Is thalidomide mutagenic?

SIR — McBride[1] has suggested a mutagenic mechanism to account for two instances of men with thalidomide-induced deformities having a deformed child among normal offspring. This suggestion was immediately challenged[2–4] on genetic and morphological grounds. Read considered the association unfounded[2] and Smithells[3] specifically cautioned that the McBride hypothesis was without any scientific foundation and should not be allowed to stir up inappropriate anxieties. However, the matter has been taken up by several newspapers, in particular by the UK *Daily Express*, in whose 4 May edition Sewards and Fuller[5] speculated on a possible third-generation effect. The status of thalidomide as an experimental mutagen was not discussed in any of these articles.

Despite a few early, sporadic reports of the posssible mutagenicity of thalidomide to onion root tips and mosquito larvae, most of the limited published literature concerns its non-mutagenicity. Negative *Salmonella* mutation data have been reported by Gordon[6] derived from experiments using a range of metabolizing tissues taken from species sensitive to the dysmorphic action of thalidomide. In a particularly relevant study, Soukup *et al.*[7] reported the absence of an increase in chromosomal aberrations in rat and rabbit embryos exposed to thalidomide *in utero*. However, Roux *et al.*[8] observed positive effects in similar experiments, noting the irregular results that thalidomide often gives in such assays and recommending further studies.

The situation was clouded at an early stage by a curious exchange that appeared in *New Scientist* in 1983. MacKenzie[9] wrote an article entitled 'Secret tests say thalidomide is mutagenic'. The unpublished work of Hagström was claimed to show that thalidomide is mutagenic to *Salmonella* and to the mouse bone marrow. The German manufacturers of thalidomide, Grünenthal, contested this and stated, again in the absence of data, that thalidomide was negative in the *Salmonella* assay, in a mouse bone-marrow micronucleus assay and in a mouse germ-cell mutation assay[10]. The negative germ-cell result is pertinent to the current debate and is consistent with earlier data[11].

At that point (1983) we decided to evaluate the mutagenicity of thalidomide ourselves. We observed negative results in extensive *Salmonella* and mouse bone-marrow assays. Several colleagues from other laboratories also contributed negative data from assays using yeast, fruit flies and grasshoppers. Being consistent with the claims made by Grünenthal, those negative data were not published. However, given the recent interest in this matter we are currently repeating and extending those earlier studies and will publish them in the near future. Pending that, and a formal review of the status of thalidomide as an experimental mutagen, public discussion of McBride's paper[1] should include reference to the responses made to it by Read, Smithells and Kida.

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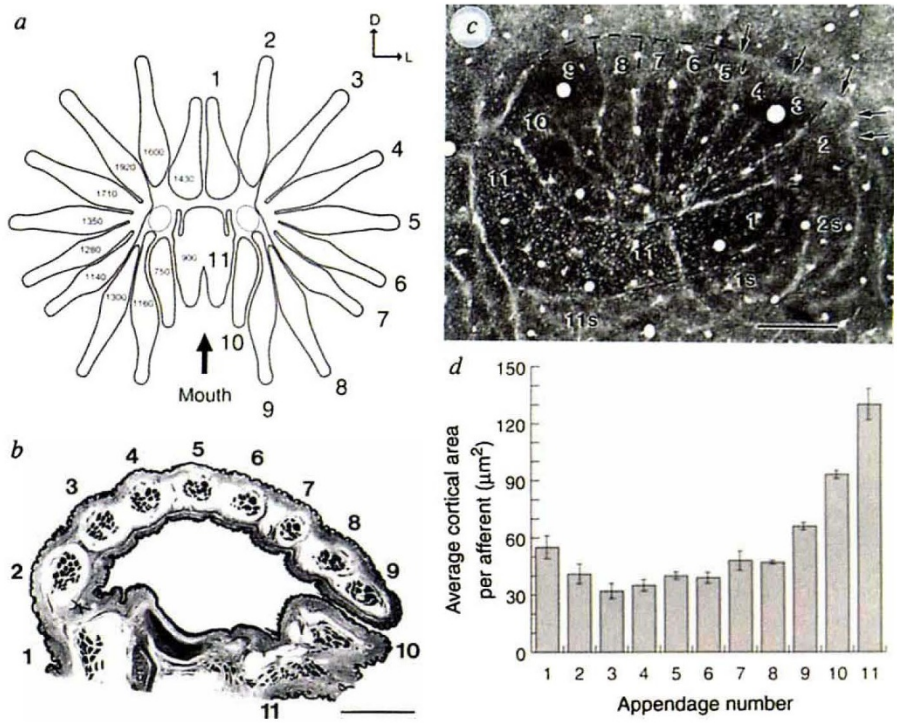
Magnified cortex in star-nosed moles

SIR — The mammalian cortex contains orderly maps of sensory surfaces with disproportionately large representations of behaviourally important areas. Are these enlarged areas proportional to their peripheral innervation densities? In the somatosensory system of rodents, the size of each cortical barrel is directly proportional to the innervation density of the corresponding whisker[1]. It has long been debated whether the large cortical representation of the retinal fovea is similarly a reflection of the increased density of ganglion cells in the fovea[2,3], or is larger than would be predicted from ganglion cell densities alone[4–6]. This question is addressed here by comparing the number of afferents from the nasal appendages of the star-nosed mole (*Condylura cristata*) with the extent of their corresponding cortical representations. The nose of this mole consists of 22 fleshy appendages (see figure), each represented in the cortex by a band visible in cytochrome oxidase



a, Diagram of the mole's nose as viewed from the front. Appendages are numbered 1–11. Left side, number of touch receptors, called Eimer's organs, located on each appendage from a single specimen. Note that the 11th appendage has relatively few sensory receptors on its surface. *b*, A 1-μm section taken caudal to the appendages reveals the 11 nerve branches from the 11 appendages from one half of the nose. There are approximately 50,000 myelinated afferents innervating each half-nose (roughly 4,000–5,000 per appendage). Bar, 1 mm. *c*, Tangential section of flattened somatosensory cortex, stained with cytochrome oxidase, reveals the representation of the 11 appendages. Note the huge representation of the 11th appendage (more than 25% of the nose field). Arrows, septa at the border of the nose field. Bar, 500 mm. *d*, Average cortical area per myelinated afferent for each appendage of the nose (means from four animals). The area of cortex devoted to each appendage is not proportional to the corresponding peripheral innervation density. Appendages 9, 10 and 11, which form an opening in front of the mouth, also have the highest cortical area per fibre. Bars, s.e.m.