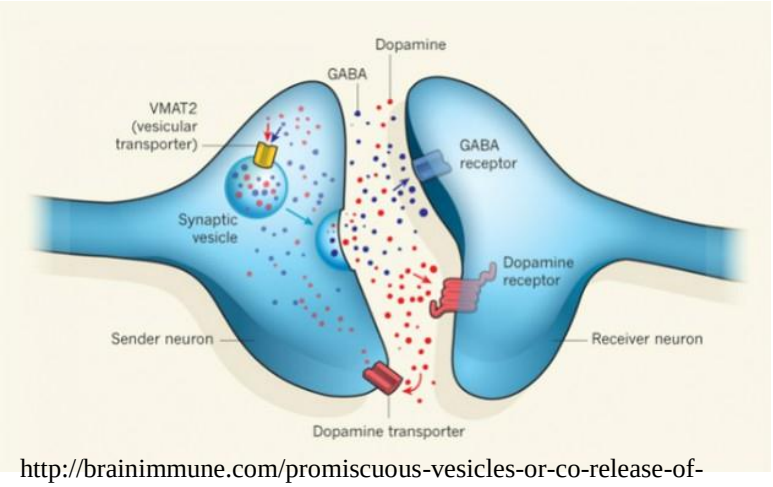
Gamma Aminobutyric Acid



http://brainimmune.com/promiscuous-vesicles-or-co-release-of-dopamine-and-gaba-in-the-brain/

Gamma Aminobutyric Acid (GABA) is a major neurotransmitter that is present in the central nervous system. It is considered an inhibitory neurotransmitter. Inhibitory neurotransmitters bind to specific GABA receptor sites on neurons. When this binding occurs, it decreases the ability of those neurons to become excited or "fire".

GABA receptor binding substances are common in human and equine medication. Often they are prescribed in cases of muscle disorders such as muscular sclerosis and as sedative/anti-anxiety medications. Example representative drugs with effects on GABA receptors include baclofen (Gablofen™), diazepam (Valium™), and etofoxine (Stresam™). It is important to note that these drugs do not contain GABA they merely work on the same receptors as endogenous GABA.

GABA is an endogenous substance found in all mammals. Accordingly, it was necessary to determine the normal concentration range in race horses.

GABA and Racing Integrity

GABA has been identified as being used on race day in several jurisdictions through records seized from veterinarians. Often, GABA is administered as a part of a substance called "Carolina Gold". It is believed that this substance is often given at or around Lasix time. The purported use is to calm a horse prior to a race so that it remains calm through the paddock and even into the post-parade.

To date, there is only one published study examining the effects of this substance on horses.[1] The researcher administered 1650 mg of GABA to 16 exercised thoroughbreds. Post administration, several select potential pharmacodynamics effects were investigated – specifically, heart rate, step count, distance of muzzle to ground, and gastro-intestinal effects.[2] For each of these parameters, no appreciable effects were noted.[3] While this was a very thorough study, it was by no means exhaustive – and the potential for other pharmacodynamics effects certainly exists.

Regardless, the administration of an intravenous medication on race-day, with the exception of those specifically allowed, is prohibited in every racing jurisdiction. No United States racing jurisdiction allows the administration of exogenous GABA in the 24 hours prior to post time.

GABA and Animal Welfare

Currently, there are no studies examining potential effects or side effects of the use of exogenous GABA. It is not an FDA approved drug for use in animals or humans. Moreover, an administration of GABA as Carolina

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[1] Knych, H.K., *et al., Endogenous concentrations, pharmacokinetics, and selected pharmacodynamics effects of a single dose of exogenous GABA in horses*, J. Vet. Pharmacol. Therap., 2014 March 12, doi: 10.1111/jvp.12146 [epub. ahead of print].
[2] *Id.*
[3] *Id.*

Gold preceded the sudden death of a show pony in December 2012.[4] Additionally, in one horse administered GABA by USEF representatives, several adverse effects were noted including shaking and near collapse.[5]

GABA has been declared a banned substance by the United States Equestrian Federation.

Setting a GABA Threshold

First and foremost, the RMTC had to ensure that the laboratories were able to attain good agreement for testing. Accordingly, the RMTC performed an administration study with the University of California Davis Maddy Laboratory. The samples obtained were used to create a ring test among laboratories. Samples were retained by the Maddy Laboratory and offered to three other United States racing jurisdiction laboratories, the USEF, France Gallop, and British Horseracing Association laboratories. All but one of the laboratories agreed to participate. All laboratories followed the published methodology referenced above. There was good agreement among the laboratories that participated.

Once good agreement among the labs submitting samples was obtained, the RMTC requested that various jurisdictions share results they had. Two jurisdictions provided samples that they had obtained. From those two jurisdictions, 325 horse samples were provided – the majority of those being from post-race testing. The samples were from a mixture of Thoroughbred horses, Standardbred horses, and Quarter Horses. The post-race samples were collected absent any regulatory control of GABA.

The raw data was not normally distributed. The mean of this data was 41.24 ppb. The standard deviation was 16.41 ppb. If we treat this as normally distributed data, which was discussed by the SAC, calculating the internationally accepted 1 in 10,000 probability of a false positive for a naturally-occurring substance, a threshold concentration of 102.27 ppb results. This value was rounded up to 110 ppb further decreasing the probability of a false positive. Like cobalt, this is similar to the approach used for TCO2. The recommended threshold errs on the side most advantageous to horsemen and trainers.

By comparison, the log transformed data – which still is not normally distributed but is closer to a normal distribution than the raw data yields similar results – the resultant recommended threshold using this analysis is approximately 76 ppb. Both the raw data and log transformed histograms are attached to this document.

Prior to this study, only one other laboratory had described normal GABA concentrations in the United States.[6]

GABA Recommendation

The RTMC SAC committee members reviewed the GABA administration data as well as the raw data in person and via conference call. After reviewing this information, the SAC committee members in attendance voted unanimously in favor of the following recommendation:

- GABA should have an endogenous threshold set at 110 ng/mL in plasma/blood and
- GABA was recommended as a Class 3 substance with a Penalty Category B.

The RMTC Executive Committee was vested with authority to approve this threshold by the RMTC Board and did so unanimously.

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[4] http://www.nytimes.com/2012/12/28/us/ponys-death-draws-notice-to-drugs-in-show-ring.html?_r=0
[5] *Id.*
[6] That laboratory was invited and chose not to participate in the ring testing for GABA. Accordingly, the results of their study, even had they been provided, could not be accepted.