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Jörg B. Schulz

Chief Editor

Journal of Neurochemistry

Ref: Ahluwalia et al., Activation of capsaicin-sensitive primary sensory neurones induces anandamide production and release. J. Neurochem., 84, 585: 591; 2003.

Dear Professor Schultz,

In 2003, we reported in the *Journal of Neurochemistry* (Ahluwalia et al., Activation of capsaicin-sensitive primary sensory neurones induces anandamide production and release. J. Neurochem., 84, 585: 591; 2003) that application of capsaicin (10nM or 100nM) or KCl (50mM) to adult rat cultured primary sensory neurons results in increased anandamide content of the superfusate of the cells. In one of our recent studies, we repeated a part of the experiment we described in that *Journal of Neurochemistry* paper. While we found that application of capsaicin or KCl indeed results in increased anandamide content of the superfusate, regrettably, I have to inform you that our current data indicate that the concentration of anandamide in the superfusate we reported in the *Journal of Neurochemistry* paper must be incorrect.

Based on our current data, we can estimate that the superfusate of 500 cultured primary sensory neurons, after incubating the cells in 100nM capsaicin for 5 minutes, could contain ~ 7 fmol/ml anandamide, in average. However, in the paper we reported

that 250µl superfusate of 500 cultured primary sensory neurons, following 3 minutes incubation in 100nM capsaicin contained 2.07pmol/ml anandamide, in average.

Based on our current data, we can also estimate that 5 minutes incubation of 500 cultured primary sensory neurons in 100nM capsaicin or 50nM KCl results, respectively, in ~47fmol/ml and ~68fmol/ml anandamide in the cells and superfusate together, in average.

Our current data are obtained from two independent experiments, and measurements were done in two laboratories using different machines and conditions (i.e. extraction, solvents, etc). Therefore, I think that our current data indicate the correct range of anandamide that 500 cultured primary sensory neurons could produce following capsaicin or KCl application.

A possible reason for the incorrect measurements, in our previous experiments, could be that instead of anandamide alone, we measured anandamide and other lipid compounds of very similar molecular mass together, because, due to the lack of internal standard and the use of single quad mass spectrometry, we could not differentiate between molecules of very similar molecular mass. Therefore, it appears that the conclusion of the *Journal of Neurochemistry* paper is based on data with a large artefactual component.

In order to correct wrong data in the public domain and maintain our reputation in the field, I believe that we should withdraw the Ahluwalia et al., Activation of capsaicin-sensitive primary sensory neurones induces anandamide production and release. *J. Neurochem.*, 84, 585: 591; 2003, paper.

I contacted all the co-authors regarding the withdrawal of this paper. To date I have received confirmation from three of the co-authors, Professor Stuart Bevan, Dr Laszlo Urban and Dr Mohammed Yaqoob that they support this course of action. I have not

yet received a response from Dr Jatinder Ahluwalia but in light of the experiments we have conducted, I still consider it appropriate to instigate the next steps to proceed with the withdrawal of the paper so we can notify the scientific community of our more recent findings.

I would be grateful if you gave me advice how to proceed.

I look forward to hearing from you.

Yours sincerely,

A handwritten signature in black ink, appearing to be 'Istvan' followed by a stylized surname.

Istvan Nagy