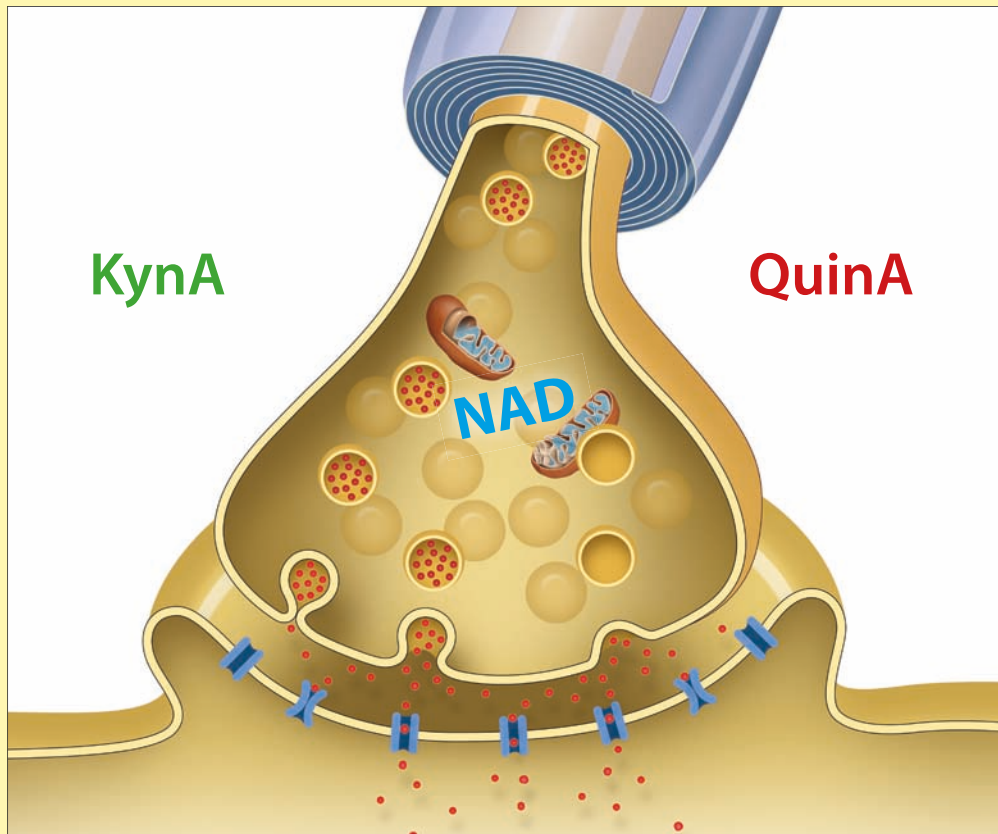


Tryptophan Metabolism



Tryptophan – an essential amino acid for health

- ▶ Indication: Depression and Neuro-Inflammation
- ▶ Diagnosis: Differential Diagnostics for Depression with and without Inflammation
- ▶ Therapy: Homeostatic levels for Kynuric acid, Quinolic acid and Kynurenine improve the Symptoms

Tryptophan metabolism – more than just serotonin

Tryptophan is today already used as a dietary supplement to support sleep and well-being, because 100% of the **serotonin** we produce comes from this essential amino acid.

Tryptophan is also the basis for two other vital substances produced by the body:

- About 45% of **nicotinamide adenine dinucleotide (NAD)** comes from tryptophan. NAD can therefore not simply be produced by absorption of a possible precursor, niacin (vitamin B3). NAD as the intermediate storage for hydrogen is essential for mitochondria. Without NAD, mitochondria cannot function and therefore cells cannot grow¹.
- **Kynurenic acid** is a super substance as it acts as a neuroprotector, antioxidant and mitochondrial growth factor. It controls (i) the function of our nervous system, to be more precise: it throttles the excitation at the glutamate receptors², it is (ii) a potent antioxidant and thus protects against radical oxygen³ and it is (iii) a true mitochondrial growth elixir and for example it stimulates fat burning⁴.

All substances therefore contribute very strongly to our well-being. For example, if tryptophan and kynurenic acid are missing, depression is threatening. This has been proven in a number of studies^{5,6,7,8}. At the same time, there is a risk of long term damages in cases of kynurenic acid deficiency, that can lead for example to Alzheimer's disease at an advanced age⁹.

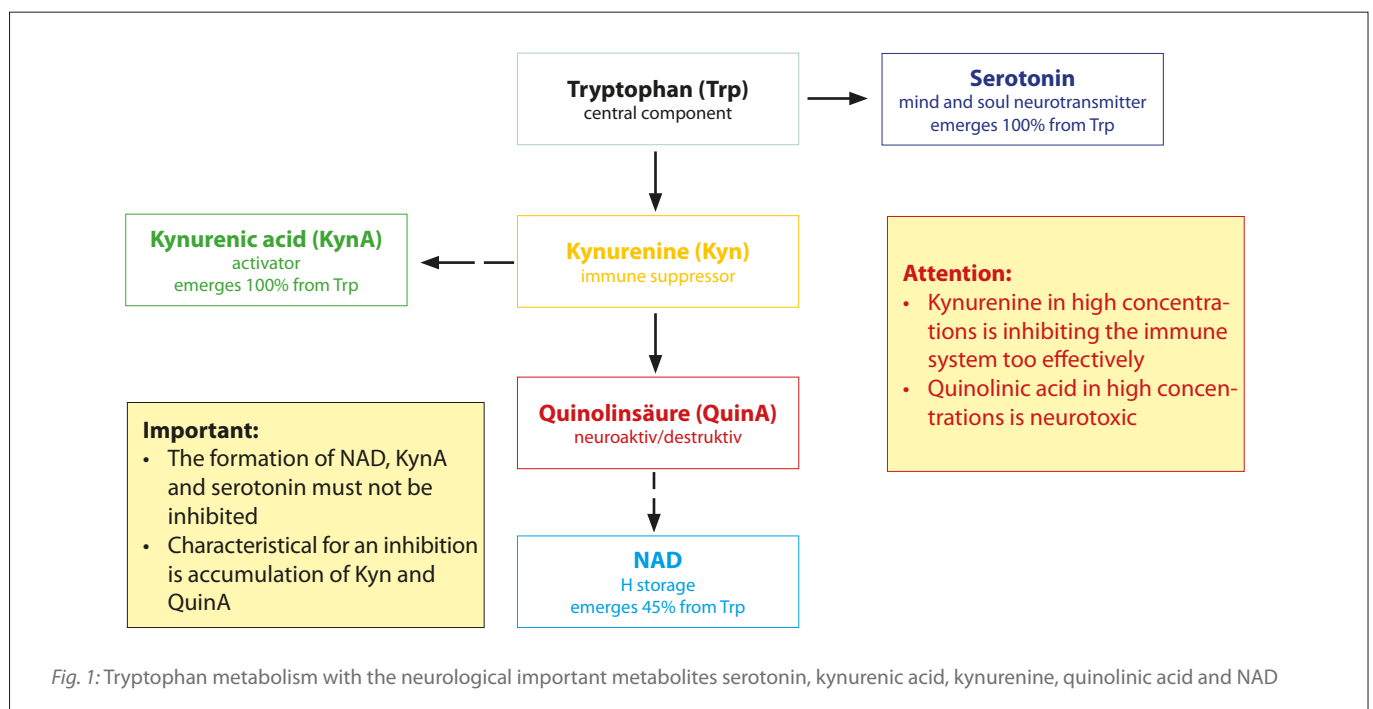
Disorders in the tryptophan metabolism

In case of inflammations, the tryptophan metabolites **kynurenine** and **quinolinic acid** play a central role.

Kynurenine is produced in the course of inflammation and is valuable as an immunosuppressant. In too high concentrations, however, it blocks our immune system and increases the risk of cancer and bad progressions in viral diseases.

Quinolinic acid has a neurotoxic effect and is a strong oxidizing agent. It damages the nerve tissue and is therefore for instance a risk factor for multiple sclerosis¹⁰ or Parkinson's disease¹¹.

Figure 1 shows the tryptophan metabolism and points out possible misalignments^{12,13,14,15}. In the case of excessive synthesis of kynurenine and quinolinic acid the formation of serotonin and kynurenic acid decreases. At the same time it is observed, that less NAD is formed, while quinolinic acid is excreted increasingly in the urine. This leads to a deficiency condition for kynurenic acid, serotonin and NAD in the central nervous system, which causes both misdirected stimulus transmission and an energy deficiency. In addition, quinolinic acid, due to its toxicity, causes disturbances in the CNS control loops.

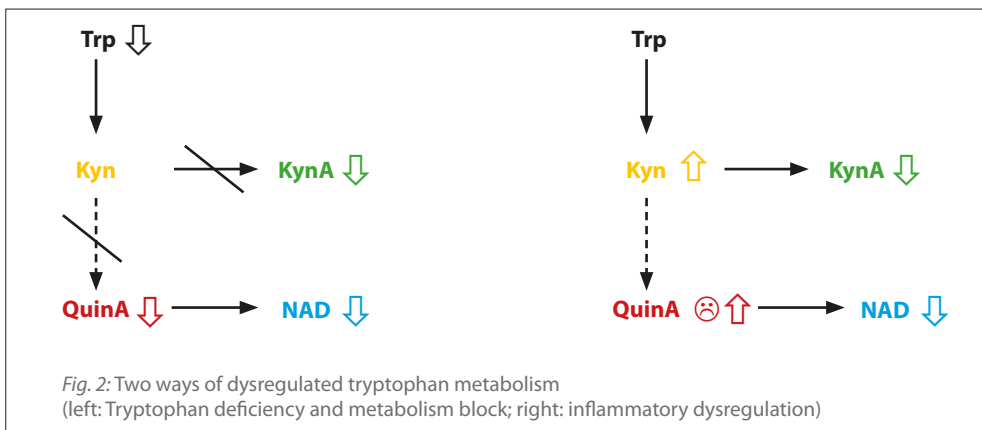


How can I detect malfunctions in the tryptophan metabolism?

By determining the tryptophan and kynurenine levels from serum and the formation of the ratio Kyn/Trp on the one hand as well as the determination of kynurenic acid and quinolinic acid and the formation of the ratio QuinA/KynA, on the other hand a malfunction of the tryptophan metabolism can be detected and therapeutic consequences can be concluded (see below).

We recognize two patterns:

1. *a lack of tryptophan and kynurenic acid **without pronounced inflammation***. This deficiency can be caused by a poor tryptophan supply, vitamin B₃ or B₆ deficiency or poisoning of relevant metabolic enzymes caused by metals^{16,17} or plasticizers¹⁸.
2. *a deficiency situation **resulting from inflammation*** in which the ratio Kyn/Trp or the ratio QuinA/KynA is increased. This is typical in primary diseases such as cancer or persistent infections¹⁹, but also with rheumatoid arthritis²⁰, multiple sclerosis²¹ or chronic inflammatory bowel disease²².



Which therapeutic intervention makes sense?

From this diagnosis possible conclusions with complementary medicine drugs can now be drawn:

1. in the case of tryptophan or kynurenic acid deficiency without clear inflammation, tryptophan and vitamin B administration²³ including a positive control of the formation of kynurenic acid by omega-3 fatty acids^{24,25} are indicated. At the same time a possible poisoning has to be clarified by diagnostic and countermeasures are to be considered in the given case.
2. in the case of simultaneous inflammation, i. e. with an increase in kynurenine or kyn/trp ratio or increased quinolinic acid or quinolinic acid/kynurenic acid ratio a tryptophan administration is only advised after the administration of substances which lower quinolinic acid and as well kynurenine, such as curcumin^{26,27}, resveratrol²⁸, or berberine²⁹. The administration of omega-3 fatty acids can in parallel, favourably shift the ratio of quinolinic acid to kynurenic acid³⁰.
3. in both cases sport is a good therapy: by regular training the formation of kynurenic acid from kynurenine is stimulated in the muscles³¹. At the same time kynurenic acid acts against quinolinic acid³². This is how sport has a positive effect on the nervous system.

	Depression	Depression mit Inflammation
Trp ↓	!	
KynA ↓ or QuinA ↓	!	
Kyn/Trp ↑ or Kyn ↑		!
QuinA/KynA ↑ or QuinA ↑		!
Therapy option (first line)	Tryptophan Ω-3 fatty acids sports	Curcumin, Berberin, Resveratrol Ω-3 fatty acids sports
Therapy option (second line)		Tryptophan

Table 1: Diagnostics and selection of therapeutic options for optimising tryptophan metabolism

Tryptophan metabolism



Additionally available:

IDK® IDO activity ELISA (K 7726)

IDK® Kynurenine high sensitive ELISA (KR3728) *

IDK® Tryptophan ELISA (Stool) (K 7729)

IDK® Tryptophan high sensitive ELISA (KR3730) *

IDK® Serotonin ELISA (Serum, Dried Blood) (K 6880)

**for research use only*

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