Scopolamine Intoxication as a Model of Transient Global Amnesia

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In Colombia (South America) during recent decades the administration of scopolamine, extracted from plants belonging to the Datura or Brugmansia genus, has become an important neurologic and toxicologic phenomenon. These extracts have been popularly known as “Burundanga.” Chemical characteristics and clinical features of scopolamine intoxication are described. Anterograde amnesia and submissive behavior found in patients intoxicated with scopolamine are analyzed. Burundanga intoxication is related to other toxic phenomena found in different countries and similitudes with transient global amnesia are emphasized.

The syndrome of sudden amnesia and confusion was first described by Bender in 1956 and has been given the name of transient global amnesia (TGA) (Fisher & Adams, 1964). It is clinically characterized by an abrupt deficit in memory for recent events usually associated with retrograde amnesia of hours, days, and even months, and is generally associated with people over the age of 50. During the episode, the patient maintains a personal identity and can perform everyday activities adequately, although

We express our gratitude to Drs. David A. Gross and Sarah Defier for their careful review of and very valuable comments on this paper. Address correspondence and reprint requests to Dr. Alfredo Ardila, Instituto Colombiano de Neuropsicología, Apartado Aéreo 17021, Bogotá, Colombia, South America.

The word “Burundanga” has an African origin. It appeared in a very popular Afro-Cuban song during the 1950’s. This word has not been incorporated into the Spanish language even in the Caribbean area. We do not know the reason for selecting this particular word to name some Datura extracts.
he/she usually shows signs of anxiety. Awareness of something strange happening is present (Steinmetz & Vroom, 1972; Heathfield, Croft, & Swash, 1973; Caplan, 1985; Kushner & Hauser, 1985; Ardila, 1989). The most outstanding characteristic is very severe anterograde amnesia, which often causes the patient to ask the same question repeatedly. Submissive behavior usually is not mentioned.

TGA has been reported in connection with angiography, migraine, arterial embolism, bilateral infarction of the mesial temporal lobe, and epileptic attacks, among others (Shuttleworth & Wise, 1973; Greene & Bennett, 1974; Fogelholm, Kivalo, & Bergstrom, 1975; Caplan, Chedru, Lhermitte, & Mayman, 1981; Cochran, Morrell, Huckman, & Cochran, 1982; Crowell, Stump, Biller, McHenry, & Toole, 1984; Kushner & Hauser, 1985). Several factors have been proposed in relation to its etiology: Most authors considered it to be a case of a reversible ischemic accident in the region of the posterior cerebral artery with a deficit in circulation in the fornicohippocampal system (e.g., Poser & Ziegler, 1960; Mathew & Meyer, 1974). This explanation has, however, been criticized (e.g., Caplan, 1985).

Some precipitant factors have been related to episode onset, such as emotional experience, fatigue, sexual activity, showers with hot or cold water, anxiety, stress, migraine, pain, and mild trauma (Ardila, 1989; Ardila & Sanchez, 1988; Haas & Ross, 1986; Heathfield et al., 1973; Fisher, 1982; Merriam, 1988). Apparently, TGA has not been reported as a result of toxic agents administration.

The effects of intoxication with extracts derived from plants belonging to the *Datura* or *Brugmansia* genus have been known for many years (Castaneda, 1968; Furst, 1976; Lockwood, 1979). All the species are native to South America, but several are widely cultivated around the world. Writings dating from colonial times indicate that promenades along streets planted with “cacao sabanero” (*Brugmansia candida* or *Datura candida*) represent an excellent treatment for insomnia (Arevalo, 1983).

In Colombia the criminal administration of *Datura* or *Brugmansia* extracts appeared during the 1950s. Since then, these extracts have been known as “Burundanga.” In the early 1980s, pure scopolamine began to be used. Most recently, *Datura* extracts or pure scopolamine have been mixed with tranquilizers (benzodiazepines and phenothiazines) and they have been known as the “new Burundanga.” However, *Datura* intoxication with ritual purposes has been reported in other countries for several centuries (Harner, 1973).

Genus *Datura* belongs to the order Solanaceae together with the mandrake (*Mandragora*), henbane (*Hyoscyamus*), and belladona (*Atropa belladonna*). Each of these botanical agents contains varying quantities of atropine, and other closely related tropane alkaloids (hyoscyamine, norhyoscyamine, and scopolamine), all of which can have hallucinogenic
effects (Harner, 1975). Scopolamine is an anticholinergic drug. Scopolamine blocks the acetylcholine muscarinic receptors; its effect is correlated with the dosage (Goodman, Goodman, & Gilman, 1980). Scopolamine easily crosses the blood–brain barrier, and this explains its efficacy in the central nervous system. Once orally ingested, it is quickly absorbed in the digestive tract and has a large volume at distribution. The majority of the drug is excreted in the urine during the first 12 hr. This rapid excretion explains the difficulty in obtaining positive toxicologic analyses (Brizer, & Manning, 1982).

Dale in 1914 showed that acetylcholine acts at two pharmacologically different receptors, according to the ability of the nicotine and muscarine to activate them. Muscarinic receptors are found in the smooth muscle and in the exocrine glands receiving parasympathetic postganglionic fibers, and represent the majority of cholinergic brain receptors (MacGeer, Eccles, & McGeer, 1978). Using pirenzepine, it has been possible to identify two different subclasses of muscarinic receptors (Hammer, Berrie, Birdsall, Burgen, & Hulme, 1985). M1 receptors have high affinity for pirenzepine and those with low affinity are called M2 receptors. The neocortex has a mixed muscarinic population with 67% M1 and 33% M2 muscarinic receptors. Muscarinic receptors in the caudate nucleus, putamen, globus pallidus, hippocampus, and amygdala nuclei are predominantly M1 (Vanderheyden, Ebiger, Dierck, & Vauquelin, 1987). Atropine and probably scopolamine are M1 antagonists (Mash, Flynn, & Potter, 1985). Increase in the number of muscarinic receptors in the hippocampus of rats has been observed as a consequence of long-term scopolamine administration (Ben-Barak & Dudai, 1980).

Scopolamine intoxication is clinically characterized by midriasis, tachycardia, dry mouth, flushed skin, blurred vision, urinary retention, disorientation, uncoordinated movements, and severe amnesia (Goodman et al., 1980; Brizer & Manning, 1982). Intoxication with other anticholinergic agents produces a similar clinical picture (Hall, Pfefferbaum Gardner, Stickney, & Perl, 1978; Baraka & Harim, 1977). There might, thus, exist a "central anticholinergic syndrome" (atropine psychosis or toxic delirium). This represents a special problem in psychotropic drug prescription; e.g., anticholinergic antipsychotics, anticholinergic antiparkinsonians, anticholinergic antidepressants. However, scopolamine delirium and other anticholinergic deliria might be different.

INTOXICATION WITH BURUNDANGA

Accurate information about the incidence of Burundanga intoxication is difficult to obtain. In Bucaramanga (population about 500,000) the university hospital Ramón Gonzalez Valencia reported 98 cases during 1980-1981 (Peña, Puentes, & Arenas, 1983). Twenty-five cases of Burundanga intoxication were received in the emergency unit of the Social
Security Hospital San Pedro Claver (Bogotá; population about 6 million) during the first 5 months of 1984 (Moreno et al., unpublished). The National Institute of Legal Medicine in Bogotá reported 122 positive toxicologic exams for pure or mixed scopolamine intoxication during June 1988–June 1989 (Moreno, Yomayusa, & Mora-Izquierdo, 1990).

Scopolamine is eliminated very quickly, and rarely are laboratory tests positive. In Peña, Puentes, and Arenas' study (1983), only 50% of the patients tested for scopolamine in urine during the first 10 hr after hospitalization were positive. In the National Institute of Legal Medicine in Bogotá, only 22% of tested cases were reported as positive (Moreno et al., 1989). When laboratory tests are performed, usually more than 12 h have elapsed after the Burundanga ingestion.

In order to study the effects of Burundanga intoxication on memory, a pilot study was carried out at the San Pedro Claver Hospital in Bogotá. Twenty-five consecutive patients (15 men, 10 women; mean age = 28.3, range = 19–48) were received at the emergency unit with the diagnosis of scopolamine intoxication were given the Wechsler Memory Scale (Wechsler, 1945). The testing was performed during the days after admission, when the chronic effect was over, the patient was oriented, and the autonomic changes had disappeared. A matched by age and educational level control group was taken. Although all the scores were decreased in the experimental group, only Logical Memory, Digits, Visual Reproduction, and Associative Learning scores were significantly decreased. This might point to a residual memory deficit after scopolamine intoxication, although longer follow-up testings are required.

Some illustrative cases will be presented. However, as usual in TGA cases, to perform psychometric testing during the amnesic period is very difficult and unlikely. *A posteriori*, a lacunar amnesia extending several hours and even days is usually observed.

**Case 1**

TG is a professional 28-year-old woman. She works in an office for the distribution of pharmacological products. After leaving her office in downtown Bogotá at 11:00 AM, an elegantly dressed man with an apparently foreign accent approached her, asking information about a particular address in the city. She does not remember anything else until 2:30 PM. During this time, from 11:00 AM to 2:30 PM, the following events occurred reconstructed *a posteriori*. She returned to her office, where she was observed to be somehow euphoric by her co-workers. She asked for her salary check, went to the bank, and cashed it. She gave the money to the offender. She went to several automatic cashiers withdrawing money. She went to her home, took her jewelry, and gave it also to the offender. She returned home, where she recovered consciousness at approximately 2:30 PM, at which point she felt anxious and had a headache, dry mouth,
and somnolence, and fell asleep. She was then taken by a relative to a local hospital, where she had a gastric washing. Her urine exam was positive for scopolamine and fenotiazine. At 10 PM she returned home. She remained at home with some somnolence during the following day.

**Case 2**

DE is a 40-year-old male cab driver by profession. The patient reports that a spray was applied to his face by an unknown person; following this, he does not remember anything for approximately 3 hr. When he recovered consciousness, he experienced a headache, nausea, disuria, blurred vision, generalized hyperalgesia, and difficulties in walking. His money and personal belongings had disappeared. He was taken to a local hospital. At the incoming neurological exam, he exhibited photophobia, miosis, tachycardia, generalized hyperesthesia, patellar hyperreflexia, and dermographism; during the exam, he vomited. Lumbar function was reported as normal. Toxicologic exam revealed the presence of scopolamine and phenothiazine. The patient remained at the hospital for 2 days.

**Case 3**

JP is a 16-year-old female high school student. After a serious argument with her father, she disappeared from her house for 1 week. Upon returning home, she was pale and behaved unusually. She reported a headache and drowsiness. A couple of hours later, she was found asleep not responding to external stimuli. She subsequently vomited and had unusual uncoordinated movements according to her family. She was taken to a local hospital. The neurological exam demonstrated that the patient was in a coma, had midriasis with pupils reacting slowly to light, and no response to painful stimulation. She had generalized hypotonia, and bilateral Babinski signs. Gastric washing was performed, and intravenous fluids and diuretics administered. A toxicologic exam reported scopolamine and benzodiazepines. The patient remained hospitalized for a week.

**DISCUSSION**

For centuries plants of the genus *Datura* or *Brugmansia* have been widely used in shamanism and witchcraft (Harner, 1973; Lockwood, 1979). Some morphological evidence, however, points to the fact the *Brugmansia* can be considered a subgenus of *Datura*, although all of the species have been referred as the “Datura trees” (Lockwood, 1979). In the Americas, several *Datura* genus plants have been used in preparing extracts and unguents for ritual purposes (Furst, 1976). Pre-Columbian inhabitants, the Chibchas, administered an extract of a *Datura* species to the widows and servants of a recently-deceased chief before burying them alive with his body (Lockwood, 1979). In Central America, *Datura* species have been widely used to produce unguents with anesthetic properties, and for
producing the feeling of levitation in ritual ceremonies (Castaneda, 1968). It has been proposed that *Datura stramonium* is used in the process for creating the so-called “zombies” in Haiti (Davis, 1988). It is believed that a toxic prepared with a base of tetrodotoxine obtained from a puffer fish (of which there are several species) produces a state of apparent death, during which the victim is declared as dead. The victim can be even buried and quickly “exhumed.” This future zombie is fed during the following days with a paste containing a significant amount of *Datura stramonium*, a plant known in Haiti as the zombie’s cucumber. The victim, in a state of amnesia, disorientation, and even psychotic delusion, is renamed by his captors and maintained in a context of virtual slavery. *Datura stramonium* extracts are further used to maintain the victim in this confusional state.

The clinical picture of intoxication with Burundanga is marked by two main characteristics: (1) the severe anterograde amnesia, and (2) the submissive behavior of the subject. Clinical observation of intoxicated patients with scopolamine disclose strong similarities to patients during TGA. Except for the autonomic changes observed with scopolamine intoxication (midriasis, dry mouth, etc.) both phenomena are quite similar: the patient maintains an apparent behavioral integrity, and he/she presents an abrupt onset of very severe anterograde amnesia. Some excitation and euphoria can be observed in cases of scopolamine intoxication; in TGA, a feeling of strangeness is most frequently observed (Caplan, 1985). This euphoria and sympathetic activation is the reason for mixing scopolamine with tranquilizers. As in the restricted amnesia observed in cases of TGA, a selective action of scopolamine on the hippocampus is suggested.

Brizer and Manning (1982) reported two cases of intoxication with scopolamine that occurred in New York, with some clinical characteristics virtually identical to those we have observed in our patients: they presented dry mouth, blurred vision, and tachycardia. Severe memory disturbances were evident.

Administration of scopolamine is known to interfere with normal memory function (Safer & Allen, 1971; Drachman & Leavitt, 1974). This effect has been related to its blocking action on the cholinergic systems. The cholinergic properties of the hippocampus are well documented (Drachman, 1977). It has been observed that experimental intake of scopolamine produces an impairment in memory performance, involving both storage and retrieval of recently presented information. Scopolamine primarily affects the storage and retrieval of new information rather than the retrieval of previously learned information (Peterson, 1977). Anterograde amnesia is consequently the result. Scopolamine effects are reversed by physostigmine, an anticholinesterase drug (Drachman, 1977). Recently, it has been demonstrated that the administration of scopolamine reduces
the ability to recall and recognize stimuli presented previously (declarative memory), but does not reduce performance in a series of reaction time tasks incorporating a repeating stimulus and response sequence (Nissen, Knopman, & Schacter, 1987). That is, scopolamine affects declarative but not procedural memory. This memory dissociation is clearly observed in cases of Burundanga intoxication.

The most intriguing phenomenon seen in Burundanga intoxication is the submissive and obedient behavior the victim presents. To the best of our knowledge, submissive behavior has not been reported in cases of TGA. The intoxicated person follows any command, does not present any resistance, and offers money and belongings to the offender. Victims return home to pick up additional money. The subject returns to the offender without any attempt to escape. The subject even spontaneously offers to give additional belongings. Sexual abuse has been sometimes found with Burundanga intoxication. Increased susceptibility and the propensity to accept or respond to specific statements have been noted with regard to some Datura hallucinogenics (Tart, 1969; Dobkin de Rios, 1972). This submissive behavior is most probably the result of scopolamine action on the brain structures normally controlling emotional behavior, particularly aggressive behavior. Dream-like dissociative states observed with Burundanga intoxication might seem very similar to temporal lobe fugues. However, the clinical picture observed with Burundanga intoxication may be not only the result of scopolamine action, but also due to benzodiazepines and often alcohol combination (Mickey Finn effect).

In addition to the Burundanga action on the hippocampus that has a cholinergic nature, a selective action on other temporal lobe limbic system structures (very likely the amygdala) should be considered. The amygdala contains several nuclei, which are divided into two main groups: corticomedial and basolateral. The corticomedial amygdala plays a role in the control of aggressive behavior (Verges, 1976) and agonistic behavior in rats (Bolhuis, Fitzgerald, Dijk, & Koolhaas, 1984). The basolateral amygdala presents an excitatory influence on affective attack: its stimulation produces affective attack whereas lesions decrease the affective attack elicited by noxious stimuli (Hilton & Zbrozyna, 1963). The amygdala has a special role in learning about avoiding dangerous stimuli; i.e., it is responsible then for the display of defense responses in cases of attack. Submissive behavior and inability to respond to aggression can be expected in cases of amygdala involvement. Cholinergic neurons mediate most amygdaline nuclei, and important input and output to the nucleus basalis of Meynert are observed (Carlson, 1986).

Consequently, a restricted action of Datura extracts on the limbic system, particularly on the hippocampus and the amygdala, is suggested. Severe anterograde amnesia and submissiveness represent the two most notorious clinical signs of Burundanga intoxication.
Scopolamine intoxication can represent an excellent model for the study of the brain organization of memory and emotional behavior. Its similitudes with TGA are provocative. More careful analysis of patients intoxicated with Burundanga is required.

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