J Med Pers (2010) 8:143–144
DOI 10.1007/s12682-010-0066-2

LETTER

A homeopathic remedy showed reproducible effects in murine behavioural models

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Received: 4 May 2010 / Accepted: 12 October 2010 / Published online: 28 October 2010

Dear Editor,

There is a wide debate regarding the scientific basis and the effectiveness of complementary medicines (complementary and alternative medicine, CAM in USA), and of homeopathy as a special case. I would like to let the readership of this Journal informed of some advancements in this field by our team working at the University of Verona composed, in addition to myself as coordinator, by Paolo Magnani, Anita Conforti, Maria Elisabetta Zanolin and Marta Marzotto of the Departments of Pathology and Diagnostics and of the Department of Public Health and Community Medicine. As part of a line of research we have been pursuing for years, we have recently shown that high dilutions of a homeopathic remedy (*Gelsemium sempervirens*) are able to modulate the behaviours and emotional responses of laboratory mice. A detailed report of these results was recently published by the authoritative scientific journal "*Psychopharmacology*" [1], and we believe that it merits attention because it may represent a milestone in the two-centuries lasting—and often conflictual—relation between homeopathy and official pharmacology.

Anxiety and behavioral disorders have a relatively high prevalence in modern society, and consume significant financial resources. The most well-known tranquilisers or anxiolytics are those of the benzodiazepine family, which act by modulating the GABAergic receptors, but many others are known, including buspirone and other drugs which act on the serotoninergic receptors. However, the clinical use of those drugs is not without its drawbacks, particularly due to the risk of side effects such as psychomotor impairment or potentiation of other central depressant drugs. Benzodiazepines are not recommended for long-term treatment of generalized anxiety disorders, due to the associated development of tolerance, cognitive and memory changes, physical dependence, and withdrawal reaction on discontinuation. Natural remedies possessing the same efficacy as conventional drugs, but with fewer side effects, would thus be a valuable addition to the treatment options for anxiety-related disorders. However, the acceptance of alternative remedies has thus far been hampered by the scarcity of pharmacological studies elucidating their indications, limitations and mechanisms of action.

In traditional Materia Medica, *Gelsemium sempervirens* is described as a remedy for a variety of anxiety-like psychological and behavioral symptoms; however, consistent evidence of its efficacy is lacking. Without needless pain or stress (all the studies were approved by the ethical committee), the mice were treated with either homeopathic solutions of *Gelsemium*, conventional anxiolytic drugs, or a placebo consisting of only the solvent (control groups). After 1 week of treatment, the behaviour of the animals was assayed using "ethological" tests which elicit a state of slight anxiety and fear (for example: being kept isolated rather than with other mice, being placed in a brightly lit area rather than in semi-darkness, or finding themselves in a novel environment different from the usual housing cages), and evaluate the movements and behavioural responses of the animals in a standardized manner, through assignment of point scores. With respect to methodology, a procedure was introduced that is only rarely used in animal studies, namely "blind" experimentation. This meant none of the researchers knew which of the remedies was being administered until after the calculations were completed, when the envelope containing the codes was opened. All the tests were recorded on DVD and analysed using the most modern statistical procedures.

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The results showed, in a rigorous and unequivocal manner, through six successive and independent repetitions on groups of eight animals for each remedy or dose, that *Gelsemium* reduced anxiety and fear in a manner quantitatively comparable to the effects of normal anxiolytic drugs, but without provoking any sedation side-effects (which instead did occur with buspirone in that experimental set-up). The effect was observed even with very high dilutions of the remedy, up to the 30th centesimal dilution. These results are consistent with those obtained by a group at the University of Strasbourg, which found that the same homeopathic remedy had a direct effect on rat neurons grown in cell culture plates [2]. It is likely that the mechanism involved is the regulation of production of endogenous neurosteroids through glycinergic receptors.

The chief innovation of this line of research lies in the fact that, until now, nearly all homeopathic remedies had been tested only on humans, but with controversial results. Since these remedies also appeared to work on animal models, this indicates that they do not have merely a "placebo" effect, and that this type of pharmacology using ultra low doses—referred also as "nanopharmacology" [3]—merits further investigation and validation. The fact that the traditional indications for the remedy are consistent with these new, significant laboratory findings helps bridge a gap between two medical disciplines generally considered to be at variance with each other, but which should instead be regarded as complementary and compatible. Of course, further scientific evidence of possible clinical benefits of homeopathy in humans is needed.

Acknowledgments Our work was carried out thanks to a joint scientific collaboration between University of Verona and Laboratories Boiron. The researchers do not have any conflicts of interest.

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