Pharmacological Approaches to Lie Detection: A Review of Scopolamine, Sodium Thiopental, and LSD

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Abstract: This research mainly focuses on ways of lie-detection, especially in the medical area. Three medicines are discussed in this paper, including their histories, chemical structures, functions, etiology and pathogenesis, clinical signs, and effectiveness. Finally, this study compares the effectiveness of these three medicines and compares the medicines to the modern technologies that have been used for lie detection.

Keywords: lie-detection; medication; histories; chemical structures; functions; etiology and pathogenesis; clinical signs; effectiveness; and modern technologies

1. Pharmacological approaches to lie detection

The lie detection serves the determination of lies, detecting the change in examinees' behavior. This passage is a review of the history of using medication to assist in lie detection, as well as the limitations of employing these drugs for this purpose. Fabricating lies included the activation of Dorsolateral prefrontal cortex and ventrolateral prefrontal cortex that serve to produce lies and inhibit real information; the activation of Anterior cingulate cortex that serves to monitor conflicts and error; the activation of Inferior parietal lobule and posterior parietal cortex that serve to search information. The medicines will influence the substance that activate these parts in people's brain which will further affect the procedure of telling lies[1]. To substantiate this passage, several studies have been reviewed that support the lie-detecting medicines. This paper includes the histories of the medicines, which the background information hides behind the pure appearance of the medicines; the functions of the medicines, which contains the specific way for the medicines to disturb human behavior and other relative side-effects; the etiology and pathogenesis, which represents how the medicines' particles interact with substances in human body to achieve the purpose of lie detecting; the clinical signs of the medicines, which shows the direct effects of using these medicines; the effectiveness of the medicines, which compares the utility of different medicines.

In conclusion, this paper establishes the results of the comparison between different medicines for lie detection and appeal indications of ethical factors.

2. Scopolamine

Scopolamine(C17H21NO4) is the first medicine that was considered the "Truth Serum". Scopolamine was manufactured from a plant called Scopola carniolica, a purple-flowered shrub that grows in calcareous soil in damp areas, discovered by a doctor called Giovanni Antonio Scopoli. Later, in the late nineteenth century, a German pharmacologist called Ernst A. Schmidt transferred the plant into medicine, scopolamine. Since this medicine can pass human recognition into narcosis, it has been discussed as an anesthetic for deliveries[2].

A doctor called Robert House, who discovered the lie detection usage of scopolamine when doing delivery, used scopolamine on two criminals. The result was successful. Later, Robert House devoted his whole life to the study of lie detection using scopolamine and even spearheaded the medication interrogation era[2].
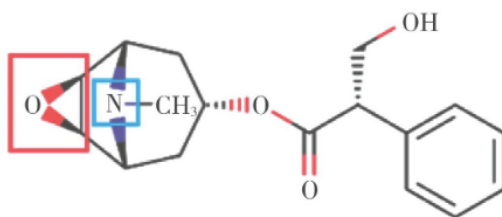

Figure 1. Chemical structure of Scopolamine.

Scopolamine is a type of anesthetic that contains acetylcholinesterase, which is constructed by an ester and alcohol polymer. The epoxycyclone in scopolamine makes it perform unique weak alkalinity and good fat solubility, which makes scopolamine effectively penetrate through the blood-brain barrier. The active center of scopolamine is the quaternary ammonium structure in the molecule, in which the nitrogen on the quaternary structure will form a hydrogen bond with the acetylcholine receptor when scopolamine floats near the acetylcholine receptor, blocking the downstream effect of ACh by competing with ACh for binding with the Acetylcholine Receptor. Since the binding of ACh and AChR participates in respiratory progress, heart rate controlling, and digestive and energy utilization, scopolamine will ultimately affect the nerve network and finally interfere with the ability of recognition, attention, and emotion for human beings[3].

The disadvantage of scopolamine is that it makes the information expressed by the respondent indistinguishable. Because scopolamine will make people over-express information, it is hard for people to identify which are lies and which are the truth. On the other hand, it also has a lot of bad influences. For example, using it with a really small amount will cause a decrease in heartbeat rate, dizziness, headache, and other issues. Indeed, employing scopolamine may cause mirage to human bodies due to damage to the pre-attentive system. Moreover, due to the blockage of the binding of ACh and AChR, the hippocampus will be damaged without opportunities for repairing it. Thus, those who have employed scopolamine may experience diseases relating to memorization, such as Alzheimer's disease[3].
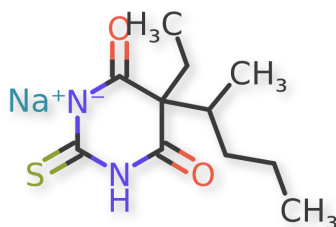
Concerning ethical factors, neither finding data nor doing scientific examinations can be acceptable. The counterinfluences will further impair the human body with non-repairable injuries and ignite drug abuse catastrophically.

3. Sodium Thiopental

Before the occurrence of Sodium Thiopental, the development of anesthesia was surrounded by ether. Being the first clinical anesthetic, ether was flammable and pungent, which caused dizziness for many patients. These unstable and dangerous properties of ether contributed to the advancement of anesthetics, in other words, the appearance of Sodium Thiopental [4].

In 1904, barbiturates entered the clinical area. Being a barbiturate medicine, Sodium Thiopental(C11H17N2NaO2S), a scientist called J. Stephen Horsley found in 1931, could make patients fall asleep quickly, have better feelings during

the operation, and recover faster than other anesthetics[5]. Doctor John Silas Lundy tested Sodium Thiopental on over 700 patients and concluded that most of them fell asleep without counting to 20 seconds. Later, Sodium Thiopental became the monumental checkpoint of the anesthetics area[4]. After being used as an anesthetic, doctors discovered Sodium Thiopental could be used as a method to cure PTSD by helping doctors to evoke the memory hidden in the human mind. The commercial value of this function then transformed the main function of this medicine from anesthetic to lie detection, which later raises ethical problems.
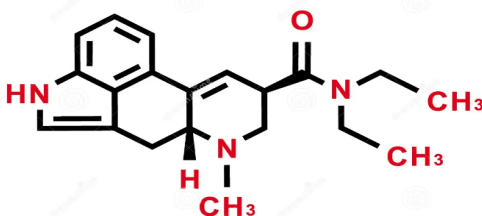
It contains alcohol and, amine polymer. It is weakly acidic because it contains a 1,3-diamino group, capable of keto and enol intermodal isomerism, and secondary ionization in aqueous solutions. Inhibition of synaptic transmission. Sodium thiopental, a noncompetitive gamma-aminobutyric acid type A receptor agonist, promotes the opening of excitatory chloride channels in the postsynaptic membrane [6] leads to hyperpolarization of the postsynaptic membrane and thus blocks inter-synaptic message transmission[7]. Without efficient message transmission, people would be less resistant to outside information interruption and become sensitive to the implications that came from their minds.

Inaccuracy is the reason making it unreliable. Since Sodium Thiopental is a CNS penetrant[6], the message blockage function of this medicine becomes influential to the brain function. In fact, the influence of Sodium Thiopental will make people's brains inert and further cause inaccurate information spoken by the patients that is not even related to reality[5].

4. Lysergsäurediethylamid(LSD)

During the Cold War, Lysergsäurediethylamid(C20H25N3O) appeared. Under the background of the Cold War, with the information concerning Eastern countries holding the technologies of brainwashing, the US government decided to conduct an experiment of human controlling by using medicines including LSD[8]. Lysergsäurediethylamid(C20H25N3O), a type of addiction drug, causes the Hippies movement, was created by Albert Hofmann. This medicine could cause acute hallucination and even trigger mental disorder [9].

After the insertion of LSD, this medicine will be brought to the brain by blood circulation. Since LSD contains an indole ring and a tertiary amine, it contains high fat solubility and an appropriate pKa. LSD then can penetrate through blood blood-brain barrier, in other words, LSD is a CNS-penetrant. When LSD gets into the brain, it serves as a blockage of the neurotransmitter 5-hydroxytryptamine, because 5-hydroxytryptamine is likely to bind with LSD[10]. Since 5-hydroxytryptamine is responsive to cognitive, sensitive, and cognition regulation works, the binding of LSD and 5-hydroxytryptamine will create a disorder that will finally evolve into a mental disorder[11].

LSD

Hallucination and perceptual distortion are the least disadvantages for using LSD. After a hallucination and perceptual distortion, an irreversible mental disorder may appear and torture those who used LSD. Furthermore, LSD is an addictive drug that even caused the Hippie Movement in history. The disaster caused by this drug inhibits the experiment relating to lie detection based on this drug. This could be proved by the action of deleting data retrieved by obligatory experiment from the US government during the Cold War [8].

5. Comparison with modern technology

Since medicines are all unstable and unreliable, new technologies are developed to achieve the lie detection function. These new technologies are recognized as better than using medicine, because new technologies are detecting lies by using methods without any uncontrollable inputs, instead of observing the changes happen in the subjects. These new technologies included polygraph, AI, and EGG.

The most famous method is based on polygraph, which detects the physical change on the subjects' bodies in order to analyze whether the change indicates the truthfulness of what the participants say. Researchers can repeat the process of using this method without harming the participants and incurring high costs.

AI can be specified into different parts, including micro face expression, sound characters, behavior checking, and multimodal models. This method is even more repeatable and has avoided harming participants. This method has been put into experiments in border places in different countries. Including three projects, none of which are stable for realistic usage, but with no harm and trainable properties for the AI method, this method is still promising[12].

EEG, electroencephalography, serves to record the data of the electric signal P300 that is released from the nerve cells in the head. This method has high accuracy in the laboratory and does not cause damage to the human body. Since it is repeatable, this method can be better than medicines. However, due to the restriction of device layout and other hardware problems, this method cannot be adopted widely easily[13]. These methods are all repeatable and more robust than using medicine. With no ethical problems, data can be generated and analyzed. The future of lie detection would be these developed technologies, instead of medicines.

6. Conclusion

Evaluation Criteria	Scopolamine	Sodium Thiopental	LSD
Reliability	Low	Moderate	Very Low
Specificity to Cognitive Function	Low	Low–Moderate	Very Low
Safety & Reversibility	Low	Moderate	Very Low
Susceptibility to Suggestibility	High	High	Very High
Ethical Acceptability	Very Low	Low	Very Low
Overall Assessment	Not suitable	Most practical among the three, but still unreliable	Not suitable
Hallucination	Yes	No	Yes
Addiction Possibility	Low	Moderate	High

In conclusion, standing on the detecting lie's perspective, Sodium Thiopental appears relatively more practical, though still not reliable. According to the graph above, Scopolamine and LSD appear to have low or very low reliability, specificity to cognitive function, and ethical acceptability, and cause hallucination in patients. By contrast, Sodium Thiopental has been used as an anesthetic for a really long time, presents moderate reliability, low-moderate specificity to cognitive function, better ethical acceptability than the other two drugs, and causes no hallucination to patients. Through

these evidences, with the history of using Sodium Thiopental as anesthetic for long period of time, Sodium Thiopental is better than the other two drugs at the area of lie detection.

Based on the fact that these medicines will cause irreversible damage to the human body, using medicines for lie detection is unethical. Scopolamine serves as a blockade of the binding of ACh and AChR that will cause defect on hippocampus and further prompts functional defects on human brain such as Alzheimer's disease; Sodium Thiopental serves as a blockade of inter-synaptic transmission that affects the function of brain; LSD serves as a blockade of neurotransmitter in brain which causes impair on human brain and furthermore attracting relying on it. All of these three medicines lead to a negative influence on the human body, which makes it unsuitable for testing on humans. With such torturing methods for important purposes, allowing the methods will definitely lead to large-scale damage to human beings. The histories demonstrated the inapplicability of the medicines. Using these medicines on criminals or prisoners of war shows the disaster the medicines can bring based on lie detection. During the Cold War, LSD appeared. If the US government had not stopped testing LSD for lie detection, more wars would have appeared later in the world, which no one would have expected.

Exposing humans to medical treatments exclusive to experiments is unethical; this paper can only extract information from historical records, concluding non-decisive results. Whether using these medicines for economic reasons or personal excuses is ethically unacceptable, not only violated the ethical rule of informed consent, but also disobeyed the no-harm rule. Wars brought us nothing but disasters. Taking LSD as an example, this drug was born to be a medicine for helping the mental recovery process, but it finally became an inhumane punishment for those who participated in the war. All of these three drugs have similar endings, becoming inhumane medicines for lie detection and then being banned due to enlightened justice. As technology developed, people should use machines and other ways to conduct experiments that do not cause irreversible harm to the human body and brain, or simply conduct the experiment under the control of official organizations and with the consent of informed participants. Abandoning unethical experiments should be the most important index of research.

Disclosure statement

The author declares no conflict of interest.

References

[1] Christ SE, Van Essen DC, Watson JM, et al., 2009, The Contributions of Prefrontal Cortex and Executive Control to Deception: Evidence from Activation Likelihood Estimate Meta-Analyses. *Cerebral Cortex*, 19(7): 1557–1566.

[2] Reis CL, 1958, In Scopolamine Veritas. *Journal of Criminal Law, Criminology, and Police Science*, 49(2): 137–151.

[3] Tang J, Wang Q, Lei P, 2023, Progress in the Study of the Central Pharmacological Mechanism of Scopolamine. *Journal of Nanjing Medical University (Natural Science Edition)*, (8):1161-1171.

[4] Orkaby A, Desai SP, 2021, The Death of Sodium Pentothal: The Rise and Fall of an Anesthetic Turned Lethal. *Journal of the History of Medicine and Allied Sciences*, 76(3): 294–318.

[5] Gvalani A, 2023, Are Truth Serums Real? *ScienceABC*. visited on December, 20, 2025, https://www.scienceabc.com/eyeopeners/are-truth-serums-real.html

[6] National Center for Advancing Translational Sciences, n.d., 2023, Thiopental Sodium. In *Inxight Drugs*. U.S. Department of Health & Human Services. visited on December, 20, 2025, https://drugs.ncats.io/drug/49Y44QZL70

[7] Anonymous, 2023, Pharmacologic Mechanism of Sodium Thiopental. *39 Drug Safety Net*. visited on December, 20, 2025, https://ypk.39.net/saftydrugs/s12oupls.html

[8] Meier LJ, 2025, Mind Control: Past and Future (Issue 2025-01b). Carr Center for Human Rights Policy, Harvard Kennedy

School.

[9]   Fusar-Poli P, Borgwardt S, 2008, Albert Hofmann, the Father of LSD (1906–2008). *Neuropsychobiology*, 58(1): 53–54.

[10]Liechti ME, 2017, Modern Clinical Research on LSD. Neuropsychopharmacology, 42(11): 2114-2127.

[11]   Rashad W, 2019, The Magic of the Serotonin Receptors. *Psychopharmacology Institute*. visited on December, 20, 2025, https://psychopharmacologyinstitute.com/publication/the-magic-of-the-serotonin-receptors-2496/

[12]   Kalodanis K, Rizomiliotis P, Feretzakis G, et al., 2025, High-Risk AI Systems—Lie Detection Application. *Future Internet*, 17: 26.

[13]   Taha BN, Baykara M, Alakuş TB, 2025, Neurophysiological Approaches to Lie Detection: A Systematic Review. *Brain Sciences*, 15(5): 519.