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LETTER TO THE EDITORS

Topiramate-induced weight loss is possibly due to the blockade of conditioned and automatic processes

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Sir,

We read with great interest the paper of Tremblay and others [1] on topiramate's effect on weight, energy balance, appetite and satiety. They studied topiramate-induced weight loss (WL) in obese males who were, however, instructed not to start any diet or exercise program intended to induce WL during the course of the study. Most interestingly, the authors investigated among other things the desire to eat, hunger, fullness and prospective food consumption. The WL that clearly appeared during the study could not be explained by a modification of energy expenditure. In absence of any dietary intervention, a general reduction in food intake was observed in patients receiving topiramate. An anorectic effect of topiramate, as reported for other anti-obesity agents [2] was, then, expected. Actually, no variations were found on hunger, fullness or desire to eat under topiramate treatment.

Thus, as neither appetite nor energy expenditure was affected, other mechanisms underlying the food intake process have to be hypothesized as being affected by topiramate. Eating behavior is not only linked to appetite mechanisms but may largely be maintained by a compulsive and/or an addictive component, both of which are generally associated with environmental cues and automatic processes [3]. These processes have been found to depend on the glutamatergic system, where the activation of the α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor is critical for their expression. The AMPA receptors (AMPAR) antagonists are known to block reinstatement of conditioned and automatic processes [4]. Topiramate has multiple mechanisms of action, including blocking the AMPA/kainate subtype of the glutamate receptor [5]. Given the role of AMPAR in the expression of conditioned responses and topiramate's AMPAR-antagonistic properties, one can hypothesize that topiramate-induced WL, which was not due to modification of energy expenditure nor to an anorectic effect, was possibly mediated by topiramate's effect on conditioned and automatic processes.

This observation is in line with observations on topiramate's effects on various addictive and/or compulsive behaviors such as alcohol addiction [6], nicotine addiction [7], sexual compulsive behavior [8], pathological gambling [9] as well as binge-eating disorder [10]. It could be of high interest to investigate the importance of automatic and conditioned processes in overeating in obese patients who probably could have better response to topiramate treatment.

A further study including an investigation of conditioned and automatic processes in eating, for example by a cognitive and behavioral analysis of eating patterns before and during topiramate treatment, could highlight this subject.

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