Dilemmas in counselling females with the fragile X syndrome

Bert B A de Vries, Hanneke M A van den Boer-van den Berg, Martinus F Niermeijer and Aad Tibben

J. Med. Genet. 1999;36;167-170

Dilemmas in counselling females with the fragile X syndrome

Bert B A de Vries, Hanneke M A van den Boer-van den Berg, Martinus F Niermeijer, Aad Tibben

Abstract

The dilemmas in counselling a mildly retarded female with the fragile X syndrome and her retarded partner are presented. The fragile X syndrome is an X linked mental retardation disorder that affects males and, often less severely, females. Affected females have an increased risk of having affected offspring.

The counselling of this couple was complicated by their impaired comprehension which subsequently impaired their thinking on the different options. The woman became pregnant and underwent CVS, which showed an affected male fetus. The pregnancy was terminated. Whether non-directive counselling for this couple was the appropriate method is discussed and the importance of a system oriented approach, through involving relatives, is stressed.

(*J Med Genet* 1999;**36**:167–170)

Keywords: fragile X syndrome; counselling; mental retardation; FMR1

Department of Clinical Genetics, University Hospital Dijkzigt and Erasmus University, PO Box 1738, 3000 DR Rotterdam, The Netherlands
B B A de Vries
H M A van den Boer-van den Berg
M F Niermeijer
A Tibben

Department of Philosophy, Medical Ethics and History of Medicine, University Hospital Dijkzigt and Erasmus University, Rotterdam, The Netherlands
H M A van den Boer-van den Berg

Department of Medical Psychology and Psychotherapy, University Hospital Dijkzigt and Erasmus University, Rotterdam, The Netherlands
A Tibben

Correspondence to Dr de Vries.

Received 10 December 1997
Revised version accepted for publication 22 June 1998

The fragile X syndrome is an X linked disorder, which may cause mental retardation in both males and females. In addition to the mental retardation, it is characterised by physical features, such as a long face with large, prominent ears and macro-orchidism, in combination with behavioural features, such as hyperactivity and avoidance of eye contact.[1–3]

The phenotype in females with fragile X chromosomes is usually less distinct than in males, as would be expected from the influence of lyonisation. Cognitive defects and behavioural problems, such as shyness, attention problems, and anxiety, are less conspicuous than in affected males.[4 5]

Molecular definition of the FMR1 gene and its specific CGG repeat mutations in 1991 allows accurate diagnosis of patients and carriers.[6–8] The FMR1 gene has a CGG repeat before the 5' exon which varies from six to 54 units in the normal population.[9] Phenotypically normal premutation carriers have a repeat in the 43 to 200 range, whereas affected subjects have more expanded CGG repeats (>200) in that position.[9] Female carriers of a premutation or full mutation have an increased risk of producing affected offspring.

Females with a full mutation have a substantial risk (52-82%) of mental impairment (IQ <85).[10–14] Their retardation is usually less severe (70<IQ<85) than in affected males. Affected females, who are often aware of their handicap, live a fairly independent life, frequently supported by their relatives or social workers, and often have relationships and the desire for offspring. It is likely that some affected females remain undiagnosed or, even if diagnosed, do not use genetic services either through choice or ignorance of their existence.

Genetic counselling is the process of comprehensively informing subjects or couples about their personal risks or the risks for their (future) offspring in order to enable them to make an informed decision that is in line with their personal opinions, values, norms, and personality.[15 16] Generally, a non-directive attitude is seen as an essential approach to this goal. A non-directive attitude means that the counsellor is able to show respect for the consultand's attitude, choices, and decisions, even if they seem undesirable from the counsellor's point of view.[17] Kessler[18] suggested the following definition: non-directiveness describes procedures aimed at promoting the autonomy and self-directedness of the client. Non-directiveness is a way of interacting and working with clients that aims to raise their self-esteem and leave them with greater control over their lives and decisions.

Here, we report on the counselling dilemmas of a mildly retarded female carrier of the full mutation in the FMR1 gene and her retarded partner. We address the psychological and ethical issues involved in counselling couples with intellectual disabilities.

Case report

The index patient (II.2, fig 1) was diagnosed with the fragile X syndrome at the age of 24 years. He still lived with his parents and was moderately/severely retarded with severe panic attacks and compulsive behaviour. His 26 year old sister (II.1) was diagnosed as a carrier of the full mutation and had mild retardation. The partner of II.1, II.1A, was mentally retarded without a specific diagnosis; he had no dysmorphic features and additional investigations, such as chromosome, FMR1 gene, and urine metabolic analyses, were normal. The couple (II.1 and II.1A) came for genetic counselling together with II.1's parents and II.1A's mother, at the request of II.1's parents, who were concerned for their daughter's future children. To support the couple's individuality, they were seen independently from their parents after the first session. In the following sessions they expressed their own questions and worries and were regarded as clients from then. Routinely, professionals, such as a psychologist, paediatrician, and ethicist, are

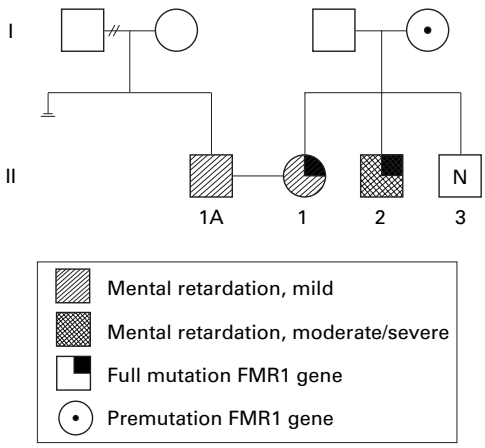

Figure 1 Pedigree of the family.

available for consultation and participation in the care of consultands and they contributed to the management of this case.

The phases in the counselling process are shown in table 1. The couple (II.1 and II.1A) had met in a sheltered workshop; they lived on the premises of II.1A's mother who took responsibility for their daily affairs. During counselling, the couple was aware of their risk of having a mentally retarded boy and the emotional problems a prenatal diagnosis might bring. II.1 was very anxious. She certainly did not want "a boy like her brother", but she also believed that she could not face a selective abortion.

Disagreement was observed among the parents. The parents of II.1 were discouraging their daughter from having a child. II.1 was told by her mother that "she would never have wanted any children if she had known the problems beforehand". However, II.1A's mother supported their wish: "one child will be fine as long as it is healthy".

In the following sessions, the couple was seen without their parents. They suggested that they would try one pregnancy and if that was affected and consequently terminated then opt for adoption. It was explained that adoption would not be possible in their case owing to the strict adoption rules. The option of a life without children was brought up. However, they repeatedly asked the counsellor "whether they were 'allowed' to get pregnant".

After the couple's marriage, the husband brought up the idea of egg cell donation which had been suggested to them by others. They had already contacted a potential donor, a mentally handicapped woman from the same sheltered workshop. In this counselling session, it became obvious that the couple was unable to understand the consequences of this procedure. They were informed that this would not be a realistic option.

Six months later II.1 was pregnant by her husband. They first considered terminating the pregnancy without prenatal diagnosis. After consultation with their GP and II.1A's mother they opted for prenatal testing for the fragile X syndrome, but were very uncertain what to do if the disorder were detected. The woman asked: "could the disorder be less severe than in my brother?". The couple agreed that the husband's mother was fully informed by the counsellor. She was willing to take care of a child (with or without a handicap) and was already planning alterations in her house. The couple and II.1A's mother remained uncertain which choice to make if a female fetus with a full mutation was detected. Eventually II.1 decided to proceed with prenatal testing by (late) CVS performed at 14 weeks as she mistimed her last menstrual period. The prenatal test result showed a 47,XXY karyotype with a full mutation on both X chromosomes. The couple were informed that the child would be severely affected, similar to II.1's brother. The couple decided to terminate the pregnancy. Follow up visits were offered, but the couple did not contact the department.

In the same period, a cousin of II.1 (the daughter of the mother's sister) was identified at 22 years as a full mutation carrier. She worked at a sheltered workshop, was single, and lived with her parents. Her parents became concerned about her future offspring and indicated that their daughter should not have children. They discussed this carefully with their daughter and helped her to cope with this.

Discussion

When counselling a couple of mildly mentally retarded people, several problems may be encountered. First, the couple may not be able fully to comprehend the possible risks for their offspring. Accurate assessment of the comprehension capacities in subjects with borderline competence is difficult. A certain level of reasoning and independent thinking is required to deal with options when there is an increased risk, such as refraining from having children, using prenatal diagnosis, or accepting the risk. The couple in this case showed some awareness of the risk, clarified by the severe mental handicap in the woman's brother which she

Table 1 From diagnosis in index patient (II.2) to risk in pregnancy of couple (II.1+II.1A)

*Time**	
0	Diagnosis of fragile X syndrome in II.1's brother (II.2)
4/12	II.1 carrier of full mutation
2 2/12	First counselling of couple II.1 and II.1A together with II.1's parents and II.1A's mother
2 6/12	Second counselling in presence of psychologist: the impact of prenatal diagnosis and selective abortion
2 9/12	II.1 and II.1A opted to try one pregnancy and later adoption
3 4/12	Marriage
3 6/12	II.1A brought up oocyte donation, suggested to them by others
4	II.1 is pregnant by husband, prenatal diagnosis
4 1/12	CVS test result: 47,XXY, both X chromosomes with a full mutation; pregnancy terminated

*Time lapse (in years) since diagnosing index patient.

knew about from childhood. However, coping with this increased risk was a great problem because they were unable to reflect on the different options and their consequences.

A second problem is how to conduct counselling when the counsellees have difficulties in perceiving their risks and options. Following the "golden rule" of non-directive counselling might leave the couple with information and responsibilities they cannot handle. Initially, in this case, the counsellor tried to help the couple to go through the various options using a non-directive attitude, that is, exploring their feelings about a pregnancy with empathy.[17] In addition, the couple received information and was helped to assimilate the information in order to enable them to make a decision that met their wishes. However, it was unclear whether the couple could handle this information. For this couple with restricted mental capacities a non-directive approach might be questionable, as it requires the ability for independent reflection and introspection. These abilities are frequently impaired in people with an intellectual disability. The couple's question "may I get pregnant now, doctor?" implies that obtaining "approval" seemed more important to them than taking an independent decision for themselves.

Non-directiveness is thought to be the most desirable attitude in genetic counselling in north west European and North American countries. However, non-directivity is not universal and justification of exceptions has been discussed.[16 17] For instance, what is the approach to a mentally retarded couple wanting a child? Is there in this case justification for a counsellor to intervene in the freedom to reproduce? The presented case raises dilemmas. The couple are both mentally disabled and there are reasonable doubts about their capacity to raise a child. Their mental handicap seemed mild, as they were able to cite suggestions made to them by others on various reproductive choices, including egg cell donation and testing during pregnancy. They were also able to express their fear about having a mentally retarded child and undergoing an abortion. Although many "normal" people express the same feelings, this couple was not able to use these feelings in order to consider their different options.

In this case, values and opinions of the woman's parents and the man's mother interacted with the couple's ideas. Her mother indicated she would have refrained from having children in retrospect. The man's mother would have opted to have children, even when retrospectively regretting having a disabled son. She obviously did not want to influence the choice of the young couple.

The counsellor's task is to inform, assist, comfort, and support a couple. The counsellor creates a working alliance, in which the couple eventually make their own choices. Should the counselling be different in this case? There was an initial difference in that not the couple but the woman's parents asked for counselling as the parents wished to prevent a pregnancy. They thought that the couple might be unable to raise children and that they should refrain from having children for their own and their children's sake. The parents felt strengthened in this because of the woman's inability to cope with either prenatal testing and a possible adverse outcome or with the upbringing of a child. Also, the counsellors experienced difficulty in expressing unconditional acceptance of the couple's wish for a child and they noticed they felt inclined to take over the responsibility for the couple's decision and, consequently, for their quality of life. This more directive attitude was induced by the wish to prevent harm to the counsellees as well as the future child. In facing this dilemma, the counsellors consulted several other professionals throughout the counselling process, which led to a multidisciplinary approach to the care of this couple. The counsellors decided that if there was a reasonable doubt about the capacities of the couple to raise a child, it was sensible to talk to them about their motives, reasons, and ideas. However, the goal of counselling may not be guiding a couple in one direction; "counselling" is different from preventing a pregnancy.

Ideally, parents of mentally impaired persons may help their sons/daughters in these decisions. Unlike her aunt (mother's sister), who helped her retarded daughter to cope with the risks and therefore the "inability" to have children, the woman's parents were not able to influence their daughter's decision. The couple's decisions would considerably affect the life of their actual parents, who were involved in their supervision and care. These caregivers might wish to be involved or informed during the counselling and decision making process. The counsellors attempted to assist the retarded couple in reproductive decisions whereas the parents of the woman were the initial applicants for counselling. In retrospect, it might have been better to counsel the parents separately on their problems with coping with their children's desire for a child. The parents' problems may reflect guilt feelings, grief, and worries about their children's future. It is difficult for parents to accept that their child will be unable to seek freedom from the parental figures (separation) and will not achieve an independent personal identity (individuation), and will experience problems in handling sexuality and interpersonal intimacy.[19–21] The parents may feel uncertain about their parental responsibilities for mentally retarded adolescents and young adults, which are different from those for children who do achieve their developmental goals. Moreover, the parents must account for an unexpected pregnancy resulting from inappropriate or uncontrolled use of contraception in the retarded couple. These issues should be extensively addressed in counselling. Therefore, parents of mentally handicapped children merit access to genetic counselling, irrespective of the age of their children.

The man's mother has supported the couple's desire for a child. It is possible that she was neither aware of the risks of recurrence nor of the couple's ability to raise a child or to cope with a pregnancy termination. After counsel-

ling the woman's parents, they might have discussed with the man's mother their common worries and those of the psychologist and tried to find a common resolution of the problem. The genetic counsellor and the psychologist could have assisted by exploring personal feelings about the children, the parental tasks and responsibilities, and seeking an acceptable attitude.

In conclusion, the issues presented require a system oriented approach, considering both parental responsibility for adult mentally retarded children and these children themselves, as the latter will be impaired in their achievement of developmental goals. The genetic counsellor has the complex task of differentiating between the needs of the mentally handicapped subjects, their requirement of support, and the needs of their parents/relatives, who might fear becoming burdened by social responsibilities for their children and grandchildren.

Conscious considerations of a counsellor about his directiveness or non-directiveness towards a couple with moderate or reduced understanding/perception of genetic risk and its implications might help to achieve a controllable balance between directiveness and non-directiveness. Genetic counsellors may feel that the modern concept of pervasive "autonomy and self determination after full information" may not meet all the needs of consultands, especially when the consultands are not able to take full responsibility for their decisions and consequences. Still, informing mentally impaired people in an appropriate fashion, without intervening in their freedom to reproduce, may help them to achieve self-reliance and self-determination. Support from their parents and other care givers may subsequently be obtained. In terms of case management, this case shows how the counselling of clients with a mental handicap may not always seem satisfactory to all the parties involved. The clinical geneticist/counsellor has the professional duty to discuss a case, as described here, with other professionals from inside and outside the field. Yet there may be pitfalls and only openness and professional reflection on those issues constitute good medical practice.

We thank Dr D J J Halley and Dr Ir A M W van der Ouweland for performing the DNA analysis and Dr J O Van Hemel for the cytogenetic studies in the fragile X family.

1 Fryns JP. X-linked mental retardation and the fragile X syndrome: a clinical approach. In: Davies KE, ed. *The fragile X syndrome*. Oxford: Oxford University Press, 1989.
2 Hagerman RJ. Physical and behavioural phenotype. In: Hagerman RJ, Cronister A, eds. *Fragile-X syndrome: diagnosis, treatment and research*. Baltimore: The Johns Hopkins University Press, 1996.
3 De Vries BBA, Halley DJJ, Oostra BA, Niermeijer MF. The fragile X syndrome. *J Med Genet* 1998;**35**:579-89.
4 Borghgraef M, Fryns JP, van den Berghe H. The female and the fragile X syndrome: data on clinical and psychological findings in 7 fra(X) carriers. *Clin Genet* 1990;**37**:341-6.
5 Sobesky W. The treatment of emotional and behavioral problems. In: Hagerman RJ, Cronister A, eds. *Fragile-X syndrome: diagnosis, treatment and research*. Baltimore: The Johns Hopkins University Press, 1996.
6 Verkerk AJ, Pieretti M, Sutcliffe JS, *et al*. Identification of a gene (FMR-1) containing a CGG repeat coincident with a breakpoint cluster region exhibiting length variation in fragile X syndrome. *Cell* 1991;**65**:905-14.
7 Yu S, Pritchard M, Kremer E, *et al*. Fragile X genotype characterized by an unstable region of DNA. *Science* 1991; **252**:1179-81.
8 Oberle I, Rousseau F, Heitz D, *et al*. Instability of a 550-base pair DNA segment and abnormal methylation in fragile X syndrome. *Science* 1991;**252**:1097-102.
9 Fu YH, Kuhl DP, Pizzuti A, *et al*. Variation of the CGG repeat at the fragile X site results in genetic instability: resolution of the Sherman paradox. *Cell* 1991;**67**:1047-58.
10 Rousseau F, Heitz D, Biancalana V, *et al*. Direct diagnosis by DNA analysis of the fragile X syndrome of mental retardation. *N Engl J Med* 1991;**325**:1673-81.
11 Rousseau F, Heitz D, Oberle I, Mandel JL. Selection in blood cells from female carriers of the fragile X syndrome: inverse correlation between age and proportion of active X chromosomes carrying the full mutation. *J Med Genet* 1991;**28**:830-6.
12 Smits A, Smeets D, Hamel B, Dreesen J, de Haan A, van Oost B. Prediction of mental status in carriers of the fragile X mutation using CGG repeat length. *Am J Med Genet* 1994;**51**:497-500.
13 Taylor AK, Safanda JF, Fall MZ, *et al*. Molecular predictors of cognitive involvement in female carriers of fragile X syndrome. *JAMA* 1994;**271**:507-14.
14 De Vries BB, Wiegers AM, Smits AP, *et al*. Mental status of females with an FMR1 gene full mutation. *Am J Hum Genet* 1996;**58**:1025-32.
15 Roberts JAF. *An introduction to human genetics*. Oxford: Oxford University Press, 1959.
16 Michie SW, Bron F, Bobrow M, Marteau TM. Nondirectiveness in genetic counseling: an empirical study. *Am J Hum Genet* 1997;**60**:40-7.
17 Rogers C. The necessary and sufficient conditions of therapeutic personality change. In: Kirschenbaum H, Henderson VL, eds. *The Carl Rogers Readers*. London: Constable, 1989.
18 Kessler S. Psychological aspects of genetic counseling. XI. Nondirectiveness revisited. *Am J Med Genet* 1997;**72**:164-71.
19 Rolland JS. Chronic illness and the family life cycle. In: Carter B, McGoldrick M, eds. *The changing family life cycle*. London: Allyn and Bacon, 1989.
20 Brown FH. The impact of death and serious illness on the family life cycle. In: Carter B, McGoldrick M, eds. *The changing family life cycle*. London: Allyn and Bacon, 1989.
21 Fanos JH. Developmental tasks of childhood and adolescence: implications for genetic testing. *Am J Med Genet* 1997;**71**:22-8.