

BURUNDANGA : MYTH OR REALITY?

Pharmacological analysis about the scopolamine

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MOTIVES

The reasons that drove me to write my Bachelor thesis about the scopolamine, also known as Burundanga, were the different news and urban legends about this. The myths about this drug, affirm that the Burundanga remove the free will and the memory of the people that take it. Other reason that made me declined for this theme was the importance that in my point of view the study of the drugs has to have. In our society is a fact that the people take drugs, and being realistic I think that can be affirmed that the people will take drugs ever, so one of the best way to combat the drug abuse and the effect that can have in the society is to inform the people of the effects that the drugs can have, so in that way the people will be able to make a more accurate choice between taking or not taking drugs.

SCOPOLAMINE PROPIERTES

The scopolamine is naturally found in different plants of Solanaceae family and other plants belonging to the same plant genera. These plants are naturally present around the world and are also used on gardening.

Scopolamine is a muscarinic antagonist structurally similar to the neurotransmitter acetylcholine and acts by blocking the muscarinic acetylcholine receptors and is thus classified as an anticholinergic. Anticholinergic agents, produce cognitive deficits in humans, rats, and monkeys. The scopolamine have different influence in the organisms. High doses of scopolamine have been shown to cause impairment in many cognitive tasks, and therefore interpreting the results is complex. Acetylcholine is widespread in the brain, and therefore scopolamine could potentially impact many different systems.

MUSCARINIC RECEPTORS:

There is a huge amount of studies that reveal the muscarinic acetylcholine receptors play an important role regulating different functions of the central and peripheral nervous system.

The muscarinic acetylcholine receptors belong to the super family of membrane-bound G-protein coupled receptors. There are five types (M1-M5) described and studied. These types are similar, in homology and identity in mouse, rat and human.

The M1, M3, and M5 muscarinic acetylcholine receptors subtypes are positively coupled to the activation of phospholipase C, leading to the release of inositolphosphate second messengers. While M2 and M4 are associated with effector channels such as ion channels and adenyl cyclase.

M1: Plays an important role in the memory and learning processes. Although, a knock out mice for this receptor show normal performance in cognition process, this may be due to the importance of this processes that some compensative processes may be developed.

M3: This receptor has an important role in the contraction of the smooth muscles, the pupil diameter and the salivation. Although that is widespread in all the brain no cognitive impairments have been found in knock out mice.

M5: is mainly found in different peripheral and cerebral blood vessels. A mice with this receptor knock out virtually lose the ability to dilate the cerebral arteries.

M2 and M4: are important in the potassium-stimulated release of acetylcholine in hippocampal.

M4: The autoinhibition of acetylcholine in striatum is mostly mediated by this receptor.

CHOLINERGIC HYPOTHESIS

The cholinergic hypothesis tries to explain the paper of acetylcholine in learning and memory processes. A model has been proposed where acetylcholine is really important in the mode shifting between encoding and retrieval in the hippocampus. With the proposed mechanism, information with high novelty content would induce dynamics in favour of learning the input, while similar to already stored patterns would induce a state that enhances retrieval of previous information.

In this model, which is explained in the, conditions for acquisition of new information are high acetylcholine concentration, and low acetylcholine concentration allow to recall previous memories. That's why encoding is impaired by low acetylcholine concentration and consolidation and retrieval would be affected by high acetylcholine concentration.

Besides the cognition area, the acetylcholine is also related with the optimization of signal-to-noise ratio in the parietal and visual striate cortex, this characteristic is considered really important in the processing of the stimulus. In some experiments in this fields was conclude that the acetylcholine plays an important role in detection and processing of the relevant stimuli and suppression of the irrelevant ones.

EFFECTS - Nonbehavioural

The non-behavioural effects of the scopolamine are mainly three, affects the pupil diameter, salivation and the function of the smooth muscle.

The scopolamine dilates the pupil and impairs lens accommodation this effect is mainly mediated by the M3 muscarinic receptor. Also, the scopolamine can reduce salivation because the muscarinic receptor M3 has an important role in the control of salivation, also the receptors M1 and M5 play a role. Other effect of scopolamine is the way that can influence on the function of the smooth muscle in the respiratory, vascular and gastrointestinal system. In these systems the smooth muscle is likely controlled by the M2 and M3 receptors.

EFFECTS - Behavioural

Stimulus discrimination:
Pharmacological inactivation of muscarinic receptors by scopolamine frequently impairs performance on discrimination tasks. The administration of scopolamine, attenuated sound sequence discrimination learning, flattened the response-gradient distribution in a temporal discrimination task and impaired visual discrimination (probably due to its peripheral effects on pupil diameter and lens accommodation).

Stimulus discrimination is very sensitive to scopolamine treatment. However, it should be noted that not all studies have reported scopolamine-induced discrimination deficits, in favour of this idea is the finding that scopolamine does not impair olfactory discrimination.

Locomotor activity:

The scopolamine in some studies increase the locomotor activity, this may be related to the lack of concentration, because the movements were spontaneous. In the other hand, there are other studies that reported decrease in motor activity.

Antidepressant:

There are studies that indicate that the muscarinic cholinergic receptor system is related with depression. The antidepressant effects mediated by scopolamine were really fast, the patients said that they felt a relief within 24 h. In the other hand, no improvement was observed 150 minutes after scopolamine infusion.

The improvements on the depression symptoms last for more than 2 weeks. The persistence of the antidepressant effect on the body after scopolamine's clearance from plasma (elimination half-life = 2-4 hours) suggests that the mechanism is beyond the direct pharmacological action on muscarinic receptors.

Learning and memory

There are several papers which have analysed the effects of the scopolamine on learning and memory, as well there are different types of memory.

Different studies demonstrate that blocking the muscarinic acetylcholine receptor by scopolamine can interfere in the encoding of new information and the short-term memory, but, in the other hand, has a small effect on retrieval of information that was already stored.

The object recognition memory in rats under the effects of the scopolamine is assessed in different papers. In these studies when the scopolamine was given before showing the sample, an impairment of the object recognition memory is found. Moreover, there is a study suggesting that scopolamine can improve the object recognition if the test is preformatted after the scopolamine injection. One possible reason for this finding is that scopolamine block the interference from other objects, because the scopolamine block the acquisition of the memories of these objects.

In a study in humans the capacity of learning word-pairs is assessed. The conclusions are that the scopolamine impair the encoding of new word paired associates. Moreover, in the study is shown that the scopolamine does not impair the retrieval of previously learned word pairs.

Also in other study the effect of the scopolamine in working memory is shown. The working memory is the capacity that we have to hold in mind and mentally manipulate an information over a short period of time. In this study, a significance disruption by scopolamine is observed. However, there are some studies that have questioned the fact that scopolamine can influence on the working memory.

There are different studies where the study of the scopolamine's effect in anxiety-related memory has been assessed. And is found a relation between the time of administration, if was before training or after, before training had more capacity to impar the anxiety-related memory.

The modification of the fear conditioning by scopolamine is also assessed in some studies. The reports in this area are quite variable, because there are reports which say that scopolamine impairs the context and cued fear conditioning. There are reports that says that scopolamine only impairs one, and there are reports which say that facilitates the fear cued conditioned.

In addition the scopolamine can impaired the spatial cognition

Attention:

Attention is a rich and complex psychological and neurobiological construct. There is ample evidence for the involvement of acetylcholine in attentional modulation. Different experiments show that the increase on the acetylcholine lead to an increase of the attention. The scopolamine modulates the concentration of acetylcholine, that's why scopolamine affect in the attention.

There have been different studies assessing this field, and the reports are different, in a study with humans the scopolamine impair the maintenance of attention. Also in a study with monkeys the accuracy was decreased. Furthermore in a study with rats performing 5-Choice Serial Reaction Time Task increase the number of omissions, but the animals which responded to the trial there was not any drug effect in the correct choice.

Anxiety

It is hard to distinguish the effect of the scopolamine in the anxiety between other effects that can have the scopolamine in the body (i.e. locomotor activity). Nevertheless, in some experiments was found that scopolamine increase the anxiety-related behaviour.



Figure 1: Datura Stramonium

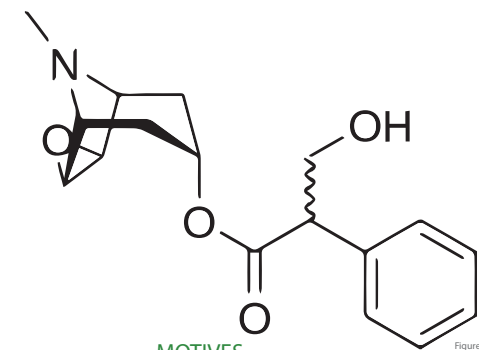


Figure 2

CONCLUSIONS

Seen this summary of effects about the scopolamine, it can be concluded that the scopolamine may make a human loose the memory, because in the different studies that are reviewed different types of memory acquisition are impaired, this possible memory loose would be easier of the memories after the taken of scopolamine, because it's shown that mostly impair the memories after the scopolamine was taken. One thing that it may be important is the dose. But, in order to be able to affirm without doubt that the scopolamine make the humans loose their memory further studies with humans subjects will have to be done.

About the effect of the scopolamine in the free will is hard to arrive to conclusions, because is it right that scopolamine may reduce the fear, and also can reduce the attention. Moreover, the people can get confused because affect the stimulus discrimination. Also the people can have less attention, can control less the motor activity, but from there arrive to the conclusion that scopolamine remove the free will is not possible. As before, further studies should be make in order to asses this possible effect. Moreover, some supposed crimes related with scopolamine are committed in night clubs where the people normally is under the effect of other drugs (i.e. ethanol).

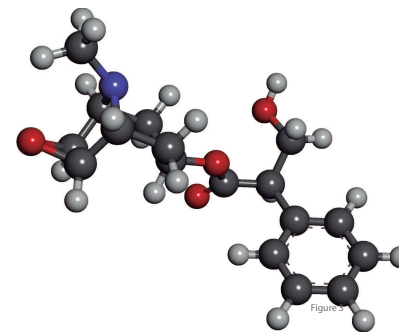


Figure 3

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Figure 2: File:Scopolamine.svg [Internet]. Wikipedia, the free encyclopedia. [citad 31 maig 2015]. Recovered from: <http://en.wikipedia.org/wiki/File:Scopolamine#/media/File:Scopolamine.svg>
Figure 3: File:Scopolamine_structure.png [Internet]. Wikipedia, the free encyclopedia. [citad 31 maig 2015]. Recovered from: http://en.wikipedia.org/wiki/File:Scopolamine_structure.png
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NON BEHAVIOURAL

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ANTIDEPRESSANT

LEARNING AND MEMORY

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