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Does GABA supplementation modulate muscle cytokine expression and inflammatory status in aged rats?

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Abstract

Aging is a multifactorial process affecting all organs and systems in the body. Specific to aging is the establishment of a chronic subacute inflammatory state in tissues underlying age-related pathologies. GABA (Gamma-Aminobutyric Acid) is an inhibitory neurotransmitter in the central nervous system. Pharmaceutical properties of Gaba on non-neuronal peripheral tissues and organs were reported from anti-hypertension, anti-diabetes, anti-cancer, antioxidant, anti-inflammation, anti-microbial, anti-allergy, hepato-protection, reno-protection, and intestinal protection. GABA was indicated as an inflamation inhibitor via decreasing pro-inflammatory mediator production and ameliorating inflammatory symptoms. This study aimed to evaluate the effect of GABA supplementation on inflammatory status in the muscle tissue of aged rats. Male Wistar rats (n=24) were put in 3 groups: CY (3 month-old controls); CO (24 month-old controls); G (24 month-old rats supplemented with GABA at dosage of 10ml/kg for 3 months). At the experiment's end, skeletal muscle, small intestine and heart material was collected for immunohistochemical analysis. Comparative analysis of the intensity of IL-10, IL-4 and IL-1β immunoreaction in different muscle tissues showed that inflammatory responses varied with age and tissue. Aged animals showed higher IL-1β levels than young animals, and these effects amplified in IL-10- and IL-4-deficient rat muscles of same group. In group of GABA-supplemented animals, the intensity of IL-1β in skeletal muscle, heart and small intestine was reduced compared to adult controls. In conclusion, GABA supplementation can influence the inflammatory status of muscle tissue in old animals by modulating pro- and anti-inflammatory cytokine levels. GABA can be used to prevent the effects of ageing.

Key Words: muscle tissue, IL-10, IL-4, IL-1β, GABA, aging.

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Aging is strongly driven by two interconnected biological processes: chronic oxidative stress and persistent low-grade inflammation, commonly referred to as "inflammaging." Excessive Reactive Oxygen Species (ROS) contribute to cellular damage, mitochondrial dysfunction, and genomic instability, while dysregulated inflammatory signaling promotes tissue degeneration and age-related pathologies. Therefore, molecules that can simultaneously suppress oxidative stress and modulate inflammatory responses are of particular interest in anti-aging research.

Gamma-Aminobutyric Acid (GABA) demonstrates a dual protective role within this context. By increasing the activity of key antioxidant enzymes and reducing lipid peroxidation products, GABA helps prevent ROS-induced cellular injury – a primary trigger of aging processes. At the same time, its ability to inhibit pro-inflammatory cytokines and NF-κB activation reduces chronic inflammation, thereby limiting tissue degradation, immune imbalance, and delayed wound healing, all of which are characteristic of aging tissues.[1] GABA has been shown to inhibit inflammation triggered by physical injury, UV exposure, microbial infection, and immune responses. It reduces the production of key pro-inflammatory mediators such as cytokines, Nitric Oxide (NO), and prostaglandin E2. In LPS-stimulated macrophages, GABA suppresses iNOS, IL-1β, and TNF-α expression, which supports faster wound healing. It also decreases cytokine production and inhibits NF-κB signaling in lymphocytes and pancreatic β-cells.[1]

GABA also exhibits significant antioxidant properties.

GABA has demonstrated the ability to neutralize reactive intermediates formed during lipid peroxidation and to reduce malondialdehyde levels while enhancing antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase. These effects have been observed in various models, including brain tissue under epileptic conditions, pancreatic cells exposed to oxidative stress, endothelial cells, and intestinal tissue damaged by radiation. Natural GABA-rich sources—such as fermented sea tangle, germinated brown rice, and pigmented rice vinegar—also exhibit strong radical-scavenging activity, supporting both direct and indirect cellular protection.[1]

Cytokines are small protein signaling molecules produced primarily by immune cells, but also by various other cell types in the body. They act as essential mediators of intercellular communication, regulating immune responses, inflammation, and hematopoiesis. Cytokines influence the growth, differentiation, activation, and migration of immune cells. Depending on the biological context, they may exert either pro-inflammatory or anti-inflammatory effects, contributing to both the initiation and the resolution of immune responses.[2] IL-1β (Interleukin-1 beta) is pro-inflammatory cytokine, produced mainly by activated macrophages, monocytes, and dendritic cells. It mediates inflammatory responses, fever, and recruitment of immune cells and plays a key role in acute and chronic inflammation IL-1β is elevated in autoimmune diseases, infections, and age-related inflammation, it also contributes to tissue damage when chronically high.[3] IL-4 (Interleukin-4) is anti-inflammatory/immunoregulatory cytokine which is secreted by Th2 cells, mast cells, and basophils. IL-4 promotes differentiation of naive T cells into Th2 cells, stimulates B-cell antibody production, and supports tissue repair. It is key in allergic responses and maintaining immune balance, also counteracts excessive pro-inflammatory signaling.[4] IL-10 (Interleukin-10) is an anti-inflammatory cytokine, produced by regulatory T cells, monocytes, macrophages, and some B cells. IL-10 suppresses the expression of pro-inflammatory cytokines (e.g., IL-1β, TNF-α), limits immune-mediated tissue damage, and promotes resolution of inflammation. IL10 is essential for controlling chronic inflammation and maintaining immune homeostasis, it is therapeutic target in autoimmune and inflammatory disorders.[5]

Increasing evidence demonstrates that GABA can attenuate inflammatory responses by suppressing the synthesis and release of the pro-inflammatory cytokine IL-1β, a key driver of tissue injury and age-related chronic inflammation.[6,7]

The data in the scientific literature on the effect of GABA on the inflammatory status of muscle tissue are limited. This determined the aim of the present study.

The aim of the study was to evaluate the effect of GABA supplementation on the inflammatory status in muscle tissue of aged rats.

Materials and Methods

This was a controlled, parallel-group preclinical study conducted in an aged rat model to evaluate the effects of chronic GABA supplementation on cytokine expression and inflammatory status in muscle tissues. Male Wistar rats (n=24) were put in 3 groups: CY – young controls (3-month-old controls); CO - old controls (24-month-old controls); G - (24-month-old rats supplemented with GABA at dosage of 10ml/kg for 3 months). The daily dose of GABA solution was diluted 1:1 with drinking water and provided to the animals in a separate bottle alongside their drinking water. After the completion of the 3-month experimental period, the animals were anesthetized with i.m. Ketamine/Xylazine (90 mg/kg/10 mg/kg) and euthanized by decapitation. Skeletal muscle, small intestine and heart tissue samples were collected for immunohistochemical analysis. The following antibodies were used for immunohistochemical examination: RPA563Hu01 Recombinant Interleukin 1 Beta (IL1b), RPA056Hu01 Recombinant Interleukin 10 (IL10) and APA077Ca61 Active Interleukin 4 (IL4), Cloud-Clone Corp., Texas, USA. The intensity of immunohistochemical staining was visually assessed and classified on a four-point scale by two independent pathologists: 0 – no reaction; + – weak intensity; ++ – moderate intensity; and +++ – strong intensity. The criterion was the presence or absence of brown granular cytoplasmic staining in smooth muscle, cardiac muscle, skeletal muscle, connective tissue macrophages, and some blood cells in the vessels. According to the intensity of the brown staining, the assessment was graded as follows: weak, where the brown staining was pale; moderate, where the brown staining was light; and strong, where the brown staining was dark brown to black. The experiment took place between October and December 2024. The animals were bred in the vivarium of the Medical University, Plovdiv under standard laboratory conditions. The rats were kept in compliance with all the experimental procedures recommended by the European Commission for protection and welfare of laboratory animals. The experimental protocol was approved by the Committee on Ethical Treatment of Animals of the Bulgarian Agency for Food Safety (No. 408/2024). All animals received humane care in compliance with the "Principles of laboratory animal care" formulated by the National Society for Medical Research and the "Guide for the care and use of laboratory animals" prepared by the National Institute of Health (NIH publication No. 86-23, revised 1996).

Results

Cardiac muscle tissue

We used immunohistochemical imaging to determine the expression level of the interleukins IL-1β, IL-4 and IL-10 in the heart tissue. Results are shown in Figure 1 and Table 1. Immunoexpression intensity for interleukins in rat heart was evaluated via semiquantitative analysis classified on a four-point scale: 0 – no reaction; + – weak intensity; ++ – moderate intensity; and +++ – strong intensity.

We found that IL-1β was expressed intensively in cardiomyocytes in the Young Controls (CY) and GABA groups, while in the Old Controls (CO) group the expression was weak. In the blood vessels, the strongest expression of IL-1 was observed in the CO and GABA groups, while in the

CY group it was weaker. In macrophages, IL-1β showed high expression in the CO and GABA groups, and moderate in CY (Figure 1, Table 1).

Analysis of IL-4 showed moderate to strong expression in all groups in cardiomyocytes. In the blood vessels, IL-4 was most strongly expressed in CO and GABA, while in CY the expression was weaker. In macrophages, IL-4 was weakly expressed in the CY group, moderately in GABA and strongly in CO.

For IL-10, we found high expression in cardiomyocytes

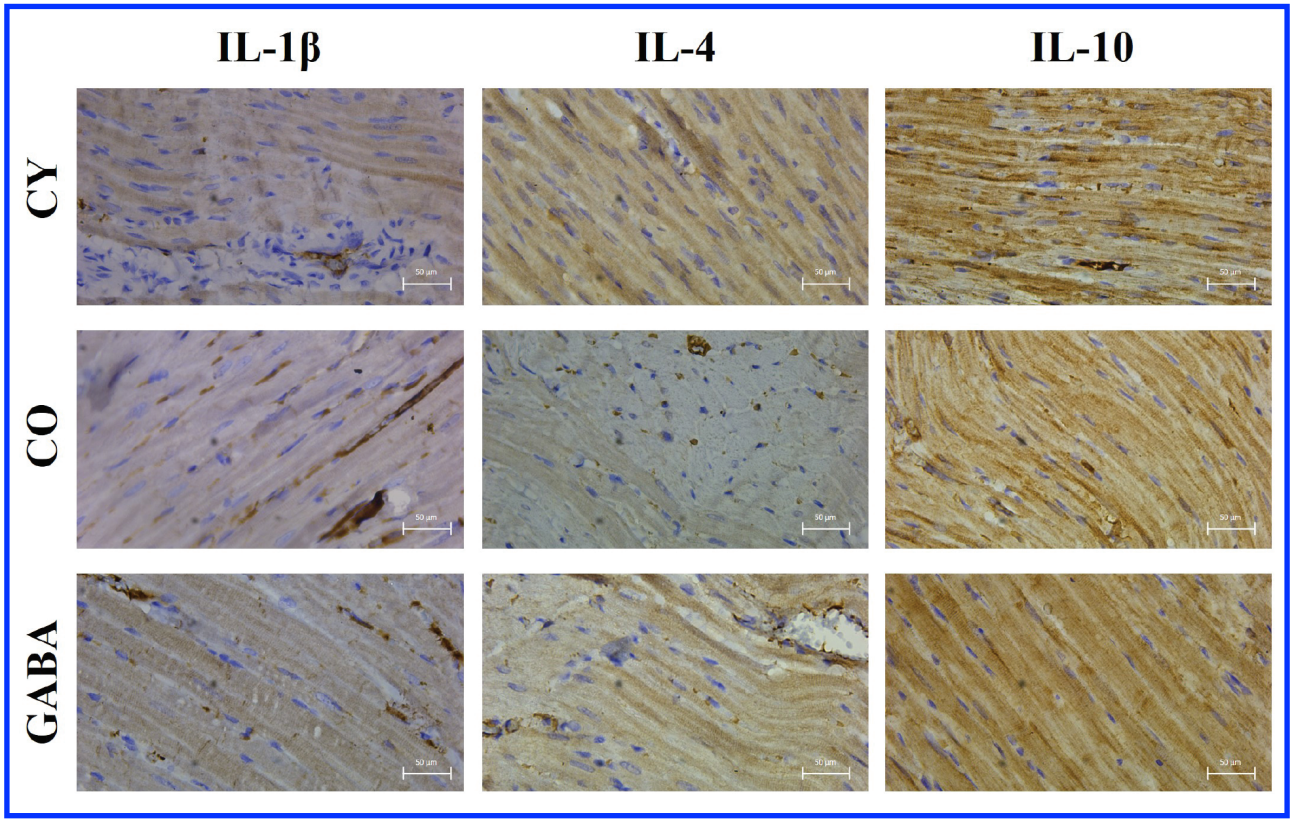

Figure 1. *Microphotographs of IL-1β, IL-4, and IL-10 immunostained sections showing the expression in heart tissue; magnification (×400). CY, young controls; CO, old controls; GABA, GABA supplemented group.*

Table 1. *Immunoexpression intensity for IL-1β, IL-4, IL-10 in rat heart. Semiquantitative analysis.*

	Location	CY	CO	GABA
IL-1β	Cardiomyocytes	+++	+/-	+++
	Blood vessels	+	+++	+++
	Macrophages	++	+++	+++
IL-4	Cardiomyocytes	++	++	++
	Blood vessels	+	+++	+++
	Macrophages	+/-	+++	++
IL-10	Cardiomyocytes	+++	+++	+++
	Blood vessels	++	++	++

-, absent; +, weak; ++, moderate; +++, strong expression; CY, young controls; CO, old controls; GABA, GABA supplemented group.

in all studied groups. In blood vessels and macrophages, IL-10 was presented with moderate intensity in all groups, with slightly lower expression in macrophages in the GABA group compared to the other two groups (Figure 1, Table 1).

Striated skeletal muscle tissue

Figure 2 and Table 2 demonstrate the immunostaining of IL-1, IL-4, and IL-10 in striated skeletal muscle tissue (rat gastrocnemius muscle), including myofibrils, blood vessels, and macrophages.

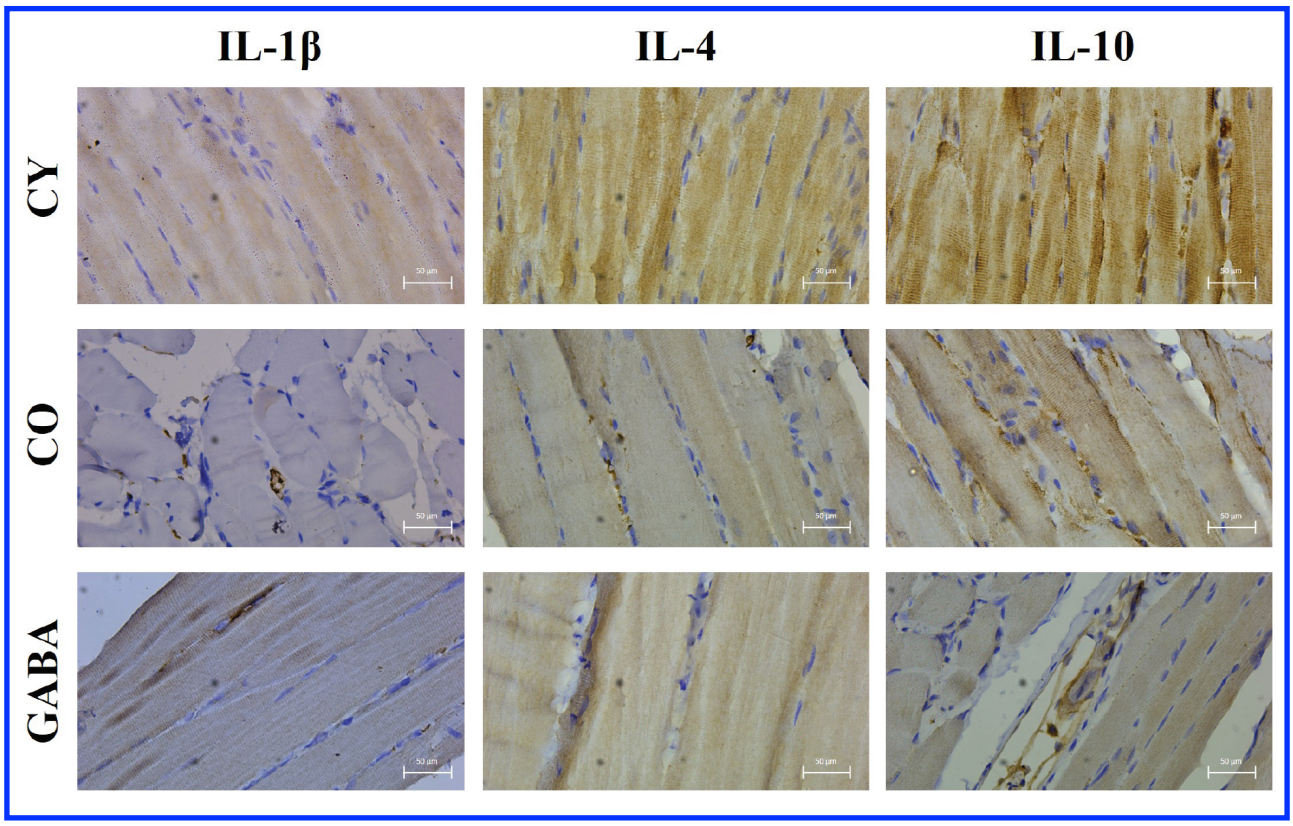

Figure 2. *Microphotographs of IL-1β, IL-4, and IL-10 immunostained sections showing the expression in striated skeletal muscle tissue (gastrocnemius muscle); magnification (× 400). CY, young controls; CO, old controls; GABA, GABA supplemented group.*

Table 2*. Immunoexpression intensity of IL-1β, IL-4, IL-10 in rat gastrocnemius muscle. Semiquantitative analysis.*

	Location	CY	CO	GABA
IL-1β	Striated skeletal muscle fibers	++	-	+++
	Blood vessels	++	+++	+++
	Macrophages	-	+	++
IL-4	Striated skeletal muscle fibers	++	+	++
	Blood vessels	-	+/-	+
	Macrophages	+/-	+/-	-
IL-10	Striated skeletal muscle fibers	+++	++	++
	Blood vessels	+	++	+
	Macrophages	+	+	+

-, absent; +, weak; ++, moderate; +++, strong expression; CY, young controls; CO, old controls; GABA, GABA supplemented group.

IL-1β showed moderate expression in striated myofibrils in the CY group, absent expression in CO, and strong expression in GABA. In blood vessels, IL-1β was highly expressed in CO and GABA, while expression was moderate in CY. In macrophages, IL-1β expression was weak in CY, weak to moderate in CO, and moderate in GABA.
IL-4 showed moderate expression in striated myofibrils of the CY group, with lower expression in CO, and absent in GABA. In blood vessels, IL-4 was not detected in the CY group, and was weakly detected in CO. In macrophages, IL-4 was weakly expressed in both groups, with no significant difference between them.
IL-10 was most strongly expressed in striated myofibrils of group CY, with slightly reduced expression in CO and GABA. In blood vessels, interleukin was weakly visualized in CY, moderately in CO, and again weakly in GABA. In macrophages, IL-10 was weak but uniformly expressed in all three studied groups, with no clear differences between them (Figure 2, Table 2).

Smooth muscle tissue

Figure 3 and Table 3 demonstrate the immunostaining of IL-1β, IL-4 and IL-10 in various structures of the small intestine samples, including Smooth Muscle cells (SM), blood vessels, macrophages and myenteric plexus.

IL-1β showed weak to absent expression in smooth muscle in the CY and CO groups, while a clear expression was observed in the GABA group. In the blood vessels, IL-1β was weakly expressed in all groups. In macrophages, IL-1β showed moderate expression in the CY group, strong expression in CO and also high in GABA. In the myenteric plexus, weak expression was observed in CY, absent in CO and strong in GABA.
IL-4 was weakly expressed in smooth muscle in all groups, with a trend towards the lowest levels in GABA. In the blood vessels, expression was moderate in the CY and CO groups, and weak in GABA. In macrophages, IL-4 was most highly expressed in CO, with moderate expression in CY and decreased in GABA. In the myenteric plexus, strong expression was reported in the CY and CO groups, while it was significantly decreased in GABA.
Analysis of IL-10 showed a lack of expression in the smooth muscle of CY and CO, while strong expression was reported in the GABA group. In blood vessels, IL-10 was moderately expressed in CY and GABA, and weakly in CO. In macrophages, IL-10 was moderately expressed in CO and GABA, and weakly in CY. In the myenteric plexus, interleukin was highly represented in all groups, without significant differences between them (Figure 3, Table 3).

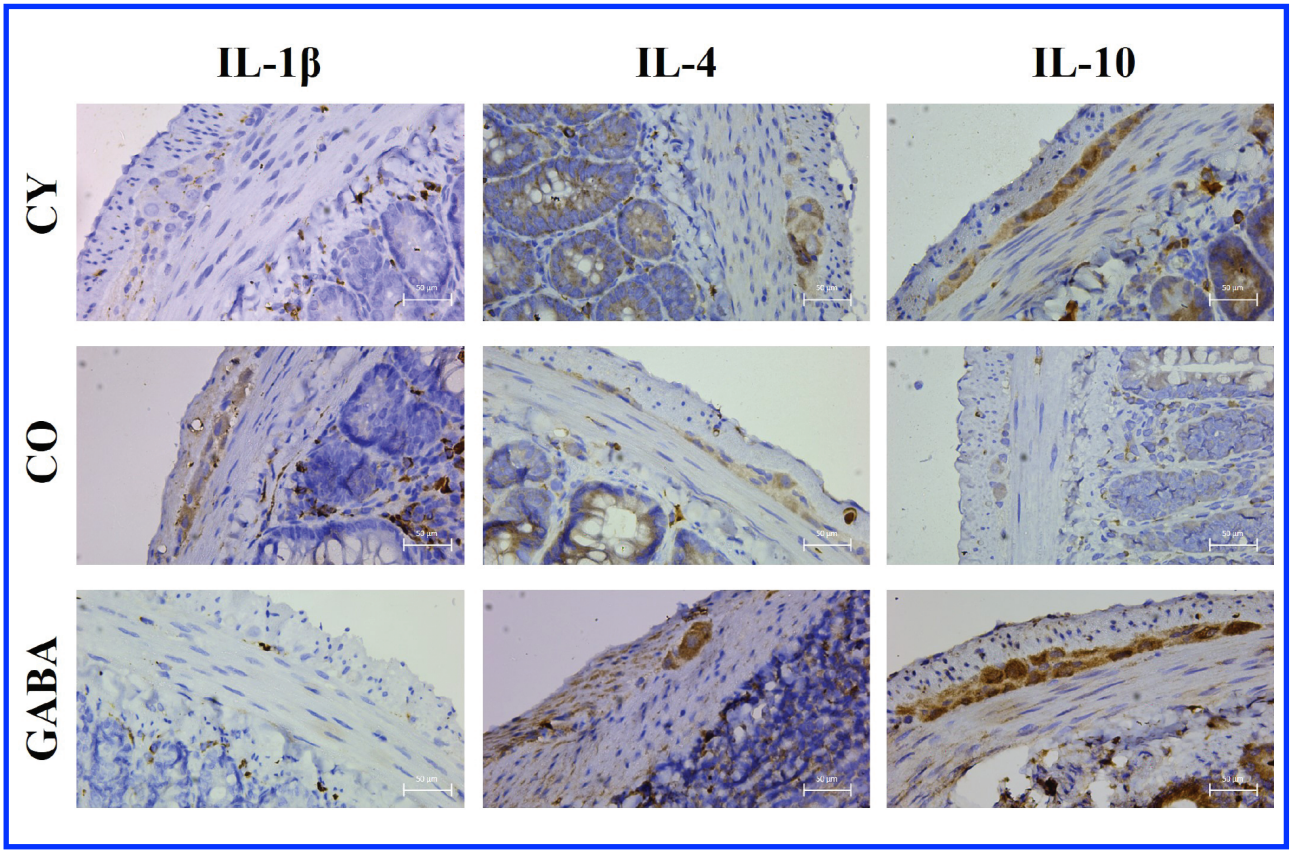

Figure 3. *Microphotographs of IL-1β, IL-4, and IL-10 immunostained sections showing the expression in smooth muscle tissue (SM); magnification (× 400). CY, young controls; CO, old controls; GABA, GABA supplemented group.*

Table 3. *Immunoexpression intensity of IL-1β, IL-4, IL-10 in rat small intestine. Semiquantitative analysis.*

	Location	CY	CO	GABA
IL-1β	Smooth muscle cells	-	-	++
	Blood vessels	+	+	+
	Macrophages	+	+++	++
	Myenteric plexus	+/-	-	+++
IL-4	Smooth muscle cells	+	+	+/-
	Blood vessels	++	++	+
	Macrophages	+	+++	+/-
	Myenteric plexus	+++	+++	+/-
IL-10	Smooth muscle cells	-	-	+++
	Blood vessels	++	+	++
	Macrophages	+	++	++
	Myenteric plexus	+++	+++	+++

-, absent; +, weak; ++, moderate; +++, strong expression; CY, young controls; CO, old controls; GABA, GABA supplemented group.

Discussion

This study demonstrates that GABA supplementation modulates cytokine expression in cardiac, skeletal, and smooth muscle tissues, indicating a role in peripheral immunoregulation during aging. The observed increase in IL-1β expression in cardiomyocytes and smooth muscle of GABA-treated older rats suggests that GABA may enhance controlled inflammatory signaling required for cellular turnover and tissue adaptation. Similar age-dependent changes in IL-1β have been reported in cardiac tissue as part of remodeling and stress-response pathways supporting vascular homeostasis.[8]

Importantly, GABA supplementation was associated with increased IL-10 expression across all analyzed tissues, particularly pronounced in smooth muscle. IL-10 is a key anti-inflammatory cytokine promoting inflammation resolution and mitochondrial protection. These findings align with previous work demonstrating GABA-dependent suppression of NF-κB signaling and promotion of IL-10 secretion in intestinal and immune cells.[9,10] Such a response may counteract inflammaging — the chronic low-grade inflammation characteristic of aging tissues.

Our data also revealed tissue-specific modulation of IL-4. In cardiac and skeletal muscle, IL-4 expression tended to decline with aging but showed partial restoration in GABA-supplemented rats, particularly in macrophages associated with vascular structures. IL-4 is involved in macrophage M2 polarization and myogenic regeneration; thus, its modulation may reflect GABA-mediated shifts toward a reparative immune environment. Comparable findings have been shown in skeletal muscle regeneration models, where GABA receptor activation enhanced satellite cell-macrophage communication.[11]

Skeletal muscle exhibited the most pronounced age-related decline in IL-1β and IL-4 expression within myofibers, consistent with reduced immune signaling contributing to sarcopenia progression. GABA supplementation selectively restored IL-1β but not IL-4 expression, suggesting that GABAergic immunoregulation in skeletal muscle may preferentially support metabolic remodeling over immune-driven regeneration. These results resemble previously reported differential cytokine responses in aging muscle under GABA influence.[12]

Smooth muscle showed the strongest immunoreactivity changes following GABA supplementation, including robust increases in IL-1β and IL-10, and reduced IL-4 expression in the myenteric plexus. These findings indicate that GABA may shift gut immune balance by promoting tolerance-associated cytokines while preventing excessive Th2-type signaling. Similar mechanisms are described in gut epithelial barrier enhancement through GABA receptor activation,[13] suggesting that GABA may support gastrointestinal health in aging.

GABA has been shown to modulate immune responses by interacting with both pro-inflammatory and anti-inflammatory cytokines. In immune cells, GABA can suppress the production of IL-1β, a key pro-inflammatory cytokine, through mechanisms involving GABA receptors and transporters, such as GAT2. For example, blocking or removing GABA transporter activity in macrophages reduces IL-1β secretion, suggesting that GABAergic signaling can dampen inflammatory responses.[6]

Conversely, activation of GABA receptors in peripheral tissues, such as the gut and lungs, is generally associated with increased anti-inflammatory cytokines, including IL-4 and IL-10. These effects have been demonstrated in models of intestinal inflammation and viral pneumonitis,

where GABAergic modulation reduced tissue damage and promoted immune resolution.[14,15]

The interaction between GABA and cytokines is bidirectional. Elevated IL-1β can impair GABAergic neurotransmission in neurons, potentially increasing excitability and decreasing inhibitory tone. Similarly, IL-10 has been shown to directly modulate neuronal GABA currents, indicating that immune signaling can influence neural function.[16]

Our findings (e.g. increased IL-1β and IL-10 with GABA in certain tissues) resonate with a recent study showing that GABA administration in old mice ameliorated "inflammaging" in skeletal muscle: GABA suppressed pro-inflammatory M1 macrophages and reduced classical pro-inflammatory cytokines (e.g., TNF-α, IL-6).[17] In that same study, GABA helped restore muscle mass, fiber size, and strength, and improved anabolic signaling (via Akt/mTOR). Thus, our observation that GABA affects interleukin expression in muscle (and presumably influences immune environment) fits with a broader pattern of GABA counteracting age- or obesity-related muscle decline.[18,19]

There is growing evidence that GABA and GABA-receptor signaling have systemic immunomodulatory effects beyond the nervous system. For example, immune cells (macrophages, antigen-presenting cells) express GABA_A receptors, and activation of these receptors shifts them toward anti-inflammatory phenotypes.[13,10] More specifically, GABA treatment can inhibit IL-1β production in inflammatory macrophages by modulating metabolic and epigenetic pathways (e.g., via LSD1-mediated histone demethylation, suppression of NLRP3 inflammasome formation, and enhanced mitochondrial oxidative phosphorylation).[6]

Our data on cardiac muscle tissue show GABA-related changes in interleukin expression. This is supported by a study demonstrating that activation of GABA_B receptors in macrophages after Myocardial Infarction (MI) promoted polarization toward M2 (anti-inflammatory) macrophages, increased IL-10 (and TGF-β1) release, and ameliorated pathological sympathetic nerve remodeling post-MI.[20] This is quite relevant: it suggests that GABA not only modulates immune cell behavior in skeletal muscle, but can also influence inflammatory and remodeling processes in heart tissue. Thus our immunohistochemical observations may reflect a genuine physiological mechanism previously demonstrated in pathologic cardiac settings.

Not all studies report solely beneficial effects. For example, a study of muscle regeneration in diabetic mice found that high-dose GABA supplementation during early inflammatory phase delayed regeneration, possibly because persistent GABA may interfere with necessary inflammatory signals (e.g. initial cytokine-mediated repair).[21] This finding suggests that GABA's effect on cytokines and tissue repair is not universally protective — timing, dose, and tissue context are critical. That aligns with our data's variability: e.g., in smooth muscle we see GABA strongly inducing IL-1β along with IL-10, which might reflect a complex balance rather than a simple suppression of inflammation. Here GABA shows dual role – not strictly anti-inflammatory. Because GABA sometimes increases IL-1β (as in smooth muscle in our data) while also increasing IL-10, its role may be modulatory rather than purely suppressive. In some tissues or situations, a transient pro-inflammatory signal (IL-1β) might be part of normal remodeling or protective adaptation, while IL-10 helps prevent chronic inflammation.

Our findings, together with prior literature, support the view that GABA does not exert a uniform anti-inflammatory action but rather rebalances cytokine patterns according to the specific physiological roles of each tissue. In the heart, GABA supports protective remodeling; in skeletal muscle, it restores inflammatory triggers necessary for adaptation; and in the intestines, it reinforces immune tolerance and barrier protection. By modulating IL-1β, IL-4, and IL-10 in a coordinated manner, GABA may contribute to slowing immunosenescence and maintaining tissue integrity during aging.

This study has certain limitations. These include the semi-quantitative assessment of immune responses, the lack of functional muscle tests and the absence of systemic cytokine measurements.

Conclusions

Overall, our findings indicate that GABA modulates both pro- and anti-inflammatory cytokines in a tissue- and cell-specific manner, enhancing IL-1β and IL-10 while variably affecting IL-4. This cytokine modulation suggests a potential role for GABA in maintaining tissue homeostasis, supporting immune balance, and mitigating age-related inflammatory changes in cardiac, skeletal, and smooth muscle tissues.

Collectively, the evidence suggests that GABA can interrupt key mechanisms underlying age-related decline. This positions GABA as a promising bioactive compound for strategies aimed at healthy ageing and the prevention of diseases mediated by inflammation and oxidative stress. The findings of this study could inform the development of therapeutic strategies for sarcopenia, cardiac inflammation and disorders of the smooth muscles.

List of abbreviations

GABA, Gamma-Aminobutyric Acid
CY, young controls
CO, old controls
IL-1β, Interleukin-1 beta
IL-4, Interleukin-4
IL-10, Interleukin-10
ROS, reactive oxygen species

Contributions

The authros contributed equally to the present paper.

Conflict of interest

The authors delare no confict of interest.

Ethics approval

The experimental protocol was approved by the Committee on Ethical Treatment of Animals of the Bulgarian Agency for Food Safety (No. 408/2024). All animals received humane care in compliance with the "Principles of laboratory animal care" formulated by the National Society for Medical Research and the "Guide for the care and use of laboratory animals" prepared by the National Institute of Health (NIH publication No. 86-23, revised 1996).

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References

1. Ngo D, Vo T. An updated review on pharmaceutical properties of gamma-aminobutyric acid. Molecules 2019;24:2678.
2. Baldo BA. Cytokines. Safety Biologics Ther 2016;13: 217-61.
3. Akdis M, Aab A, Altunbulakli C, et al. Interleukins, from 1 to 37, and interferon-γ: receptors, functions, and roles in diseases. J Allergy Clin Immunol 2016; 138:984-1010.
4. Li B, Cheung PCK. The immunoregulatory role of interleukin-4 in immune responses. J Cell Physiol 2019; 234:4217-4227.
5. Ouyang W, O'Garra A. IL-10 family cytokines: from basic biology to disease therapy. Immunity 2019;50: 871-891.
6. Fu J, Han Z, Wu Z, et al. GABA regulates IL-1β production in macrophages. Cell Rep 2022;41:111770.
7. Xia Y, He F, Wu X, et al. GABA transporter sustains IL-1β production in macrophages. Sci Adv 2021;7: eabe9274.
8. Narayan P, Trikantzopoulos E, Mezzaroma E, Mauro A, Vohra H, Abbate A, Toldo S. The interleukin-1 receptor type I promotes the development of aging-associated cardiomyopathy in mice. Cytokine 2022;151: 155811.
9. Ngo DH, Tran QT, Kim YS, Hang NTN, Ngo DN, Vo TS. GABA-enriched rice bran inhibits inflammation in LPS-stimulated macrophages via suppression of TLR4-MAPK/NF-κB signaling cascades. J Food Biochem. 2022;46(12):e14421
10. Tian J, Lu Y, Zhang H, Chau CH, Dang HN, Kaufman DL. Gamma-aminobutyric acid inhibits T cell autoimmunity and the development of inflammatory responses in a mouse type 1 diabetes model. J Immunol 2004; 173:5298-304.
11. Park J, Lee H. GABA receptor involvement in skeletal muscle regeneration. Cells 2020;9:1324.
12. Benarroch EE. Muscle immune–metabolic interactions and aging. Neurology 2020;95:705-14.
13. Bhandage AK, Barragan A. GABAergic signaling in gut immunity and inflammation. Front Immunol 2022; 13:1020053.
14. Deng Z, Li D, Wang L, et al. Activation of GABA-BR attenuates intestinal inflammation by reducing oxidative stress through modulating the TLR4/MyD88/NLRP3 pathway and gut microbiota abundance. Antioxidants 2024;13:1141.
15. Tian J, Kaufman DL. The GABA and GABA-receptor system in inflammation, anti-tumor immune responses, and COVID-19. Biomedicines 2023;11:254.
16. Llansola M, Arenas YM, Sancho-Alonso M, et al. Neuroinflammation alters GABAergic neurotransmission in hyperammonemia and hepatic encephalopathy. Front Pharmacol 2024;15:1358323.
17. Song G, Oh HJ, Jin H, et al. GABA prevents sarcopenia by regulation of muscle protein degradation and inflammaging in aged mice. J Cachexia Sarcopenia Muscle 2024;15:2852-64.
18. Ji Y, Li M, Chang M, et al. Inflammation: roles in skeletal muscle atrophy. Antioxidants 2022;11:1686.
19. Jin H, Oh HJ, Lee BY. GABA prevents age-related sarcopenic obesity in mice with high-fat-diet-induced obesity. Cells 2023;12:2146.
20. Liu Q, Li Y, Shi Y, et al. Protective effect of GABA-B receptor activation on sympathetic nerve remodeling via regulation of M2 macrophage polarization after myocardial infarction. Rev Port Cardiol 2023;42:125-35.
21. Horii M, Bumrungkit C, Yanaka N, et al. Effects of oral γ-aminobutyric acid intake on muscle regeneration in diabetic mice. Am J Physiol Cell Physiol 2025; 328: C967-85.

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