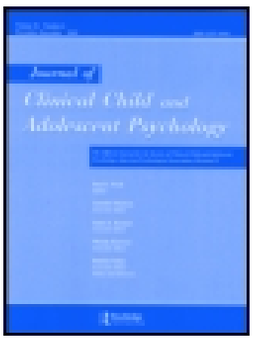

Routledge
Taylor & Francis Group

Journal of Clinical Child Psychology

ISSN: 0047-228X (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/hcap19

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To cite this article: Rachel Levy-Shiff , Eli Vakil , Lilly Dimitrovsky , Miriam Abramovitz , Norith Shahar , Dov Har-Even , Schlomo Gross , Maya Lerman , Izhak Levy , Lea Sirota & Benjamin Fish (1998) Medical, cognitive, emotional, and behavioral outcomes in school-age children conceived by In-Vitro Fertilization, Journal of Clinical Child Psychology, 27:3, 320-329, DOI: 10.1207/s15374424jccp2703_8

To link to this article: https://doi.org/10.1207/s15374424jccp2703_8

Journal of Clinical Child Psychology
1998, Vol. 27, No. 3, 320–329

Medical, Cognitive, Emotional, and Behavioral Outcomes in School-Age Children Conceived by In-Vitro Fertilization

Rachel Levy-Shiff, Eli Vakil, Lilly Dimitrovsky, Miriam Abramovitz, Norith Shahar, and Dov Har-Even
Bar-Ilan University, Israel

Shlomo Gross, Maya Lerman, Izhak Levy, Lea Sirota, and Benjamin Fish
Rabin Medical Center, Israel

Assessed long-term effects of assisted reproduction technologies of in-vitro fertilization (IVF) and related techniques of embryo transfer (ET) on children's adjustment. 51 school-age Israeli children conceived by IVF/ET were compared with 51 control-matched children conceived spontaneously. The assessment included a comprehensive medical evaluation, a psychological examination, teachers' reports, parents' reports, and children's self-reports. As compared with controls, IVF/ET children did not reveal significant differences in physical and neurological status or on cognitive measures of IQ, visual-motor coordination, visual memory, and verbal comprehension. Nevertheless, the IVF/ET children were scored lower by teachers on measures of socioemotional adjustment in school and on self-report measures of anxiety, aggression, and depression. Among IVF/ET children, the tendency to be at a greater risk for emotional disturbances was exacerbated among boys and among children whose parents were older.

Advances in assisted reproductive techniques of in-vitro fertilization (IVF) and related procedures of embryo transfer (ET) help approximately 16–20% of couples with infertility problems who use these methods to conceive a child (DeCherney & Lavy, 1986). The registries of different nations include data, up to 1987, for more than 40,000 newborns conceived by these technologies (Fertilization In Vitro Nationale, 1989). Since then, the numbers have being growing rapidly. Information on developmental outcome is only slowly emerging in the literature, and consensus on what constitutes the major outcomes has yet to be achieved. Previous studies and surveys of national IVF/ET registries have focused mainly on the obstetric and parental outcome and on mental and psychomotor development in infancy. The aim of the present study was to assess the physical, neurological, cognitive, emotional, and behavioral outcomes of IVF/ET children in middle childhood, hitherto uninvestigated.

Researchers have raised concern regarding the increased biological and psychological risk associated with IVF/ET pregnancies (e.g., Biggers, 1981; Dennerstein & Morse, 1988; D'Souza, Rivlin, Buck, & Liberman, 1990; Mushin, Spensley, & Barreda-Hanson, 1985). From a biological perspective, various mechanisms that increase the potential risk have been suggested. These include induction of chromosomal aberrations, increased rate of fertilization by abnormal spermatozoa, the induction of point mutations, nondisjunction resulting in nullisomy, monosomy, and trisomy, and structural abnormalities such as haploidy and diploidy (e.g., Angell, Templeton, & Aitken, 1986; Biggers, 1979, 1981; Edwards, 1983). Other factors have also been suggested, such as the genetic or medical profile of the couples who use fertility treatments and the medications used to induce ovarian superovulation (e.g., Marrs, 1986; Ron-El et al., 1994). The significance of these concerns is as yet unclear, but their presence indicates the need for careful evaluation of children conceived by IVF/ET (Beral & Doyle, 1990; Yeh, Leipzig, Friedman, & Seibel, 1990).

Researchers have suggested that psychological risk factors may also be at play. Successful resolution of psychological conflicts concerning infertility may not occur. Thus, even though couples successfully conceive by IVF/ET, they may still regard themselves as infertile. When conflicts regarding infertility are resolved, they may resurface during certain stressful periods (Kemeter, Eder, & Springer-Kremser, 1983). Moreover, participants in IVF programs are often couples who have persisted in their attempts to successfully conceive despite significant hardship, inconvenience, and expense (Callan & Hennessey, 1988; Mahlstedt, Macduff, & Bernstein, 1987). One might postulate that such couples

Requests for reprints should be sent to Rachel Levy-Shiff, Department of Psychology, Bar-Ilan University, Ramat-Gan 52900, Israel. E-mail: levyra@mail.biu.ac.il

possess good coping skills, that they are highly motivated to have children, and that their commitment to parenting will be strong (Golombok, Cook, Bish, & Murray, 1995). These would be positive factors when considering this group of prospective parents. However, they may also be overanxious when raising a child who is often thought of as "precious," particularly by couples who are older and cannot conceive more children (Raoul-Duval, Bertrand-Servais, & Frydman, 1993). Furthermore, it has been suggested that parent–child relations and family climate may differ in IVF and non-IVF families (Mushin et al., 1985), in turn affecting child adjustment. Indeed, IVF/ET parents' style was found to be altered (Golombok et al., 1995).

A review of empirical studies has revealed that IVF pregnancies were, indeed, associated with an increased risk for pregnancy complications, fetal loss, and parental and neonatal morbidity and mortality. In addition, they were found to be associated with preterm delivery, low birth weight, Caesarian sections, required transfer to neonatal intensive care units, and higher incidence of induced multiple pregnancies. The latter predispose to preterm birth and low birth weight. Nevertheless, the frequency of preterm deliveries and low-birth-weight babies was not entirely accounted for by the high frequency of multiple births. Measurements of head circumference and length, both at birth and at two years of age, were lower than normal. These data are consensual, reflecting both the results of studies that used control groups and surveys of IVF/ET national registries (e.g., Andrews et al., 1993; Australian In-Vitro Fertilisation Collaborative Group, 1985; Beral & Doyle, 1990; Brandes et al., 1992; Friedler, Mashiach, & Laufer, 1992; Lancaster, 1985; Leiblum, Kemmann, Colburn, Pasquale, & Delisi, 1987; Medical Research International Society, 1992; National Perinatal Statistics Unit, 1987; Nygren, Bergh, Nylund, & Wramsby, 1991; Raoul-Duval, Bertrand-Servais, Letur-Konirsch, & Frydman, 1994; Rizk et al., 1991; Rufat, Olivennes, De Mouzon, Dehan, & Frydman, 1994; Steptoe, Edwards, & Walters, 1986; Sutcliffe et al., 1995; Tan, Doyle, & Campbell, 1992; Wennerholm, Janshon, Wennergren, & Kjellmer, 1991; Yeh et al., 1990).

Although some studies have indicated somewhat higher rates of malformations (e.g., National Perinatal Statistics Unit, 1987), most pointed to malformation rates comparable to those of national surveys and control groups (e.g., Lancaster, 1987; Morin et al., 1989; Rufat et al., 1994). Sporadic cases of major congenital malformations during the first weeks of life were reported; the types of malformations varied and the number of each specific type was small (Beral, Doyle, Tan, Mason, & Campbell, 1990) .

With regard to mental and psychomotor development evaluated by various scales (e.g., Bayley, Griffith, Stanford–Binet) during infancy and early childhood, research has not shown the IVF/ET children to differ significantly from children conceived spontaneously (e.g., Brandes et al., 1992; Ron-El et al., 1994; Sutcliffe et al., 1995). Developmental and neurological problems that were discovered were found to be related mainly to multiple births, prematurity, and low birth weight (Brandes et al., 1992; Mushin, Barreda-Hanson, & Spensley, 1986).

Few studies have documented the social, emotional, and cognitive development of IVF/ET children during the preschool years. Golombok, Bhanji, Rutherford, and Winston (1990) found adequate developmental progress, with most children performing above chronological age norms. Nevertheless, the IVF/ET participants, and particularly the boys among them, showed a higher incidence of behavioral and emotional problems than did the control group children.

No study has explored IVF/ET children's developmental outcome during the school years. Previous research has focused on adjustment in early childhood, a period when a number of dimensions of functions cannot be accurately assessed. The school years are of particular importance because, as has been shown with other high-risk groups, children who apparently have had reasonable development up to this point can manifest more subtle difficulties in various domains (e.g., learning disabilities) that necessitate longer follow-up to be detected (e.g., Aylward, Pfeiffer, Wright, & Verhulst, 1989; McCormick, 1989).

Hence, the present study was designed to assess developmental outcome in school-age children conceived by IVF/ET by comparing them with children conceived spontaneously. The assessment included a medical evaluation of the physical and neurological status, as well as a psychological evaluation of the cognitive, emotional, and behavioral aspects manifested at home and in school. Given the aforementioned delineated biological and psychological risks that may be encountered by the IVF/ET children, as well as previous research findings on IVF/ET children in early childhood, they were hypothesized to be at a higher risk for medical, cognitive, and emotional difficulties, as compared with their control counterparts.

Possible differential effects of parental age and number of siblings on the adjustment of the IVF/ET and control groups were also explored. It was thought possible that IVF/ET children who had fewer siblings and whose parents were older might be considered more precious (Mushin et al., 1985; Raoul-Duval et al., 1993). This could perhaps affect parental style (Golombok et al., 1995) and in turn increase the risk for emotional difficulties. Effects regarding sex were also explored as there is some evidence that IVF/ET boys may be at a higher risk than IVF/ET girls (Golombok et al., 1990) and that school-age boys may be more vulnerable to various biological and psychological risks than girls (e.g., Arnold, 1996; Brown & Rife, 1991; Del'Homme,

Kasari, Forness, & Bagley, 1966; LaBuda & Defries, 1989; McDermott, 1996; Webster-Stratton, 1966).

To prevent confounding the effects of prematurity and IVF/ET pregnancy variables (Brandes et al., 1992), this study was confined to children who were born full term.

Method

Participants

The sample consisted of 51 Israeli children conceived by IVF/ET and 51 control-matched children (for sample characteristics, see Table 1).

The only additional criterion for selection of the IVF/ET children was that they were born with gestational age over 36 weeks (full term), about 80% of the total screened IVF/ET conceived children.

The children in the control group were conceived spontaneously, and the course of pregnancy and birth was normal. The sampling procedure for selection of the control group children was matched-pair. The children were matched one-to-one for age, sex, birth order, and socioeconomic status, including maternal and paternal education, maternal and paternal professional status (classified according to the index of occupational prestige in Israel on a 9-point scale, 1 = *unemployed*, 9 = *lawyers, medical doctors*), and family income (classified according to five categories, 5 = *much more than the average salary in Israel*, 1 = *far less than the average salary in Israel*). The samples of both groups were heterogeneous, and their socioeconomic profile was similar to that of the general Israeli population.

Table 1. *Description of Children's and Parents' Characteristics*

	Pregnancy			
	IVF/ET		Spontaneous	
Characteristic	*M*	*SD*	*M*	*SD*
Children				
Gestational Age (Weeks)	37.51	2.35	40.28	1.58
Birth weight (g)	3,015.20	675.16	3,380.02	442.33
Age	9.75	0.81	9.66	0.73
Male(%)	56.86		56.86	
Firstborn(%)	54.90		54.90	
Mothers				
Age	43.52	3.68	36.11	5.89
Education (Years)	13.08	2.67	12.98	2.71
Professional Status	3.83	2.28	4.01	1.96
Fathers				
Age	46.25	4.25	39.57	5.41
Education (Years)	13.63	3.56	13.52	3.76
Professional Status	4.44	1.86	4.75	1.89
Family				
Number of Siblings	1.94	0.88	2.89	0.63
Income	3.48	0.71	3.42	0.76

Note: IVF/ET = in-vitro fertilization/embryo transfer.

A comparison of the IVF/ET and non-IVF/ET samples indicated that although the IVF/ET children were born full term, their birth weight and gestational age were lower, $F(1, 100) = 6.51$, $p < .001$ and $F(1, 100) = 5.60$, $p < .001$, respectively; more IVF/ET children were born through Caesarean section (61% versus 18%), $\chi^2 = 12.82$, $p < .001$; they had fewer siblings, $F(1,100) = 17.64$, $p < .001$; and their mothers' and fathers' mean age was higher, $F(1,100) = 9.87$, $p < .001$ and $F(1,100) = 12.79$, $p < .001$, respectively. Because paternal age was highly correlated with maternal age ($r = .87$), they were averaged and a composite score of parental age was used in subsequent analyses.

Procedure

The children were recruited when they were 9–10 years old. The IVF/ET children were selected from two hospitals in central regions of Israel. First, their medical records were screened, and approximately 80% of the children were found qualified to participate in the study (i.e., their gestational age was over 36 weeks). The qualified families were then contacted and were asked to participate in the study; all agreed to participate. Those who did not qualify for the study were IVF/ET children who were born prematurely with gestational age less than 36 weeks. An analysis conducted to compare the IVF/ET children born prematurely and full term indicated that the former had a lower birth weight, were in intensive care units more frequently, and stayed longer in the hospital. These findings are congruent with previous ones (e.g., Brandes et al., 1992). A comparison of the demographic variables did not reveal any significant difference between the two groups.

The control group children were recruited through the IVF/ET children's schools. Questionnaires were distributed to the children in class asking for their parents to provide information regarding the criteria relevant for matching (e.g., parental education). About 75% of the families returned the questionnaires. Families suitable according to the matching criteria were then contacted. Of the families approached, 92% agreed to participate in the study. A comparison of the information we had of those who agreed and those who did not agree to participate revealed no significant difference.

After the initial screening procedure, evaluations were then performed by a multidisciplinary team of pediatricians, specializing in neurology and child development, and clinical child psychologists. The evaluations were conducted using a standard checklist protocol and included interviews with the mothers regarding the course of pregnancy and child development, as well as medical examinations and psychological assessments of the children. Several measures were taken in order to assure that assessment was blind as to

the status of the child (i.e., IVF/ET or non-IVF/ET conceived): The pediatrician examining the child was unaware of the information obtained from the medical record or of the results of the psychological assessment, and children's names were withheld from the medical charts reviewed.

The psychological tests were administered to the children in a counterbalanced order. Each test was scored by two clinical child psychologists separately. The agreement between the two raters ranged between .98 and 1.00. Had there been scoring differences, a third senior clinical psychologist would have coded the data as well, and discussions would have been held until resolution, thereby reaching 100% agreement. A similar procedure was employed with regard to the review of the medical charts and maternal interviews relating to pregnancy and child development. These were reviewed and coded by two different pediatricians. The agreement between the two raters ranged between .96 and 1.00. Had there been scoring differences, a third senior pediatrician would have coded the data as well, and discussions would have been held until resolution, thereby reaching 100% agreement. All team members were trained to reach a high reliability before actual data collection by assessing cases that did not participate in the actual study.

The study was approved by the institutional review boards of the respective medical centers, and all parents signed informed consent forms.

Measures

Medical assessment. This included pregnancy history data obtained from hospital charts. Parental data included mode of delivery, gestational age, birth weight, parental complications, and psychomotor developmental milestones. The medical evaluation included a general pediatric examination of respiratory, cardiovascular, gastrointestinal, genital-urinary tracts as well as orthopedic and dermatological assessment. A neurological examination evaluated the child's coordination, handedness, symmetry of movement, deep tendon reflexes, cranial nerve function, muscle tone, and muscle strength. Cerebellar function was assessed by observing the gait, posture, and coordination of the children. Physical indices of weight and height were taken.

Wechsler Intelligence Scale for Children–Revised (WISC–R). The standard Hebrew version of the WISC–R was administered (Wechsler, 1976). Scores on all the subscales were examined, and full-scale IQ scores were reported. The full-scale IQ scores ranged from 83 to 142.

It is noteworthy that previous studies and practitioners' observations have suggested that the WISC IQ scores of Israeli children are somewhat high relative to Israeli standardization norms (e.g., Alla, Greenbaum, Wilensky, & Ornoy, 1992; Levy-Shiff et al., 1994), suggesting a problem with the Israeli norms. The problem of high scores relative to the standardization norms has also been reported in other countries (e.g., Michelsson, Lindahl, Parre, & Helenius, 1984). Therefore, in reporting the IQ scores, the focus should be on the comparison of the research and the control groups and not on the comparison with the standardization norms.

Visual Motor Gestalt Test (Bender, 1946). The test, designed to assess visual-motor coordination, was administered and scored according to the system developed by Koppitz (1975): A composite score consisted of the number of errors made in the copying stage (e.g., rotation, integration, perseveration). In the present study the scores ranged from 1 to 9.

Visual Retention Test (Benton, 1963). This instrument, designed to assess visual memory, comprises 10 cards on which one or more geometrical forms are marked. The participant is shown the card for 10 seconds and must then sketch the forms from memory. The score is based on the number of cards correctly recalled and, therefore, possible scores range from 0 to 10. The scores in the present study ranged from 3 to 9.

Reading Comprehension Test (Orthar & Ben Shahar, 1976). This test is designed to assess the level of reading comprehension using booklets adapted to age, school curriculum, and school type (socially integrated/nonintegrated). The booklet used in the study comprises 35 questions regarding various paragraphs and sentences. Each question has four possible answers, only one of which is correct. A composite score was calculated on the basis of the incorrect answers. The range of possible scores is 0–35. The scores in the present study ranged from 6 to 24.

School adjustment. Data were obtained from school teachers via the Rating Scale for School Adjustment (Smilansky & Shephatia, 1976). An initial validity and reliability study was conducted with 388 children in 68 school classes of all grades. Factor analysis of the scale items revealed two main factors: (a) socioemotional adjustment, including discipline, emotional balance, moodiness, likeability, aggression, sociability, leadership, and independence; and (b) learning adjustment, including comprehension, interest, concentration, scholastic ambition, and scholastic self-confidence. Responses for each item were given on a 5-point

rating scale on which each point is assigned a descriptive label (e.g., points for sociability were: 1 = *usually keeps to himself*, 2 = *has trouble creating social ties*, 3 = *active to a certain degree in the company of children*, 4 = *possesses numerous social ties*, and 5 = *always spends time in the company of others*). For middle-school-age children, the authors reported test–retest reliability of .91 for the whole scale (the retest was conducted after 8 weeks). In the present study, scores ranged from 1.98 to 5 for the learning scale and from 1.85 to 4.83 for the socioemotional scale. Cronbach's alpha coefficients were .82 and .89 for the socioemotional and learning adjustment, respectively.

Conners Symptoms Questionnaire (Conners, 1973). This rating scale was designed to assess hyperactive behavior among children (e.g., "shows unpredictable behaviors"). The various behaviors were rated by the teachers on a 4-point scale (0 = *not at all*, 3 = *very much*). In the present study, the scores ranged from 8.00 to 26.00. The Hebrew version was translated by a team of bilingual clinical child psychologists versed in both Hebrew and English. Back translations were used to ensure consistency of meaning with the English original (Bidel, 1988). The Hebrew version questionnaire accurately discriminated, in a theoretically consistent fashion, between clinical and nonclinical populations (e.g., children diagnosed as ADHD) and correlated well ($r = .87$) with observed class behavior in a sample of Israeli elementary school children. Further, a pilot study on a population of 60 elementary school children yielded correlations of $r = .85$ between scores reported by children's mothers and teachers for the summed total score. In a sample of middle-school-age children, test–retest reliability was .89 and internal consistency was .85 (Levy-Shiff et al., 1994). In this study, Cronbach's alpha was .83.

State–Trait Anxiety Inventory for Children (Spielberger, 1973). This self-report questionnaire was designed to assess state and trait anxiety in children. In the present study, only the Trait 20-item questionnaire was employed (e.g.,"I worry too much"; "Deep in my heart, I am afraid"). Children rated their answers on a 3-point scale. A higher anxiety score reflects a higher level of anxiety. The range of possible scores is 1–60, and in this study scores ranged from 22.00 to 52.00. Using the Hebrew version (Tichman & Melnik, 1984) in a sample of school-age children, internal consistency was found to be .84, test–retest reliability was .85, and validity as assessed by correlation with Cattel's questionnaire of anxiety was .76. It was also found to differentiate significantly between children with different patterns of attachment (secure, ambivalent, and avoidant) in a theoretically consistent fashion (Finchy, Har-Even, Wizman, Tiano, & Shnit, 1996). Cronbach's alpha in this study was .86.

Children's Depression Inventory (Kovacs, 1978; Kovacs & Beck, 1977). This self-report questionnaire consists of 27 items that assess depression manifested in four areas: emotional, cognitive, motivational, and physical. Within each item, there is a choice of three statements on a 3-point scale, the child choosing that which best describes himself/herself (e.g., "I am sad sometimes," "I am sad often," "I am sad all the time"), and a higher depression score reflects a higher level of depression. In the present study, scores ranged from 2 to 16. The translation to Hebrew (Bidel, 1988) used the same procedure described previously, and for middle-school-age children, internal consistency was .80, test–retest reliability was .84, and concurrent validity as measured by correlation with a psychiatric interview was .82. The Hebrew questionnaire was found to differentiate significantly between clinical and nonclinical samples of children and to highly correlate with a psychiatric interview based on the *Diagnostic and Statistical Manual of Mental Disorders* (3rd edition, rev.; American Psychiatric Association, 1987; Kronenberg, Blumensohn, & Apter, 1988). In the present study, Cronbach's alpha was .85.

Children's Aggression Inventory (Feshbach, 1966). This self-report 20-item questionnaire was designed to assess aggressive behaviors in children. The answers are given on a two-point scale (true or false) (e.g., "I sometimes get angry," "Sometimes there are good reasons to beat another child," "In comparison to others I bicker a lot"). A higher aggression score reflects a higher level of aggression. In the present study, scores ranged from 1 to 9. The translation to Hebrew (Bidel, 1988) used the same procedure described previously, and for middle-school-age children, internal consistency was found to be .85, test–retest reliability was .87, and concurrent validity as assessed by correlation with teachers' reports of aggression was .78 and with parents' reports was .81. It was found, for example, to differentiate between late-adopted and nonadopted children (Zoran, 1996). In the present study, Cronbach's alpha was .81.

Child's Behavior Inventory (Shepherd, Oppenheim, & Mitchell, 1971). This 32-item questionnaire was designed to assess behavioral disturbances at home as reported by parents. The behavioral difficulties are related to various domains: emotional difficulties (e.g., "behaves in a childish way, younger than his age"), fears (e.g., "afraid of darkness"), somatic complaints (e.g., "has stomach pains"), sleep disturbances (e.g.,

"has nightmares"), and antisocial behavior (e.g., "takes money without permission"). Answers were given on a 4-point scale. A higher behavioral disturbances score reflects more frequent behavioral disturbances. The range of possible scores is 1–4, and in the present study scores ranged from 1.03 to 2.94. The Hebrew adaptation of the questionnaire (Bidel, 1988) used the same translation procedure described previously for the aggression and depression questionnaires. For middle-school-age children, internal consistency was found to be .82, and test–retest reliability .84. The questionnaire was reported to differentiate between clinical and nonclinical samples, such as premature versus full-term school-age children (Einat, 1994). In this study, Cronbach's alpha coefficient for the entire questionnaire was .83.

Results

To examine the differences between children conceived by IVF/ET and children conceived spontaneously on the various measures of medical evaluation and psychological evaluation, we conducted multi variate analyses of variance (MANOVAs) with one factorial (Pregnancy Status: IVF/ET pregnancy or spontaneous pregnancy), followed by invert analyses of variance (ANOVAs) for the continuous measures and chi-square tests for the categorical measures. In addition, we tested effect size as one of the determinants of the power of analysis of variance, using Cohen's (1988) formula. Effect size up to .10 is considered small, up to .25 is considered medium, and up to .45 or more is considered large.

The results regarding the medical evaluation did not reveal any significant difference between the two groups. Yet the MANOVA conducted on all the psychological adjustment measures, including cognitive measures (IQ, visual-motor coordination, visual memory, and language comprehension); school adjustment measures (learning, socioemotional, and hyperactive behavior); emotional adjustment measures (aggression, depression, anxiety); and a measure of behavioral disturbances, indicated a significant main effect for pregnancy status, $F(11, 90) = 2.37$, $p < .05$.

The follow-up ANOVAs indicated that the IVF/ET children, as compared with control group children, showed poorer socioemotional adjustment to school and reported themselves to be more aggressive, more anxious, and more depressed (see Table 2).

The analyses were repeated with demographic variables that were found to differ in the two groups as covariates—parental age and number of siblings. The results of the MANCOVA and the follow-up ANCOVAs were quite similar, and the significant between-group differences remained.

To explore the possibility that various familial variables, namely parental age and number of siblings, as well as child sex, contribute differentially to the adjustment of the IVF/ET children as compared with the spontaneously conceived children, we generated additional linear regression analyses using a two-step hierarchical procedure. In the first step, we entered pregnancy status as a discrete variable as well as child sex, parental age, and number of siblings into the regression equations as main effects; in the second step, the interaction terms of IVF/ET by each of the three variables entered the equations in a stepwise procedure. An F-entry minimum was established for interaction term entry ($p < .01$) to keep the number of variables entered to only those with a meaningful contribution. Where a significant interaction was revealed, regression analyses were carried out separately for the IVF/ET and control

Table 2. *Psychological Outcome Measures in In-Vitro Fertilization/Embro Transfer (IVT/ET) and Spontaneously Conceived Children*

	Pregnancy					
	IVF/ET		Spontaneous			
Measure	*M*	*SD*	*M*	*SD*	*F*(1, 100)	Effect Size
Cognitive						
Full-Scale IQ	123.39	12.94	120.31	10.95	1.16	.13
Visual-Motor Coordination	5.17	2.41	4.90	1.67	0.92	.11
Visual Memory	6.35	2.23	6.84	2.43	0.93	.11
Language Comprehension	12.05	7.42	12.16	6.38	0.65	.08
School Adjustment						
Learning	3.80	0.55	3.81	0.51	0.01	.01
Socioemotional	3.22	0.46	3.96	0.32	4.16*	.24
Hyperactive Behavior	16.35	4.69	15.53	4.68	0.49	.06
Emotional Adjustment						
Aggression	5.49	2.46	4.12	2.01	4.70*	.27
Depression	12.64	7.84	9.52	6.85	4.93*	.28
Anxiety	39.02	6.53	34.40	5.66	5.62**	.33
Behavioral Disturbances at Home	1.96	0.64	1.77	0.50	2.06	.17

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

groups in order to interpret the interaction (Cohen & Cohen, 1984).

The analyses revealed significant interaction effects of Pregnancy Status × Child Sex that added 9% to the explained variance of anxiety ($\beta = .32$, $p < .01$). Child sex had a significant effect on anxiety in the control group but not in the IVF/ET group (βs = .01 and .39, respectively). In the control group, girls were found to be much more anxious than boys but only slightly so in the IVF/ET group, mainly due to the increase of anxiety in the IVF/ET boys. Hence, the IVF/ET boys were much more anxious than the non-IVF/ET boys, whereas IVF/ET girls were only slightly more anxious than non-IVF/ET girls on this measure.

In addition, significant interaction effects of Pregnancy Status × Parental Age added 12% to the explained variance of socioemotional adjustment in school ($\beta = .40$, $p < .001$), 8% to the explained variance of behavioral disturbances at home ($\beta = .31$, $p < .01$). The higher the parental age, the more difficulties the IVF/ET children revealed in school and the more behavioral disturbances at home (βs = –.38 and .34, respectively); no such link was found for the control group children (βs = –.16 and –.06, respectively).

Discussion

Our findings suggest that the children conceived by IVF/ET reproductive techniques did not suffer from significant long-term detrimental sequelae related to physical, neurological, and cognitive development. In the emotional sphere, however, the IVF/ET children were revealed to be at a higher risk for emotional difficulty than controls.

With regard to physical and neurological outcomes, no significant pathological differences were reported; with regard to cognitive development, IVF/ET children's scores fell within normal ranges and did not differ from those of controls on visual-motor coordination, visual memory, reading comprehension, full-scale IQ scores, or on any of the subscales of the Wechsler Intelligence Scale. The latter finding is particularly important, because profile differences within subscales have been found both clinically and empirically to be indicative of learning disabilities (e.g., Breslau, 1992; Kaufman, 1979).

Though not reaching statistical significance, it is noteworthy that the IVF/ET school-age children scored somewhat higher on the IQ test than did control children. This is in accordance with previous results among younger IVF/ET children, who scored somewhat higher on the Mental Developmental Scales (Bayley) during early childhood than did controls (e.g., Morin et al., 1989; Mushin et al., 1986). The higher scores on the Mental Development Index (MDI) were found to be related to such variables as those labeled *wantedness* and *personality dynamics* of the couples selecting IVF/ET over adoption (Mushin et al., 1986). The aforementioned findings, both on the MDI and IQ, may be explained by the quality of parenting among the IVF/ET group, qualified as superior in terms of expression of warmth and extent of parental involvement (Golombok et al., 1995). Yet other studies reported somewhat lower MDI scores of the IVF/ET children as compared with controls (e.g., Brandes et al., 1992). A possible explanation for this conflicting trend is that in these studies, IVF/ET children born prematurely were also included, and prematurity and low birth weight have been linked to more widespread developmental difficulties (Aylward et al., 1989; Hoy, Bill, & Sykes, 1988; McCormick, 1989). This inclusion thus confounds the effect of IVF/ET pregnancy and prematurity on numerous outcome measures.

It is notable that the means of the IQ were relatively high in the IVF/ET group as well as in the control group. We attribute this to the problem of the Israeli standardization of the WISC–R. Similar high scores were revealed in various Israeli studies (e.g., Alla et al., 1992; Levy-Shiff et al., 1994). This emphasizes the need to use a control group and the danger in relying on a comparison of the research group scores with published norms.

In contrast, IVF/ET children, especially boys, were found to be doing more poorly than the spontaneously conceived children in the emotional domain. In school, teachers assigned them lower scores on the socioemotional dimension. Self-reports revealed them to be more anxious, depressed, and aggressive.

The fact that different and independent sources of information indicated that IVF/ET children were at a higher risk for emotional difficulties lends further support to these results. These findings are also consistent with those of Golombok et al. (1990) pointing to a higher incidence of behavioral and emotional problems among IVF/ET preschool children, particularly boys.

It seems possible that the findings in the emotional domain may be related to parenting style. The parents of IVF/ET children have typically struggled for years with infertility, difficult treatments, failures to conceive a child, and they have had to invest considerable efforts into bringing a child to term (Cemeter et al., 1983; Leiblum et al., 1987). The parents are usually older than parents of children conceived spontaneously, and the chances of having more children are low. Understandably, therefore, these children may be seen precious and special, often perceived by their parents to be both physically and psychologically vulnerable (Mahlstedt et al., 1987; Mushin et al., 1985). In consequence, these parents are highly involved (Golombok et al., 1995), yet their parenting style may tend to be more anxious and overprotective and may foster unreal concerns or expectations of their children. When addressing either physical or psychosocial problems, parents may tend to place undue emphasis on the IVF/ET

conception as an explanation of the problem, hampering the family's ability to resolve conflicts (Mushin et al., 1985; Sokoloff, 1987). This parental style may reflect on the child's emotional adjustment. The findings of our study lend some support to these speculations, as the older the parents of the IVF/ET children were, the greater the children's risk for emotional and behavioral difficulties. The speculation that parental style is the explanatory underlying mechanism as well as the possibility that there are other mediating variables should be further investigated.

In summary, controlling for the prematurity factor, our findings suggest that IVF/ET pregnancy has no detrimental long-term effects on children's physical, neurological, and cognitive development. However, IVF/ET children tend to be at a somewhat higher risk for emotional difficulties than those born of spontaneous pregnancies. Among the IVF/ET children, the tendency to be at a higher risk for emotional disturbances is greater among boys and among children of older parents. Moreover, various factors within the family have a differential effect on IVF/ET children and on children spontaneously conceived, again highlighting possible dynamics contributing to the IVF/ET children's potential adjustment vulnerability. These findings should raise the clinician's attention to the IVF/ET–conceived children, whose number is rapidly growing.

Finally, the results of the present study should be qualified. As noted, IVF/ET children born prematurely were excluded. Their inclusion could have altered the results, especially in the medical and cognitive domains. The findings should also be qualified in terms of their generalizability. Across-samples, across-countries, and across-cultures validation is needed.

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Manuscript received July 14, 1997
Final revision received February 2, 1998