## Intro

A few people I've talked to lately have been interested in learning more about intranasal insulin ("**INI**"), which led to me tweeting about it, which led to my inbox being absolutely flooded with requests for more info so I'm putting this short doc together. The goal is just to provide a simple and balanced high-level overview summarizing some very dense blog posts and studies so you don't have to read those and I can give people a single link instead of rambling at them like a lunatic. This doc is a work in progress, and over time I hope to expand it to include all of the major studies including their findings, duration, dose, and my thoughts on the conclusions.

INI became fashionable on nootropics forums and subreddits about 8 years ago for its cognitive effects. I am fairly risk averse when it comes to experimenting with biohacking, but began using INI myself about a year ago when dealing with severe brain fog after getting COVID. **I believe this to be extremely safe based on the current research, which I will summarize later along with my own experiences, but I'm not a health expert. It's obviously an unusual thing to do and you should absolutely not take my word for it. This is provided purely for informational purposes.**

If you want more in depth explanations, I recommend the following from a biohacker blog called Lostfalco:

- The Benefits of Intranasal Insulin and How to Make It Legally at Home Without a Prescription
- Intranasal Insulin: A Revolutionary New Treatment for Alzheimer's
- Intranasal Insulin Studies on Cognitive Enhancement, Alzheimer's, Traumatic Brain Injury, Etc.
- Rodent Study: Intranasal insulin improves cognitive deficits, ameliorates defective brain insulin signaling, strongly reduces β-amyloid (Aβ) production and plaque formation, and enhances hippocampal neurogenesis
- What types of intranasal insulin have been used in the scientific studies?
- Is Intranasal Insulin Safe?
- Is Zinc in Intranasal Insulin Safe?

These are a bit old so some image links are broken, and they are missing a few more recent studies, but still remain some of the best overviews of the topic written in normal non-jargon language. Lostfalco is both very smart and much more willing to do risky things with his body than I am. I take what he writes with a grain of salt, but it's a great research resource and I rely on research review for determining my own safety profile.

## Protocol

**Items required:**

1. Novolin R. It looks like this:


2. A nasal spray bottle that meters 10 IU, or 0.1ml, per spray.
   I prefer this one because the nozzle helps to get a good angle when there is less liquid at the bottom.
3. Small pliers, the type that would be on a multitool. Underneath that orange plastic cap is a metal ring that holds down a piece of rubber. When used for injectables you would stick a needle through the rubber, but we need to remove the cap to pour the insulin into our spray bottle. It's a bit finicky the first time but you get used to it.

Pour the insulin into the spray bottle and seal the lid. spray into the air to make sure you're getting a good flow before using. Always keep your Novolin refrigerated. If traveling it will be fine at room temp for a bit but if it gets warm it will start to break down. This will not present any danger but will reduce effectiveness.

**Where to source Novolin R**

In the US, by far the easiest way to get Novolin R is at a WalMart pharmacy. They charge $20-25 per vial and will sell you up to 3 at a time without a prescription or even health insurance. You just need to make sure they give you the vials and not the pen injectables. Each vial contains 1000 IU, so at a 20 IU per day dose this will last you 5 months and cost about $10-15 per month.

CVS, Duane Reade, Walgreens, Costco, Rite Aid, and Amazon Pharmacy all have Novolin R for $50-65 per vial. I have heard they sometimes also run out more quickly than WalMart but that's anecdotal. Although it is 3x the cost, it's pretty cost effective especially for something you may only do for the short term, so if you live somewhere like NYC where these are much easier to access than WalMart it's probably worth just going and seeing if they have it in stock.

**How to start using INI**

As mentioned before, this should not be used as a casual nootropic and I am providing this info to help others with chronic brain fog, cognitive degeneration, traumatic brain injuries, or other forms of neuroinflammation - so they can research for themselves whether to try this, and do it safely if they decide to do so.

If you decide to try INI:

- Day 1: Take a partial spray to test for allergies
- Day 2: Try 1 full spray (10 IU) in the morning
- Day 3: 1 full spray in the morning and 1 in the evening

You can stay there or work your way to a higher dose if you feel you need it. If you want to be extra careful you can eat 10g of carbs or sugar along with it although hypoglycemia was not reported in any studies, even at higher doses. It's a pretty strange smell at first and stings a bit; I grew to sort of enjoy it.

**Is INI safe?**

Doses up to 160 IU have been tested for as long as 18 months without any reports of severe adverse effects that I have seen. The only side effects I have seen reported are some sporadic cases of rhinitis (aka nasal irritation) and mild dizziness.

Based on all of the available literature, short term use done properly is incredibly safe. With this being said, you should absolutely not do this over the long term until more studies come out. This works best as a short term way to moderate neuroinflammation from specific causes, or at the very least something you cycle on and off.

## Research Summary

There is a lot of specific research that I would like to summarize here eventually, but will start with a broader summary and a bunch of links. There are a  bunch of ongoing studies and research projects going on now as well, and I will try to keep tabs on those as they come out. As with many cutting edge therapies, especially to do with the brain, the results are broadly positive but a bit over the place when it comes to replication, etc. Certain positive effects are seen in specific demographic sections, ages, or are missing from people who carry a specific gene. The good news is that the safety profile for short to medium term use seems quite airtight, which means that you can feel relatively comfortable in trying it for yourself and seeing if it has positive effects or none at all. It is also much more accessible than many other promising treatments that may require a prescription, be prohibitively expensive, or not available at all in certain countries. As will be obvious, I partially used GPT (o1-preview) to generate this summary of the studies I provided it. I have other shit to do but will come back to this at some point and flesh this section out.

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**1. Cognitive Enhancement and Improvement on Cognitive Tests**

**Memory and Cognitive Function:**

- **Healthy Individuals:** Several studies have demonstrated that INI can enhance memory consolidation and recall in healthy adults. For instance, a double-blind, placebo-controlled study showed that participants receiving INI performed better on verbal memory tests compared to those receiving a placebo.
- **Mechanism of Action:** INI is thought to enhance hippocampal activity, a brain region crucial for memory formation, by increasing insulin levels directly in the central nervous system without affecting peripheral insulin levels.

**Attention and Executive Function:**

- Participants using INI have shown improvements in attention span and executive functions, including better performance on tasks requiring sustained attention and quick decision-making.

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**2. Reduction of Diet- or COVID-Induced Neuroinflammation and Brain Fog**

**Neuroinflammation Reduction:**

- **Diet-Induced Neuroinflammation:** High-fat or high-sugar diets can lead to neuroinflammation, contributing to cognitive deficits. Animal studies indicate that INI can mitigate these effects by reducing inflammatory markers in the brain and improving insulin signaling pathways.
- **COVID-19-Related Brain Fog:** Emerging research suggests that COVID-19 can cause neuroinflammation leading to brain fog and cognitive impairments. While direct studies on INI's effects on COVID-19-induced brain fog are limited, the anti-inflammatory properties of INI may offer potential benefits. INI could theoretically reduce neuroinflammation by modulating cytokine production and improving neuronal resilience.

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**3. Reduction of Risk for Alzheimer's Disease and Dementia**

**Alzheimer's Disease (AD) Intervention:**

- **Improved Insulin Signaling:** Impaired insulin signaling in the brain is a feature of Alzheimer's disease, sometimes referred to as "Type 3 diabetes." INI has been shown to enhance insulin signaling pathways in the brain, potentially slowing AD progression.
- **Amyloid-beta Plaque Reduction:** Studies have found that INI can decrease the accumulation of amyloid-beta plaques, a hallmark of AD pathology, by promoting their clearance and reducing their production.

**Clinical Trials:**

- **Memory Improvement in AD Patients:** Clinical trials involving AD patients have reported that those treated with INI showed stabilization or improvement in memory tests over several months compared to declining performance in placebo groups.
- **Delay in Cognitive Decline:** Some long-term studies suggest that INI may slow the rate of cognitive decline in individuals with mild cognitive impairment (MCI), a precursor to AD.

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**4. Regulation of Mood and Appetite**

**Mood Regulation:**

- **Depression and Anxiety:** Preliminary research indicates that INI may have mood-stabilizing effects. By enhancing insulin signaling in brain regions associated with emotion regulation, INI could potentially alleviate symptoms of depression and anxiety.

**Appetite Control:**

- **Satiety Enhancement:** INI has been shown to influence the hypothalamus, a brain region that regulates hunger and satiety. Studies report that INI administration can lead to reduced appetite and decreased caloric intake in healthy adults.
- **Weight Management:** Due to its potential to suppress appetite, INI is being explored as a therapeutic option for obesity management.

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**5. Positive Effects on Metabolism and Blood Sugar Levels**

**Metabolic Regulation:**

- **Peripheral vs. Central Effects:** While INI does not significantly affect peripheral blood glucose levels, it can influence central metabolic processes. By acting on brain regions that regulate metabolism, INI may improve insulin sensitivity and energy homeostasis.
- **Improved Glucose Tolerance:** Some studies suggest that INI can enhance whole-body insulin sensitivity, leading to better glucose tolerance, which is beneficial for metabolic health.

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**6. Reduction of Cerebral Insulin Resistance**

**Enhancing Insulin Sensitivity in the Brain:**

- **Mechanism:** Cerebral insulin resistance is associated with cognitive decline and neurodegenerative diseases. INI directly delivers insulin to the brain, bypassing the blood-brain barrier, and can restore insulin sensitivity in neuronal tissues.
- **Cognitive Benefits:** By reducing cerebral insulin resistance, INI may improve neuronal function, synaptic plasticity, and overall cognitive performance.

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**7. Prevention of Type 1 Diabetes via Immune Modulation**

**Immune System Interaction:**

- **Autoimmune Response Modulation:** Type 1 diabetes is an autoimmune condition where the immune system attacks pancreatic beta cells. There is emerging research on the potential of INI to modulate immune responses.
- **Immune Tolerance Induction:** Some studies propose that INI may promote immune tolerance to insulin-producing cells by presenting insulin to the immune system in a way that reduces autoimmune activity.

**Clinical Trials:**

- **Preventative Measures:** Early-phase clinical trials are investigating whether INI can delay or prevent the onset of Type 1 diabetes in high-risk individuals, particularly in children with a family history of the disease.

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**8. Neuroprotective Effects**

- **Traumatic Brain Injury (TBI):** INI has been shown to reduce neuronal damage and improve functional outcomes in animal models of TBI by decreasing oxidative stress and inflammation.
- **Stroke Recovery:** Preliminary studies suggest that INI may enhance recovery after ischemic strokes by promoting neurogenesis and angiogenesis.

**Psychiatric Disorders**

- **Schizophrenia and Bipolar Disorder:** Research is exploring INI as an adjunct therapy for psychiatric conditions, with some studies indicating potential benefits in cognitive deficits associated with these disorders.

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## Mechanisms of Action

**Blood-Brain Barrier Bypass:**

- **Direct Delivery:** INI allows insulin to be delivered directly to the brain by bypassing the blood-brain barrier (BBB), which insulin struggles to cross when administered peripherally (e.g., through subcutaneous injection). Because INI delivers insulin directly to the central nervous system with minimal absorption into the bloodstream, it minimally impacts peripheral blood glucose and insulin levels. This means that it does not significantly alter blood sugar levels or increase the risk of hypoglycemia (low blood sugar), which is a common concern with systemic insulin administration.

**Neuronal Function Enhancement:**

- **Synaptic Plasticity:** Insulin plays a role in synaptic plasticity, essential for learning and memory. INI enhances insulin availability in the brain, supporting these processes.

**Anti-Inflammatory Effects:**

- **Cytokine Modulation:** Insulin has anti-inflammatory properties, and INI can reduce the production of pro-inflammatory cytokines in the brain.

## Conclusion and Future Directions

Intranasal insulin presents a promising avenue for treating a variety of neurological and metabolic disorders. The ability to deliver insulin directly to the central nervous system opens up potential therapeutic strategies for conditions previously considered challenging to treat.

**Ongoing Research:**

- **Large-Scale Clinical Trials:** More extensive and longer-term clinical trials are underway to confirm the efficacy and safety of INI in different populations.
- **Combination Therapies:** Researchers are exploring the use of INI in combination with other treatments to enhance therapeutic outcomes.

**Considerations for Use:**

- **Medical Supervision:** It is crucial to use INI under medical guidance to ensure appropriate dosing and monitoring.
- **Personalized Medicine:** Future applications may involve tailoring INI treatments based on individual genetic profiles, disease states, and specific metabolic needs.

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## References

For those interested in exploring the research further, here are some key studies and reviews:


- Intranasal insulin improves memory in humans
- Intranasal insulin therapy for Alzheimer disease and amnestic mild cognitive impairment: a pilot clinical trial
- Intranasal Insulin for Alzheimer's Disease
- Effect of intranasal insulin on cognitive function: a systematic review
- Role of Insulin in Neurotrauma and Neurodegeneration: A Review
- Efficacy of intranasal insulin in improving cognition in mild cognitive impairment or dementia: a systematic review and meta-analysis
- Intranasal insulin enhances brain functional connectivity mediating the relationship between adiposity and subjective feeling of hunger
- Intranasal Insulin Administration to Prevent Delayed Neurocognitive Recovery and Postoperative Neurocognitive Disorder: A Narrative Review
- Intranasal Insulin: a Treatment Strategy for Addiction
- A Comprehensive Review of Intranasal Insulin and Its Effect on the Cognitive Function of Diabetics
- Hot Spots for the Use of Intranasal Insulin: Cerebral Ischemia, Brain Injury, Diabetes Mellitus, Endocrine Disorders and Postoperative Delirium
- Intranasal insulin ameliorates neurological impairment after intracerebral hemorrhage in mice
- Safety and efficacy of intranasal insulin in patients with Alzheimer's disease: a systematic review and meta-analysis
- The effect of intranasal insulin on appetite and mood in women with and without obesity: an experimental medicine study
- Intranasal Insulin Improves Age-Related Cognitive Deficits and Reverses Electrophysiological Correlates of Brain Aging