of .52 between the behavioral indexes at 21 months and 5½ years).

Discussion

When children are selected in the second or third years to be extremely inhibited or uninhibited in their behavioral reactions to the unfamiliar, there is preservation of these two behavioral profiles over a period of 4 years. There is also a theoretically consistent association between inhibited behavior and peripheral physiological processes that originate in activity in the limbic lobe, especially the amygdala and the hypothalamus. These facts imply that a small proportion of children, estimated to be about 10%, has a low threshold of reactivity in those parts of the limbic lobe that are responsive to unfamiliarity and challenge, while another 10% has a higher threshold in these areas.

The use of an aggregate index of responsivity across the eight physiological variables

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does not presume an abstract state of general arousal. A study of eight endocrine and physiological variables in adult phobic women exposed to psychological stress revealed that very few women showed increased reactivity on all of the biological indexes, and the correlations among the variables were generally low (Nesse et al., 1985). The aggregate score is useful, and often yields more robust relations than any single index, because any single variable can be the product of a factor unrelated to the hypothetical mechanisms mediating inhibited and uninhibited temperaments. Pooling several indexes dilutes the contribution of any one of these extraneous factors. For example, a child who did not have an inhibited temperament but was highly motivated to solve the cognitive problems might show a high and stable heart rate and a large pupil, but this child should show low levels of cortisol and high variability in the vocal perturbation index.

Inhibition of motor activity is the biologically prepared initial response to states of uncertainty and to discharge of one or more of the stress circuits in infants and young children, and if assimilation is not possible, crying or other signs of distress may occur. The prepared behavioral reaction in 2–3-year-olds is cessation of play and speech and seeking a target of attachment. That is why the second year, especially 20–30 months, is a sensitive time to detect the behavioral tendencies toward inhibition or lack of inhibition to the unfamiliar. In the final section of the article we turn to three general issues related to this research.

Biological mechanisms.—Explanations of individual differences in behavior that involve temperamental constructs have become more popular during the last decade. Two of the most popular are, first, the tendency either to approach or to avoid challenge and unfamiliarity and, second, the ease with which the emotional states of uncertainty, anxiety, and fear are generated. These qualities are different and, in adults, are statistically independent. Introversion-extraversion and neuroticism emerge as independent factors in the questionnaire responses of unselected samples of adults (Eysenck, 1982). However, these dimensions are moderately correlated in young children who fall at the extremes on the tendency to approach or to withdraw from unfamiliarity. Therefore, there is a potential utility, at least for young children, to a conjunctive construct for young children that we might call “variation in the ease of generation of psychological uncer-

tainty and physiological arousal and, as a consequence, withdrawal, rather than approach, to unfamiliar or challenging situations.”

There are several possible explanations of the variation among children in this complex quality or qualities. During the 40 years when behaviorism and psychoanalytic theory shared popularity, many American and European psychologists viewed the variation in fearful behavior as learned. The American behaviorists offered a logically consistent and intuitively appealing argument based on the conditioning of a state of fear and the biologically prepared response of avoidance to formerly neutral events. The popular textbook example is of the infant who acquired a fear of a white rat. In this model, a child who was consistently shy with unfamiliar adults must have had painful experiences with adults in the past. Thus many psychologists teaching during that era explained intense stranger anxiety in the infant as a consequence of unpleasant experiences with strangers. In a similar vein, an extreme degree of separation anxiety was the result of experiences of hunger or pain when the mother was away from the home; hence, the mother’s absence became the conditioned stimulus for an anxiety reaction. Although this explanation seemed reasonable 30 years ago, only a small number of contemporary psychologists continue to favor a version of this argument.

Two related explanations that are gaining initial consensus do not deny the influence of learning from experience but implicate the role of inherent individual differences in central nervous system functioning. One explanation holds that children differ in ease of excitability—or threshold of response—in those parts of the central nervous system that contribute to states of psychological uncertainty and physiological arousal. Most investigators assume that limbic structures play a central part in this phenomenon (Gray, 1982). A more specific variant of this hypothesis is that some infants are born with low thresholds of reactivity in amygdala and hypothalamus when the child encounters unfamiliarity or challenge for which there is no immediate coping response. A related, complementary, explanation emphasizes the effectiveness of processes that inhibit the discharge of limbic structures. As Rothbart and Derryberry (1981) note, these two mechanisms are different, even though investigators working with humans cannot measure each separately at the present time. Pavlov chose to emphasize the inhibition function, suggesting that organisms differed in the “strength of the central ner-

vous system," where strength meant the ability to inhibit the buildup of excitation. Pavlov implied that fearful dogs and shy children had a "weak nervous system." The Polish psychologist Jan Strelau (1985) is responsible for a modern version of Pavlov's ideas.

The environment presents children with at least three classes of events that invite some form of response. The first refers to unfamiliar events that provoke attempts at assimilation (e.g., an unfamiliar sound or sight). The second class includes events, usually the actions of people, to which the child must issue some action (e.g., an unfamiliar person approaches and offers a toy). Finally, the environment presents problem situations to which the child must generate cognitive solutions (e.g., test questions in our battery). Most of the time children and adults assimilate unfamiliar events easily, issue socially effective actions to others, and generate correct cognitive solutions with minimal delay and, therefore, minimal limbic lobe arousal. But when there is a delay in the generation of a coping response, the child is simultaneously alerted psychologically and aroused physiologically. We believe that this state should be treated as a special psychological cum physiological condition mediated in part by limbic structures. We choose to call this state *uncertainty*; others may prefer a different word.

The state of uncertainty often has peripheral physiological consequences because the amygdala and hypothalamus mutually influence each other, and the latter influences the pituitary-adrenal axis, reticular activating system, and sympathetic chain. Hence, the physiological signs that are characteristic of inhibited children could be due to tonically lower thresholds of reactivity in these brain structures. As a result, the inhibited children show increases in muscle tension, a rise and stabilization of heart rate, pupillary dilation, or increased cortisol to minimally unfamiliar or challenging events, whereas most children would not show these physiological reactions to the same relatively innocuous experiences. This speculative suggestion is in accord with results of neurobehavioral studies of the amygdala and the hypothalamus over the last 20 years. One primary function of the amygdala is to receive evaluated, meaningful information from secondary, or associative, sensory areas and the hippocampus, and through projections to the hypothalamus and the autonomic nervous system generate visceral reactions that are often accompanied by behavioral signs of fear and feelings of increased emotionality (Aggleton & Passingham, 1981; Gloor, 1978; Sarter & Markowitsch, 1985;

Turner, Mishkin, & Knapp, 1980). Indeed, one team of investigators has suggested that a person's conscious awareness of internal feeling tone is generated in the amygdala (Hebben, Corkin, Eichenbaum, & Shedlack, 1985).

The idea that inhibited and uninhibited children differ in the excitability of the amygdala and the hypothalamus finds support in studies of domestic cats differing in degree of defensive, nonaggressive behavior with rats. The descriptions of the defensive, in contrast to the nondefensive, cats resemble closely our descriptions of inhibited and uninhibited children. The defensive cats are less likely to attack rats and are more inhibited in novel environments, as well as with humans. These behavioral qualities are stable over periods as long as 3 years (Adamec & Stark-Adamec, 1986). Stimulation of the basal amygdala evoked stronger multiple unit activity in the limbic structures of defensive compared with nondefensive animals. Further, when the amygdala was stimulated with single pulses of increasing intensity, the peak height of the evoked potential in the ventromedial hypothalamus was significantly greater in defensive than in nondefensive cats. Finally, while orienting to rats, the defensive cats showed both larger and more prolonged increases in multiple unit activity in the amygdala than did the nondefensive animals. The authors, who believe that the behavioral differences between defensive and nondefensive cats may be due, in part, to a lower threshold of response in the amygdala, wrote, ". . . Some form of synaptic potentiation underlies [this] behavioral disposition [or bias] . . . the behavioral outcome may be determined by the normally occurring excitatory status of limbic substrates" (p. 142), . . . "some form of potentiation of synaptic transmission" (p. 132; Adamec & Stark-Adamec, 1986). This suggestion, together with data indicating that the amygdala appears to mediate the state of conditioned fear in the rat (Hitchcock & Davis, 1986), renders a bit more credible the idea that differences in responsivity of limbic structures make an important contribution to the contrasting behaviors of inhibited and uninhibited children.

The reasons for the lower thresholds of reactivity in the amygdala and hypothalamus are unclear, but one possible contributing factor is high levels of central norepinephrine. Central norepinephrine appears to amplify the brain's reaction to novelty by suppressing background neural activity and, therefore, increasing the psychological salience of an incentive stimulus (Aston-Jones & Bloom, 1981; Charney, Heninger, & Breier, 1984;

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Charney & Redmond, 1983; Reiser, 1984). Further, rats who are unable to avoid shock show increased norepinephrine activity, especially in the amygdala and the hypothalamus (Tsuda & Tanaka, 1985), and assays of a large number of autonomic and hormonal variables in phobic women exposed to the sources of their fear reveal that blood levels of norepinephrine have the largest number of correlations with the other physiological indexes (Nesse et al., 1985) (see also Bandura, Taylor, Williams, Mefford, & Barchas, 1985).

The locus coeruleus is a major source of central norepinephrine and its axons synapse on many parts of the brain, including the amygdala and the hypothalamus. The fact that neurons of the locus coeruleus of rats fire to the novelty of unexpected tones and lights led Aston-Jones and Bloom (1981) to suggest that the increased state of vigilance to novelty is accompanied by increases in the concentration of central norepinephrine, as if the locus coeruleus-norepinephrine system "rendered ordinarily neutral innocuous stimuli anxiety provoking" (Reiser, 1984). Thus, one possible hypothesis, albeit speculative, is that inhibited children have tonically higher levels of norepinephrine than uninhibited children due to enhanced reactivity of the locus coeruleus. As a result, a mildly unfamiliar or challenging event is more likely to produce activity in the amygdala and hypothalamus of inhibited children and, during the early years, an accompanying disposition to become quiet, to cease playing, and to withdraw from the event.

The role of experience.—Although there may be an inherited biological contribution to the profile of behaviors we have described, there is also an important role for learning. First, most American families regard consistent fear and withdrawal to challenge as undesirable qualities (Singer, 1984). Hence, parents reward their children for inhibition of excessive fear and may discourage consistent display of its outward manifestations. Second, by 4 years of age, most inhibited children have become aware of their behavioral reactions to novelty and the fact that they might be afraid, and want to control these responses. One 5½-year-old inhibited boy in our study told his mother, "I know I am afraid, but I'm trying to not be." Many inhibited children who are motivated to control behavioral signs of fear learn to react to the states of uncertainty and arousal with less fearful, timid behavior. These children may gradually acquire the ability to interrupt the prepared response of inhibition. As these coping behaviors be-

come stronger, they might even mute the uncertainty and arousal that occur in unfamiliar settings. This suggestion may explain why the index of inhibition at 5½ years of age was a slightly poorer correlate of the aggregate biological index than inhibited behavior at 21 months ($r = .58$ vs. $.70$). Just as knowledge about the reversibility of a Necker cube makes it easier to see it in both perspectives, so, too, might knowledge about one's physiological and behavioral reactions to unfamiliarity make it easier to influence them. Whether this alteration is context specific or can become more general is still not clear.

Although there is no question that inhibited children can become uninhibited in surface behaviors, it is less clear if these behavioral changes are accompanied by changes in the thresholds of responsivity in the limbic system. However, we suspect these changes are also possible, for a few older children who had been very inhibited at 21 months were both behaviorally uninhibited and showed minimal signs of physiological arousal when seen at 5½ years. It is possible, of course, that if more serious stressors had been used, these children would be more likely than the average child to react with the physiological signs they displayed at a younger age.

Inhibition: A quality or a quantity?—Finally, these data invite consideration of a choice between continuous quantities or discrete qualities in describing these children. The traditional strategy is a return to the popular concept of general arousal as a continuum with individuals varying in magnitude of the state. Hence, the small group of children who showed reactivity in all of the target systems originating in limbic structures would be regarded as highly aroused; those who showed reactivity in only a few would be moderately aroused. However, one can also regard the children as falling into qualitatively different groups. Those who show reactivity in most of the target systems are coherently aroused; those who show reactivity in none are coherently nonaroused; those who show reactivity on only a few indexes are not coherently aroused. These groups of children are to be regarded as differing in "quality of arousal," not in "degree of arousal." When we treated heart rate, heart rate variability, and inhibited behavior at 21 and 48 months in Cohort 1 as continua and used these variables as predictors in a multiple regression equation with the index of inhibition at 5½ years as the criterion, neither heart rate nor variability had any significant amount of unique variance over and above the variance attributable to behavioral inhibition at 21 and 48 months.

However, when we created four discrete groups—inhibited with a high and stable heart rate, inhibited with a low and variable heart rate, uninhibited with a high and stable heart rate, and uninhibited with a low and variable heart rate—the 13 children who were inhibited and had a high and stable heart rate were significantly different from the other three at 5½ years. These children stared more at the unfamiliar peer and spent significantly more time close to the mother in the peer play session and, in another room, avoided contact with novel objects that suggested risk of harm. During the first year of life these children showed at least one of the following symptoms: chronic constipation, allergy, extreme irritability, and sleeplessness. Thus, treating inhibited children with a high and stable heart rate as a qualitatively special category yielded results that did not emerge when behavior and heart rate variability were treated as continua reflecting degree of arousal.

Scientists can choose among many possible dimensions when they summarize the similarities and differences between two classes of events they believe to be related theoretically. Prior premises, the question of interest, and the sources of evidence will determine whether the dimensions selected imply a continuum or qualitatively different categories. We chose to emphasize the qualitative differences between inhibited and uninhibited children because we selected children at the behavioral extremes and, therefore, minimized behavioral overlap in the original groups. Additionally, the forms of the distributions of the behavioral data gathered subsequently (e.g., time proximal to the mother and time staring at an unfamiliar child) did not suggest a continuous trait, for very few uninhibited children spent a long time near their mother or staring at the unfamiliar child. The pattern of behavioral stabilities and the intercorrelations also favored the hypothesis of qualitatively discrete groups because inhibited children with a high and stable heart rate at 21 months were different at 5½ years from inhibited children with a low and variable heart rate. Further, the fact that some obviously uninhibited children had a high and stable heart rate led us away from the notion of a continuum of arousal. If there were such a continuum, inhibited behavior and a high and stable heart rate should have covaried better than they did, and there should have been fewer uninhibited children with a high and stable heart rate. As our work proceeded, we began to develop the hypothesis that an inhibited tem-

perament might be influenced by biological factors. As a result, we were tempted to emphasize dimensions that were unique to inhibited children, like their later-born ordinal position, high cortisol levels, and presence of infant symptoms such as colic, allergy, and constipation. These characteristics imply qualitative differences between inhibited and uninhibited children. However, if we had believed that experience was the primary cause both of inhibited behavior and the correlated physiological signs, we would have selected dimensions implying constructs such as strength of conditioned anxiety, motivation to control fear, and ability to deal with uncertainty. These concepts can be applied to all children to differing degrees. As a result, we would have treated the differences between inhibited and uninhibited children as continuous.

Many readers may feel, with us, that pragmatic factors will decide which descriptive category—qualitative categories of children or quantity of arousal in children—is theoretically more profitable for a given corpus of data. The description that leads to the more robust predictions and the more satisfying explanations is always the one to be preferred. For those who wish to emphasize the important environmental contributions to the formation of and change in inhibited and uninhibited behavior, the major dimensions will refer to experiences and imply continua. For those who wish to emphasize the possibility of a biological contribution to these profiles, and especially genetic influences, the dimensions selected will emphasize qualities. Each perspective has validity, given the investigator's initial assumptions and intentions, and, of course, the form of the evidence.

This conclusion is the central theme in Bohr's famous essay on complementarity, which attempted to resolve the debate as to whether electromagnetic energy should be treated as a continuous wave or as discrete quanta. Bohr (1950) suggested that the frame adopted depended upon the question and mode of data analysis. Each perspective was valid in its own domain of inquiry, leading the physicist J. J. Thomson to suggest the metaphor of a tiger and a shark to represent the two perspectives; each animal was potent in its own ecological niche, but impotent in the niche of the other (Wheaton, 1983).

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