Finding the optimal dosage for nootropic agent Noopept: An analysis of available literature

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Abstract

Noopept is a novel nootropic agent with various potential uses: as a neuroprotective agent, as a memory enhancer in older people with mild cognitive impairment, and as a way to significantly increase wakefulness and focus. However, recommendations for the correct dosage of Noopept rely largely on animal studies and anecdotal data, as well as rough estimates based on comparisons to less potent Piracetam. This article will attempt to draw together all available evidence regarding proper dosing of Noopept to arrive at a more precise and safer figure for users of this nootropic.

Keywords: Noopept, Noopept dosage, nootropics, cognition, cognitive decline, memory, focus

1. About Noopept

Noopept, more properly known as N-phenylacetyl-L-prolylglycine ethyl ester, is a synthetic nootropic first synthesized in Russia, where it was initially (and sometimes still is) referred to as GSV-111.

Noopept is a widely used nootropic agent. Often wrongly described as a racetam, Noopept is a compound similar to but chemically distinct from Piracetam. However, comparisons between the two compounds are apt; Noopept has similar effects to most racetams [1] – including Piracetam – but is drastically more potent, requiring just a fraction of the dose to achieve the same effects.

Today Noopept is widely available for purchase around the world. Few jurisdictions list Noopept as a controlled substance. It is commonly used by a variety of demographics, particularly college students and young professionals in cognitive demanding jobs.

However, Noopept is far from a safe nootropic substance. Dosing Noopept is difficult. The compound is much more potent than most nootropics; users typically find that just 10mg is enough to produce significant effects. There is also a dearth of robust human clinical trials done on Noopept. Most recommendations regarding correct dosing of Noopept are extrapolations from animal studies and anecdotal reports from users.

2. What does Noopept do?

Noopept is unusual among synthetic nootropics in that its mechanism of action is quite well understood. All of Noopept's nootropic effects result from the fact that it is a prodrug of cycloprolylglycine. Cycloprolylglycine is a neuropeptide which has two primary neurological functions: stimulating the release of Brain derived Neurotrophic Factor (BDNF) and potentiating various neurotransmitter systems.

2.1 Noopept and BDNF

The main benefits of Noopept are the result of the drug's ability to increase the release of Brain Derived Neurotrophic Factor, or BDNF. This is a neurotrophic factor responsible for governing the growth, differentiation and proliferation of neurons, synapses, and the dendrite branches which connect them. Increased levels of BDNF lead to greater rates of brain cell structure growth, maintenance and proliferation, while decreased expression of BDNF stifles brain cell structure development.

Clinical trials have found that Noopept significantly increases the expression of BDNF in the brain by increasing

levels of cycloprolylglycine [2]. Cycloprolylglycine is a neuropeptide which directly triggers the release of BDNF in the human brain. So Noopept has a somewhat indirect effect on BDNF; it stimulates cycloprolylglycine release, which in turn stimulates the release of BDNF.

This is important for a number of reasons. The clinical evidence makes it abundantly clear that increasing BDNF levels reliably improves almost every aspect of cognitive performance, including memory recall and retention, attention, focus, mood, and long-term brain health. This maps onto the effects reported by Noopept users; generally users report enhanced learning capacity while on the drug.

While some researchers have posited that increasing BDNF expression may help reduce the severity, or possibly even the incidence, of degenerative brain disease, it is unclear how BDNF would be implicated in diseases such as Alzheimer's Disease or dementia which are often caused by vascular restriction and myriad other problems. However, the role played by BDNF in neuronal restoration means Noopept has at last some potential as a treatment for degenerative brain disease [3].

2.2 Noopept and AMPA receptors

Another mechanism of action proposed for Noopept is that of AMPA receptor agonist. AMPA receptors are glutamate receptors. Glutamate is the principle excitatory neurotransmitter in the human body. By acting on AMPA receptors, Noopept increases nerve excitability. This greatly increases perceived mental energy, alertness, focus, and reaction times.

It must be said that Noopept is not chiefly known as a stimulant or fatigue reducing supplement. The effect of Noopept on AMPA receptors has not been properly validated by robust clinical trials with large numbers of participants. Yet it remains an interesting potential effect of this popular nootropic.

3. Issues with Noopept dosing

Supplementing with Noopept is commonplace, but safety concerns are significant. Not only is Noopept a synthetic nootropic designed to treat specific cognitive impairments, but safe dosing recommendations for Noopept are far from well established.

The problem with the dosing guidelines for Noopept is not the substance itself, but rather a marked lack of targeted scientific investigation. As it stands, the standard dosing recommendation for Noopept of 10-30mg per day is almost entirely derived from limited studies that did not investigate lower doses. What's more, these studies have typically been limited to a small number of participants with measurements taken over 30 days or less. This hardly constitutes a good yardstick for judging the safest and most effective dose of Noopept for people to use on a daily basis. A better approach is to amalgamate long-term user dosing data for Noopept and compare it to outer dosing limits established by human and animal trials of sufficient duration.

3.1 Establishing a correct dosage for Noopept

The current recommended dose for Noopept is 10-30mg per day for most users. However, most of the available clinical literature on Noopept talks of doses measured in mg/kg. In terms of balancing efficacy with toxicity, this is a far more useful way of dosing a drug than simply having a blanket recommendation.

In one good animal study [4], for instance, Noopept is dosed at 0.1mg per kg of bodyweight. Here, researchers found that 0.1mg/kg was a highly effective dose for improving learning and reducing anxiety in older male and female rats. It is worth quoting the findings here in full:

"In the period from 8th to 20th day, both drugs (Noopept and Piracetam) suppressed the horizontal and vertical activity and the anxiety in test animals as compared to the control group treated with 0.9 % aqueous NaCl solution. Early postnatal injections of the nootropes influenced neither the morphology development nor the behavior of adult female rats in the plus maze, extrapolational escape, passive avoidance, and pain sensitivity threshold tests. Animals in the "intact" group (having received neither drugs not physiological solution, that is, developing in a poor sensor environment), showed less pronounced habituation in the open field test as compared to the control and drug treated groups."

In some higher quality human trials, clinicians have given participants 0.5-1.2mg/kg of Noopept. Interestingly, one trial [5] found that 0.5-0.7mg/kg of Noopept per day was effective for enhancing memory while the higher dose of 1.2mg/kg did not (the even larger dose of 10-20mg/kg was also effective although potentially dangerous). Importantly, the 0.5-0.7mg/kg dose range was found to be safe and well tolerated by all users in the trial. It is worth quoting the paper in full:

"Effective doses were 0.5-10 mg/kg. Experiments on a specially-developed model of active avoidance (massive one-session learning schedule) showed that GVS-111 stimulated one-session learning after single administration, while after repeated administration it increased the number of successful learners among those animals who failed after initial training. In this respect, GVS-111 principally differs from its main metabolite cycloprolylglycine and standard nootropic piracetam."

In practical terms, this would give us a 30mg dose for a 60kg individual. While this is in line with many of the doses

used in clinical trials, it does not match what we see from the anecdotal data reported by users. Of course, this data is far from reliable, but it is meaningful. Many regular users of Noopept take no more than 10mg per day and report significant cognitive benefits. New Noopept users have long been devised to begin with 10mg per day and increase the dosage slowly over time when some degree of tolerance is evident.

No human studies have used more than 30mg of Noopept per day for any meaningful length of time. As such, 30mg per day represents a good outer limit for Noopept dosing. However, there seems to be no reason to ever approach 30mg per day. The best clinical trials indicate that Noopept has rapidly diminishing returns when doses increase. One study found that larger doses actually perform worse than lower doses by a significant degree. The lowest dose that this trial tested was 0.5mg/kg, which would give a 30mg dose for a 60kg individual. Looking at the other data, it seems highly likely that an even lower dose would deliver similar, if not more pronounced benefits while reducing the risks of side effects as well as lowering end user costs.

The lowest Noopept dose used in an animal study is 0.1mg/kg. For a 60kg person, this produces a dose of 6mg. For many people this is a sufficient dose to produce meaningful cognitive enhancements. The standard 5mg tablets of Noopept do indeed produce sizeable effects in most users, particularly new users, those with a relatively low body weight, and those with a low tolerance for the drug.

So, it appears that the standard recommended range for Noopept dosing of 10-30mg is perhaps too generous. A dosage range of 6-20mg is more appropriate for most users, with 30mg/day being the absolute maximum dose to stay within safe limits.

3.2 Noopept cycle length

The longest trial on Noopept conducted to date, on humans, lasted for 56 days [6]. There are no clinical studies examining the effects of prolonged Noopept usage. There is no reliable clinical data on the effects of chronic, long-term Noopept use in people of any age at any dose.

4. Conclusion: What is the ideal Noopept dosage?

When amalgamating the data on Noopept dosing, it becomes clear that 30mg represents a sound upper limit on what constitutes a sensible dose for an individual seeking cognitive enhancement. The vast majority of users should experience significant benefits from 10mg per day of Noopept, with some needing to raise this to 20mg per day depending on tolerance, body weight, metabolism, etc.

Animal studies have found that 0.1mg/kg is sufficient to produce significant cognitive improvements (or 6mg per day for a 60kg individual). This is the ideal dose to start at for new users, rising to 10-20mg/kg as required, with 20mg being a good safe upper limit for all body weights.

In terms of the ideal length of a Noopept cycle, the clinical studies currently available do not extend beyond 56 days (these trials found no severe adverse effects). Given the popularity of Noopept and the length of time it has been widely available, long-term side effects or health risks are unlikely. However, until long-term trials are done, 56 days represents the longest safe Noopept cycle. A cycle of this length, using 10mg per day, should be followed by at last 60 days abstinence for a maximum of three cycles before an extended break from the drug is taken.

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