Chair’s introduction

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The presentations at this meeting break down into five areas. The first is the characterization and definition of nicotine and tobacco addiction. The second deals with nicotinic receptors. The third involves brain pathways and neurotransmitters involved in nicotine and tobacco addiction. Genetic susceptibility is a fourth issue, and the fifth is medications for nicotine and tobacco addiction.

In terms of characterizing nicotine and tobacco addiction, there are some immediate issues that need discussion. How do we define nicotine and tobacco addiction? In my opinion, resolution of this is something that should be high on our list of priorities. If we look across the range of current definitions, there are disparate elements, factors and dimensions being used.

How do we reduce tobacco and nicotine addiction to studiable elements? Is there a single concept or definition for the disease but various sub-dimensions, the study of which is logical to advance the field and to advance medication development? What cellular or animal models can we use to achieve such advances in basic biology? How can we deconstruct the disease into logical models for human experimental research? And what are appropriate components of the disease in clinical trials?

We need to turn our attention to the full set of nicotinic receptors that could be involved in nicotine addiction. An extensive focus on the mid-brain dopamine system has guided some of the focus on the nicotinic receptor subtypes involved in addictive processes. This is only sensible. As the span of neurochemical targets is broadening, however, we should look at how other nicotinic receptors might be involved. Where is this full set of receptors located in the CNS? How do they influence local CNS function, both at the individual cell level and at the local circuitry level? What are the response dynamics of these receptors when ligand binding occurs?

At the last of these meetings on this topic, 16 years ago (Ciba Foundation 1990), there was clearly a focus on the midbrain dopamine system. This focus has remained, as indeed it has with drug abuse in general. The present meeting affords a good opportunity for us to review where we have been and where we might go with this concept, while at the same time broadening our focus to other neurochemical targets.
What are the new approaches that exist by which we might make progress in understanding neurochemical pathways involved in nicotine addiction?

With regard to genetic susceptibility, the obvious issue is the question of what underlies the high heritability of nicotine addiction. What are the phenotypes of interest? What are the polymorphisms of interest? These relate to the neurochemical substrates that have been discovered. However, we have not yet accounted for all of the variance, and there must be other key elements.

Finally, we come to medications for nicotine and tobacco addiction. Here we need to examine the mechanisms of the various nicotine-replacement therapies that account for their effectiveness. Also, what is their effectiveness? What are the mechanisms of other non-nicotinic medications? Do all existing medications have essentially the same effectiveness? What are the prospects for medications that have a non-CNS base of action, such as a nicotine vaccine or medications that interfere with the metabolism of nicotine? Also, how can we improve the translation of science to practice? Are there realistic ways to proceed today to help move discovery science to development more expeditiously?

Through these five key themes of this symposium, there are a number of overarching issues. The one I would raise at the outset is that we are talking about both nicotine and tobacco. Nicotine addiction may be a large or small part of tobacco addiction. We need to recognize this in medication development. Behavioural influences and sociocultural factors are also important. Is the tobacco-addicted individual in the same situation as a person addicted to cocaine or opioids, for example?

A second issue relevant to the whole is that substantial resources will be needed for us to advance this work. This is an issue both for funding agencies and also for those of us who practise in the field. As a part of the research community, we need to think about ways we can contribute to making progress with existing funding realities. And finally it would be valuable to give some thought to how we as a community can help to effect the substantial agreement that will be required to resolve different points of view? These are some of the questions that I hope we will consider at this meeting.

Reference

Ciba Foundation 1990 The biology of nicotine dependence. Wiley, Chichester (Ciba Found Symp 152)