LONG-TERM BEHAVIOURAL EFFECTS OF BLASTOMERE BIOPSY

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Manipulations and culture of embryos are widely used in human assisted reproductive technology. Such techniques can cause micro-environmental perturbations during pre-implantation development and epigenetic modifications. In this study we wanted to determine whether removal of one blastomere from 8-cells-embryo alters the expression of imprinted genes (Snrpn, Peg1 and Ube3a) in preimplantation embryos and if this alteration is maintained through development. The imprinted genes, highly expressed in both the blastocyst and the brain, are involved in multiple neuronal mechanisms, shaping behavioural phenotype of offspring. Real-Time PCR analysis revealed significant down-regulation of Peg1 (P<0, 05), Snrpn and Ube3a (P<0, 01) in blastocysts derived from the biopsed embryos, compared to controls. One-month-old mice derived from the biopsed embryos were subjected to a battery of behavioural tests. The animals displayed an increased locomotor and exploration activity (P<0, 05) and increased anxiety-like behaviour. Interestingly, the depression-like behaviour in the tail suspension test was observed only in female offspring (P<0,001). The results suggest that blastomere biopsy causes a reduced expression of imprinted genes in preimplantation embryo. The reduction of expression of these transcripts can cause anxiety- or depression-like behaviour and alteration of locomotory activity in offspring obtained following biopsy of early embryos.