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Impairments of number processing induced by prenatal alcohol exposure

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Abstract—Prenatal alcohol exposure causes a variety of cognitive deficits, notably in mathematics and higher order processes such as abstraction. An exploratory battery was developed to examine specific types of number processing impairments in 29 adolescent and adult patients with Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Effects (FAE) relative to controls matched for age, gender, and educational level. The battery included 11 tests: number reading and writing, exact calculation (addition, multiplication, subtraction), approximate calculation (selecting a plausible result for an operation), number comparison, proximity judgment, and cognitive estimation. The results indicated particular difficulties in calculation and estimation tests, with intact number reading and writing ability. The greatest impairment was found in the cognitive estimation test, which is sensitive to frontal lobe lesions. The patterns of deficit described may reflect either the diffuseness of brain damage incurred from prenatal alcohol exposure, or a cumulative deficit in comprehension which may be important for the acquisition of higher-order mathematical abilities. Copyright © 1996 Elsevier Science Ltd

Key Words: cognitive deficits; Fetal Alcohol Syndrome; cognitive estimation; number processing; prenatal alcohol exposure.

Introduction

In the last two decades, it has become clear that alcohol is a teratogen. A teratogen is defined as any agent capable of inducing abnormal or atypical fetal development. The first evidence of the teratogenic effects of alcohol came from the identification of the Fetal Alcohol Syndrome (FAS), the diagnostic term for a birth defect caused by prenatal alcohol exposure. Patients with FAS were first identified in France in 1968 [17] and in the United States in 1973 [16]. Since that time, thousands of patients with FAS have been identified in many countries [6, 7, 18, 20, 31, 32].

FAS is defined by three criteria: (1) growth deficiency of prenatal origin for height or weight; (2) a pattern of specific minor anomalies that includes characteristic facial features, e.g. short palpebral fissures, thin upper lip, smooth and/or long philtrum; and (3) central nervous system dysfunction, including microcephaly, delayed development, hyperactivity, attention deficits, learning disabilities, intellectual deficits, and so forth [6, 29]. Patients are often described as having possible Fetal Alcohol Effects (FAE) when they are heavily exposed to alcohol *in utero* and have some, but not all, of the hallmark features of FAS [6].

Both clinical case studies and large epidemiologic studies have found alcohol-affected individuals to be impaired in standardized arithmetic achievement tests and IQ tests [7, 26, 32, 33]. While deficits with visual sequencing, visual spatial reasoning, attention, and memory have also been described [5, 11, 19, 24, 35], some of the most striking deficits are evident on number processing tasks. The exact nature of these deficits, however, has not been adequately studied. The purpose of the present study is to determine which components of number processing are impaired in patients with FAS and FAE by utilizing more specific tests and theories derived from cognitive neuropsychology.

Recently, there have been several careful studies of brain-lesioned patients with selective impairments in the numerical domain [10, 22, 25, 37]. This has led to the development of detailed models of the cognitive architecture of number processing [3, 8, 21]. It is beyond the scope of this paper to describe these models in detail. However, two general principles of number processing were particularly relevant in guiding the present study.

The first principle is that number-related processes appear to be largely modular. Single-case studies indicate that a focal brain lesion can have a highly selective effect on number processing. For example, knowledge of arithmetical tables may be impaired, while number reading and writing to dictation may be spared [22]. The results from multiple single-case studies suggest that at least three components must be distinguished: number comprehension and number production components (with distinct sub-components for Arabic, spelled-out or spoken numerals), and a calculation component. Whether these components are to be seen as strictly disjoint modules or as parts of a flexible interactive system remains a matter of some debate [3]. However, the fact that each component may be selectively affected by a brain lesion implies that they are implemented within at least partially distinct brain areas. Within this framework, one goal of the present study was to better describe the selective impairments of number processing that may be observed in alcohol-affected individuals. This was accomplished by using tasks focusing on specific components of number processing, an improvement over standardized, global tests of arithmetic ability. A similar strategy has been used by others to study the calculation impairments of learning disabled children [14, 15] and of children who suffered from a brain lesion at an early age [1].

A second tentative principle of numerical organization is the classification of number processing operations into two distinct sets which have been termed "two mental calculation systems" [10]. Most adult number processing abilities, such as reading, writing or calculating, rely on formal symbol-processing algorithms taught at school, that can be applied blindly without reference to the actual quantities denoted by the numbers. In contrast, approximation of numerical magnitudes, e.g. selecting the larger of two Arabic numbers, is very elementary, appears to be largely independent of language or formal instruction, and is found in preverbal infants and animals [9, 13].

The notion that language-based versus magnitude-based numerical abilities constitute two dissociate systems was originally based on a single case study of patient N.A.U. [10]. Following a major lesion of the left posterior brain, this patient had lost the ability to read aloud, write, or calculate, yet abilities in tasks requiring some knowledge of approximate number magnitudes were preserved. Dehaene and Cohen argued that, in this patient, symbolic number processing was completely abolished, but that approximate magnitude processing was intact.

The present study examined whether the concept of a distinct magnitude processing system could be applied to the numerical deficits observed in alcohol-affected individuals. Clinical observations of patients with FAS describe long-term problems with number-related situations, such as the handling of money, timing of daily activities, or other daily situations depending on number quantities and estimation [4, 12, 34]. Even so, these patients often attend school (typically with the support of special education) and have little difficulty in acquiring language and verbal skills. Such clinical observations might suggest a deficit of number magnitude processing in alcohol-affected subjects, perhaps with preserved formal calculation, a pattern representing the dissociation opposite to that of patient N.A.U.

In order to test these theories, a short battery of number processing tests, designed by S. Dehaene, was administered to 29 patients with either FAS or FAE and to 29 control subjects. The battery included a number of classical tests of symbolic number processing: reading Arabic numerals aloud, writing Arabic numerals to dictation, and computing the results of simple additions, multiplications, and subtractions, and tests assessing the understanding of number magnitudes.

In addition, the subjects were administered a cognitive estimation task in which they had to give a reasonable estimate of unknown quantities (e.g. "What is the length of a dollar bill?"). A similar task was demonstrated in studies by Shallice and Evans [28] and by Smith and Milner [30], which both showed the selective effects of frontal lobe lesions on cognitive estimation. Frontal patients produced wildly unreasonable answers, suggesting impairments in preparing an adequate answer-finding strategy, verifying a given answer, or both. Since alcohol-affected patients with some degree of brain impairment have difficulties in understanding numerical quantities, they would also be expected to produce answers which differ significantly from controls on the cognitive estimation task.

Research has indicated that prenatal alcohol exposure results in rather diffuse brain damage, as opposed to the focal damage seen in other types of adult impairment, such as vascular cases. Deficits of response inhibition, visual spatial planning, attention and concentration, and executive processing have been demonstrated in both clinically diagnosed individuals with FAS as well as individuals exposed to lower levels of alcohol prenatally. Interestingly, some of these same deficits have been observed in clinical case studies of patients with specific frontal lobe lesions or closed head-injury cases [23, 27, 36].

Method

Subjects

The 29 patients who participated in this study were a subsample of those enrolled in a larger study examining secondary disabilities in alcohol-affected individuals. They included all available patients participating in the larger study aged 12 years or older who were tested between October 1993 and March 1994, and who had previously been evaluated by a dysmorphologist trained in recognizing fetal alcohol effects. As depicted in Table 1, patients ranged in age from 12 to 44 years (mean = 20.0 years), and 11 were diagnosed FAS, while 18 were described as FAE. All patients had a history of maternal alcohol abuse during pregnancy. The comparison group ($N = 29$) was matched for age, gender, and educational level to the patient group, and consisted of individuals reporting no prior history of learning disabilities.

Table 1. Demographic characteristics for patients and comparison group

Characteristics	Patients ($N=29$)	Comparison group ($N=29$)
Age	20.0 (6.9)	20.4 (7.1)
Education (years)	10.2 (2.7)	10.6 (2.8)
Gender (percentage male)	55.2	55.2
Diagnosis:		
Percentage FAS	37.9	—
Percentage FAE	62.1	—

Note: values are means (standard deviations), except where percentages are indicated.

Measures

Number processing battery. This consisted of 11 pencil-and-paper number-processing tasks. In order of task presentation, they were:

1. *Number reading.* Twenty Arabic numerals, one- or two-digits long, were presented vertically on a page, and the respondent was asked to read them aloud.
2. *Number writing to dictation.* Twenty numbers ranging from 1 to 99 were read aloud to the respondent, who wrote them down in Arabic notation.
3. *Number comparison.* Twenty pairs of Arabic numerals of the same length (either one or two digits) were presented in a vertical column. The respondent was asked to circle the largest number of each pair.
4. *Exact calculation for addition, subtraction, and multiplication.* Twenty each of the three types of exact calculation problems were presented visually, in horizontal format (e.g. $3+5=$——). The respondent was asked to compute and write down the result in Arabic notation. For addition and subtraction, the operands were either single digits or two-digit numerals, and the result was a one- or two-digit numeral not exceeding 68. For multiplication, the operands were always single digits.
5. *Approximate calculation for addition, subtraction, and multiplication.* The same 20 addition, 20 subtraction, and 20 multiplication problems were presented in a different random order accompanied by two proposed results (e.g. $4+5=10$ or 20). The respondents were told that they should not calculate the exact answer, but should just choose the number that seemed closest to the actual answer. The two proposed answers were always of the same length (one or two digits). Both were false, but one of them was within a few units of the actual answer, whereas the other was more distant.
6. *Proximity judgment.* A list of 30 Arabic numerals was presented, with each numeral accompanied by two other numerals of the same length (e.g. 18: 20 or 30?). The subject was asked to circle the one that represented "about the same quantity" as the target number.
7. *Cognitive estimation.* Thirty questions requiring a numerical answer were presented visually and read aloud to the respondent. By design, their exact answer was unlikely to be known, and the respondent was therefore asked to make a reasonable guess (e.g. "What is the length of an average man's spine?"). Some questions were modified from those of Shallice and Evans [28].

Procedure and analysis

The patients with FAS/FAE were administered the number processing battery as part of a 3-hr laboratory examination. The control group was administered only the number processing battery. Two scores were derived for each of the 11 tests in the number processing battery: error rate and a dichotomous impairment score.

Error rates represent the number of items answered incorrectly on each test. For the first nine tests, this represents the percentage of errors out of 20 items, and, for the last two tests, the percentage of errors out of 30 items.

Since the exact answers for the items on the cognitive estimation test were unlikely to be known to either patients or controls, an *a-priori* decision regarding an acceptable range of 'correct' responses was determined by a panel of nine 'judges' aged 11–40 years old. Responses on the Cognitive Estimation Test were scored as incorrect if the respondent failed to give a response, gave a non-numerical answer, used an inappropriate unit of measurement, or gave a response that fell outside the acceptable range of 'correct' responses. The 30 questions in the cognitive estimation test, the corresponding acceptable intervals, and the range of patient and control group responses are presented in Table 2.

Impairment scores are dichotomous scores on each test determined by either of these two criteria: (1) having an error rate of 20% or higher, or (2) having an error rate equal to, or higher than, the poorest performing control. This latter criterion was adopted to avoid attributing occasional inattentional errors to an arithmetic deficit.

Results

Comparison of number-task performance between groups

Distribution statistics for error rates for the patient and control group on each number test are displayed in Fig. 1. In six out of 11 tasks, the differences in error rates between patients and controls attained significance (Mann–Whitney Z-scores ranging from 2.62 to 4.15, respective P values<0.01). Patient error rates differed significantly from controls in exact calculation of addition, subtraction, and multiplication, approximate subtraction, proximity judgment and cognitive estimation. However, error rates for the two groups did not differ significantly in number reading, number dictation, number comparison, and approximate addition and multiplication tasks. Patients performed more poorly than controls on all tasks, except for the number reading, dictation, and comparison tasks.

Patterns of impairment among patients on number tasks

Given the poor performance of the patients relative to controls on the majority of the number tasks, further analysis focused on particular patterns of impairment which may be evident. The Cognitive Estimation task had the highest percentage of subjects with impaired performance (14 impaired patients out of 29 patients). The rank-ordering of the remaining tasks in terms of the number of patients with impaired scores is as follows: approximate subtraction, exact multiplication (eight patients each), approximate multiplication (five patients), exact addition, subtraction, and approximate addition

Table 2. Cognitive estimation questions, range of acceptable responses, and response ranges of patients and controls

Items	Acceptable range	Patient range	Controls range
How many rooms are there in a typical apartment?	2–6	1.5–6.0	2–18
On average, how many frying pans does a restaurant need?	4–130	4–130	2–40
How many days do you think it took Columbus to sail across the Atlantic?	17–240	2 hr–2016 days	21 days–2 years
On average, how many children are there in a classroom?	15–40	15–130	20–35
What is the normal length of a bus?	6–200 ft.	3.3–58 ft.	7–609 ft.
How fast do race horses gallop?	10–50 m.p.h.	3–2000 m.p.h.	5–99 m.p.h.
How long does it take to cook a fish?	7–30 min	2.5 min–5 hr	3 min–2 hr
How old is the oldest woman on earth?	96–115	75–600 years	93–150 years
How much does it cost to have your shoes repaired?	$3.75–$40	25 cents–$2000	$2.50–$40
What is the size of the largest kitchen knife that can be found?	6–60 in.	6 in.–6.5 ft.	1.5 in.–5 ft.
What is the height of the White House in Washington?	12–432 ft.	9.2–500 ft.	30–250 ft.
How many months are there in a year?	12–12	6–12	12–12
On average, how many TV programs are there on any one TV channel between 6 pm and 11 pm?	5–12	3–20	2–15
How much does a compact car cost?	$1600–$50,000	$100–$200,000	$2000–$60,000
How many slices are there in a sliced loaf?	11–30	6–40	10–30
What is the length of a dollar bill?	3–8 in.	2 in.–5 ft.	3.75–10 in.
How heavy is the heaviest dog on earth?	11–319 lbs	15–2000 lbs	60–378 lbs
What is the length of an average man's spine?	2–4 ft.	1 in.–24 ft.	2–4.5 ft.
How long did it take the astronauts to go to the moon?	6 hr–180 days	2 hr–10 years	45 min–4 years
What is the size of the largest object that you can find in a house?	5–30 ft.	1.42–36 ft.	5–148 ft.
How heavy is a typical chair?	2–50 lbs	1–75 lbs	2–100 lbs
What is the average annual salary per year for a doctor?	$30,000–$200,000	$200–$300,000	$1500–$300,000
How many spectators will come to a major football match?	6000–2000,000	200–1,500,000	100–200,000
How much does a commercial airplane cost?	$22,000–$60,000,000	$3–$1,500,000,000	$275–$1,000,000,000
How many children can a schoolbus carry?	30–80	20–100	30–80
What is the height of the tallest tree in the world?	100–1500	10–7000 ft.	40–800 ft.
How long would it take to drive from San Francisco to New York?	4–25 days	1 hr–30 days	2–30 days
How much does a regular TV-set weigh?	3–70 lbs	4–200 lbs	4–100 lbs
How many pages are there in a daily newspaper?	8–100	4–90	10–100
What is the size of the largest bird in the world?	5–20 ft.	10 in.–18 ft.	10 in.–40 ft.

Note: values represented as the 'acceptable range' were determined by judges before the study was carried out. Values for patients and controls indicate the minimum and maximum response obtained.

(four patients each), proximity judgment (three patients), and larger–smaller comparison (two patients). No patients were impaired on number reading and writing to dictation. This finding suggests that cognitive estimation, and, to a lesser extent, approximate subtraction, pose special difficulties for alcohol-affected individuals. These two tasks heavily involve processing of numerical quantities. Additionally, knowledge of multiplication tables also appeared to be impaired, suggesting additional problems with arithmetical memory.

The analysis also indicated that the degree of number processing impairment varied considerably from one individual to the next. See Table 3 for a listing of patients' error rates on number tasks. Two-thirds of the patients evidenced some degree of impairment on the number tasks, and one-third (five FAS and five FAE) evidenced no impairment whatsoever, according to our criteria. Discounting reading and number dictation, on which no patients fell into the impaired range, three patients (two FAS and one FAE) were impaired on eight or nine of the remaining tasks, eight patients (three FAS and five FAE) were impaired on two or three tasks, and six patients (three FAS and three FAE) showed isolated impairment on only one task. Interestingly, the pattern of impairment seemed to be relatively independent of the diagnosis of the patient (FAS vs FAE), thus suggesting varied degrees of impairment in the processes underlying arithmetic problem-solving for both patient groups.

Table 3 also indicates those tasks that were the most sensitive in terms of identifying impairment among patients. Cognitive estimation identified six patients as 'impaired' who were not identified as 'impaired' on other tasks; approximate subtraction and multiplication each identified only one patient not otherwise identified as impaired.

Cognitive estimation task

The cognitive estimation results were analyzed further in order to understand better the nature of the difficulties manifested by alcohol-affected subjects. Qualitatively, the patients gave very different responses compared to the controls. Examples of patients' unrealistic responses include "6.5 ft." for the length of the largest kitchen knife that one can buy, "1 hr" for the drive from San Francisco to New York, "6" for the number of months in the year, and "5 ft." for the length of a dollar bill. Curiously,

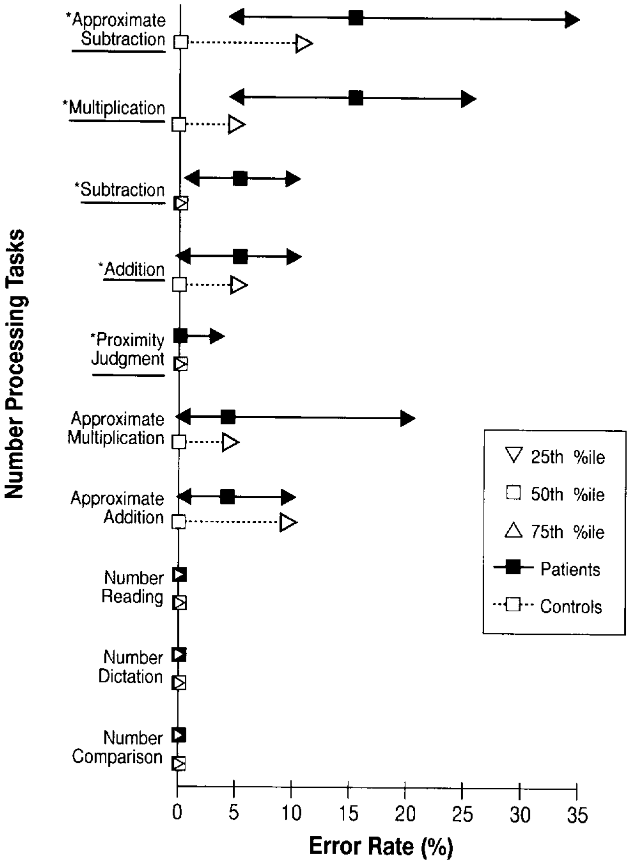

Fig. 1. Performance of patient and control groups on each of the number processing tasks. The number processing tasks are rank-ordered from left to right according to the greatest magnitude of difference in means between the groups. Items with significantly different group means, as tested by the Mann–Whitney test, are underlined and identified with an asterisk. The following items significantly differentiated patients from controls: Approximate Subtraction, Multiplication, Subtraction, Addition, and Proximity Judgment.

although their numerical answers were often very different from those produced by controls, the patients almost always selected appropriate units of measurement (e.g. inches or feet for length, miles per hour for speed, etc.) without any prompting from the examiner. Sometimes there were even indications that the subjects knew the answers but selected an inappropriate number. For instance, when asked for the height of the tallest tree in the world, one patient correctly answered "redwood", but then gave it a size of 23 ft. and 2 in.!

Table 2 lists the response ranges for the patient and control groups across all 30 items. On 19 items, the patients exhibited a wider range of responses when compared to controls. The patients produced both higher and lower number responses relative to the controls; in 23 out of 29 items (one tie), the minimum answer was lower for the patients than for the controls, and in 21 out of 28 items (two ties), the maximum answer was higher. This discrepancy in response range is clearly portrayed in Fig. 2, where the actual numerical responses to the items have been standardized to the geometric mean and plotted for both groups to aid in the comparison of items. For example, patients produced similar responses to controls on the item involving the number of TV programs on a given channel between 6 and 11 p.m., but markedly discrepant responses to the item inquiring the age of the oldest woman on earth. However, we could not find any obvious single explanation for why certain items appeared to pose particular problems for the patients. Neither familiarity nor the type of question, e.g. distance, nor the magnitude of the numbers involved seemed to account fully for the pattern of discrepant responses.

Relationship between background variables and task performance

Given the differences found between patients and controls on the number tasks, Pearson correlation coefficients were computed separately in order to examine the relationships between certain background variables and number task performance. Interestingly, neither a patient's age, diagnostic category, nor gender was related to error rate performance on any of the number-processing tasks. A patient's intellectual level was negatively related to error rates on seven out of 11 number tasks: number comparison, exact calculation for multiplication and subtraction, approximate addition and multiplication, proximity judgment, and cognitive estimation (r's ranging from 0.39 to 0.49). Surprisingly, a higher mathematical achievement (defined as larger standard scores on an achievement test) was related to only three number tasks (exact calculation for multiplication, approximate multiplication, and proximity judgment; r's ranging from 0.44 to 0.58). Examination of the correlations between tasks revealed a positive correlation between all three exact calculation tasks (addition, subtraction and multiplication) and the corresponding approximation tasks. Thus, there was no evidence of a dissociation between approximation and exact calculation in patients taken as a group.

A similar correlation analysis was performed for the controls. Cautious interpretation is warranted as there was often little variation in performance, with most controls scoring at floor level in terms of error rates. Nevertheless, gender was significantly related to approximate addition, multiplication, and subtraction performance, with female controls performing worse on the three approximation tasks. There was also a significant association between education and cognitive estimation ($r = -0.49$, $P < 0.01$). A positive correlation structure again emerged among the three approximation tasks and the exact addition task, but not with the exact multiplication and exact subtraction tasks (perhaps because exact calculation yielded very few errors in controls).

Discussion

The present investigation was conducted in order to examine deficits of number processing in alcohol-affected

Table 3. Error rates and impairment scores on number tasks for individual patients and error rates for control group mean and patient group mean on number tasks

	Number tasks:											Total tests
	Number reading	Number dictation	Compare	Add	Subtraction	Multi-plication	Approximate addition	Approximate subtraction	Approx. multiplication	Proximity judgment	Cognitive estimation	in impaired range
Control group mean	0.00	0.00	0.69	1.90	1.38	3.28	5.69	6.55	6.72	0.34	8.85	
Patient group mean	0.34	0.34	3.28	7.59	9.14	17.24	10.00	19.31	13.28	6.09	21.38	
Patients												
1	0	5	5	5	15	5	10	25	0	0	13	0
2	5	0	0	0	5	5	0	25	0	3	17	0
3	0	0	0	10	0	0	5	15	0	0	7	0
4	0	0	0	5	5	0	10	20	0	3	10	0
5	0	0	0	0	0	15	0	0	0	0	10	0
6	0	0	0	**25**	**25**	**30**	**40**	**50**	**40**	**43**	**33**	8
7	0	0	0	0	0	0	0	25	0	3	**27**	1
8	0	0	0	5	0	15	0	5	0	0	10	0
9	0	0	0	0	5	5	5	**40**	0	0	7	1
10	0	0	5	0	0	20	5	5	15	3	10	0
11	0	0	0	0	10	5	0	**35**	0	3	**23**	2
12	0	0	0	5	5	15	10	5	0	3	**27**	1
13	5	0	0	5	**35**	**40**	15	15	20	0	**20**	3
14	0	0	0	10	0	15	5	5	0	0	**33**	1
15	0	0	0	5	0	**25**	5	15	15	0	17	1
16	0	0	0	5	0	15	5	15	10	0	13	0
17	0	0	0	0	0	15	0	5	5	3	13	0
18	0	0	**20**	10	**35**	**55**	**60**	**45**	**55**	**30**	**43**	8
19	0	0	0	5	0	5	**30**	25	**45**	0	10	2
20	0	0	0	10	10	**25**	10	10	15	0	**20**	2
21	0	0	0	0	10	0	0	0	0	0	**33**	1
22	0	0	0	0	0	0	0	**35**	5	0	**33**	2
23	0	0	0	10	5	**45**	5	**35**	**40**	3	13	3
24	0	5	0	**20**	10	5	10	**40**	25	3	13	2
25	0	0	**55**	**65**	**80**	**100**	**50**	**40**	**65**	**67**	**60**	9
26	0	0	0	**20**	10	**25**	10	20	20	3	**33**	3
27	0	0	0	0	0	5	0	5	5	3	13	0
28	0	0	0	0	0	0	0	0	0	0	**37**	1
29	0	0	10	0	0	10	0	0	5	0	**20**	1

Note: impaired performance on a given task is indicated by **bold-face** error rates. Impaired performance was defined as (a) exhibiting an error rate of at least 20% on a given task; and (b) having an error rate equal to, or worse than, the poorest performing control. An underline indicates that the test was the only one in which a given patient had impaired performance.

patients. Two principles of number processing architecture were emphasized: the modularity of number processing systems, and the notion of two mental calculation systems, one for symbolic calculation and the other for approximate magnitude processing. We will consider these two principles in turn.

The present results supported the notion of modularity in that the patients were able to perform the number reading and number writing tasks quite well, yet exhibited difficulty with the calculation and estimation tasks. This broad dissociation between intact number transcoding and impaired calculation and/or estimation is consistent with previous neuropsychological findings [21] and clinical observations [34], and suggests that the effects of prenatal alcohol exposure on cognitive processing can leave basic verbal tasks, such as reading and writing, intact while impacting other processes. However, we cannot fully preclude the possibility that an undetected transitory deficit in number reading and writing was totally overcome by the time our sample of teenagers and adult subjects was tested.

Even on the calculation and estimation tasks, impairment was not uniform. In particular, most subjects performed extremely well on the number comparison task. Only two subjects were impaired on number comparison, and those also showed impairments in all but the transcoding tasks. This selective preservation of a larger–smaller comparison replicates previous neuropsychological findings, which indicate that even drastically-impaired acalculic patients, such as patient N.A.U. (who could not compute 2+2) are able to master number comparison [10]. It supports the view that number comparison is an elementary operation which does not require any instruction and is relatively independent of other forms of number processing [8, 9].

The cognitive estimation task appeared to be one of the best measures in discriminating between patients and controls. Alcohol-affected patients were often unable to

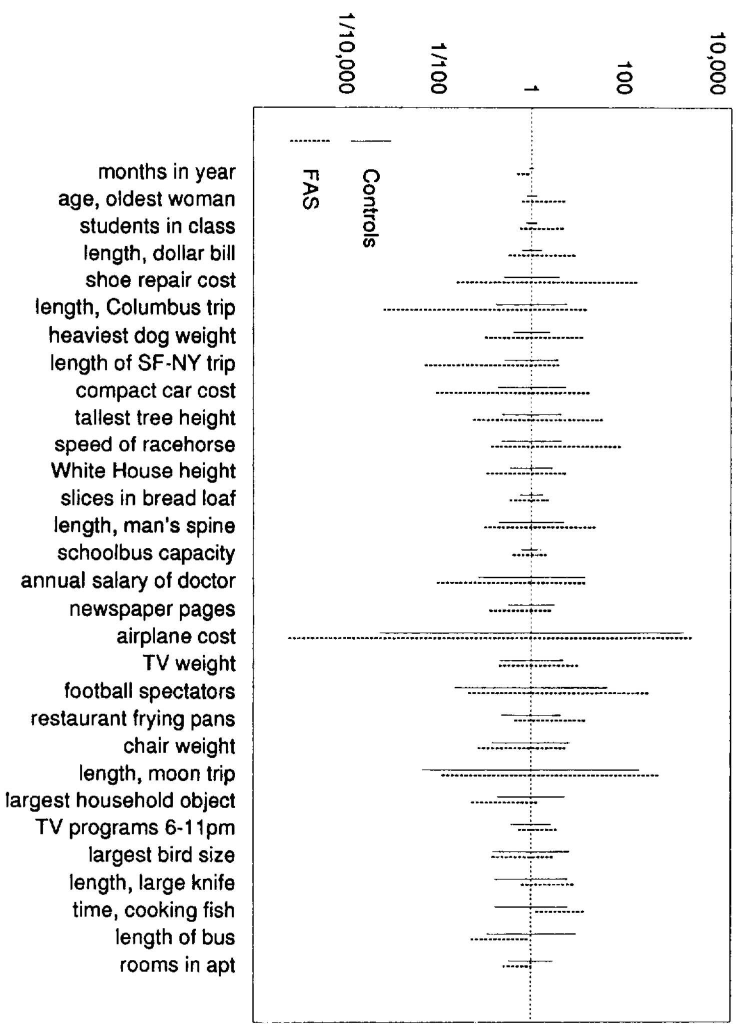

Fig. 2. Range of responses for patient and control groups on each of the cognitive estimation items. For comparison purposes, numerical responses to each item were standardized to the geometric mean.

produce even vaguely reasonable numerical answers to unfamiliar questions such as "What is the height of the White House?". This cognitive estimation difficulty might even be said to be a characteristic of alcohol-affected individuals in that 14 patients out of 29 (48%) gave impaired responses on cognitive estimation. Six patients appeared to have particular difficulty with the cognitive estimation task, despite adequate performance on the other number tasks. Thus, cognitive estimation appeared to be the most sensitive test in the battery for detecting impaired number processing performance. Given that the patients could almost always give the appropriate unit of measurement or even show some knowledge of the non-numerical answer, their difficulty was in producing a quantity that constituted a reasonable value in this unique problem-solving context. This meshes well with previous clinical observations of inadequate understanding of quantities in alcohol-affected individuals, for example, the inability of some patients with FAS to manage money [34].

Based on the notion of "two mental calculation systems", we initially speculated that alcohol-affected patients might show a selective deficit of approximate magnitude processing abilities. The results provided only limited support for this hypothesis. As a group, the patients were indeed impaired in their processing of number magnitudes (as shown by significant deficits in cognitive estimation, subtraction approximation, and proximity judgment). However, the proximity judgment deficit in patients was minimal and only reached significance because of a floor effect in the controls. Thus, most patients could determine which of two numbers is closest to a third one, a finding which is consistent with their adequate performance in number comparison, yet somewhat incompatible with the hypothesis of a basic deficit in understanding number magnitudes.

Likewise, patients and controls did not differ significantly in approximate addition and approximate multiplication, two tasks that were expected to tax the putatively impaired approximate representation of number magnitudes. Examination of the error rates (Fig. 1) revealed that, while patients did perform slightly worse than controls, the controls themselves averaged errors of between 5 and 7% in these tasks. Thus, the approximation tasks might have been difficult for some controls as well.

Finally, there was no evidence of a selective preservation of exact calculation tasks. On the contrary, the exact multiplication task, which probed rote memory of the multiplication table, was quite difficult for patients relative to controls. Exact addition and exact subtraction were also significantly impaired, but to a lesser extent. Thus, even though the deficit of alcohol-affected patients spared number transcoding and was broadly restricted to calculation and/or estimation tasks, there was no sharp dissociation between exact and approximate calculation in alcohol-affected patients when considered as a group. Clearly, not all of their deficits in mathematics could be attributed to faulty processing of approximate magnitudes. Impaired memory for simple arithmetical facts may have contributed to their difficulties.

Nevertheless, these results do not necessarily invalidate the notion of two mental calculation systems for at least three reasons: (1) diffuse brain damage may affect several number processing systems; (2) impairments at an early age may have a cumulative effect on subsequent number development; and (3) specific processing deficits may be masked when combining groups of individuals with various areas of impairment.

First, the degree of impairment in alcohol-affected individuals may simply reflect the diffuseness of brain damage, which is likely to affect several tasks simultaneously. A working hypothesis is that prenatal alcohol exposure results in a bilateral impairment of frontal functions, left lesions being responsible for exact calculation deficits and right lesions impacting the cognitive estimation and approximate subtraction abilities. This notion is compatible with observations of cognitive estimation deficits in cases of left or right frontal lesions [28] and of price estimation deficits in cases of right lesions [30].

Second, an early deficit in understanding number magnitudes may hinder the subsequent acquisition of other higher-order mathematical abilities such as exact calculation. It has been suggested that a preverbal representation of number magnitudes, which supports number comparison among other things, serves as a foundation for the later acquisition of more advanced language-based calculation routines [8, 13]. In this case, isolated deficits of numerical magnitude processing should not be observable in developmental cases, because they would cause a global retardation in other sectors of mathematics. Only in adult cases with localized brain lesions would there be any chance of observing a selective deficit of the processing of numerical quantities.

Third, selective impairments may not be visible when considering patients as a group, especially if their pathology results in a diffuse pattern of brain damage. Individual cases may exhibit very selective dissociations which may not be seen when combining cases. Even though our study was exploratory and not designed for individual analysis, there was some suggestive evidence of selective impairments in estimation and approximation tasks. Six patients, as mentioned above, had problems exclusively with cognitive estimation. Four other patients exhibited selective difficulties with the approximation tasks, in the absence of any deficit in exact calculation, number approximation, or proximity judgement. In two of them, there was also a difficulty with cognitive estimation.

To consider a rather striking example of the selective impairments in approximation and estimation observed, one patient performed at, or close to, chance level in approximate addition (30% errors), approximate multiplication (45%) and approximate subtraction (25% errors), yet this patient made no error in comparison, proximity judgment and exact subtraction and only one error (5%) in exact multiplication and exact addition. This pattern is very suggestive of a selective impairment of approximate calculation. It may even seem paradoxical because, in solving the approximation tasks, nothing prevented the patient from computing the exact result and selecting the closest of the two proposed numbers, using the intact exact calculation and proximity judgment abilities. Some patients seem to know how to perform mathematical operations mechanically without knowing how to deal with numerical magnitudes in a less familiar context.

Interestingly, even in controls, approximate calculation seemed to pose special difficulties, with females performing significantly worse than males on the three approximation tasks only. Thus, the approximation tasks may, indeed, constitute a distinct set which poses special difficulties for females. Other sex differences in mathematical abilities have been described, and the reader is referred to Benbow [2] for a review.

In conclusion, the present study has contributed to the specification of arithmetic impairments observed among alcohol-affected adolescents and adults. Our results demonstrate preserved number comprehension as indexed by number reading and writing, with particular difficulty in cognitive estimation, and approximate and exact calculation. The pattern of impairment is clearly variable among patients, with ten of the patients exhibiting no measurable impairment in any of the numerical tasks used. Subsequent research should combine neuroimaging techniques with cognitive neuropsychological tests in order to understand better the causes of such variability. Correlation of cognitive impairments with specific lesion sites may provide insights into the specific neural mechanisms impaired by prenatal alcohol exposure.

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