Reviewer's report

Title: A defined 4q subtelomeric deletion identified in a screen of patients with co-morbid psychiatric illness and mental retardation

Version: 1 Date: 12 May 2004

Reviewer: Nicholas R Dennis

Reviewer's report:

General Primarily a report of a single case which may corroborate the suggestion from elsewhere of a gene at 4q35.2 which when mutated or deleted can lead to a high risk of bipolar affective disorder (or, as in this patient, schizoaffective disorder). Of secondary interest is the observed prevalence of submicroscopic subtelomeric abnormalities in a sample of patients with mild to moderate learning disability and psychiatric disorders, but the value of this is reduced by the lack of detail on ascertainment of the sample (see below).

Methods adequately referenced.

The paper seems longer than it needs to be- eg the general discussion of telomeres in the Background section is easily available elsewhere, and over half of page 9 is devoted to a comparison of MAPH and FISH which is not directly relevant to this paper.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Testing of the deleted patient's parents to see whether the deletion was inherited or de novo should be done if possible, and if not possible, this should be explained.

2. It should be mentioned whether or not the deleted subject had any family history of psychiatric disorder.

3. DUX4 in table 2 does not appear on figure 1, and it is not immediately obvious that a-f on the fig refer to the genes listed in table 2. MTNR1A is on figure 1 twice, and BC012432 on the fig does not appear in table 2. These apparent discrepancies should be corrected or explained.

4. The authors should explain why FISH was not done on the patient found to have a 4q deletion by MAPH, especially as they comment in the paper on the comparability of these 2 methods.

5. It is stated on page 6 that there were 3 "confident" diagnoses of deletions on MAPH, plus one of the 4 "possible" deletions was not discounted but details are subsequently given of only one deleted case. We need to know what was concluded about the other 3 cases- were these eventually thought to be real deletions?

6. The word "stereotypical" on page 10 should, I think, be "typical".

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Discretionary Revisions (which the author can choose to ignore)

1. The title would be more informative if 4q35.2 was included rather than just 4q, and the word "defined" could be omitted.
2. There should be more detail on ascertainment of the series of subjects—e.g., were they ascertained via a learning disability service or via psychiatry? It is implied that all subjects had normal results on standard cytogenetic analysis as a condition of entry but this needs to be stated and if possible some indication should be given of how long ago these analyses were performed.

3. More detail on the level of learning disability in the group as whole and in the deleted patient would be helpful.

4. A brief comment could be made in the discussion on whether there are other patients reported with 4q35 deletions, and if so, whether they have a defined phenotype.

5. A value of theta could be given for the lod score mentioned at the bottom of page 9.

6. The association between 22q11 deletions and psychiatric disorders should be discussed in the Background section rather than appearing for the first time in the Discussion.

**What next?:** Accept after minor essential revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

None