Background

- Plants have been an integral compound in the development of what we know as modern medicine, with written texts concerning medicinal plants dating back approximately 5000 years. Ancient Ayurvedic, Chinese, Arabian, Egyptian, and Sumerian texts all have references to compounds whose indications is to improve cognition. The modern “nootropic” market has grown to include plant and lab-prepared compounds that are unregulated by the FDA. These supplements are available to the consumer regardless of age or education, as evidenced by a Google search for “nootropic store” netting over 2 million results.

What is a nootropic?

- Nootropic, of Greek origin, has a basic translation of “to bend or shape the mind,” also called cognitive enhancers or “cognitive stimulants,” are compounds that both plant and lab derived that aim to improve one’s neurocognitive abilities.  These are both; FDA approved, such as modafinil and methylphenidate, and not FDA approved, such as piracetam, sesame, or ashwagandha.  

- Commonly administered as a pill, but some as a tea, tincture, cream, or ointment.

- With these compounds both referenced as “brahmi” in Sanskrit Ayurvedic literature, there is discord whether “brahmi” is Bacopa monnieri, Centella asiatica, or a combination of the two.

Bacopa Monnieri

- Plant: Water hyssop
- Mechanism of action: Bacoides, the proposed active compound of Bacopa monnieri is proposed to increase GABA and modify “acetylcholine release, choline acetylase activity, and muscarinic cholinergic receptor binding.” Inhibition of acetylcholinesterase has been documented in vitro studies.
- Proposed neuropsychological indications: Greatest effectiveness is proposed in the language neurocognitive domain. Among the many domains that Bacopa monnieri has been proposed to affect learning and memory, attention, and executive functioning are three cognitive domain where Bacopa monnieri has literature to support its claims. Multiple studies, including systematic reviews, randomized, double blind, placebo controlled,iron (crossover) trials, phase 2 trials, open label trials and reviews have shown improvement in language domains, some even obtaining results similar to donepezil. Multiple animal studies1-4 and case report5 show positive antipsychotic properties.

- Do[ing these theoreitical doses demonstrated in studies and not FDA approved]:
  - Adult: Up to 600 mg daily for max 12 weeks.
  - Children: Up to 225 mg for 6 days.
  - Neurological adverse reactions: drowsiness, headache, insomnia, and vivid dreams.

Centella Asiatica

- Plant: Gotu kola or Indian pennywort, is a member of the parsley family.
- Mechanism of action: Theorized to be protective from glutamate-induced oxidative damage and combat build of beta-amyloid. In vitro, activity has been shown at cholecystokinin and GABA receptors.
- Proposed neuropsychological indications: Neutrophilinogenesis, depression, “nootropic activity,” epilepsy, and as a sedative. Randomized, placebo controlled, double blind study revealed improvements in mood and cognitive function, a double blind placebo controlled study reveal anecdotical anesthetics and a paper label study showed improvement in mild cognitive impairment and “well being.”

- Do[ing these theoreitical doses demonstrated in studies and not FDA approved]:
  - Extract or tincture: up to 10 mg daily for 12 months or 1 g daily for 50 days.
  - Dried plant: up to 2.2 g daily for 4 weeks.
  - Also available in creams and ointments.
- Adverse reactions: No neurological adverse reactions found, however night eating syndrome was seen in one case report. Proposed moderate interaction resulting in sedation from increased effect of central nervous system depressants.

Bacopa monnieri and Centella asiatica use as a Possible Nudivs for Psychosis?

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Case Report

Chief Complaint: Trying to figure out what my memories are

HPI: 22-year-old Caucasian male presents for voluntary psychiatric hospitalization, at the prompting of his mother, with symptoms including poor sleep, paranoia, and religious preoccupation. Utilizing Bacopa monnieri 5 g daily for six months and an unknown amount of Centella asiatica daily. Reports taking these medications to feel “unbend and calm,” promote “neuromasticity,” and help “figure out what my memories are.” Reports 3-4 hours of poor sleep night and poor appetite. Describes eructomatic delusions, paranoia, thought disorganization, religious preoccupation and passive suicidal ideation with no plan or intent. Endorses delusions of reference involving social media posts from old friends that he believes are speaking directly to him, becoming fixated on these individuals. Reports significant anxiety with rumination, intrusive, and raking thoughts described as “obsessive.” Self reports a down and sad mood, though denies feelings of worthlessness or hopelessness. Negative for past manic symptoms or hallucinations.

Current Medications: Only taking nootropic supplements

Past Psychiatric History:

Diagnoses: Major Depressive Disorder, Generalized Anxiety Disorder and Attention Deficit Hyperactivity Disorder, and Dyslexia.

Medication trials: escitalopram, paroxetine, bupropion, alprazolam, lidocamfetamine and amphetamine/dextroamphetamine mixed salts

Family Psychiatric History: Maternal and paternal anxiety

Social History: Has a bachelor’s degree and currently is an intern. He is single with no children. Denies all substance use including illicit drugs, tobacco and alcohol.

Diagnostic Testing:

Vitals (at intake): hypertensive (145/87), otherwise unremarkable.

Labs: U/L, COVID-19, TSH, CMP, and CBC were unremarkable.

Imaging: CT head was unremarkable.

Mental status exam: Patient was disheveled with slow rate of speech and flat affect. Reported eructomistatory delusions, paranoia, delusions of reference. Thought process was illogical and disorganized and he was perseverative. Fair insight as he was aware of his symptoms but unable to discern whether his delusional thoughts were reality. Appeared internally preoccupied and repeated questions before responding. Fair memory as he recalled some but not all biographical information. Endorsed passive suicidal thoughts with no plan or intent.

Assessment: Working diagnoses included Unspecified Schizophrenia Spectrum and Other Psychotic Disorder and Substance/Medication-Induced Psychotic Disorder, ruled out social suicidal thoughts.

Clinical Pearls

- Nootropics are widely available but not FDA-approved or regulated
- Patients may seek out nootropics as a less burdensome and less expensive route to treatment (Figure 1)
- Routine screening for nootropic and other supplement usage is important as part of a psychiatric assessment
- Nootropic use, especially beyond typical dosing ranges, may contribute to psychosis and other psychiatric symptoms

References


Discussion

Patients may not understand the ramifications of using widely available over the counter nootropics. While some of these compounds have been used for millennia, many do not have established pharmacologic properties. Furthermore, the sellers of nootropics advertise the proposed effects of the compounds using verbiage such as “quality,” “pure,” and “guaranteed.” Many also provide dosing guidelines, while stating that the Food and Drug Administration has not assessed these compounds. Lastly, these sellers do not typically list adverse effects of their products.

When applying this to our patient, he was ingesting levels of Bacopa monnieri and Centella asiatica well beyond recommended doses. With theoretical or controversial mechanisms of action for these compounds it is difficult to explain how they would influence psychotic symptoms. GABA has been seen to be in higher levels in actively manic patients, with each of these compounds being linked to elevated levels of GABA or binding to GABA receptors. Was our patient experiencing a mixed episode? Or did the Centella asiatica’s possible increase of dopamine lead to psychotic symptoms? Without well vetted pharmacokinetics and FDA oversight, we are unable to point to any one etiology. Thus, we present this case to highlight a possible connection between Bacopa monnieri or Centella asiatica and psychotic symptoms. We hope to add to the body of literature on the compounds while encouraging providers to inquire about usage in their own patients.

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Figure 1. Patient dilemma of a lengthy and costly route to FDA approved medications or widely available inexpensive nootropics

No indication for medications

Primary care

Corentin A. 

Testing and lab work

Primary care or specialist

FDA approved medications