for ^{10}Be and argon for ^{36}Cl. After production both nuclides become attached to aerosols and are removed by precipitation. The ^{10}Be concentrations in samples of the same ice block No. 2995 differ by ~60%. The average accumulation rate for the Allan Hills area is ~4 cm (ice equivalent) yr^{-1} (ref. 3). If the age of the ice is a simple function of depth, each ice sample contains 2–3 years accumulation of snow. Precipitation may not accumulate continuously, however, due to the strong wind. The difference of ^{10}Be concentrations in the top and bottom of the ice block can be explained by the variation of ^{10}Be production rate during the solar cycle and terrestrial influences such as a change in precipitation rate. However, the higher ^{10}Be concentrations in the ice compared to fresh snow in the same area (about a factor of 6–9) cannot be explained by the solar cycle.

Our measurement of the age of surface ice in the Allan Hills Far Western icefield, 11,000 yr, is the time of the end of the Glacial/Holocene transition. An increase of ^{10}Be concentration by more than a factor of two between about 11,000 yr and 14,000 yr is well known in both Antarctic and Greenland ice cores (for example refs 13,14). Raisbeck found ~$10–12 \times 10^4$ atoms ^{10}Be g^{-1} in a Dome C ice core from the last ice age[13]. Although Dome C is located ~1,000 km inland from the Allan Hills, the data for Dome C could apply because the climate change was world wide. □

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1. Fireman, E. L. *Antarct. J. U.S.* **XXII,** 75–77 (1987).
2. Nagata, T. *Mem. Natn. Inst. Polar Res., Spec. Iss.* No. 8, 70–92 (1978).
3. Nichio, F. & Annexstad, J. O. *Mem. Natn. Inst. Polar Res., Spec. Iss.* No. 17, 1–13 (1980).
4. Whillans, I. M. & Cassidy, W. A. *Science* **222,** 55–57 (1983).
5. Gow, A. J. & Cassidy, W. C. *Smithson. Contr. Earth Sci.* **28,** 87–91 (1989).
6. Suter, M. *et al. IEEE Trans. Nucl. Sci. NS-30* 1528–1531 (1983).
7. Jull, A. J. T., Donahue, D. J. & Linick, T. W. *Geochim. cosmochim. Acta* (in the press).
8. Elmore, D. *et al. Nature* **277,** 22–25 (1979); and erratum, *Nature* **277,** 246 (1979).
9. Drewry, D. J. *Nature* **287,** 214–216 (1980).
10. Nishiizumi, K., Elmore, D. & Kubik, P. W. *Earth planet. Sci. Lett.* (in the press).
11. Fireman, E. L. *Antarct. J. U.S.* (in the press).
12. Jull, A. J. T., Donahue, D. J. & Linick, T. W. abstr. *Lunar Planet. Sci* **XX,** 488–489 (1989).
13. Raisbeck, G. M. *et al. Nature* **292,** 825–826 (1981).
14. Beer, J. *et al. Radiocarbon* **25,** 269–278 (1983).
15. Evans, J. C. & Reeves, J. H. *Earth planet. Sci. Lett.* **82,** 223–230 (1987).

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Assessment of effects of socio-economic status on IQ in a full cross-fostering study

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AN important question in studies of mental ability concerns the effect of parental socio-economic status (SES) on the IQ of their offspring. Only a full cross-fostering study, including children born to biological parents from the most highly contrasting SES and adopted by parents with equally constrasting SES, can answer this question. Previous adoption studies using incomplete cross-fostering designs[1–3] have indicated an effect of postnatal environment on the IQ of children born to low-SES backgrounds and adopted by high-SES parents. They have not shown whether a low SES reduces the IQ of children born to high-SES parents or whether the SES of biological parents has an effect on IQ, or whether the effect of the SES of adoptive parents is independent of the SES of biological parents. We present a full cross-fostering study dealing with IQ, and find that children adopted by high-SES parents score higher than children adopted by low-SES parents; children born to high-SES parents score higher than children born to low-SES parents; and that there is no evidence for an interaction between these two factors on children's IQ.

Data reported elsewhere in the literature[1,2,4] have been arranged *a posteriori* in the form of full designs (refs 5 and 6; and S. Scarr, personal communication). The results of two of these designs[5,6] where the two factors (biological and adoptive parents) were defined by the same variable—number of years schooling (NYS)—are contradictory. One study showed an effect on children's IQ only for NYS of biological parents[5], whereas the other reported an effect for the NYS of adoptive parents[6]. This contradiction probably results from the arbitrary definition of levels of the independent variables. In addition, the contrast in levels between the characteristics of the groups of biological parents, as for the adoptive parents in the samples, tends to be low. This is why an *a priori* cross-fostering study was designed.

The sample was composed of four groups of adopted children (Table 1). The two-by-two factorial design includes two independent variables (SES of the two biological parents and of the two adoptive parents) each split into two highly contrasted levels (highest versus lowest). The two factors were defined operationally in terms of SES, by a combination of NYS and occupational status. Subjects were selected from two private adoption agencies and six public agencies according to the stringent procedure[7] developed for French adoption studies[3,8]. Subjects were born between 1 January 1970 and 31 December 1974. The range of birth dates was later extended to 31 December 1980 to obtain B+/A− subjects as these are extremely rare (1 of 600 files). The extension of the birth-date range for this latter group does not introduce a bias because all the subjects meeting the requirements in the total population of each agency were included in the study. Before beginning the screening, we decided that 10 subjects per group was statistically sufficient. The strict selection procedure will be described as it justifies the use of small sample sizes. Of 380 children relinquished at birth in the first adoption agency, 10 files met the requirements for group B−/A−, 10 for group B−/A+, 8 for group B+/A+ and 3 for group B+/A−. The search for B−/A− and B−/A+ subjects was, therefore, stopped. In Agency 2, out of the 146 children relinquished within the time period set by the study, 1 B+/A− and 10 B+/A+ subjects met the criteria. Only 2 B+/A+ were selected after matching with characteristics of A+ parents of the B−/A+ group. Four B+/A− were selected from six other public agencies. The likelihood of introducing non-systematically controlled variables having an impact on IQ is extremely low with this procedure. Furthermore, the two-way analysis of variance allows for calculating factor effects by augmenting the number of degrees of freedom.

The occupations of each of the two biological and adoptive low-SES parents corresponded to the lowest level on the scale, and the occupations for each of the two biological and adoptive upper-SES parents corresponded to the highest level (Table 1). Graduates (at least 13 years of schooling) were included in the group of highest biological background parents. NYS means are identical for the two groups of B− parents and the two groups of A− parents, and identical for the two groups of B+ parents and the two groups of A+ parents, whereas the differences were considerable between the + and − groups. Moreover, within-group variance of NYS was extremely low for all groups (Table 1). Control for possible bias showed no evidence of

selective placement: the age of the child at the time of relinquishment and age at adoption did not differ between the four groups; and as the within-group variance for SES and NYS was very low, no selective placement could have taken place on the basis of these criteria in this study. No significant differences were observed for the four groups for length of gestation, birthweight, or the prevalence of neo- or perinatal disorders. All the subjects selected from their files were subsequently tested. Therefore there was no bias due to loss of subjects. The mean age of subjects at the times of testing (168.10 ± 3.28 months) did not differ among groups.

Testing and scoring for calculation of the Full IQ were carried out using a blind procedure, as the testers did not know that the study dealt with adopted children. Each adoptee and one classmate were individually administered the Wechsler Intelligence Scale for Children-Revised (WISC-R[9]) in his or her regular school. Each test was scored twice; first by the tester, and secondly by another psychologist uninformed of the aims of the study. Only the second scoring was included in data analysis.

Full IQ scores (Table 2) show an effect for SES of the adoptive parents on their adopted children's IQ. Children reared by high-SES parents have significantly higher IQs than those reared by low-SES parents. Thus, there is a postnatal environmental effect on IQ performance which is independent of the SES of the biological parents. Partial comparison (Table 2), which reproduces the change of background comparable to the first partial French adoption study[3], show the same directional effect as those in this study[3]. The previous study indicated that mean full IQ WISC[12] scores for children born to low-SES parents and adopted by high-SES parents are significantly higher than those obtained by their non adopted half-siblings who remained in their original backgrounds. This partial design, however, is uninformative as to whether the improvement in observed scores was due to postnatal environment as assessed by the parental SES, or to the adoptive parents providing a more stimulating child-rearing environment. By testing adopted children only, the present study provides new and original data showing that improvement in performance is clearly caused by change—low SES versus high SES—in the postnatal environment.

The data show an effect for the biological parents' background on IQ independently of the SES of the adoptive parents (Table 2); that is, children born to parents with high SES have significantly higher scores than children born to low-SES parents. Although these findings clearly indicate that the biological parents' background contributes to observed differences in IQ between extreme groups, as does that of the adoptive parents, more detailed interpretation is difficult. The adoption method provides a means of dissociating the pooled effects of genetic and prenatal factors from factors related to the postnatal environment. But it is not equipped to differentiate prenatal from genetic factors[10]. This precludes interpreting the effects of the biological parents' background solely in genetic terms, or concluding that observed effects could be prenatal or prenatal acting either in additive or interactive manner with genotype. On the contrary, the effect attributed to the adoptive parents is clearly environmental.

The absence of an interaction effect calls for comment. The groups selected for this study represent extremes, that is, those with the greatest likelihood of exhibiting an interaction, if indeed one is present. The fact that there is no interaction is convincing evidence that changes in IQ resulting from changes in postnatal environment are of similar magnitude and exhibit the same general trend independently of the SES of the adopted children's biological parents. □

TABLE 1 SES of parents

Measure of SES	Groups of adopted children B+/A+ $n=10$	B+/A− $n=8$	B−/A− $n=10$	B−/A+ $n=10$
Biological parents				
NYS	15.3 (1.4)	14.8 (1.2)	6.7 (1.1)	6.6 (0.8)
	14–18	13.5–17.5	5–5.9	5–7
OS	Student	Student	Worker	Worker
	Physician	Physician	Diverse	Farmworker
		Senior executive	unskilled	Diverse unskilled
Adoptive parents				
NYS	16.8 (2.4)	6.8 (1.2)	6.3 (0.7)	17.3 (1.3)
	14.5–23	5–8	5–7	15–19
OS	Physician	Worker	Worker	Physician
	Senior executive	Small farmer	Small farmer	Senior executive
	Professor	Diverse unskilled	Diverse unskilled	Professor

NYS, number of years of schooling—mid-parent value, standard deviation and range. OS, occupational status of biological and adoptive parents. Groups were composed of children who fulfilled the following conditions: 1, relinquished at birth; 2, placed for adoption at no more than 6 months of age; 3a, born to two high SES biological parents B+; 4a, adopted by two high (A+; the B+/A+ group) or two low (A−; B+/A−) SES parents; or; 3b, born to two low SES biological parents B−; 4b, adopted by two high (B−/A+) or low SES parents (B−/A−). The mean NYS for both biological and adoptive parents corresponds to the minimal NYS between the first year of mandatory education and the level of education attained when leaving the school system (repeated years were not counted). NYS ranged from a maximum of 9 for low SES parents (A− and B−) and a minimum of 13 for the high SES (B+ and A+). Occupations were defined as high or low according to the French Occupational Status Classification Scale[11]. Adopted children B+/A− and B−/A+ changed postnatal environment, whereas control group children B+/A+ and B−/A− were adopted by parents having an SES identical to the SES of their biological parents.

TABLE 2 IQ of adopted children

SES of biological parents		SES of adoptive parents: High A+	SES of adoptive parents: Low A−	
	High B+	$n=10$ $\bar{x}$, 119.60 σ, 12.25 Range, 99–136	$n=8$ $\bar{x}$, 107.50 σ, 11.94 Range, 91–124	113.55
	Low B−	$n=10$ $\bar{x}$, 103.60 σ, 12.71 Range, 91–125	$n=10$ $\bar{x}$, 92.40 σ, 15.41 Range, 68–116	98.00
		111.60	99.95	

An analysis of variance (unweighted means) on full IQ scores indicates significant effects of both biological and adoptive parents SES. Effect of adoptive parents' SES, ($F(1, 34)=7.31$; $P=0.010$), mean difference 11.6 IQ points in favour of children adopted by high SES parents. Effect of biological parents' SES, ($F(1, 34)=13.02$; $P<0.001$), mean difference 15.5 IQ points in favour of children born to high SES parents. The interaction for these two factors is not significant ($F(1, 34)=0.011$). Nevertheless, a partial analysis of B−/A− and B−/A+ subjects is warranted since a directional hypothesis based on results of a previous study[3] can be formulated. The results show a partial effect for the adoptive parents' SES on the IQ of B− children: $t(18)=1.773$; $P<0.05$, one tailed-t-test.

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1. Skodak, M. & Skeels, H. M. *J. genet. Psychol.* **75,** 85–125 (1949).
2. Scarr, S. & Weinberg, R. A. *Am. Psychol.* **31,** 726–739 (1976).
3. Schiff, M. *et al. Science* **200,** 1530–1504 (1978).
4. Scarr, S. & Weinberg, R. *Am. social. Rev.* **43,** 674–692 (1978).
5. Plomin, R., DeFries, J. C. & Loehlin, J. C. *Psychol. Bull.* **84,** 309–322 (1977).
6. Scarr, S. & Weinberg, R. in *Race, Social Class and Individual Differences in IQ* (ed. Scarr, S.) (Lawrence Erlbaum, Hillsdale, N.J., 1989).
7. Schiff, M. *et al.* in *Education and Class* (eds Schiff, M. & Lewontin, R.) 41–54 (Oxford University Press, 1986).

8. Duyme, M. *Devl Psychol.* **24,** 203–209 (1988).
9. Wechsler, D. L. in *Manuel: Echelle d'Intelligence de Wechsler pour Enfants Forme Révisée* (Centre de Psychologie Appliquée, Paris, 1981).
10. Roubertoux, P. & Nosten, M. *Behavl Brain. Sci.* **10,** 36–37 (1987).
11. INSEE, *Nomenclature des Professions et Catégories Socioprofessionnelles* (Imprimerie Nationale, Paris, 1983).
12. Wechsler, D. in *Manuel: Echelle d'Intelligence pour Enfants* (Centre de Psychologie Appliqué, Paris, 1965).

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An essential role for postsynaptic calmodulin and protein kinase activity in long-term potentiation

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THE phenomenon of long-term potentiation (LTP), a long lasting increase in the strength of synaptic transmission which is due to brief, repetitive activation of excitatory afferent fibres, is one of the most striking examples of synaptic plasticity in the mammalian brain. In the CA1 region of the hippocampus, the induction of LTP requires activation of NMDA (*N*-methyl-D-aspartate) receptors by synaptically released glutamate[1] with concomitant postsynaptic membrane depolarization[2–5]. This relieves the voltage-dependent magnesium block of the NMDA-receptor ion channel[6,7], allowing calcium to flow into the dendritic spine[8–10]. Although calcium has been shown to be a necessary trigger for LTP (refs 11, 12), little is known about the immediate biochemical processes that are activated by calcium and are responsible for LTP. The most attractive candidates have been calcium/calmodulin-dependent protein kinase II (CaM-KII) (refs 13–16), protein kinase C (refs 17–19), and the calcium-dependent protease, calpain[20]. Extracellular application of protein kinase inhibitors to the hippocampal slice preparation blocks the induction of LTP (refs 21–23) but it is unclear whether this is due to a pre- and/or postsynaptic action. We have found that intracellular injection into CA1 pyramidal cells of the protein kinase inhibitor H-7, or of the calmodulin antagonist calmidazolium, blocks LTP. Furthermore, LTP is blocked by the injection of synthetic peptides that are potent calmodulin antagonists and inhibit CaM-KII auto- and substrate phosphorylation. These findings demonstrate that in the postsynaptic cell both activation of calmodulin and kinase activity are required for the generation of LTP, and focus further attention on the potential role of CaM-KII in LTP.

Figure 1*a* shows a comparison between the tetanus-induced potentiation of the intracellular excitatory postsynaptic potential (e.p.s.p.) in cells recorded with electrodes filled with normal control recording solution, and cells recorded with electrodes which contained in addition 20 mM H-7, a potent but non-specific kinase inhibitor[24] (see Table 1). Control cells showed robust potentiation at 60 min, whereas H-7 filled cells showed a decremental potentiation which returned to baseline after ~30–40 min. The time course of this potentiation is similar to that seen following extracellular application of H-7 (ref. 21). Figure 1*b* shows that the magnitude of the LTP induced in the cells surrounding those which were impaled, as measured by monitoring field e.p.s.ps, was similar in the two populations of hippocampal slices.

Both CaM-KII and protein kinase C (PKC) have been proposed to play a role in LTP. A number of calmodulin (CaM) antagonists have been reported to block LTP, following bath application, to the entire hippocampal slice[22,25–27]. As was the case with H-7, however, it is unclear whether these compounds acted pre- and/or postsynaptically. To test whether activation of calmodulin in the postsynaptic cell is required for LTP, we recorded from cells with electrodes filled with 0.5 mM calmidazolium. Calmidazolium blocked LTP (Fig. 1*c*) in a manner similar to that seen when cells were filled with H-7. This could not be attributed to the effects of dimethyl sulphoxide (DMSO), the solvent for calmidazolium, as the control cells recorded with electrodes filled with 1% DMSO exhibited LTP. Figure 1*d* shows that the magnitude and time course of the LTP induced in the two populations of slices were again very similar. This set of experiments suggests that activation of CaM within the postsynaptic cell is required for the generation of LTP.

Calmidazolium, however, like other calmodulin antagonists tested on LTP, has actions in addition to its ability to antagonize calmodulin[28,29]. Furthermore, both H-7 and calmidazolium could slowly cross neuronal membranes, making it difficult to rule out absolutely effects on adjacent presynaptic terminals. It was therefore important to examine further the role of postsynaptic calmodulin in LTP using inhibitors of calmodulin that are more specific and less membrane-permeable. Recently a synthetic CaM-binding peptide (CBP), the sequence of which is based on the CaM-binding domain of CaM-KII, has been shown to bind potently to CaM and inhibit the CaM-dependent activation of CaM-KII (Table 1)[30]. In an initial set of experiments, we compared the effects on LTP of intracellularly applied CBP and CTP_2, a control peptide that shares sequence homology with CBP and has a similar isoelectric point, but is not a CaM antagonist (Table 1). For all experiments involving intracellular application of peptides, the same sample of peptide used for electrophysiological experiments was also tested biochemically, as described in Table 1. Figure 2*a* shows that LTP was blocked in cells recorded with electrodes containing CBP, whereas CTP_2 had no apparent effect on LTP. The simultaneously recorded field e.p.s.ps are plotted in Fig. 2*b* and demonstrate that there was no observable difference in the LTP induced in the two populations of hippocampal slices.

If the three N-terminal amino acids are removed from CBP, a peptide is obtained (CBP_{-3}) which has the same CaM antagonistic activity but, unlike CBP, does not block Ca^{2+}/CaM-independent substrate phosphorylation by previously autophosphorylated CaM-KII (Table 1)[30]. Thus, if CBP_{-3} differed from

TABLE 1 Inhibition of substrate phosphorylation

	CaM-KII		PKC
	Ca^{2+}/CaM-dependent IC_{50} (μm)	Ca^{2+}/CaM-independent IC_{50} (μm)	IC_{50} (μm)
CBP	0.090	2.0	>150*
CBP_{-3}	0.090	>150*	>150*
CTP_2	170	>2,000*	—
H-7	20	32	8

The substrates for the two forms of CaM-KII were synapsin I (4–50 μM per assay) or the synthetic peptide MHRQETVDG-amide (single-letter amino-acid code; 15 μM); for PKC the substrate was syntide (15 μM) (ref. 30). IC_{50} values were determined as described previously[30]. The Ca/CaM-independent form of CaM-KII was prepared by autophosphorylation as described[30]. PKC was purified and assayed as described[38], except that chromatography on protamine-agarose was omitted. Final ATP concentration in all assays was 15 μM. The sequence of CBP is MHRQETVDCLKKFNARRKLKGAILTTMLA, that of CBP_{-3} is QETVDCLKKFNARRKLKGAILTTMLA, and that of CTP_2 is ILTTMLATRNFSGGK. CTP_2 was a gift from Ruthann Masarachia.

* No inhibition of kinase activity was observed at this concentration.

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