Seeking new methods to treat heroin addiction

September 26 2013, by Elin Fugelsnes

"Heroin itself is an inactive substance," explains Jørg Mørland, Norwegian forensic medicine and toxicology researcher. "The substances that heroin forms in the body are mainly what enter the brain and cause the narcotic effects."

The heroin high and feelings of pain relief manifest themselves almost immediately after the drug has been injected. Yet it was shown many years ago that heroin is inactive at the opioid receptors in the brain.

So what is it about heroin that brings about such a pronounced effect? A number of research projects funded under the Programme on Alcohol and Drug Research (RUSMIDDEL) at the Research Council of Norway may help to solve the mystery.

"Gaining a thorough understanding of the effects of heroin and of the neurobiological mechanisms involved will be a valuable basis for the development of new treatments for addiction," states Jørg Mørland, who is the project manager of an ongoing project on this important subject, the most recent in a long line of such Norwegian projects which he has headed.

Dr Mørland is a senior researcher at the Norwegian Institute of Public Health and Professor emeritus at the University of Oslo. Through studies on rats and mice, he and his colleagues have come up with new findings that may be significant to the development of new treatment methods.

Heroin metabolises rapidly

One widely-held theory has been that heroin passes quickly into the brain where it is converted into morphine, and that what users are actually experiencing are the effects of morphine. As it turns out, however, heroin undergoes a number of important transformations on its way to the brain. Just a few minutes after injection, the conversion of heroin into the metabolite 6-MAM is almost complete.

"Our research shows that it is primarily 6-MAM that crosses the blood-brain barrier and that heroin as such only enters the brain to a small degree. Thirty minutes after injecting heroin, 6-MAM is the predominant substance both in the blood and in the brain," Dr Mørland explains.

The presence of 6-MAM also results in a sharp increase in the signalling molecule, dopamine, in certain areas of the brain. This plays a pivotal role in the rewarding effect.

"This points towards 6-MAM as the main substance behind all the acute effects of heroin," says Dr Mørland.

"After about an hour, most of the 6-MAM has been converted into morphine. Morphine acts rapidly on the body and is the dominant component for the next hours, but from six to twelve hours after injection the effects observed are mostly consequences of a metabolite formed from morphine, morphin-6-glucuronide.

Looking for a new treatment

"We are working to understand the roles of all these metabolites and to investigate potential treatments to counter their effects," Dr Mørland

states.

The current approach to treating heroin addiction in Norway is pharmacotherapy – using methadone, subutex or subuxone. These are synthetic substances that all work in the same way as heroin, however, and are addictive in their own right.

"The treatment method involves administering these substances over the course of a day to reduce the rewarding effect. The intent is to diminish the patient's preoccupation with finding heroin in order to lead a more normal life," Dr Mørland points out.

Researchers at the Norwegian Centre for Addiction Research (SERAF) in Oslo are examining sustained-release naltrexone – a non-addictive opioid antagonist that blocks the effects of opiates in the brain. Dr Mørland is hopeful that his research will make it possible to affect opiates even before they reach the brain.

An opiate roadblock

"It may be possible to block these substances from ever entering the brain, thereby modifying the effect of heroin," Dr Mørland adds.

As part of a new project, he and his colleagues will study the effect of a 6-MAM antibody developed by a Norwegian company. The antibody binds to the 6-MAM in the blood, making the 6-MAM molecule too large to cross the blood-brain barrier.

"If we succeed in getting this antibody to work it could block much – and maybe even all – of the effect of heroin," the researcher concludes.