

Dehydroepiandrosterone replacement in elderly individuals: Still waiting for the proof of beneficial effects on mood or memory

Sir,

In the September issue 1998 of this Journal Polleri *et al.* (1) comment on our recent opinion paper, in which we express our critical view of the current state of DHEA research (2). We completely agree with the authors, that long-term treatment studies are needed, although this does not have a bearing on our opinion concerning the (neurosteroidal) effects of DHEA in humans.

Polleri *et al.* leave the readers of the journal with a somewhat skewed view of our position. First, our expectation that DHEA effects should be obvious after two weeks was not only based on electrophysiological evidence but is also supported by a number of animal studies showing immediate effects of DHEA(S) on memory (e.g. 3, 4). In addition other steroid hormones have rapid effects on memory performance in humans. For example we previously demonstrated that a single cortisol administration impairs memory in young subject (5), which fits to the known effects of this steroid on hippocampal plasticity (LTP) as demonstrated in rodents. Second, we pointed out the possibility of intermediate DHEA effects mediated via IGF-I (2). However, only Morales *et al.* (6) observed an increase in IGF-I after three months of DHEA replacement which was paralleled by a decrease in IGFBP-1. Diamond *et al.* (7) observed only the decrease in the binding protein while a recent study by Casson *et al.* (8) reported on a transient increase in the IGF-I to IGFBP-1 ratio after three months which disappeared after six months of treatment. Moreover in this study deleterious effects on high density lipoprotein occurred, thereby pinpointing to possible negative side effects of long-term DHEA replacement (8).

In sum, our studies were aimed to investigate whether the discussed direct neuroactive effects of DHEA are strong enough to produce beneficial effects on cognition in elderly individuals. Our data clearly do not support this idea (2). The hypothesis that positive (indirect?) long-term effects occur after DHEA replacement awaits future experimental demonstration since currently the empirical evidence for this is still weak - at best. This is in sharp contrast to the media "hype" of DHEA in certain countries. In addition, we all should probably be critical about the possible negative side effects of a long-term DHEA replacement.

Last but not least, a note for the protocol: The presentation in Pavia mentioned by Polleri *et al.*, was given by our colleague Brigitte Kudielka - the first author of the opinion paper (Oliver Wolf) is actually a man.

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