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Migraine, Big and Small

The article published by Lipton et al.1 has special meaning to me. First of all, it provides the first scientific evidence for a statement often made by my mentor in headache management, John Ruskin Graham, MD, MACP, that there are two types of migraine, big and small. Dr. Graham, the father of the vascular mechanism of migraine,2 did not believe in the existence of tension headaches. He thought that all headaches were vascular in nature and treated them accordingly, with great success. This particular idea was not based on research but on his vast experience in treating patients with headache, which, by the time of his (final) retirement in 1987,3 spanned half a century. The kind of patients he used to see were very much the same as we see nowadays in a specialized headache practice like my own. They suffer either from severe, episodic headaches or from daily headaches with severe ones superimposed.4 The great majority of them suffer, or suffered at one point,5 from migraine in the traditional sense, with severe episodic headaches associated with nausea, sometimes vomiting or diarrhea, photophobia, photophobia, and occasionally osmophobia. Over the last decade, with the advent of the International Headache Society (IHS) classification,6 when these headaches are mild and lack certain features, such as a pulsating quality or lack of aggravation by physical activity, we have called them "tension-type headaches." Lipton et al have proven this wrong by showing that the so-called tension-type headaches in migraineurs respond to (sumatripant) treatment in the same way as migraine headaches do and, therefore, are, in actual fact, small migraine headaches.

Secondly, I have maintained that the IHS classification lacks biological/clinical validity7 and, therefore, undermines advancement in our understanding of headache. It is a waste of time, money, and effort as well as potentially misleading to study from a biological/clinical perspective a condition, which, as in the classification, is defined purely on arbitrary grounds. In this regard, the Ad Hoc Committee classification8 was more highly evolved; it advanced a vision related to the mechanisms underlying the headaches, leaving room for change that experience and scientific advancement might bring. Lipton et al are again the first to demonstrate scientifically the lack of biological/clinical validity of the condition that is defined as "episodic tension-type headache" in the IHS classification. Thus, we now have two biologically/clinically distinct types of "episodic tension-type headache," identically named and defined, of which one applies to migraineurs1 and the other to nonmigraineurs.9 It is likely that this is but the tip of the iceberg with regard to the problem, which the questionable biological/clinical validity of the IHS classification has presented us with. It is an issue of paramount importance as it may well have already set us back in general in advancing our understanding of headache.
There is, however, also a word of caution that needs to be directed towards the study and, in particular, the statistical analysis applied to it. First of all, the groups are considerably out of balance in terms of the number of headaches included, ranging from 870 in the sumatriptan-treated group to 17 in the placebo-treated group. Secondly, the number of observations for the statistical analysis (N) is the number of patients in each group and not the number of headaches treated by the patients. It is common sense, if not statistical wisdom, that one cannot enlarge N by increasing the number of observations per subject. Otherwise, one could do a valid randomized, double-blind, placebo-controlled study with just 2 subjects, having each of them treat a number of headaches. Interestingly, in the accompanying article by Cady et al., based on the same study and with very much the same authors, statistical analysis was deferred because "...some patients contributed more than one treated attack." If this was the case in the article by Cady et al., which included 92 patients who treated 118 headaches, it is certainly the case in the article by Lipton et al., in which 249 patients treated 1,576 headaches!

Finally, with regard to the article by Cady et al., "early intervention" is not the same as treatment at mild headache intensity. Treatment at that level of headache intensity can take place only when the headache comes on during the day and slowly builds to its maximum intensity. Not uncommonly, migraine headaches develop during the night and awaken the patient or, already at a significant intensity, are present on awakening in the morning. It is important to understand that early intervention in this scenario still relates to treatment of moderate or severe headache. Therefore, rather than "early intervention," it is better to speak of low-intensity headache treatment, in order to avoid confusion. "Early intervention," or rather low headache-intensity treatment, is also not a new paradigm, as some like to refer to it, but has been common knowledge since the (not-so-good) "old days" when the (oral) ergots prevailed. In addition, in the 1970s, Volans provided a scientific rationale for it when he demonstrated that migraine is associated with impaired oral absorption, correctable by parenteral administration of metoclopramide, a gastrokinetic medication. The delayed gastric emptying during migraine was subsequently shown to have a strong positive correlation with the intensity of the headache ($r_s = 0.84$, $P < .01$),13 closing the circle.

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