

Discussion #3

NICHOLSON, UK: With the authors who are dealing with modafinil and with amphetamines, I felt that quite a large number of the tests were rather mechanical and that issues such as decision making and judgement and interpersonal relations were not assessed. I wonder if they could indicate what their view is of these more subtle effects on performance as far as those drugs are concerned, because both modafinil and amphetamines are, of course, amphetamine-like compounds (in reference to Papers #8, 9 & 10).

CALDWELL, US: We didn't look at a judgement task per se because of the psychometric problems that that entails. If one introduces an emergency procedure into the task a sufficient number of times for subjects to do it consistently, then it is no longer an emergency procedure. So it's hard to know how they would respond to such a task. What was clear was that for those subjects that were on the placebo condition what was often seen were these huge lapses in performance as observed if you broke down the flight performance, for instance, and just graphed how well they were able to maintain altitude for a period of a minute. They seemed to be doing just fine and then there would be this large deviation in performance, then they would get their mind back on the task and correct the problem. In the operational environment, if they're not in one of those lapses when they have to do something; for example, make a quick decision, then maybe they can do it just fine. However, they seem to spend a lot of their time in those lapses once they become sleep deprived, especially in the morning hours between about 4:00 am and 11:00 am. Then there is also the command and control issue of being able to interact with others. I was quite viciously attacked verbally a couple of times by some of our subjects by just simply walking in and saying: "Could you focus on the TV screen a little bit better during

the EEG recordings?" I got yelled at and was told: "I'm doing the best I can, leave me alone." So they can become very difficult to get along with and, often, just withdraw interpersonally from the situation when they are in the placebo condition. In contrast, subjects on dextroamphetamine essentially maintained their performance at a reasonably normal level even though they were significantly sleep deprived.

NICHOLSON, UK: One of the issues with amphetamine that I have noticed over many years - research going on for over 50 years - is that it may have detrimental effects, particularly at high doses. I know of subjects that ingested 30 mg over a period of eight hours - very high doses of the drug - and, although performance on well-learned tasks or mechanical tasks was improved, higher level activities, perhaps, could easily have been prejudiced. That's what worries me most.

CALDWELL, US: There seems to be this concern that people under the influence of amphetamines will respond faster but are not able to think as well about what they want to do. There is very little statistical evidence that that is the case. We certainly didn't see any evidence that people were becoming more careless so that being alert made them awake but yet they couldn't do their job any better. In fact, we saw just the opposite: They were more awake, were able to interact with others and did their jobs better.

JONES, US: I have some comments for Dr Caldwell and, perhaps also, for Dr Nicholson. I too came up in the era when dextroamphetamine was a lot more commonly used than it is today. I was assigned for two years to a base that routinely used dextroamphetamine for fighter squadrons rotating across the Atlantic where they had very early morning rises and then had two or

three or even four mid-air re-fuelings before they landed at dusk. Giving dextroamphetamine to twenty or thirty pilots at a time was an operational commonality in those days. To my recollection, we never had any adverse medical effects. We used 100 mg of secobarbital to help them sleep. Today, I think it was a very poor thing to do, but it did work very well, and we never had any ill effects. The protocol that we used for that operation is given in Keynote Address #2 in which we discuss how we did it, what we did to ground test the fighter squadrons and how we documented it with the squadron commanders and so on. It was also used before the raid on Libya in the mid-80s in an operational setting without any difficulty.

JONES, US: I have some comments/questions for Dr French also. You mentioned in passing that you were developing a series of drug test protocols for the US Air Force. I've had a number of discussions with the US Federal Aviation Agency (FAA) about that because of questions we have about the use of Prozac, Zoloft and other drugs in civil aviation. I wonder if what you are doing could be published as a technical note, perhaps indicating how one can test any drug, and the philosophy behind the use of positive controls. One of the basic scientific questions that needs to be answered is: To what are you comparing the outcome of the drugs? I think that in the use of anti-emetic drugs one should compare the performance to airsick aviators who didn't take the drug. Like the use of dextroamphetamine, the time to use it is when it's more dangerous not to use it. That is, we use it in spite of its side effects because the alternative is even less acceptable. So I wonder if you have any feeling about the performance of very nauseated vomiting aviators doing that task (in reference to Paper #13)?

FRENCH, US: In response to the first question, we have a paper in press on our

Phase I and Phase II studies in Aviation Space and Environmental Medicine. The use of the technique as a drug screen will be published in the RTO Conference Proceedings resulting from this meeting. Your second comment is a very good point. I can think of nothing more disgusting than pilots throwing up while one is trying to measure their performance. Fortunately, I think one can almost guarantee that an effect would be seen because the pilots are completely prevented from being able to respond correctly. It's a condition that we have considered, but decided against, because it would be a little too messy. Perhaps this is something that could be done with animals rather than pilots.

NICHOLSON, UK: Dr French, I think one of the problems of simulation is that it may itself be a relatively insensitive technique compared with working with psychometric tests. So I am rather surprised that, when you moved on to simulation, you didn't need a positive control. I would have thought, because of the complexity of the analysis, that it's much less likely to prove an effect on a simulation and that a positive control was even more necessary.

FRENCH, US: It's a good point. I can't address it because we didn't use it. We have an AWAC simulator at Brooks AFB that would allow us to test team dynamics and team decision making in an information warfare environment. We are planning to add that to our profile for the next compound that we are interested in testing, and we will certainly include a positive control. We felt confident that if the two drugs that we tested (granisetron and ondansetron) had shown us an effect on simple laboratory tests under very carefully controlled conditions, we would have seen it. However, you are correct that we should have used a positive control in the simulator.