MEMORY FUNCTIONS IN CHILDREN RECOVERED FROM REYE'S SYNDROME

Ellen J. Quart, Ph.D.
Teacher Consultant
Ann Arbor Public Schools

Henry A. Buchtel, Ph.D.
Psychology Service
Ann Arbor V.A. Medical Center
and
Departments of Psychiatry and Psychology
University of Michigan

Ashok P. Sarnaik, M.B.B.S.
Director, Intensive Care Unit
Children's Hospital of Michigan

It was our contention that memory functions are at risk in children who have recovered from Reye's Syndrome (RS). This is based on, (1) evidence from similar types of damage that result in memory impairment and, (2) investigation of memory processes themselves.

RS is similar to other types of diffuse insult that result in memory and attentional deficits. For example, chronic alcoholism and closed head injuries cause memory impairments among other neuropsychological deficits.

One might ask, why memory? Two theories are offered: (1) over years of research, Milner has established the importance of the medial temporal lobe area in memory function. With closed head injuries, it may be that the medial temporal lobes receive a disproportionate amount of damage. The skull is constructed such that the temporal lobes rest somewhat on a shelf. Being encased in a boney framework make them more liable to be bruised and have their blood supply altered. Under increased CPP, as is the case with RS, one might expect that the temporal lobes are more vulnerable to sustaining damage.

The second theory offered is related to the global nature of memory functions. Should the temporal lobes not receive more damage than other regions, there are further reasons why memory is at risk when damage is diffuse. Memory is an extremely complex function, requiring large areas of association cortex in

addition to the temporal lobes. Since memory involves large parts of the brain, diffuse damage would have to affect it.

But as we have heard from other researchers, most survivors of RS retain a normal IQ and function quite well in school. However, IQ testing alone may not reveal deficits of practical significance, for example in school progress, and it may not be sensitive to declines from levels that were initially above-average. In addition, there are many well documented cases of individuals with global amnesia who score in the average range on IQ tests.

Therefore we designed a memory battery to test RS survivors seen at Children's Hospital of Michigan in Detroit since 1977. Each of the 26 children was given a measure of intelligence (the (Peabody Picture Vocabulary Test [PPVT]) that is based on receptive vocabulary and is accepted as an indicator of premorbid IQ, two depth of processing tests, and the Wechsler Memory Scale (WMS) which yields an MQ (memory quotient) score. An individual with an IQ of 100 is expected to have an MQ of 100 with 6 points either way being the expected variation.

We then matched each RS subject to a control subject. Children were drawn from the Ann Arbor Public Schools and matched to have the same race, age, sex, SES, and estimated IQ with the RS children. The prospective control children were given the same battery and if they scored within 6 points on the PPVT as their RS partner, they were selected as a control. Table I reports a description of these groups.

There is no difference between the two groups on IQ since the subjects were individually matched on that measure. However, when the MQ was calculated, the scores for the RS group (even though they were within the normal range), were significantly lower than those of the control group.

Keeping in mind that the MQ and IQ are expected to be within 6 points of each other, the difference between the two scores was computed for each subject. The mean MQ-IQ difference for the RS group was -14 while that difference for the control group was +2. Since the mean MQ score for the RS group is in the normal range, it is unlikely that these children would appear to have memory problems. However, given an IQ of 110, they should score much higher.

Several clinical observations were noted during the course of testing which helps account for the discrepancy between the two groups. It was observed that children in the RS group did not demonstrate the use of memory strategies such as chunking, rehearsal, and mnemonics as the control group did. This more

TABLE I

Descriptive Statistics of the Reye's Syndrome Group and the Control Group on Various Analytical Variables

Reye's Syndrome Group

Variable	Minimum	Maximum	Mean	Standard Error
Age at onset	3.25	15.42	9.55	.74
Age at testing	7.25	18.83	12.94	.65
Years since RS	0	6.00	3.35	.28
RS stage on admission	1	4	2.04	.18
Peak RS stage	1	5	3.15	.23
Days in hospital	3.00	60.00	9.48	2.24
Hours in coma	0	192.00	56.75	10.03
IQ	83.00	138.00	110.12	2.86

CONTROL GROUP

Variable	Minimum	Maximum	Mean	Standard Error
Age at testing	7.50	18.42	13.06	.61
IQ	82.00	139.00	111.50	2.70

active involvement to retain information is assumed to aid in recall.

The most significant differences between the two groups were on the three subtests Logical Memory, Digits Forward, and Visual Reproduction. Logical Memory (memory for stories) and Visual Reproduction subtests were also administered approximately 45 minutes later to test long-term memory. Not only did the RS group remember less material originally, but the proportion of material retained was also significantly less than the control group.

We attempted to identify any independent measures that might predict performance on the memory battery but none of them had a significant relationship to outcome as measured by our tests. Of the children with more than a 10 point discrepancy between their IQ and MQ, the only significant characteristic was their IQ. Students with higher IQ's had a larger negative difference. One possible explanation is that in order to score a superior MQ, the use of memory strategies is necessary.

In the course of this study, two unexpected findings emerged: a large number of left-handed subjects in the RS group (23%), and a large number of children who were diagnosed learning disabled before contracting RS (27%). The mean MQ for the left-handed RS children was significantly lower than for the right-handed RS children. However, there was no correlation between a prior history of learning disabilities and MQ scores. This is an area that needs further investigation to determine whether certain children are more at risk to developing RS than other children.

In conclusion, these data reveal good news and bad news about the memory skills of RS survivors. These children have lower MQ's than one would expect given their IQ's. However, they are still within the average range and therefore would not be seen by teachers as having memory problems. One possible cause of their lower scores is that they do not employ effective strategies to aid in recall and this may have implications for rehabilitation and a return to optimal levels of performance.

RESPONSES TO QUESTIONS FROM UNINDENTIFIED PARTICIPANTS

We decided to use normals for our control group (as opposed to children who had had meningitis, encephalitis, or learning disabled children) because we wanted to know how the RS survivors would have performed had they not contracted RS. It would be valuable however to have results of this battery on other children who have had brain damage to compare the effects of different types of diffuse insult. We did not use siblings because we wanted to very carefully match for age and IQ and thought we could also pay attention to SES without using siblings.

The question was raised whether there might have been teacher bias in the selection of the control group. The director of research for the Ann Arbor Public Schools was given a list describing the needed children. He supplied us with a computer

printout of possible matches. These families were then contacted and asked to participate. At no time were teachers contacted or asked to recommend students.

We attempted to contact all children seen at Children's Hospital of Michigan since 1977. Of those able to be located, there was an 87% positive response rate. Those are the 26 we tested. All of these children had the same treatment protocol.

For children through the age of 9, the children's stories developed by L.B. Taylor (Montreal) were substituted for the adult stories. Age corrections, also developed by Taylor, were used with all the children.

Further questions and correspondence can be directed to:

Dr. Ellen Quart
1645 Miller Avenue
Ann Arbor, Michigan 48103

QUESTIONS AND ANSWERS TO DR. QUART'S PRESENTATION.

Question: How did you handle computing the memory quotients in younger children?

Answer: Laughlin Taylor in Montreal, working with Brenda Milner has devised children's stories that we used below the age of 10. The stories and norms are published in Kimura and McGlone (Neuropsychological Test Manual). In scoring the Memory Scale we corrected for age using corrections suggested by Taylor.

Question: When you look at the large number of LD children and those with attention deficient related disorders prior to the development of RS, could that also have factored into these lower scores?

Answer: When we looked at the group of learning disabled students, there was not even a trend for their memory scores to be less than the rest of the Reye's syndrome group. We did look at that quite carefully.

Question: Did you decide to look randomly at 26 Reye's survivors and found all 26 or did you look for 50 and found 26?

Answer: That's a good question. We attempted to contact the families of all the children above the age of 7, who had been treated at Children's Hospital of Michigan in Detroit since 1977. Of the 30 who could be reached, 26 responded positively, and we tested all of them. Some children had moved and we were unable to contact them. One child was severely retarded and the parents did not wish anymore testing and I think there were a couple that didn't want the testing, but typically, as with other centers, the positive response rate is really quite high.

Question: I have a couple of questions concerning the selection of the controls. You selected them on a pretty sound basis, but I was wondering if the selection wasn't biased anyway because the teachers or whoever selected them may have given those names because they were good children. I also wonder why you didn't use the nearest age sibling as a control subject. Finally, if you are going to look at brain insulted children, I would think another control would have been children who have had meningitis or encephalitis and/or head trauma because what we want to know is, is this specific for Reye's or is it merely a reflection of head injury or brain insult irrespective of the insult.

Answer: About the control group. How that was selected is as follows: We gave the director of research for the public school a list of the ages, sex, race and the estimated IQ of the students that we needed. For example, we needed two 10-year-old boys, one with an IQ of 110 and the other with an IQ of 115. He then gave us a list of names of students that potentially matched this description. We then went to the schools to try to determine the socioeconomic status from the counselors or from the principals and then we started testing and we tested almost 100 to get 26 successful matches who were within 6 points on our IQ measure. So I don't think there could have been any bias on the part of teachers because they really didn't have anything to do with the selection. It was done pretty anonymously and letters went out to the parents asking if they wanted to participate in the study.

In response to your question about using the nearest age sibling as a control. We did consider choosing sibs but many of the students didn't have siblings around their age or their performance in school was quite different and we really wanted to have a very carefully matched control with the same age, sex and IQ.

Regarding your question about using other brain insulted children to discover whether the Reye's effects

are different from those of other illnesses. My experience with encephalitis and meningitis has been that they may not retain a normal IQ. We did consider choosing, for example, a learning disabled population that might have had anoxia at birth or some other kind of trauma and still retain a normal IQ because as with the Reye's syndrome children, they function quite well in school and they seem to havre good concept formation and logical thought. However, we really wanted to specifically look at memory in light of the fact that the Reye's survivors were functioning so well in school. So, that is why we chose a normal control group, but I agree it would be worthwhile to look at other groups as well with this same paradigm.

Question: My question also has to do with the selection of controls. It seems to me that just as the number of left-handed Reye's children is disproportionately high, the number of left-handed controls is disproportionately low.

Answer: That's correct.

Question: Regarding the choice of controls, it seems to me that you would also want to match for learning disabilities and maybe use a disease control that is non-neurological but had an exposure to the ICU.

Answer: That is a good point and you are right. Having just one left-hander in the control group is disproportionately low but 6 out of 26 in the Reye's syndrome group is higher than what you would find in the general population. With an N of only 26, it is not significantly different from the expected value, but it is noteworthy that this group of 6 scored significantly worse on the memory quotient battery.

Question: Did all these children receive the same medical treatment?

Answer: Yes. That is why we chose them from the period since 1977. They were all treated personally by Ashok Sarnaik who is the director of the Intensive Care Unit at Children's Hospital of Michigan. For all Stage III or more, they had a Richmond Screw put in to monitor the intracranial pressure.

Question: Have you done any correlations with respect to the actual length of time of post-Reye's or severity of

the illness and some of these demographic factors that we talked about? And, also, are there any trends that might be associated with age?

Answer: Yes, we looked at all those factors and did not find a trend. It could be that with an N of only 26, the numbers of children at different age levels is too small to show a trend in either of those.