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Letter to the Editor

Rapid decline in motor symptoms in HD neural transplant patients prior to surgery

Several clinical studies have been published recently examining the effects of cell-based neural transplantation approaches for the treatment of Parkinson's disease (PD) and Huntington's disease (HD). Most of these open-label studies aimed to test the safety as well as the efficacy of this approach. One criticism of such open-label trials is that they are open to experimenter bias and placebo effect and in this respect it is interesting to observe that recent double-blind studies using sham operated control groups in PD showed less dramatic results [2,3], although it should be noted that there were also significant methodological differences between one of these studies [2] and the earlier open-label studies.

In 2000, Bachoud-Levi and colleagues presented data on five patients who had undergone neural transplantation surgery for HD [1]. Patients were followed for 2 years preoperatively then grafted with human foetal striatal tissue into the right striatum followed by a similar graft in the left striatum 1 year later. Results were reported 2 years after the second transplant. Figs. 1 and 2 in their paper (reproduced below) shows the motor scores for the Unified Huntington Disease Rating Scale (UHDRS)—with higher numbers indicating more advanced disease. The graph illustrates that most of the patients improved after the first or second graft (vertical dashed lines), especially when compared to a control group of HD patients at a similar stage of disease.

Of interest though is the difference in the rate of symptom progression prior to surgery—from assessment number 2 to 3—between control and grafted patients. The mean score change for the control group was 4.3 (S.D. = 6.1) compared to a grafted score change of 17.0 (S.D. = 4.4; Fig. 2; $t_{(10)} = 3.96$, $P = 0.003$). The rate of decline in the control group from assessment 2–3 (1 year) was comparable to previously published UHDRS values of 5.97 [5] and 4.8 [4]. Therefore, whilst the control and experimental groups were of equal disease severity at entry into the trial (control: $M = 20.2$, S.D. = 16.3; transplant: $M = 24.0$, S.D. = 17.9), they behaved very differently thereafter. These differences in disease progression may be due to a

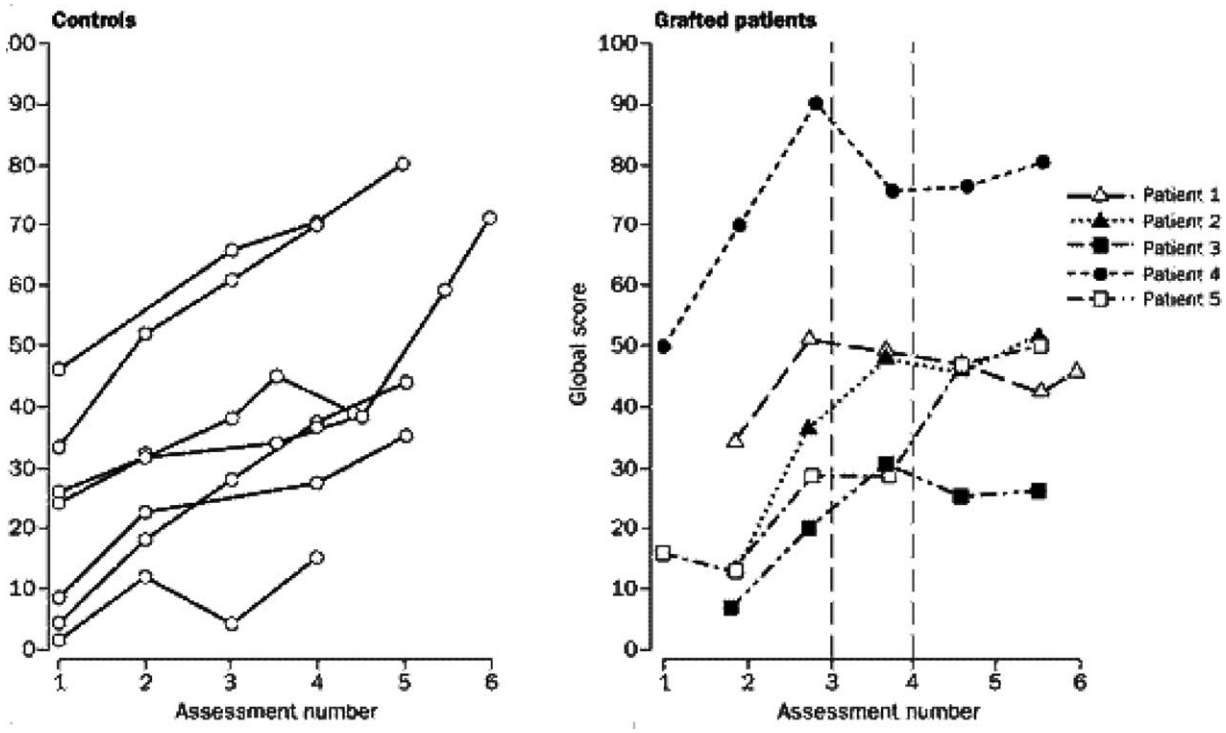

Fig. 1. Reproduction of Fig. 2 from Bachoud-Levi et al. (2000) showing total UHDRS motor scores for grafted patients and controls. Vertical dashed lines indicate time of transplantation. Reprinted with permission from Elsevier (Lancet, 2000, vol. 356, pp. 1975–1979).

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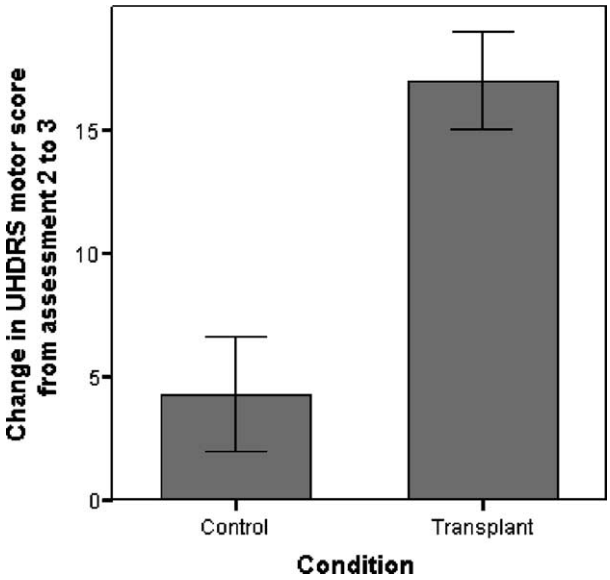

Fig. 2. An independent sample *t*-test was used to compare the change in UHDRS motor score between assessment 2 and 3 for the control and transplanted HD patients ($t_{(10)} = 3.96$, $P = 0.003$). Bars show means ± S.E.M.

host of possible factors (e.g., CAG repeat length), but does make the point that even when control groups of patients are recruited to neural transplant studies they may progress differently from expected, making interpretation of any effect difficult.

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Stanley E. Lazic*
Roger A. Barker
Department of Neurology, Addenbrooke's Hospital
Center for Brain Repair, University of Cambridge
Cambridge CB2 2QQ, UK
*Corresponding author
E-mail address: SEL33@cam.ac.uk (S.E. Lazic)
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