Long-term methadone treatment can affect nerve cells in brain

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Long-term methadone treatment can cause changes in the brain, according to recent studies from the Norwegian Institute of Public Health. The results show that treatment may affect the nerve cells in the brain. The studies follow on from previous studies where methadone was seen to affect cognitive functioning, such as learning and memory.

Since it is difficult to perform controlled studies of methadone patients and unethical to attempt in healthy volunteers, rats were used in the studies. Previous research has shown that methadone can affect cognitive functioning in both humans and experimental animals.

Sharp decrease in key signaling molecule

Rats were given a daily dose of methadone for three weeks. Once treatment was completed, brain areas which are central for learning and memory were removed and examined for possible neurobiological changes or damage.

In one study, on the day after the last exposure to methadone, there was a significant reduction (around 70 per cent) in the level of a signal molecule which is important in learning and memory, in both the hippocampus and in the frontal area of the brain. This reduction supports findings from a previous study (Andersen et al., 2011) where impaired attention in rats was found at the same time. At this time, methadone is no longer present in the brain. This indicates that methadone can lead to

cellular changes that affect cognitive functioning after the drug has left the body, which may be cause for concern.

No effect on cell generation

The second study, a joint project with Southwestern University in Texas, investigated whether methadone affects the formation of nerve cells in the hippocampus. Previous research has shown that new nerve cells are generated in the hippocampus in both adult humans and rats, and that this formation is probably important for learning and memory. Furthermore, it has been shown that other opiates such as morphine and heroin can inhibit this formation. It was therefore reasonable to assume that methadone, which is also an opiate, would have the same effect.

However, the researchers did not find any change in the generation of new nerve cells after long-term methadone treatment. If the same is true in humans, this is probably more positive for methadone patients than continuing with heroin. However, the researchers do not know what effect methadone has on nerve cells that have previously been exposed to heroin.

Large gaps in knowledge

Since the mid-1960s, methadone has been used to treat heroin addiction. This is considered to be a successful treatment but, despite extensive and prolonged use, little is known about possible side effects. There are large knowledge gaps in this field.

Our studies show that prolonged methadone treatment can affect the nerve cells, and thus behaviour, but the results are not always as expected. Many more pre-clinical and clinical studies are needed to understand methadone's effect on the brain, how this can result in altered

cognitive function, and, if so, how long these changes last. Knowledge of this is important - both for the individual methadone patient and the outcome of treatment.

More information: Andersen JM, Klykken C, Mørland J. (2012) Long-term methadone treatment reduces phosphorylation of CaMKII in rat brain. *J Pharm Pharmacol.* 64(6):843-7.

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