could be demonstrated that the animals were not paralyzed, since quick movements in the animals' visual field or loud noises elicited startle and struggle (8).

Following surgery, brain stimulation was discontinued. Some residual skin analgesia was noted for several minutes, but vigorous aversive responses to hemostat-applied pressure returned fully within 5 minutes. After 24 hours, all animals were killed and their brains were removed for histological verification of electrode placement. After a 2week period in 10 percent formalin, the brains were frozen, sectioned at 50  $\mu$ , and stained with cresyl violet. Figure 1 is a composite diagram showing the brain region where stimulation induced analgesia to hemostat-applied pressure and to abdominal surgery. The circled numbers are the r.m.s. currents required for electrical analgesia. Circles without numbers are points at which stimulation did not induce electrical analgesia at the maximum current used (35  $\mu$ a r.m.s.). As shown in this figure, effective stimulation sites are clustered at the dorsolateral perimeter of the central gray. One noneffective electrode tip was not located with certainty at histology and does not appear in the diagram.

These effects have been interpreted as analgesic since all animals could move about during brain stimulation and exhibited startle to sound and visual stimuli, but none struggled in response to hemostat-applied pressure or surgical procedures. The analgesia was attributed to electrical stimulation and not to tissue damage, which might have been caused either by electrode implantation or during the application of electrical currents, since the analgesia occurred only during and shortly after stimulation, and was entirely reversible.

This demonstration of analgesia induced by focal brain stimulation raises the possibility that electroanesthesia, typically induced by "whole-brain" stimulation, may not require undifferentiated current flow through multiple brain regions. Of all the current diffusely applied, only a small portion, passing through specific brain areas, may be required to induce analgesic effects. The remaining current may either serve no purpose or produce adverse cardiac, respiratory, and other effects encountered during the induction of electroanesthesia (1). Obviously, for both ethical and practical reasons, human electroanesthesia must continue to be induced from surface and not depth electrodes. However, by identifying brain systems where stimulation induces analgesia, and other regions that do not, efforts can be made to develop techniques for directing externally applied currents to "effective" brain regions. If progress is made in this direction, a safe, reliable, surgical-level electroanesthesia may eventually be developed for use in man.

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## **References and Notes**

 A. Flach, Anesthetist 7, 180 (1958); V. Stephen, Med. J. Australia 1, 831 (1959); L. W. Fabian, J. D. Hardy, M. D. Turner, F. J. Moore, Anesth. Analg. Curr. Res. 43, 87 (1964); L. A. Geddes, Med. Elec. Biol. Eng. 3, 11 (1965); R. H. Smith, Electrical Anesthesia (Theorem 5.14, 111, 1065) (Thomas, Springfield, Ill., 1963).

- 2. D. V. Reynolds, "A preliminary study of decreased sensitivity to aversive foot-shock dur-ing brain stimulation in the rat: Electrical analgesia," presented at California State Psy-oblesional Association Martine Networks chological Association Meeting, Los Angeles, Dec. 1964
- W. H. Mehler, in *Pain*, R. S. Knighton and P. R. Dumke, Eds. (Little, Brown, Boston, 3. 1966) 1966), p. 11. 4. R. Melzack, W. A. Stotler, W. K. Livingston,
- . Neurophysiol. 21, 353 (1958); D. D. Kelly,
- thesis, Columbia University (1966).
  N. F. Miller, E. E. Coons, M. Lewis, D. D. Jensen, in *Electrical Stimulation of the Brain*, D. E. Sheer, Ed. (Univ. of Texas Press, Austin 1961) Austin, 1961)
- 6. J. DeGroot, Koninkl. Ned. Akad. Wetenschap. Proc. Ser. C, 52, 1 (1959).
- 7. C. A. Kreele and R. Smith, Eds. The Assessment of Pain in Man and Animals (Latimer, Trend, Plymouth, England, 1962).
- 8. D. V. Reynolds, Surgery in the Rat under Electrical Analgesia, 16-mm film presented at the Federation of American Societies of Ex-perimental Biology meetings, Atlantic City, 1965.
- 9. The work reported here was conducted while D.V.R. was research associate for NAS at Ames Research Center, NASA, Mountain View, California.

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## Sex Differences in Verbal and Performance IO's of Children Undergoing Open-Heart Surgery

Abstract. Boys with congenital heart defects had essentially normal Verbal and Performance IQ's on preoperative and postoperative tests; but girls' Verbal IQ's were significantly lower than those of boys, and significantly lower than girls' own Performance IQ's. This sex difference among congenital heart cases reverses the usual finding that girls excel on Verbal tests.

A project designed to evaluate the effect of heart disease and open-heart surgery on mental development finds a sex difference in the mental abilities of children with congenital heart defects. In normal, nonpathologic samples, sex differences are seldom significant. This result is due in part to the initial test construction or standardization procedure of eliminating specific test items which are "unfair to one sex or the other" (1, 2). In spite of efforts to avoid "unfair" tests, investigations frequently report male superiority on arithmetic tests and tests of spatial relations, and female superiority on vocabulary and other aspects of language development (3). The superiority of girls in verbal ability is interpreted as due in part to the more rapid maturation of girls which is quite marked in the years of language acquisition (4), but this superiority continues into the adult years (5). Boys' higher scores on tests of spatial relations is attributed to sexlinked inherited ability, judging by the patterning of parent-child resemblance on this trait (6). Further evidence for a genetic basis of the patterning of test performance is found in children with

chromosomal aberrations such as trisomy-21 and Turner's syndrome. Girls with this latter genetic makeup (a single X chromosome instead of the usual two) have IQ's covering the entire range of the normal curve, but there is a significant difference between their Verbal and Performance IQ's. Their Verbal scores are high relative to normal samples, and their Performance scores, especially those involving perceptual organization, are definitely low. This difference between their Verbal and Performance IQ's is significant beyond the .01 level of probability (7). We have found a difference in precisely the reverse direction for girls with congenital heart disease, both before and after open-heart surgery. Girls with congenital heart difficulties have low Verbal scores relative to their own Performance scores, and relative to the Verbal scores of boys.

The sample of the present study included initially 60 boys and 58 girls with congenital heart defects. These children, ranging in age from 5 to 16 years, were tested before and after surgery. More than three-fourths of the total sample had their surgery between 4 and 9 years of age. The age distributions were similar for the two sexes. The socioeconomic background of the sample was such as to expect a normal distribution of test scores.

The procedure called for the administration of alternate forms of the Stanford-Binet tests before and within a month after surgery. Since this was a developmental study, with additional follow-up testing 6 months after surgery and at yearly intervals thereafter, the Wechsler Intelligence Scale for Children (WISC) was substituted for the Stanford-Binet at the follow-up testing approximately 6 months after surgery in order to avoid practice effects and provide information on the patterning of abilities.

The Stanford-Binet tests (S-B), described as tests of abstract thinking, contain a fairly large proportion of verbal test items. On this test, the average preoperative IQ's of the 60 boys and 58 girls were 105 and 101, respectively. This sex difference is larger than is usually found but is not statistically significant. A similar sex difference was found for the IQ's on the Stanford-Binet given within a month after surgery. However, the sex difference on the postoperative full-scale WISC is larger (mean IQ for boys, 105.1; girls, 97.4) and is significant at the .01 level (Table 1). WISC subscales yielding sex differences significant at the .01 level were Information, Vocabulary, and Arithmetic. The boys' superiority in Arithmetic was in the expected direction, but the relatively low scores of the girls on the Information and Vocabulary scales were unexpected. None of the sex differences on the Performance subtests were significant at the .01 level (Table 1). The sex differences on the Information and Vocabulary subtests were striking because the patterning differed from that reported for normal samples; for example, Wechsler (2) noted that "boys tend to do better on Arithmetical Reasoning and girls better on Vocabulary tests."

Our next question was whether the sex difference was the result of a few girls earning very low Verbal scores. We found that whereas 47 percent of the boys had Verbal IQ's which were higher than their own Performance IQ's, this was true for only 33 percent of the girls. Thus, not only were the girls' *mean* Verbal IQ's lower than those of the boys, but a disproportionate *number* of girls did poorly on the Verbal tests. Table 1. Sex differences in mean postoperative test scores on the Wechsler Intelligence Scale for Children.

| Test            | Boys*          | Girls† | t<br>ratios |
|-----------------|----------------|--------|-------------|
| Full scale IQ   | 105.1          | 97.4   | 3.05        |
| Verbal IQ       | 104.2          | 95.8   | 3.20‡       |
| Performance IQ  | 105.2          | 99.5   | 2.20§       |
| Verbal subtests |                |        |             |
| Information     | 11.2           | 9.1    | 3.97        |
| Comprehension   | 10.2           | 8.9    | 2.47§       |
| Arithmetic      | 10.5           | 9.2    | 2.62        |
| Similarities    | 11.3           | 10.7   | 1.20        |
| Vocabulary      | 10.4           | 8.8    | 2.97‡       |
| Performance     |                |        |             |
| subtests        |                |        |             |
| Picture         |                |        |             |
| completion      | 11.1           | 10.3   | 1.78        |
| Picture ar-     |                |        |             |
| rangement       | 11.1           | 9.9    | 2.26§       |
| Block design    | 10.9           | 9.6    | 2.52§       |
| Object          |                |        |             |
| assembly        | 10.8           | 9.9    | 1.57        |
| Coding          | 9.8            | 9.8    |             |
|                 | 58. ‡ <i>P</i> | < .01. | § $P < .05$ |

The distribution of Verbal IQ's shown in Fig. 1 suggests greater variability in the boys' scores. This was tested and found to be significant at the .01 level. This sex difference in variance was taken into account in testing the significance of the difference between means. Thus, the girls with heart difficulties had Verbal IQ's which were not only low on the average but were less variable than those of the boys.

The effect of the sex of the examiner was explored and found to be irrelevant, since the proportion of the girls with low Verbal IQ's was similar for the male and female examiners.

Another possibility checked was that

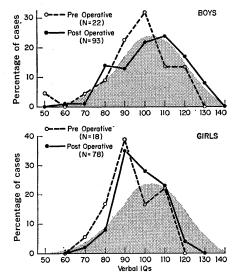


Fig. 1. Preoperative and postoperative Verbal IQ's of boys and girls compared with a normal distribution of IQ's.

variations in socioeconomic status might account for the sex differences. The Verbal and Performance scores of boys and girls within each socioeconomic level were computed and the sex difference was found to hold up for all levels.

We also considered the cardiac diagnoses. The number of children with each defect was not large but, in spite of the small number of cases, the boys' Verbal scores were higher than the girls' for all diagnostic categories: tetralogy of Fallot (P < .10), atrial septal defect secundum (P <.05), pulmonic or aortic stenosis (P <.10), and ventricular septal defect (difference not significant). The sex differences in Performance IQ's were not statistically significant for any of these diagnoses. In other words, the sex difference was most marked on the Verbal scores where the girls' scores were relatively low.

Comparisons thus far have been between the scores of boys and girls. It is also possible to compare the within sex Verbal and Performance IQ's. For boys, the mean Verbal IQ is 104.2 and mean Performance IQ is 105.2. This difference is not significant (Table 1). In marked contrast, the mean Verbal IO of girls is 95.8 and the mean Performance IQ is 99.5. This difference is statistically significant at the .05 level. This difference between the Verbal and Performance IQ's of girls is as great as that found for girls with a missing X chromosome [Turner's syndrome (7)], but in the reverse direction. However, chromosomal counts of the heart sample revealed no observable aberrations.

A major question is whether the girls' low Verbal scores on the WISC are the result of the operative procedures or whether this deficit simply became more visible on the postoperative WISC test. In order to answer this question, we altered the usual procedure of giving the Stanford test preoperatively and administered the WISC to a new sample of 22 boys and 18 girls before their surgery. The sex differences in the mean preoperative Verbal and Performance IQ's for this group are in the same direction as for the postoperative group but for this small sample they are not statistically significant. The one statistically significant sex difference was on the Vocabulary subtest. The boys' mean score on the vocabulary test was 10.2 and the girls' was 8.6. This difference is significant at the .05 level.

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Figure 1 compares the Verbal IO distributions for the preoperative sample tested on the WISC and an enlarged postoperative sample of 93 boys and 78 girls. This postoperative sample includes the initial group of 60 boys and 58 girls and an added group of 33 males and 20 females tested more recently. The boys' Verbal IQ's closely approximate the normal curve. This is especially true for the large group of boys tested postoperatively. In marked contrast, the Verbal IQ distributions of the girls are clearly below normal for both the preoperative and postoperative samples. These comparisons strongly suggest that the Verbal deficit in the girls did not result from the operative procedures but is in some way associated with the heart defects.

The results are clear but they are not easily explained. A differential mortality rate has been suggested as a causal factor but it is difficult to see why the surviving girls should perform so much better on Performance than on Verbal tests. Recent studies have increased our knowledge of the far-reaching effects of early experience on the developing brain. We know that the maturation of the central nervous system proceeds more rapidly in girls than in boys, so that periods of maximum susceptibility to experience might differ for boys and girls (4). We are becoming increasingly aware of the effects of specific environments in infancy and early childhood on later abilities (8). We know, for example, that severe paranatal anoxia or Western encephalitis occurring in early infancy may seriously affect mental growth (9). And we know that there are sex differences in the relevant family interactions as they relate to specific mental abilities (8, 10). The basis for the deficiency in verbal storage in girls with congenital heart difficulties possibly lies in one or a combination of the above factors. The question is which if any of these experiential factors is relevant, or is the deficiency due to a sex-associated genetic factor? These hypotheses should be tested and considered by other investigators, many of whom neglect to report results for boys and girls separately (11).

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## **References and Notes**

- 1. L. M. Terman and M. A. Merrill, Stanford-Binet Intelligence Scale Manual for the 3rd Revision Form L-M (Houghton Mifflin, Bos-1960). ton, 1960). 2. D. Wechsler. The Measurement of Adult In-
- telligence (Waverly Press, Baltimore, 1944), pp. 106–107.
- 3. E. E. Maccoby, The Development of Sex Differences (Stanford Univ. Press, Stanford, 1966). 4. M. P. Honzik, J. Educ. Psychol. 54(5), 231
- (1963)
- N. Bayley, in Theory and Methods of Re-search on Aging, K. W. Schaie, Ed. (West Virginia Univ. Press, Morgantown, in press).
- R. E. Stafford, Percept. Mot. Skills 13, 428 (1961).

- J. Money, Psychiat. Res. 2, 223 (1964).
  M. P. Honzik, Child Develop. 38(2), 337 (1967).
- M. P. HONZIK, Child Develop. 38(2), 337 (1967).
  J. J. Hutchings, S. R. Burnip, Amer.
  J. Dis. Child. 109, 416 (1965); K. Finley, L.
  Fitzgerald, R. W. Richter, N. Riggs, Arch. Neurol. 16, 140 (1967).
  M. P. Unrith, Encountries, 26th, Americano, 26th, 26th,
- 10. M. P. Honzik, in Proceedings, 75th Annual M. P. Honzik, in *Proceedings, 75th Annual Convention* (American Psychological Assoc., Washington, D.C., 1967), p. 151. M. Campbell and G. Reynolds, *Arch. Dis. Childhood* 24, 294 (1949); L. M. Linde, B.
- Rasof, O. J. Dunn, J. Pediat. 71(2), 198 (1967).
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## **Encephalic Cycles during Sleep and Wakefulness** in Humans: A 24-Hour Pattern

Abstract. Twenty-four-hour polygraphic tracings from normal humans indicate that a pattern of alternating periods of the presence and absence of rapid eye movement, shown to exist for normal sleep, exist over all 24 hours of the daily period. This finding suggests that the so-called sleep-dream cycle of human sleep is not specific to sleep, but is a general activity pattern of the brain.

Rapid eye movement (REM), a phenomenon which has been linked to dream activity (1), occurs with rhythmic periodicity of about every 90

minutes during human sleep. Thus, certain researchers have concluded that human sleep consists of alternating periods of sleep, during which REM

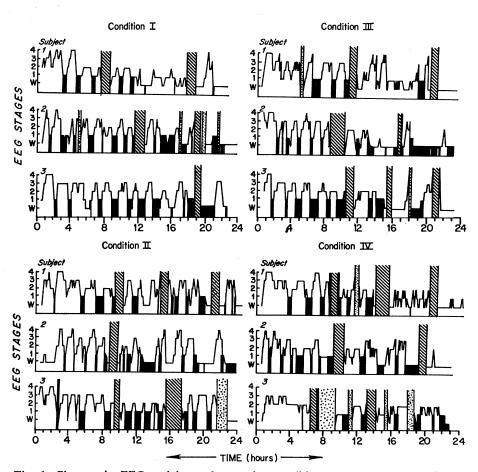


Fig. 1. Changes in EEG activity under varying conditions, recorded over 24 hours, showing alternating presence (solid areas under curve) and absence of REM. Striped areas, meal breaks; dotted areas, interruptions due to technical problems; and 0 time, equivalent of approximately 10 p.m.