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Review:

An overview of studies on psychological well-being in children born following assisted reproductive technologies*

Qi-tao ZHAN, Pei-pei PAN, Xiang-rong XU, Hang-ying LOU, Yi-yun LOU, Fan JIN†‡

(*Department of Reproductive Endocrinology, Women's Hospital, School of Medicine, Zhejiang University, Hangzhou 310006, China*)

†E-mail: jinfan@zju.edu.cn

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Abstract: Over the course of the past 35 years, assisted reproductive technologies (ARTs) have been increasingly used worldwide, while debates on their safety have been generated. Birth defects and imprinting disorders were reported in previous research. Thus, the psychological development of children born following ARTs has become a major concern nowadays. This review gives a systematic view of psychological well-being of children conceived by different types of ART, including in vitro fertilization, intracytoplasmic sperm injection (ICSI), preimplantation genetic diagnosis/screening, and in vitro maturation. The previous studies are analyzed in three sections: (1) cognitive, motor, and language developments, (2) behavior problems and socio-emotional development, and (3) parent-child relationship. We conclude that although the majority of the studies on cognitive, motor, and language developments reported comparable achievements in the ART group vs. the naturally conceived group, lower intelligence quotient (IQ) scores, worse visual-motor ability or locomotor development, and delayed receptive language competence were found in the ART group. The results on the socio-emotional development were reassuring. As for the behavior problems, a higher prevalence of behavior problems existed in ART children; moreover, ICSI children were found to be at a higher risk of autism than the general population. Meanwhile, ART parents tended to have positive parental attitudes and be more protective of their children. Some suggestions for further research are also given in this review.

Key words: Assisted reproductive technologies, Psychological well-being, Behavior problems, Parent-child relationship
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1 Introduction

Worldwide, couples view infertility as "a tragedy which carries social, economic, and psychological consequences" (World Health Organization, 2010). Since the first child conceived by in vitro fertilization (IVF) was born in Britain in 1978 (Steptoe and Edwards, 1978), assisted reproductive technologies (ARTs), which cover IVF, intracytoplasmic sperm injection (ICSI), preimplantation genetic diagnosis/screening (PGD/PGS), in vitro maturation (IVM), and other technologies, have become widely-accepted medical treatments for human infertility.

These interventions are scientifically innovative, and they have revolutionized concepts of generational identity, family, and human reproductive potential. According to the data from the Centers for Disease Control and Prevention of USA, the number of pregnancies obtained by ARTs has been steadily increasing. A total of 61426 ART infants, over 1% of all infants, were born in the United States (Centers for Disease Control and Prevention *et al.*, 2010), but these children were not always accompanied by extensive follow-up programs. Thus, the clarity on potential psychological disorders after ARTs was in need of further evaluation.

ARTs are supposed to be accompanied with an

‡ Corresponding author

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increase in psychological developmental problems for several reasons in our paper. Firstly, early development of the human nervous system is a complex and neatly orchestrated process which can be affected easily by invasive interventions like ARTs (de Graaf-Peters and Hadders-Algra, 2006). Secondly, ARTs carry a significantly increased risk of multiple pregnancies, which are associated with a higher rate of prematurity and low birth weights, and carry increased neonatal intensive care admissions (Schieve *et al.*, 2002; Helmerhorst *et al.*, 2004; Jackson *et al.*, 2004; Fauser *et al.*, 2005; Basatemur and Sutcliffe, 2008; Lu *et al.*, 2013). Thirdly, imprinted disorders, including Beckwith-Wiedemann syndrome, Angelman syndrome and Prader-Willi syndrome, and hyperthyrotropinemia tended to happen more frequently in the ART group than in the natural conception (NC) group (Cox *et al.*, 2002; DeBaun *et al.*, 2003; Gicquel *et al.*, 2003; Maher *et al.*, 2003; Halliday *et al.*, 2004; Chang *et al.*, 2005; Sutcliffe *et al.*, 2006).

Previous reviews focused on subgroups of children, such as only on children born following IVF, or took into account only a part of the psychological development, e.g., neurodevelopment. Therefore, the aim of the present review is to try to give a systematic evaluation of psychological development of ART children. Here, we restricted ourselves to the techniques of IVF, ICSI, PGD/PGS, and IVM as a substantial number of follow-up studies had been reported before in these areas. In order to identify relevant articles, we conducted an extensive search using the databases PsycINFO, PubMed, and Web of Science, with the terms "assisted reproduction OR IVF OR ICSI OR PGD/PGS OR IVM" and "child development OR child psychology OR cognition OR language OR psychomotor OR motor skills OR intelligence OR behavior OR parenting", which were chosen on the basis of preliminary exploratory literature searches and keywords in published studies. Potentially relevant studies were identified and screened based on title and abstract. We searched for articles published between 1995 and Oct. 9, 2012. Excluded from the search results were studies (1) which did not include a naturally conceived control group, (2) in which the follow-up did not figure out the conception type of ART; (3) not published in English. Two authors of this paper assessed titles, abstracts, full articles, and quality of the articles independently. Sample size, age of the children at evaluation, methods used in the assessments, and outcomes were also recorded. The scope of this research is broken down into three sections: (1) cognitive, motor, and language developments, (2) behavior problems and socio-emotional development, and (3) environment for development.

2 Cognitive, motor, language developments

There are 21 reports of early psychological functioning in children born after assisted reproduction (Table 1), 14 of this reported data from ICSI children, 7 from IVF children, and 3 from children born after PGD which was developed for couples at the high risk of having a child with genetic disease.

2.1 Cognitive development

Children must find a way to understand, to remember, to solve problems, and to organize their environment. The method that leads to the maturation of their mental activity constitutes cognitive development. Cognition was assessed in 19 studies, and it was conceptualized most often in terms of the intelligence quotient (IQ), Griffiths quotient, mental or intellectual development, and cognitive competence. Most studies used standardized scales, and some used structured interviews (Table 1).

Through an age-matched study, Knoester *et al*. (2008) observed a slightly but significantly reduced IQ in 5- to 8-year-old children born after ICSI, though the mean IQ was within the normal range. Leunens *et al*. (2006) also found a difference of IQ in 8-year-old ICSI children. However, their results are significantly increased for IQ compared with natural controls.

In contrast, the follow-up study by Leunens *et al.* (2008) revealed that the previously reported difference of cognitive development between children born after ICSI and NC had disappeared when they reached the age of 10 years. The result probably indicates that the effect of the maternal educational level or home environment decreased in the ICSI group over time. Similarly, there was no indication of a lower Griffiths quotient in ART vs. NC children in four papers (Sutcliffe *et al.*, 1999; 2001; 2003; Banerjee *et al.*, 2008) using the Griffiths Scales of Mental Development (Griffiths, 1996; Huntley, 1996). By means of the

Table 1 Outcomes on cognitive, motor, and language developments

Study	Age of children	ART group(s)	Control group	Method	Outcome
Banerjee *et al.*, 2008	4 years	49 PGD	66	Griffiths Scales of Mental Development (0–8 years) (Griffiths, 1996)	Griffiths quotient: A=C; locomotor development: A<C (p=0.0001); hearing language: A>C (p=0.03)
Gibson *et al.*, 1998	1 year	65 IVF	63	Bayley Scales of Infant Development, 2nd edition (BSID II) (Bayley, 1993); Receptive-Expressive Emergent Language Test, 2nd edition (REEL-2) (Bzoch and League, 1991)	Mental & psychomotor development: A=C; competence of receptive language: A<C (p=0.006)
Golombok *et al.*, 1996	4–9 years	116 IVF	120	Pictorial Scale of Perceived Competence & Social Acceptance for Young Children (Harter and Pike, 1984)	Cognitive competence: A=C
Knoester *et al.*, 2008	5–8 years	86 ICSI	85	Revised Amsterdam Child Intelligence Test (RAKIT; short form) (Bleichrodt *et al.*, 1987)	Intelligence quotient (IQ): A<C (p<0.05)
Koivurova *et al.*, 2003	1–3 years	299 IVF	558	Age-Related Psychomotor Developmental Milestones	Psychomotor development: A=C
Leslie *et al.*, 2003	5 years	97 ICSI; 80 IVF	110	Wechsler Preschool and Primary Scales of Intelligence-Revised (WPPSI-R) (Wechsler, 1989)	IQ (full, verbal & performance): A=C
Leunens *et al.*, 2006	8 years	151 ICSI	153	Wechsler Intelligence Scale for Children-Revised (WISC-R) (Wechsler, 1974; van der Steene *et al.*, 1986); Movement Assessment Battery for Children (ABC) (Henderson and Sugden, 1998)	IQ (full, verbal & performance): A>C (p<0.05); motor development: A=C
Leunens *et al.*, 2008	10 years	109 ICSI	90	WISC-R (Wechsler, 1974; van der Steene *et al.*, 1986); Movement ABC (Henderson and Sugden, 1998)	IQ: A=C; balance skill: A>C (p=0.044)
Ludwig *et al.*, 2009a	5.5 years	276 ICSI	273	Zimmer/Volkamer Motor Test (MOT; 4–6 years) (Zimmer and Volkamer, 1987); Kaufman-Assessment Battery for Children (K-ABC) (Kaufman, 2001)	Neuromotor development: A=C; intelligence: A=C
Mu *et al.*, 2006	6–24 months	21 IVM	21	A general physical & neurological examination; BSID II (Bayley, 1993)	Growth: A=C; mental & psychomotor development: A=C
Nekkebroeck *et al.*, 2008a	2 years	70 PGD; 70 ICSI	70	BSID II (Dutch version) (van der Meulen *et al.*, 2002)	Mental & psychomotor development: A=C
Nekkebroeck *et al.*, 2008b	3 years	41 PGD/S; 35 ICSI	53	McArthur Communicative Development Inventories (M-CDI) (Zink and Lejaegere, 2003)	Language development: A=C
Papaligoura *et al.*, 2004	12 months	34 ICSI	29	BSID II (Bayley, 1993)	Mental & psychomotor development: A=C
Place and Englert, 2003	0–5 years	66 ICSI	59	Standardized interviews with mother; Revised Brunet-Lézine Scale (Josse, 1997); WPPSI-R (Wechsler, 1995)	Psychomotor & intellectual development: A=C
Ponjaert-Kristoffersen *et al.*, 2004	5 years	296 ICSI	259	WPPSI-R (Wechsler, 1990; 1999); Peabody Developmental Motor Scales (PDMS) (Folio and Fewell, 2000)	IQ (full, verbal & performance): A=C; motor development: A<C (p<0.05)
Ponjaert-Kristoffersen *et al.*, 2005	6 years	511 ICSI; 424 IVF	488	WPPSI-R (Wechsler, 1990); McCarthy Scales of Children's Abilities Motor Scale (MSCA) (McCarthy, 1972)	IQ (full, verbal & performance): A (IVF & ICSI)=C; motor development: A=C

To be continued

Table 1

Study	Age of children	ART group(s)	Control group	Method	Outcome
Sutcliffe *et al.*, 1999	12–24 months	123 ICSI	123	Griffiths Scales of Mental Development-Revised (UK version) (Huntley, 1996)	Griffiths quotient: A=C; eye-hand coordination: A<C (p<0.05)
Sutcliffe *et al.*, 2001	17 months	208 ICSI	221	Griffiths Scales of Mental Development-Revised (UK version) (Huntley, 1996)	Neurodevelopment: A=C
Sutcliffe *et al.*, 2003	13–15 months	58 ICSI	38	Griffiths Scales of Mental Development-Revised (UK version) (Huntley, 1996)	Neurodevelopment: A=C
Wagenaar *et al.*, 2008a	8–18 years	233 IVF	233	The levels of the Dutch school system; a national test of educational achievement (CITO)	School functioning: A=C
Wagenaar *et al.*, 2009b	9–18 years	139 IVF	143	A national test of educational achievement (CITO); Trailmaking Test (Reitan, 1979); Amsterdam Neuropsychological Tasks (ANT) (de Sonneville, 1999); Beery-Buktenica Test for Visual Motor Integration, Visual Perception & Motor Coordination (Beery, 1989; Beery and Buktenica, 1989)	General cognitive ability: A=C; information processing, attention: A=C; visual-motor function (visual perception, Purdue pegboard, & tapping task): A<C (p<0.05)

A=C, no statistically significant differences between ART group and control group; A>C, higher scores in ART group than in control group; A<C, lower scores in ART group than in control group

Bayley Scales of Infant Development (BSID) (Bayley, 1993; van der Meulen *et al.*, 2002) or the Wechsler Intelligence Scales (WIS) (Wechsler, 1974; 1989; 1990; 1995; van der Steene *et al.*, 1986), neither delayed mental development nor worsening IQ scores between the ART children and the control group were found (Gibson *et al.*, 1998; Leslie *et al.*, 2003; Place and Englert, 2003; Papaligoura *et al.*, 2004; Ponjaert-Kristoffersen *et al.*, 2004; 2005; Mu *et al.*, 2006; Nekkebroeck *et al.*, 2008a). In addition, another four studies (Golombok *et al.*, 1996; Wagenaar *et al.*, 2008a; 2009b; Ludwig *et al.*, 2009a) focusing on cognitive abilities found comparable achievement between the ART and NC groups by using the standardized test.

The conclusion drawn is that there was only one report that presented a lower IQ score in the ART group, and the majority of the investigations showed similar cognitive development between the ART children and the control group. One possible reason for the different findings might be evaluation measurements, that is, the Revised Amsterdam Child Intelligence Test (RAKIT) (Bleichrodt *et al.*, 1987) was used by Knoester *et al.* (2008), while the more widely-used scales such as BSID and WIS were used in other investigations. Sample size might also account for the different results as well. In the research of Knoester *et al.* (2008), the sample size of ICSI children was relatively small, while in the research of Ponjaert-Kristoffersen (2005), which used a well-matched and controlled design, the large sample size of ICSI children might potentially induce more reliable findings.

2.2 Motor development

Two skills, locomotion and handedness, are acquired throughout the motor development process. Locomotion is the ability to navigate the environment, while handedness is the ability to reach and grasp objects (Benjamin *et al.*, 2009). Fourteen studies reported findings on motor development being assessed in terms of locomotor, psychomotor, neuromotor, balance skill, eye-hand coordination, and motor skills, with the help of common inventories, such as the Griffiths Scales of Mental Development (Griffiths, 1996; Huntley, 1996), BSID, and the Movement Assessment Battery for Children (ABC) (Henderson and Sugden, 1998) (Table 1).

On one hand, 10-year-old ICSI children were identified by Leunesns *et al*. (2008) to have higher balance skills than naturally conceived children. On the other hand, lower scores on eye-hand coordination in ICSI children and worsened visual-motor competence in IVF adolescents were observed, although these scores were still within the normal range (Sutcliffe *et al.*, 1999; Wagenaar *et al.*, 2009b). Ponjaert-Kristoffersen *et al.* (2004) additionally presented a trend indicating that ICSI children did worse on motor development than spontaneously conceived children when they were at the age of

5 years, though selection bias, educational level, age of the mother, and cultural differences might account for the differences that were found. With regard to PGD children, worse achievement on locomotor was also found when they were at age of 4 years (Banerjee *et al.*, 2008).

However, four investigations (Gibson *et al.*, 1998; Papaligoura *et al.*, 2004; Mu *et al.*, 2006; Nekkebroeck *et al.*, 2008a) found no differences of psychomotor development between the ART and NC groups by means of BSID. Similarly, Koivurova *et al*. (2003) using the psychomotor developmental milestones and Place and Englert (2003) using the Revised Brunet-Lézine Scale (Josse, 1997) presented no differences between the ART and NC groups for psychomotor development. In another three reports (Ponjaert-Kristoffersen *et al.*, 2005; Leunens *et al.*, 2006; Ludwig *et al.*, 2009a) on motor development of ICSI children, there were also no worsening performances.

In summary, worse visual-motor competence or delayed locomotor development was observed in the ART group, although more than half of the studies showed that motor development in the assisted group was similar to that in the natural group. The worse performance at early ages, but not at adolescence, might be induced by the higher rating of premature and lower birth weight in the ART group. Selection bias like educational level, age of the mother, and cultural differences might also partially account for the differences.

2.3 Language development

Language refers to the ability to communicate as well as the capacity to use symbolic thought in the speech process, that is, to produce sounds and words. There have only been three investigations of the language development in the children born after ART (Table 1).

The study of Gibson (1998) presented lower scores on receptive language skills in IVF infants. However, Banerjee *et al.* (2008) reported higher hearing language development in children born following PGD.

Another investigation (Nekkebroeck *et al.*, 2008b) found no differences between the two ART groups (PGD and ICSI) and the spontaneously control group, and both the ART groups were within the normal range.

We can conclude that previous studies presented no worse performance on language development in the ART group as compared to the NC group, except for worse receptive language competence in IVF infants. Conception after embryo biopsy in the case of PGD and PGS had no adverse impact on language development compared with the natural control group.

In general, lower IQ scores in the ICSI group were reported in one study, but fortunately, the majority of studies reported comparable achievement on cognitive development in the ART group vs. the NC group. Meanwhile, worse visual-motor competence or locomotor development was reported in the ART children, and delayed receptive language competence was found only in IVF infants. The higher rating of premature and lower birth weight in the ART group might accout for the worse performance, and the higher educational level and decent home environment might contribute to the better achievement. Based on the results in Table 1, studies on motor and language developments only followed the children up to middle childhood, and long-term follow-up research is still in need as disorders may become more obvious after middle childhood.

3 Socio-emotional development and behavior problems

There are 15 reports in children born after assisted reproduction in this section, 12 of these reports concerning IVF children, 5 concerning ICSI children, and 1 concerning PGD (Table 2).

3.1 Socio-emotional development

Once children have formed a sense of self, they can think about and interpret their experiences in other situations. That is the process of social development. Nine studies aimed to provide insight into the socio-emotional development of ART children compared with the spontaneously conceived control group (Table 2).

There was only one report (Golombok *et al.*, 2009) that found lower self-esteem in adolescents born following IVF than in the control group. And the difference of self-esteem was not from a general tendency in IVF adolescents, as the result was not significant when excluding two outliers.

Table 2 Outcomes on socio-emotional development and behavior problems

Study	Age of children	ART group(s)	Control group	Method	Outcome
Barnes *et al.*, 2004	5 years	514 ICSI; 424 IVF	488	Difficult Child Subscale (DC) (Abidin, 1990); Child Behavior Checklist (CBCL/4–18) (Achenbach, 1991a)	DC & CBCL: A (ICSI=IVF)=C
Colpin and Bossaert, 2008	15–16 years	24 IVF	21	CBCL/4–18 (Achenbach, 1991a); Youth Self-Report (YSR/11–18) (Achenbach, 1991b)	CBCL: A=C; psychosocial adjustment: A=C
Colpin and Soenen, 2002	8–9 years	27 IVF	23	CBCL/4–18 (Achenbach, 1991a); Teacher's Report Form (TRF) (Achenbach, 1991b)	CBCL: A=C; total problem behavior from teachers: A>C (p=0.06)
Gibson *et al.*, 1998	1 year	65 IVF	63	Vineland Adaptive Behavior Scales (Sparrow *et al.*, 1984); Bayley Behavior Rating Scale (BRS) (Bayley, 1993); Behavior Checklist (BCL) (Richman *et al.*, 1982)	Social development: A=C; test-taking behavior: A=C; behavior problems: A>C (p=0.005)
Golombok *et al.*, 1995	4–8 years	41 IVF	43	A standardized interview with the mother (Graham and Rutter, 1968)	Social and emotional adjustment: A=C
Golombok *et al.*, 1996	4–9 years	116 IVF	120	Rutter "A" Scale & "B" Scale (Rutter *et al.*, 1970; 1975; Goodman, 1994); Pictorial Scale of Perceived Competence and Social Acceptance for Young Children (Harter and Pike, 1984)	Socio-emotional development: A=C
Golombok *et al.*, 2001	12 years	34 IVF	38	A standardized interview with the mother; Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1994; 1997); Social Adjustment Inventory for Children and Adolescents (SAICA) (John *et al.*, 1987)	School functioning: A=C; social and emotional adjustment: A=C
Golombok *et al.*, 2002	11–12 years	102 IVF	102	Child and Adolescent Functioning and Environment Schedule (CAFÉ) (John and Quinton, 1991); SDQ (Goodman, 1994; 1997); SAICA (John *et al.*, 1987)	School functioning: A=C; social and emotional adjustment: A=C; physical aggression: A<C (p<0.05)
Golombok *et al.*, 2009	18 years	26 IVF	56	CAFÉ (John and Quinton, 1991); Inventory of Peer and Parent Attachment (IPPA) (Armsden and Greenberg, 1987); Symptoms Checklist-90-Revised (SCL-90-R) (Derogatis, 1994); Self Perception Profile for College Students (Neemann and Harter, 1986)	Peer relationships: A=C; psychological problems: A=C; physical aggression: A>C (p<0.05); suspended or expelled from school: A>C (p<0.05); self-esteem: A<C (p<0.01)
Knoester *et al.*, 2007	5–8 years	87 ICSI; 92 IVF	85	CBCL/4–18 (Achenbach, 1991a)	Behavior disorders: ICSI=C; ICSI=IVF; autism: ICSI>general population
Ludwig *et al.*, 2009a	5.5 years	276 ICSI	273	Kaufman-Assessment Battery for Children (K-ABC) (Kaufman, 2001)	Emotional & behavioral development: A=C
Nekkebroeck *et al.*, 2008b	2 years	41 PGD/S; 35 ICSI	53	CBCL (Achenbach and Rescorla, 2000)	CBCL total problem & external problem: A<C (p<0.05)
Ponjaert-Kristoffersen *et al.*, 2004	5 years	296 ICSI	259	CBCL (Achenbach and Edelbrock, 1983; Verhulst *et al.*, 1996); DC (Abidin, 1990)	CBCL total problem & external problem: A<C (p<0.05); DC: A<C (p<0.05)
Wagenaar *et al.*, 2009a	9–18 years	139 IVF	143	CBCL, TRF (Achenbach and Rescorla, 2001)	CBCL external and syndrome scale (thought problems & aggressive behavior): A<C (p<0.05); TRF: A=C
Wagenaar *et al.*, 2011	11–18 years	86 IVF	97	YSR (Achenbach and Rescorla, 2001)	Behavior problems & socio-emotional development: A=C

A=C, no statistically significant differences between ART group and control group; A>C, higher scores in ART group than in control group; A<C, lower scores in ART group than in control group

The socio-emotional development was also assessed in terms of psychosocial adjustment and peer relationship in the other eight studies. All of the eight studies were in line with each other, in which the authors reported no differences between the groups.

Taken together, the results were reassuring, that is, there were no significant differences between the ART children and control children regarding their socio-emotioanl development.

3.2 Behavior problems

Behavior problems mainly include the internal and the external aspects. Problems such as withdrawn, somatic complaints, and anxious or depressed states comprise the internalizing aspect, and behaviors like rule breaking and aggression belong to the externalizing aspect. Thirteen studies reported on behavioral problems (Table 2).

On one hand, a lower prevalence of behavioral problems, especially external problems, in the ART-conceived children were reported (Golombok *et al.*, 2002; Nekkebroeck *et al.*, 2008b; Wagenaar *et al.*, 2009a) according to Child Behavior Checklist (CBCL) (Achenbach and Rescorla, 2000; Achenbach and Rescorla, 2001) or Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1994; 1997). Ponjaert-Kristoffersen *et al.* (2004) found similar results indicating less problematic behavior in the ICSI group. However, variables such as cultural differences and selection bias were not excluded in the study.

On the other hand, Gibson *et al.* (1998) indicated that IVF mothers tended to report more children's behavioral problems. The follow-up research performed by Golombok *et al.* (2009) also revealed higher incidences of physical aggression and higher rates of being suspended or expelled from school in IVF adolescents than in the matched control group, which did not occur when they were teenagers (Golombok *et al.*, 2002). For further analysis of this research, the above described change in adolescence largely resulted from the behavior of two outliers rather than from the general performance of the IVF adolescents (Golombok *et al.*, 2009). In Colpin and Soenen (2002)'s research, marginally significant behavior problems were reported according to the Teacher's Report Form (TRF) (Achenbach, 1991b) in IVF children vs. the control group. However, according to the CBCL, the scores were similar in the two groups. It was interesting to consider why teachers' ratings tended to show slight differences from parents' ratings. First, social desirability might prevent IVF parents from observing or reporting disorders; second, it was possible that the IVF children had problems that manifested at school, but not at home. In addition, Knoester *et al.* (2007) reported a higher prevalence of autism in ICSI-conceived children vs. the general population (3.4% vs. the general population ±0.3%) (Williams *et al*., 2006).

On the contrary, Barnes *et al.* (2004), Colpin and Bossaert (2008), and Wagenaar *et al.* (2011) found no differences in self- or parent-reported behavioral problems between the ART children and NC children according to the CBCL or Youth Self-Report (YSR/11–18) (Achenbach, 1991b). Meanwhile, neither Golombok *et al*. (2001) nor Ludwig *et al*. (2009a) reported any higher prevalence of behavioral problems in the ART children.

In summary, there were two studies that reported more behavioral problems in the ART group than in the control group, and the majority of those studies found that the ART children perform similarly or were even less likely to be physically aggressive than the NC children. Additionally, a higher prevalence of autism in ICSI children was found, which warrants more research of high methodological quality and long-term follow-up.

Overall, ART children were functioning well and did not differ from the NC children on the measures of socio-emotional development. Two studies found a higher prevalence of behavioral problems in ART children, but fortunately, most of the studies did not report more behavioral problems in the ART group vs. the control group. Meanwhile, ICSI children were reported to be at a higher risk of autism than the general population. Since the birth of the first ICSI child in 1992, children born after ICSI have just reached their adulthood. Follow-up research of ICSI-conceived children, consequently, becomes an urgent need.

4 Environment for development

The home environment of ART families was assessed in 14 studies in terms of parent-child interaction, parent-child relationship, parenting style, and attachment. Eleven of these studies provided data on IVF families, 3 on ICSI families, and 1 on a PGD family (Table 3).

Table 3 Outcomes on environment for development

Study	Age of children	ART group(s)	Control group	Method	Outcome
Banerjee *et al.*, 2008	4 years	49 PGD	66	Parental Acceptance Rejection Questionnaire (Rohner and Khaleque, 2005)	Warmth-affection to child: A>C (p=0.042); aggression-hostility and rejection: A<C (p=0.03)
Barnes *et al.*, 2004	5 years	514 ICSI	488	Parent-Child Dysfunctional Interaction Subscale (P-CDI) (Abidin, 1990); Parental Acceptance-Rejection Questionnaire (PARQ) (Rohner, 1999)	Difficulties in the relationship: A=C; mother's negative feeling to child: A<C (p=0.0001); father's response: A=C
Colpin *et al.*, 1995	24–30 months	31 IVF	31	Rating Scales for Structured Tasks (Erickson *et al.*, 1985); Questionnaire for Parental Attitudes and Emotions (Engfer and Schneewind, 1976)	Parent-child relationship: A=C
Colpin and Bossaert, 2008	15–16 years	24 IVF	21	Louvain Adolescent Perceived Parenting Scale (LAPPS) (Soenens *et al.*, 2004)	Parenting style: A=C
Colpin and Soenen, 2002	8–9 years	27 IVF	23	Nijmegen Child-Rearing Questionnaire-adapted version (NCRQ) (Gerris *et al.*, 1996); Questionnaire Parenting Goals (QPG) (Gerris *et al.*, 1993)	Parenting goal of adjustment: A>C (p=0.03)
Knoester *et al.*, 2007	5–8 years	87 ICSI; 92 IVF	85	Dutch Children TON AZL Quality of Life questionnaire (Dux 25); TNO AZL Child Quality of Life questionnaire (TACQoL) (Theunissen *et al.*, 1998; Vogels *et al.*, 1998; Verrips *et al.*, 1999)	Quality of life: A=C
Gibson *et al.*, 2000	1 year	65 IVF	61	Strange Situation procedure (SS) (Ainsworth *et al.*, 1978); Emotional Availability Scales (Biringen *et al.*, 1993)	Attachment: A=C; mother-child interaction: A=C
Golombok *et al.*, 1995	4–8 years	41 IVF	43	A standardized interview with the mother (Graham and Rutter, 1968); questionnaire for parents	Mother's warmth to child & emotional involvement: A>C (p<0.01); parent-child interaction: A>C (p<0.05)
Golombok *et al.*, 1996	4–9 years	116 IVF	120	A standardized interview with the mother (Quinton and Rutter, 1988); Family Relations Test (Bene and Anthony, 1985)	Mother's warmth & emotional involvement: A>C (p<0.01); father-child interaction: A>C (p<0.01); quality of family relationship & parenting: A=C
Golombok *et al.*, 2001	12 years	34 IVF	38	A standardized interview with parents; Child and Adolescent Functioning and Environment Schedule (CAFÉ) (John and Quinton, 1991); Expression of Affection Inventory (EAI) (Hetherington, 1992); Conflict Tactics Scale (CTS) (Straus, 1979)	Warmth: A>C (p<0.05)
Golombok *et al.*, 2002	11–12 years	102 IVF	102	A standardized interview with parents; CAFÉ (John and Quinton, 1991); EAI (Hetherington, 1992); CTS (Straus, 1980)	Warmth: A>C (p<0.01); criticism & discipline: A<C (p<0.05)
Golombok *et al.*, 2009	18 years	26 IVF	56	CAFÉ (John and Quinton, 1991); Inventory of Peer and Parent Attachment (IPPA) (Armsden and Greenberg, 1987)	Warmth & control: A=C
Owen and Golombok, 2009	18 years	26 IVF	63	A standardized interview; parent-adolescent warmth scale	Mother's warmth: A>C (p<0.05); mother's control & discipline: A<C (p<0.05); father's response: A=C
Ponjaert-Kristoffersen *et al.*, 2004	5 years	296 ICSI	259	P-CDI (Abidin, 1990)	Parent-child dysfunctional interaction: A<C (p<0.05)

A=C, no statistically significant differences between ART group and control group; A>C, perform significantly better or more in ART group than in control group; A<C, perform significantly worse or less in ART group than in control group

In the research of Banerjee *et al.* (2008) and Golombok *et al.* (2001; 2002), ART parents showed more positive feeling (i.e., warmth and affection to children) and less negative feeling (i.e., aggression and hostility to children) than naturally conceived children's parents. It was notable that these feelings were especially true for mothers (Golombok *et al.*, 1995; 1996; Barnes *et al.*, 2004; Owen and Golombok, 2009). Moreover, a lower rating of discipline in IVF parents vs. NC parents was reported (Golombok *et al.*, 2002; Owen and Golombok, 2009). Nevertheless, ART parents expected their children, more than naturally conceived children's parents, to adjust to their own and others' expectations (Colpin and Soenen, 2002). As for the parent-child interaction, more healthy interactions in IVF families and less dysfunctional interactions in ICSI families were indicated vs. their control group (Golombok *et al.*, 1995; 1996; Ponjaert-Kristoffersen *et al.*, 2004).

In contrast, neither Gibson *et al.* (2000) nor Golombok *et al.* (2009) reported that warmth to child or attachment in IVF families differed from that in NC families. Quality of life, parent-child relationship, or parenting style of the ART families was also similar to that of NC families. The explanation for the absence of differences might be that, nowadays, for some couples, NC is also as heavily planned as assisted conception; meanwhile, ART has become a widely used and accepted reproduction technique.

In brief, the parent-child relationship serves as the first context for the developments of cognition, language, social, and moral values. The vast majority of the data above suggested that ART parents, especially ART mothers, showed positive parental attitudes and more protection to their children throughout their development. Duncan and Edwards (1999) also identified that ICSI mothers, but not fathers, were more committed to being a parent than the naturally conceived children's mothers, which, to a certain extent, explained the mothers' performances. In addition, reviews of issues on psychological impact of ART suggested that firstly the inability to conceive children was experienced as a stressful situation by individuals and couples, and secondly, parents who conceived using ART experienced additional stress and anxiety during the assisted conception procedure (Cousineau and Domar, 2007; Basatemur and Sutcliffe, 2008). Either of them might affect adaptation to the parental role, influence how parents view their children, and then affect the child-parent relationship and child development.

5 Conclusions

First of all, although the majority of the studies on cognitive, motor, and language developments reported comparable achievement in the ART group vs. the NC group, different performances between the two groups also existed. Lower IQ scores in the ICSI group were reported in one study, and worse visual-motor ability or locomotor development and delayed receptive language competence were found in the ART group as well.

Then, the results on socio-emotional development were reassuring. With regard to behavioral problems, two studies found a higher prevalence of behavioral problems in ART children; moreover, ICSI children were found to be at a higher risk of autism than the general population.

Finally, the vast majority of the data on home environment suggest that ART parents, especially ART mothers, show positive parental attitudes and more protection of their children throughout their development.

6 Suggestions in further researches

Previous reviews stated that potential problems of ART children perhaps emerged during adolescence, and therefore, continuing follow-up is undoubtedly recommended to make sure that ART children continue to do well (Basatemur and Sutcliffe, 2008; Izat and Goldbeck, 2008; Middelburg *et al.*, 2008; Wagenaar *et al.*, 2008b). Some studies have been conducted to estimate the psychological well-being of IVF children who were close to their 18th birthday (Wagenaar *et al.*, 2008a; 2009a; 2009b; Golombok *et al.*, 2009; Owen and Golombok, 2009), but, till now, few have focused on adolescent born following other technologies, such as ICSI, PGD/PGS, or IVM. Besides, the higher risk of autism reported in ICSI children calls for more research and long-term follow-up.

It was estimated that the blinded examiners in ART studies could intuit the mode of conception in

three out of four children. So, children would be better to be accompanied by only one family member and the examiners should not be permitted to request information about siblings, which are suggestions in future research to reduce the bias (Ludwig *et al.*, 2009b).

Compliance with ethics guidelines

Qi-tao ZHAN, Pei-pei PAN, Xiang-rong XU, Hang-ying LOU, Yi-yun LOU, and Fan JIN declare that they have no conflict of interest.

This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Abidin, R., 1990. Parenting Stress Index Test Manual. Pediatric Psychology Press, Charlottesville, Virginia.

Achenbach, T.M., 1991a. Manual for the Child Behavior Checklist/4–18 and 1991 Profiles. Department of Psychiatry, University of Vermont, Burlington, Vermont.

Achenbach, T.M., 1991b. Manual for the Youth Self-Report and 1991 Profiles. Department of Psychiatry, University of Vermont, Burlington, Vermont.

Achenbach, T.M., Edelbrock, C., 1983. Manual for the Child Behavior Checklist and Revised Child Behavior Profile. Department of Psychiatry, University of Vermont, Burlington, Vermont.

Achenbach, T.M., Rescorla, L.A., 2000. Manual for ASEBA Preschool Forms & Profiles. Research Center for Children, Youth, & Families, University of Vermont, Burlington, Vermont.

Achenbach, T.M., Rescorla, L.A., 2001. Manual of the ASEBA School-Age Forms & Profiles. Research Center for Children, Youth & Families, University of Vermont, Burlington, Vermont.

Ainsworth, M., Blehar, M.C., Waters, E.C., Wall, S., 1978. The Strange Situation. Lawrence Erlbaum, Oxford, England.

Armsden, G.C., Greenberg, M.T., 1987. The inventory of peer and parent attachment: individual differences and their relationship to psychological well-being in adolescence. *J. Youth Adolesc.*, **16**(5):427-454. [doi:10.1007/BF02202939]

Banerjee, I., Shevlin, M., Taranissi, M., Thornhill, A., Abdalla, H., Ozturk, O., Barnes, J., Sutcliffe, A., 2008. Health of children conceived after preimplantation genetic diagnosis: a preliminary outcome study. *Reprod. Biomed. Online*, **16**(3):376-381. [doi:10.1016/S1472-6483(10)60599-8]

Barnes, J., Sutcliffe, A.G., Kristoffersen, I., Loft, A., Wennerholm, U., Tarlatzis, B.C., Kantaris, X., Nekkebroeck, J., Hagberg, B.S., Madsen, S.V., *et al.*, 2004. The influence of assisted reproduction on family functioning and children's socio-emotional development: results from a European study. *Hum. Reprod.*, **19**(6):1480-1487. [doi:10.1093/humrep/deh239]

Basatemur, E., Sutcliffe, A., 2008. Follow-up of children born after ART. *Placenta*, **29**:S135-S140. [doi:10.1016/j.placenta.2008.08.013]

Bayley, N., 1993. Bayley Scales of Infant Development, 2nd Ed. Harcourt Brace and Company, San Antonio, p.374.

Beery, K.E., 1989. Developmental Tests of Visual-Motor Integration with Supplemented Developmental Test of Visual Perception and Motor Coordination. Modern Curriculum Press, Cleveland, Ohio.

Beery, K.E., Buktenica, N.A., 1989. The VMI Developmental Test of Visual-Motor Integration. Modern Curriculum Press, Cleveland, Ohio.

Bene, E., Anthony, J., 1985. Manual for the Family Relations Test. NFER-Nelson, Windsor, UK.

Benjamin, J.S., Virginia, A.S., Pedro, R., 2009. Normal Child Development. Lippincott Williams & Wilkins, Philadelphia.

Biringen, Z., Robinson, J., Emde, R.N., 1993. Emotional Availability Scales, 2nd Ed. Department of Human Development and Family Studies, Colorado State University, Fort Collins.

Bleichrodt, N., Resing, W.C.M., Drenth, P.J.D., Zaal, J.N., 1987. Intelligentie-Meting Bij Kinderen: Empirische en Methodologische Verantwoording van de GeReviseerde Amsterdamse Kinder Intelligentie Test. Swets & Zeitlinger, Lisse, the Netherlands (in Dutch).

Bzoch, K.R., League, R., 1991. Receptive-Expressive Emergent Language Test, 2nd Ed. Examiner's Manual. PRO-ED, Austin, p.48.

Centers for Disease Control and Prevention, American Society for Reproductive Medicine, Society for Assisted Reproductive Technology, 2010. 2008 Assisted Reproductive Technology Success Rates: National Summary and Fertility Clinic Reports. Department of Health and Human Services, Atlanta.

Chang, A.S., Moley, K.H., Wangler, M., Feinberg, A.P., DeBaun, M.R., 2005. Association between Beckwith-Wiedemann syndrome and assisted reproductive technology: a case series of 19 patients. *Fertil. Steril.*, **83**(2):349-354. [doi:10.1016/j.fertnstert.2004.07.964]

Colpin, H., Soenen, S., 2002. Parenting and psychosocial development of IVF-children. A follow-up study. *Hum. Reprod.*, **17**(4):1116-1123. [doi:10.1093/humrep/17.4.1116]

Colpin, H., Bossaert, G., 2008. Adolescents conceived by IVF: parenting and psychosocial adjustment. *Hum. Reprod.*, **23**(12):2724-2730. [doi:10.1093/humrep/den297]

Colpin, H., Demyttenaere, K., Vandemeulebroecke, L., 1995. New reproductive technology and the family. The parent-child relationship following in vitro fertilization. *J. Child Psychol. Psyc.*, **36**(8):1429-1441. [doi:10.1111/j.1469-7610.1995.tb01673.x]

Cousineau, T.M., Domar, A.D., 2007. Psychological impact of infertility. *Best Pract. Res. Clin. Obstet. Gynaecol.*, **21**(2):293-308. [doi:10.1016/j.bpobgyn.2006.12.003]

Cox, G.F., Bürger, J., Lip, V., Mau, U.A., Sperling, K., Wu, B.L., Horsthemke, B., 2002. Intracytoplasmic sperm injection may increase the risk of imprinting defects. *Am. Soc. Hum. Genet.*, **71**(1):162-164. [doi:10.1086/341096]

DeBaun, M.R., Niemitz, L., Feinberg, A.P., 2003. Association of in vitro fertilization with Beckwith-Wiedemann Syndrome and epigenetic alterations of LIT1 and H19. *Am. J. Hum. Genet.*, **72**(1):156-160. [doi:10.1086/346031]

de Graaf-Peters, V.B., Hadders-Algra, M., 2006. Ontogeny of the human central nervous system: what is happening when? *Early Hum. Dev.*, **82**(4):257-266. [doi:10.1016/j.earlhumdev.2005.10.013]

de Sonneville, L.M.J., 1999. Amsterdam Neuropsychological Tasks: A Computer-Aided Assessment Program. *In*: DenBrinker, B.P.L.M., Beek, P.J., Brand, A.N., Maarse, F.J., Mulder, L.J.M. (Eds.), Cognitive Ergonomics, Clinical Assessment and Computer-Assisted Learning: Computers in Psychology. Swets & Zeitlinger, Lisse, the Netherlands, p.187-203.

Derogatis, L.R., 1994. SCL-90-R Symptoms Check List: Administration, Scoring and Procedures Manual. National Computoer Systems, Minneapolis, Minnesota.

Duncan, S., Edwards, D., 1999. Lone Mothers, Paid Work and Gendered Moral Rationalities. Palgrave Macmillan Publishers Ltd., Basingstoke, UK. [doi:10.1057/9780230509689]

Engfer, A., Schneewind, K.A., 1976. Ein Fragebogen Selbstperzipiertes Elterlichen Erziehungseinstellungen. Trier University, Trier, Germany (in German).

Erickson, M., Sroufe, L.A., Egeland, B., 1985. The Relationship Between Quality of Attachment and Behavior Problems in Preschool in a High Risk Sample. University of Chicago Press, Chicago.

Fauser, B.C., Devroey, P., Macklon, N.S., 2005. Multiple birth resulting from ovarian stimulation for subfertility treatment. *Lancet*, **365**(9473):1807-1816. [doi:10.1016/S0140-6736(05)66478-1]

Folio, M.R., Fewell, R.R., 2000. Peabody Developmental Motor Scales, 2nd Ed. PRO-ED, Austin, Texas.

Gerris, J.R.M., Vermulst, A.A., Boxtel, D.A.A.M., van Janssens, J.M.A.M., van Zutphen, R.A.H., Felling, A.J.A., 1993. Parenting in Dutch Families: A Representative Description of Dutch Family Life in Terms of Validated Concepts Representing Characteristics of Parents, Children, the Family as a System and Parental Socio-cultural Value Orientations. Institute of Family Studies, University of Nijmegen, Nijmegen, the Netherlands.

Gerris, L.A.W., Dekovic, M., Groenendaal, J.H.A., Noom, M.J., 1996. Parenting Behavior. *In*: Rispens, J., Hermanns, J.M.A., Meeus, W.H.J. (Eds.), Childrearing in the Netherlands. van Gorcum, Assen, p.41-69.

Gibson, F.L., Ungerer, J.A., Leslie, G.I., Saunders, D.M., Tennant, C.C., 1998. Development, behaviour and temperament: a prospective study of infants conceived through in-vitro fertilization. *Hum. Reprod.*, **13**(6):1727-1732. [doi:10.1093/humrep/13.6.1727]

Gibson, F.L., Ungerer, J.A., McMahon, C.A., Leslie, G.I., Saunders, D.M., 2000. The mother-child relationship following in vitro fertilisation (IVF): infant attachment, responsivity, and maternal sensitivity. *J. Child Psychol. Psychiatry*, **41**(8):1015-1023. [doi:10.1111/1469-7610.00689]

Gicquel, C., Gaston, V., Mandelbaum, J., Siffroi, J.P., Flahault, A., le Bouc, Y., 2003. In vitro fertilisation may increase the risk of Beckwith-Wiedemann syndrome related to the abnormal imprinting of the *KCNQ1OT* gene. *Am. J. Hum. Genet.*, **72**(5):1338-1341. [doi:10.1086/374824]

Golombok, S., Cook, R., Bish, A., Murray, C., 1995. Families created by the new reproductive technologies: quality of parenting and social and emotional development of the children. *Child Dev.*, **66**(2):285-298. [doi:10.2307/1131578]

Golombok, S., Brewaeys, A., Cook, R., Giavazzi, M.T., Guerra, D., Mantovani, A., van Hall, E., Crosignani, P.G., Dexeus, S., 1996. The European study of assisted reproduction families: family functioning and child development. *Hum. Reprod.*, **11**(10):2324-2331. [doi:10.1093/oxfordjournals.humrep.a019098]

Golombok, S., MacCallum, F., Goodman, E., 2001. The "test-tube" generation: parent-child relationships and the psychological well-being of in vitro fertilization children at adolescence. *Child Dev.*, **72**(2):599-608. [doi:10.1111/1467-8624.00299]

Golombok, S., Brewaeys, A., Giavazzi, M.T., Guerra, D., MacCallum, F., Rust, J., 2002. The European study of assisted reproduction families: the transition to adolescence. *Hum. Reprod.*, **17**(3):830-840. [doi:10.1093/humrep/17.3.830]

Golombok, S., Owen, L., Blake, L., Murray, C., Jadva, V., 2009. Parent-child relationships and the psychological well-being of 18-year-old adolescents conceived by in vitro fertilisation. *Hum. Fertil.*, **12**(2):63-72. [doi:10.1080/14647270902725513]

Goodman, R., 1994. A modified version of the Rutter Parent Questionnaire including extra items on children's 608 child development strengths: a research note. *J. Child Psychol. Psychiatry*, **35**(8):1483-1494. [doi:10.1111/j.1469-7610.1994.tb01289.x]

Goodman, R., 1997. The Strengths and Difficulties Questionnaire: a research note. *J. Child Psychol. Psychiatry*, **38**(5):581-586. [doi:10.1111/j.1469-7610.1997.tb01545.x]

Graham, P., Rutter, M., 1968. The reliability and validity of the psychiatric assessment of the child: II. Interview with the parent. *Br. J. Psychiatry*, **114**(510):581-592. [doi:10.1192/bjp.114.510.581]

Griffiths, R., 1996. The Griffiths Mental Development Scales 1996. Association for Research in Infant and Child Development, the Test Agency, UK.

Halliday, J., Oke, K., Breheny, S., Algar, E., Amor, D.J., 2004. Beckwith-Wiedemann syndrome and IVF: a case-control study. *Am. J. Hum. Genet.*, **75**(3):526-528. [doi:10.1086/423902]

Harter, S., Pike, R., 1984. The pictorial scale of perceived competence and social acceptance for young children. *Child Dev.*, **55**(6):1969-1982. [doi:10.2307/1129772]

Helmerhorst, F.M., Perquin, D.A.M., Donker, D., Keirse, M.J.N.C., 2004. Perinatal outcome of singletons and twins after assisted conception: a systematic review of controlled studies. *BMJ*, **328**(7434):261-265. [doi:10.1136/bmj.37957.560278.EE]

Henderson, S.E., Sugden, D.A., 1998. Movement Assessment Battery for Children. Handleiding. Swets & Zeitlinger B.V., Lisse, the Netherlands.

Hetherington, E.M., 1992. Coping with marital transitions: a family system perspective. *Monogr. Soc. Res. Child Dev.*, **57**(2-3):1-14. [doi:10.1111/j.1540-5834.1992.tb00300.x]

Huntley, M., 1996. The Griffiths Mental Development Scales. 1996 Revision, the Test Agency, Henley, UK.

Izat, Y., Goldbeck, L., 2008. The development of children from assisted reproduction—a review of the literature. *Prax. Kinderpsychol. Kinderpsychiatr.*, **57**(4):264-281 (in German).

Jackson, R.A., Gibson, K.A., Wu, Y.W., Croughan, M.S., 2004. Perinatal outcomes in singletons following in vitro fertilization: a meta-analysis. *Obstet. Gynecol.*, **103**(3):551-563. [doi:10.1097/01.AOG.0000114989.84822.51]

John, K., Quinton, D., 1991. Child and Adolescent Functioning and Environment Schedule (Revised). MRC Child Psychiatry Unit, London.

John, K., Gammon, G.D., Prusoff, B.A., Warner, V., 1987. The Social Adjustment Inventory for Children and Adolescents (SAICA): testing of a new semistructured interview. *J. Am. Acad. Child Adolesc. Psychiatry*, **26**(6):898-911. [doi:10.1097/00004583-198726060-00015]

Josse, D., 1997. Brunet-Lézine Révisé: Echelle de Developpement Psychomoteur de la Première Enfance. Issy-Les-Moulineaux, EAP, France (in French).

Kaufman, A.S., 2001. Kaufman Assessment Battery for Children, Deutsche Version. Leiden University, Leiden.

Knoester, M., Helmerhorst, F.M., van der Westerlaken, L.A.J., Walther, F.J., Veen, S., 2007. Matched follow-up study of 5–8-year-old-ICSI singletons: child behaviour, parenting stress and child (health-related) quality of life. *Hum. Reprod.*, **22**(12):3098-3107. [doi:10.1093/humrep/dem261]

Knoester, M., Helmerhorst, F.M., Vandenbroucke, J.P., van der Westerlaken, L.A.J., Walther, F.J., Veen, S., 2008. Cognitive development of singletons born after intracytoplasmic sperm injection compared with in vitro fertilization and natural conception. *Fertil. Steril.*, **90**(2):289-296. [doi:10.1016/j.fertnstert.2007.06.090]

Koivurova, S., Hartikainen, A., Sovio, U., Gissler, M., Hemminki, E., Järvelin, M.R., 2003. Growth, psychomotor development and morbidity up to 3 years of age in children born after IVF. *Hum. Reprod.*, **18**(11):2328-2336. [doi:10.1093/humrep/deg445]

Leslie, G.I., Gibson, F.L., McMahon, C., Cohen, J., Saunders, D.M., Tennant, C., 2003. Children conceived using ICSI do not have an increased risk of delayed mental development at 5 years of age. *Hum. Reprod.*, **18**(10):2067-2072. [doi:10.1093/humrep/deg408]

Leunens, L., Celestin-Westreich, S., Bonduelle, M., Liebaers, I., Ponjaert-Kristoffersen, I., 2006. Cognitive and motor development of 8-year-old children born after ICSI compared to spontaneously conceived children. *Hum. Reprod.*, **21**(11):2922-2929. [doi:10.1093/humrep/del266]

Leunens, L., Celestin-Westreich, S., Bonduelle, M., Liebaers, I., Ponjaert-Kristoffersen, I., 2008. Follow-up of cognitive and motor development of 10-year-old singleton children born after ICSI compared with spontaneously conceived children. *Hum. Reprod.*, **23**(1):105-111. [doi:10.1093/humrep/dem257]

Lu, Y.H., Wang, N., Jin, F., 2013. Long-term follow-up of children conceived through assisted reproductive technology. *J. Zhejiang Univ.-Sci. B (Biomed. & Biotechnol.)*, **14**(5):359-371. [doi:10.1631/jzus.B1200348]

Ludwig, A.K., Katalinic, A., Thyen, U., Sutcliffe, A.G., Diedrich, K., Ludwig, M., 2009a. Neuromotor development and mental health at 5.5 years of age of singletons born at term after intracytoplasmatic sperm injection ICSI: results of a prospective controlled single-blinded study in Germany. *Fertil. Steril.*, **91**(1):125-132. [doi:10.1016/j.fertnstert.2007.11.030]

Ludwig, A.K., Katalinic, A., Entenmann, A., Thyen, U., Sutcliffe, A.G., Diedrich, K., Ludwig, M., 2009b. Can we sense ART? The blinded examiner is not blind—a problem with follow-up studies on children born after assisted reproduction. *Fertil. Steril.*, **92**(3):950-952. [doi:10.1016/j.fertnstert.2009.01.086]

Maher, E.R., Brueton, L.A., Bowdin, S.C., Luharia, A., Cooper, W., Cole, T.R., Macdonald, F., Sampson, J.R., Barratt, C.L., Reik, W., *et al.*, 2003. Beckwith-Wiedemann syndrome and assisted reproduction technology (ART). *J. Med. Genet.*, **40**(1):62-64. [doi:10.1136/jmg.40.1.62]

McCarthy, D., 1972. Manual for the McCarthy Scales of Children's Abilities. Psychological Corporation, New York.

Middelburg, K.J., Heineman, M.J., Bos, A.F., Hadders-Algra, M., 2008. Neuromotor, cognitive, language and behavioural outcome in children born following IVF or ICSI: a systematic review. *Hum. Reprod. Update*, **14**(3):219-231. [doi:10.1093/humupd/dmn005]

Mu, S.C., Hwang, J.L., Lin, Y.H., Sung, T.C., Lin, M.I., Yeh, T.F., 2006. Growth and development of children conceived by in-vitro maturation of human oocytes. *Early Hum. Dev.*, **82**(10):677-682. [doi:10.1016/j.earlhumdev.2006.01.012]

Neemann, J., Harter, S., 1986. Manual of the Self-perception Profile for College Students. University of Denver, Denver.

Nekkebroeck, J., Bonduelle, M., Desmyttere, S., van den Broeck, W., Ponjaert-Kristoffersen, I., 2008a. Mental and psychomotor development of 2-year-old children born after preimplantation genetic diagnosis/screening. *Hum. Reprod.*, **23**(7):1560-1566. [doi:10.1093/humrep/den033]

Nekkebroeck, J., Bonduelle, M., Desmyttere, S., van den Broeck, W., Ponjaert-Kristoffersen, I., 2008b. Socio-emotional and language development of 2-year-old children born after PGD/PGS, and parental well-being. *Hum. Reprod.*, **23**(8):1849-1857. [doi:10.1093/humrep/den179]

Owen, L., Golombok, S., 2009. Families created by assisted reproduction: parent-child relationships in late adolescence. *J. Adolesc.*, **32**(4):835-848. [doi:10.1016/j.adolescence.2008.10.008]

Papaligoura, Z., Panopoulou-Maratou, O., Solman, M., Arvaniti, K., Sarafidou, J., 2004. Cognitive development of 12 month old Greek infants conceived after ICSI and the effects of the method on their parents. *Hum. Reprod.*, **19**(6):1488-1493. [doi:10.1093/humrep/deh270]

Place, I., Englert, Y., 2003. A prospective longitudinal study of the physical, psychomotor, and intellectual development of singleton children up to 5 years who were conceived by intracytoplasmic sperm injection compared with children conceived spontaneously and by in vitro fertilization. *Fertil. Steril.*, **80**(6):1388-1397. [doi:10.1016/j.fertnstert.2003.06.004]

Ponjaert-Kristoffersen, I., Tjus, T., Nekkebroeck, J., Squires, J., Verté, D., Heimann, M., Bonduelle, M., Palermo, G., Wennerholm, U.B., 2004. Psychological follow-up study of 5-year-old ICSI children. *Hum. Reprod.*, **19**(12):2791-2797. [doi:10.1093/humrep/deh511]

Ponjaert-Kristoffersen, I., Bonduelle, M., Barnes, J., Nekkebroeck, J., Loft, A., Wennerholm, U.B., Tarlatzis, B.C., Peters, C., Hagberg, B.S., Berner, A., *et al*., 2005. International collaborative study of intracytoplasmic sperm injection-conceived, in vitro fertilization-conceived, and naturally conceived 5-year-old child outcomes: cognitive and motor assessments. *Pediatrics*, **115**(3):E283-E289. [doi:10.1542/peds.2004-1445]

Quinton, D., Rutter, M., 1988. Parenting Breakdown: The Making and Breaking of Intergenerational Links. Avebury Gower Publishing, Aldershot, UK.

Reitan, R.M., 1979. Trail Making Test: TMT. Testzentrale, Germany.

Richman, N., Stevenson, J., Graham, P.J., 1982. Pre-school to School: A Behavioural Study. Academic Press, London, p.225.

Rohner, R.P., 1999. Handbook for the Study of Parental Acceptance and Rejection. University of Connecticut, Storrs, Connecticut.

Rohner, R.P., Khaleque, A., 2005. Handbook for the Study of Parental Acceptance and Rejection. Rohner Research, Storrs, Connecticut.

Rutter, M., Tizard, J., Whitmore, K., 1970. Education, Health and Behaviour. Longman, London.

Rutter, M., Cox, A., Tupling, C., Berger, M., Yule, W., 1975. Attainment and adjustment in two geographical areas—the prevalence of psychiatric disorder. *Br. J. Psychiatry*, **126**(6):493-509. [doi:10.1192/bjp.126.6.493]

Schieve, L.A., Meikle, S.F., Ferre, C., Peterson, H.B., Jeng, G., Wilcox, L.S., 2002. Low and very low birth weight in infants conceived with use of assisted reproductive technology. *N. Engl. J. Med.*, **346**(10):731-737. [doi:10.1056/NEJMoa010806]

Soenens, B., Beyers, W., Vansteenkiste, M., Sierens, E., Luyckx, K., Goossens, L., 2004. The "Gross Anatomy" of Parenting Styles in Adolescence: Three or Four Dimensions? 18th Biennial Meeting of the International Society for the Study of Behavioural Development (ISSBD), Ghent, Belgium.

Sparrow, S.S., Balla, D.A., Cicchetti, D.V., 1984. Vineland Adaptive Behavior Scales. American Guidance Service, Circle Pines, Minnesota.

Steptoe, P., Edwards, R., 1978. Birth after the reimplantation of a human embryo. *Lancet*, **312**(8085):366. [doi:10.1016/S0140-6736(78)92957-4]

Straus, M., 1979. Measuring intrafamily conflict and violence: the Conflict Tactics (CT) Scales. *J. Marr. Fam.*, **41**(1):75-88. [doi:10.2307/351733]

Straus, M., 1980. Victims and aggressors in marital violence. *Am. Behav. Sci*., **23**(5):681-704. [doi:10.1177/000276428002300505]

Sutcliffe, A.G., Taylor, B., Li, J., Thornton, S., Grudzinskas, J.G., Lieberman, B.A., 1999. Children born after intracytoplasmic sperm injection: population control study. *BMJ*, **318**(7185):704-705. [doi:10.1136/bmj.318.7185.704]

Sutcliffe, A.G., Taylor, B., Saunders, K., Thornton, S., Lieberman, B.A., Grudzinskas, J.G., 2001. Outcome in the second year of life after in-vitro fertilisation by intracytoplasmic sperm injection: a UK case-control study. *Lancet*, **357**(9274):2080-2084. [doi:10.1016/S0140-6736(00)05180-1]

Sutcliffe, A.G., Saunders, K., McLachlan, R., Taylor, B., Edwards, P., Grudzinskas, G., Lieberman, B.A., Thornton, S., 2003. A retrospective case-control study of developmental and other outcomes in a cohort of Australian children conceived by intracytoplasmic sperm injection compared with a similar group in the United Kingdom. *Fertil. Steril.*, **79**(3):512-516. [doi:10.1016/S0015-0282(02)04701-5]

Sutcliffe, A.G., Peters, C.J., Bowdin, S., Temple, K., Reardon, W., Wilson, L., Clayton-Smith, J., Brueton, L.A., Bannister, W., Maher, E.R., 2006. Assisted reproductive therapies and imprinting disorders—a preliminary British survey. *Hum. Reprod.*, **21**(4):1009-1011. [doi:10.1093/humrep/dei405]

Theunissen, N.C.M., Vogels, T.G.C., Koopman, H.M., Verrips, G.H., Zwinderman, K.A., Verloove-Vanhorick, S.P., Wit, J.M., 1998. The proxy problem: child report versus parent report in health-related quality of life research. *Qual. Life Res.*, **7**(5):387-397. [doi:10.1023/A:1008801802877]

van der Meulen, B., Ruiter, S., Spelberg, H., Smrkovsky, M., 2002. Bayley Scales of Infant Development-II. Dutch Version of the BSID-II, Specific Dutch Norms Included. Nederlandse Versie, the Netherlands.

van der Steene, G., van Haasen, P.P., de Bruyn, E.E.J., Coetsier, P., Pijl, Y.L., Poortinga, Y.H., Spelberg, H.C., Spoelders-Claes, R., Stinissen, J., 1986. Wechsler Intelligence Scale for Children-Revised (English Version). Swets & Zeitlinger B.V., Lisse, the Netherlands.

Verhulst, C., van der Ende, J., Koot, H.M., 1996. Handbook of CBCL/4-18 (Netherland Version). Erasmus University Rotterdam, the Netherlands.

Verrips, G.H.W., Vogels, T.G.C., Koopman, H.M., Theunissen,

N.C.M., Kamphuis, R.P., Fekkes, M.I.N.N., Wit, J.M., Verloove-Vanhorick, S.P., 1999. Measuring health-related quality of life in a child population. *Eur. J. Public Health*, **9**(3):188-193. [doi:10.1093/eurpub/9.3.188]

Vogels, T., Verrips, G.H., Verloove-Vanhorick, S.P., Fekkes, M., Kamphuis, R.P., Koopman, H.M., Theunissen, N.C., Wit, J.M., 1998. Measuring health-related quality of life in children: the development of the TACQOL parent form. *Qual. Life Res.*, **7**(5):457-465. [doi:10.1023/A:1008848218806]

Wagenaar, K., Huisman, J., Cohen-Kettenis, P.T., Delemarre-van de Waal, H.A., 2008a. An overview of studies on early development cognition, and psychosocial well-being in children born after in vitro fertilization. *J. Dev. Behav. Pediatr.*, **29**(3):219-230. [doi:10.1097/DBP.0b013e318173a575]

Wagenaar, K., Ceelen, M., van Weissenbruch, M.M., Knol, D.L., Delemarre-van de Waal, H.A., Huisman, J., 2008b. School functioning in 8- to 18-year-old children born after in vitro fertilization. *Eur. J. Pediatr.*, **167**(11):1289-1295. [doi:10.1007/s00431-008-0677-2]

Wagenaar, K., van Weissenbruch, M.M., Knol, D.L., Cohen-Kettenis, P.T., Delemarre-van de Waal, H.A., Huisman, J., 2009a. Behavior and socioemotional functioning in 9–18-year-old children born after in vitro fertilization. *Fertil. Steril.*, **92**(6):1907-1914. [doi:10.1016/j.fertnstert.2008.09.026]

Wagenaar, K., van Weissenbruch, M.M., Knol, D.L., Cohen-Kettenis, P.T., Delemarre-van de Waal, H.A., Huisman, J., 2009b. Information processing, attention and visual-motor function of adolescents born after in vitro fertilization compared with spontaneous conception. *Hum. Reprod.*, **24**(4):913-921. [doi:10.1093/humrep/den455]

Wagenaar, K., van Weissenbruch, M.M., van Leeuwen, F.E., Cohen-Kettenis, P.T., Delemarre-van de Waal, H.A., Schats, R., Huisman, J., 2011. Self-reported behavioral and socioemotional functioning of 11- to 18-year-old adolescents conceived by in vitro fertilization. *Fertil. Steril.*, **95**(2):611-616. [doi:10.1016/j.fertnstert.2010.04.076]

Wechsler, D., 1974. Wechsler Intelligence Scale for Children-Revised: Manual. The Psychological Corporation, New York.

Wechsler, D., 1989. WPPSI-R: Wechsler Preschool and Primary Scale of Intelligence. Psychological Corporation, New York.

Wechsler, D., 1990. Manual for the Wechsler Preschool and Primary Scale of Intelligence-Revised. Psychological Corporation, New York.

Wechsler, D., 1995. Manuel: Echelle d'intelligence de Wechsler Pour la Période Préscolaire et Primaire. Forme Réviseé. ECPA, Paris (in French).

Wechsler, D., 1999. Wechsler Abbreviated Scale of Intelligence. Psychological Corporation, New York.

Williams, J.G., Higgins, J.P., Brayne, C.E., 2006. Systematic review of prevalence studies of autism spectrum disorders. *Arch. Dis. Child*, **91**(1):8-15. [doi:10.1136/adc.2004.062083]

World Health Organization, 2010. Infertility. Available from http://www.who.int/reproductivehealth/topics/infertility/en/index.html [Accessed on Sept. 5, 2010].

Zimmer, R., Volkamer, M., 1987. MOT 4–6, Motoriktest fvr 4–6 Jahrige Kinder. Hogrefe, Gottingen (in German).

Zink, I., Lejaegere, M., 2003. N-CDI's Lijsten Voor Communicatieve Ontwikkeling: Korte Vormen. Acco, Leuven/Leusden (in Dutch).