consequences of surgical incision and rib retraction, and as mentioned in the title, that these results represent "clinical evidence of neuroplasticity contributing to postoperative pain."

Although we agree that the concept of preemptive analgesia is extremely interesting for the understanding and potential improvement of postoperative pain treatment, we find the paper and conclusion of Katz *et al.* to be an overinterpretation of their rather minimal findings.

First, Katz *et al.* accidentally were unlucky in their randomization, since the preemptive group was significantly older than the postincisional fentanyl group. This is a problem because it is well known that pain and postoperative opioid requirements decrease in old age.[2-4] Katz *et al.* tried to remove the two youngest patients from their data set in the postincisional fentanyl group and mentioned that this did not alter the outcome of the statistical analyses, although they did not show exact date. This does not change the fact that the preemptive group was elderly compared to the control group (significant or not significant).

Second, the preemptive group was overrepresented by female patients: 9 of 15 *versus* 3 of 15 in the control group. Katz *et al.* mention this difference to be nonsignificant, but the actual P value is 0.06, which may be of potential clinical significance, since postoperative opioid consumption is less in females than males.[2] Thus, the composition of the patient material in the preemptive group with both more old patients and more females may result in less pain and opioid requirements, thereby hindering interpretation of the study (or, in fact, explaining their results!).

Third, Katz *et al.* used 5–10 ml 2% lidocaine as a test dose but did not provide information about the magnitude of this dose in the two groups. We will postulate that the test dose in fact may provide "preemptive analgesia" and that the exact dose given either should have been similar or at least should have been presented in their results.

Finally, the results on pain and opioid consumption are quantitatively of such a small magnitude that the conclusions, in our opinion, represent an overinterpretation of the data regarding the potential clinical value of their efforts. In this context, other double-blind studies on the potential effects of preemptive analgesia on postoperative pain or need for analgesics have mostly been negative[5,6] or only slightly positive.[7]

Therefore, more well designed studies on effective preemptive analgesic regimens, which may *really* prevent noxious neural impulses from getting into the central nervous system, should be performed. Furthermore, the role of the continuous afferent input during the postoperative period, as long as the inflammatory response in the wound exists, needs to be evaluated. Also, interpretation of the existing literature of preemptive analgesia should be less biased than in the past, thereby clarifying the exact role of and potential for preemptive analgesia to improve postoperative pain treatment.[8]

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In Reply:—Dahl and Kehlet raise four points concerning the results and interpretation of our study.[1] We will address each of these points in turn. First, Dahl and Kehlet suggest that the difference in postoperative pain 6 h after surgery may have been due to the age difference between the groups since pain and opioid consumption have been shown to decrease with age. They make this argument notwithstanding our statement that removing the two patients in group 2, whose ages (22 and 24 yr, respectively) were each more than 2 standard deviations below the mean age of the entire sample of 30 patients, produced a nonsignificant age difference without altering the significant difference in pain or morphine consumption.

To correct any misunderstanding surrounding our results, we pro-

vide the data and results of the tests of significance with these two patients removed. The mean age (± SD) of groups 1 and 2 was 61.8 ± 10.9 yr and 53.5 ± 15.9 yr, respectively ($t(26) = 1.64$; $P = 0.11$). Visual analog scale pain scores at 6 h were significantly lower in group 1 (2.6 ± 1.7 cm) when compared with group 2 (4.4 ± 2.2 cm) ($F(1, 26) = 5.96$; $P = 0.02$), and patient-controlled analgesic (PCA) morphine consumption between 12 and 24 h after surgery was significantly lower in group 1 (11.7 ± 8.4 mg) when compared with group 2 (24.2 ± 16.4 mg) ($F(1, 26) = 6.66$; $P = 0.02$). These results suggest that the differences in pain and morphine consumption are not attributable to age.

Dahl and Kehlet's second point concerns the distribution of males and females in the two groups. We would like to point out that the difference in the number of males and females between the groups did *not* reach the minimum conventional level of significance (*i.e.*, $\alpha = 0.05$) that we and others most frequently adopt. Furthermore, the literature on the relationship between postoperative PCA requirements and sex is by no means as unequivocal as Dahl and Kehlet imply. There are at least two studies that fail to find any significant differences between males and females in PCA opioid consumption after surgery.[2,3] The means and standard errors from our study show that, between 12 and 24 h after surgery, males in group 1 (n = 6) self-administered 13.8 ± 3.5 mg morphine and females in group 1 (n = 9) self-administered 10.3 ± 2.8 mg. Males (n = 12) and females (n = 3) in group 2 self-administered 28.7 ± 6.2 mg morphine and 15.7 ± 6.4 mg morphine, respectively. This pattern of results suggests that there may be an interaction of treatment and sex, but it does not support Dahl and Kehlet's claim of an overall effect of sex.

The third criticism concerns the test dose of 5–10 ml 2% lidocaine that we used and the possibility that this dose may in fact have provided preemptive analgesia. For Dahl and Kehlet to raise this point is somewhat confusing to us, since it is inconsistent to argue that our results are, on the one hand, due to the effects of age or sex (their points 1 and 2 above) and, on the other hand, due to preemptive analgesia (the very point we raise and discuss in our paper). Nevertheless, if we assume for the sake of argument that the test dose of lidocaine was different for the two groups (remembering that there is no evidence to support this assumption), then there are two possibilities.

One possibility is that group 1 received a larger dose that contributed to the density of the epidural blockade at the time of incision (which occurred 85 min after the fentanyl infusion in group 1). We raised a similar point in our paper (page 443) when discussing the possible synergism between the test dose of lidocaine and the subsequent epidural infusion of fentanyl in group 1. We agree with Dahl and Kehlet that, *if* this occurred, the differences in postoperative pain and morphine consumption we observed could be attributed to the combined effects of preemptive lidocaine and fentanyl. Nevertheless, the important point to realize is that the intergroup differences in postoperative pain and morphine consumption occurred long after the clinical duration of action of the lidocaine and fentanyl.

There is, of course, another possibility: namely, that group 2 received a larger test dose than did group 1, which contributed to minimizing the afferent barrage in the former group. That is, the control group also may have benefited from preemptive analgesia. Although unlikely (since more than 65 min had elapsed between the lidocaine test dose and incision as shown in table 2 of our paper), this possibility would add a fourth reason to the three we already outlined in our paper (page 444) supporting our contention that the reduced pain and morphine consumption we observed in group 1 underestimate the true potency of preemptive analgesia.

Finally, in discussing the magnitude of our findings, Dahl and Kehlet question the clinical value of the results and cite the negative results of other studies[4,5] that purport to assess the effectiveness of preemptive analgesia. To this we would respond that the clinical value of a technique should be evaluated first and foremost from the patient's perspective. A technique that reduces postoperative pain and morphine consumption should not be ruled out because the increases in patient comfort and safety it confers does not meet the rather arbitrary definitions of the anesthesiologist and surgeon. Furthermore, the two negative studies[4,5] of preemptive analgesia cited by Dahl and Kehlet have each been criticized on methodologic grounds.[6,7] Based on our results, we stand by our conclusion that preemptive analgesia may attenuate or prevent the development of central sensitization induced by surgical incision and later maintained by inputs from the wound. We agree with Dahl and Kehlet that further studies are needed to determine the factors that contribute to preemptive analgesia.[8]

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