

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



# Cytokines pattern of Multiple Sclerosis patients treated with Apitherapy



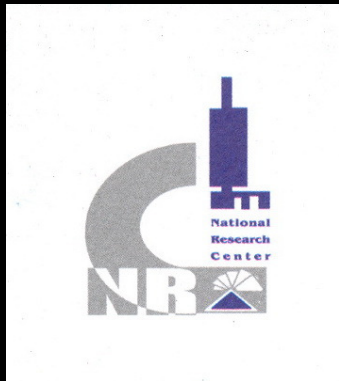
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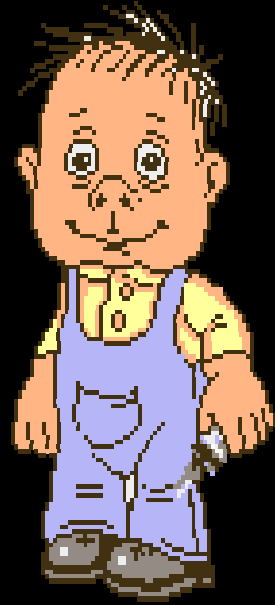
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**4<sup>rd</sup> International Conference and Exhibition  
on Clinical & Cellular Immunology  
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Houston, USA**



**Cytokines pattern of Multiple  
Sclerosis patients treated with  
Apitherapy**



سُورَةُ النَّحْلِ

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ وَأَوْحَىٰ رَبُّكَ إِلَى النَّحْلِ  
أَنِ اتَّخِذِي مِنَ الْجِبَالِ بُيُوتًا وَمِنَ الشَّجَرِ وَمِمَّا يَعْرِشُونَ ﴿٦٨﴾ ثُمَّ كُلِي  
مِن كُلِّ الشَّجَرِ فَأَسْلكِي سُبُلَ رَبِّكِ ذُلُلًا يَخْرُجُ مِنْ بُطُونِهَا  
شَرَابٌ مُخْتَلِفٌ أَلْوَانُهُ فِيهِ شِفَاءٌ لِلنَّاسِ إِنَّ فِي ذَٰلِكَ لَآيَةً لِّقَوْمٍ  
يَتَفَكَّرُونَ ﴿٦٩﴾



# Multiple Sclerosis



# What is Multiple Sclerosis?

- ❑ It is an Auto Immune Disease which is when the body starts to destroy itself.
- ❑ It is a life-long disease with no cure.
- ❑ In MS, the body attacks and destroys the fatty tissue called myelin that insulates an axon/nerve, and is called demyelination.
- ❑ If damage is severe it can also destroy the nerve/axon itself.
- ❑ MS affects the central nervous system and inflames the white matter in the brain which creates plaques.



# Definition of Multiple Sclerosis

- An inflammatory demyelinating disease of the CNS where there is:
  - Dissemination in space
  - Dissemination in time
  - No alternative neurologic disease
- MS is a clinical diagnosis

# Multiple Sclerosis Epidemiology

- The most common progressive neurologic disease of young adults
- Affects 350,000 persons in the USA
- Risk Factors:
  - Female sex
  - White race
  - Northern latitude (USA)
  - High socioeconomic status
  - Scandinavian ancestry



# MULTIPLE SCLEROSIS FEATURES

- two stages disease: inflammation and neurodegeneration
- 4,000,000 people affected worldwide
- Women:men 2:1
- Age of disease onset: 25-30 ys (young adulthood)

## •Neurological impairments:

- blindness,
- loss of sensation,
- lack of coordination,
- incontinence,
- paralysis
- Relapsing-remitting (80%);
- chronic progressive (10%);
- benign (10%)

# **Disease Overview: Autoimmunity**

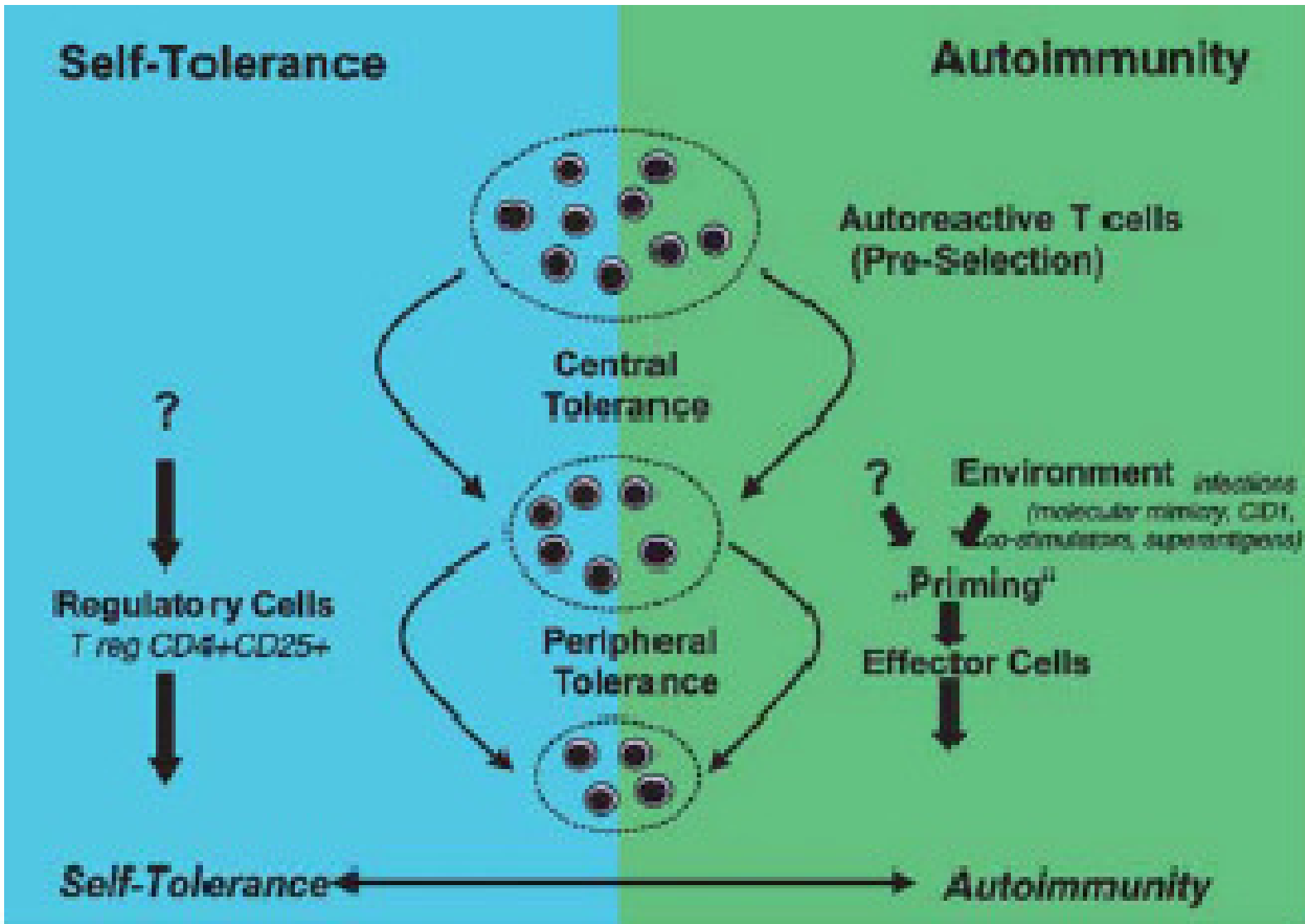
**Peripheral tolerance involves a populations of regulatory T cells which maintain autoreactive T cells in a “dormant” state in the circulation in adults.**

**The autoreactive T cells can be awoken from this state by local or environmental stimuli such as exposure to endogenous or exogenous antigens in the circulation.**

**In MS these cells becomes activated either because of failure of the mechanism of peripheral tolerance or due to priming by antigens.**

## Self-Tolerance

## Autoimmunity



## **MULTIPLE SCLEROSIS FEATURES**

**Once activated autoreactive T •  
cells release a cocktails of  
cytokines that are important for  
migration and homing of the  
cells to the target sites and for  
initiation of the inflammatory  
process**

## Disease Overview: Multiple Sclerosis

Multiple Sclerosis (MS) is an inflammatory disease of the Central Nervous System (CNS) affecting the brain and spinal cord. Predominantly, it is a disease of the "white matter" tissue.

The white matter is made up of nerve fibers which are responsible for transmitting communication signals both internally within the CNS and between the CNS and the nerves supplying rest of the body.

# Etiology

- Possible precipitating factors include
  - Infection
  - Physical injury
  - Emotional stress
  - Excessive fatigue
  - Pregnancy
  - Poor state of health



# Multiple Sclerosis

## Etiology and Pathophysiology

- Myelin can be replaced by glial scar tissue
- Without myelin, nerve impulses slow down
- With destruction of axons, impulses are totally blocked
- Results in permanent loss of nerve function

## Main symptoms of Multiple sclerosis

### Central:

- Fatigue
- Cognitive impairment
- Depression
- Unstable mood

### Visual:

- Nystagmus
- Optic neuritis
- Diplopia

### Speech:

- Dysarthria

### Throat:

- Dysphagia

### Musculoskeletal:

- Weakness
- Spasms
- Ataxia

### Sensation:

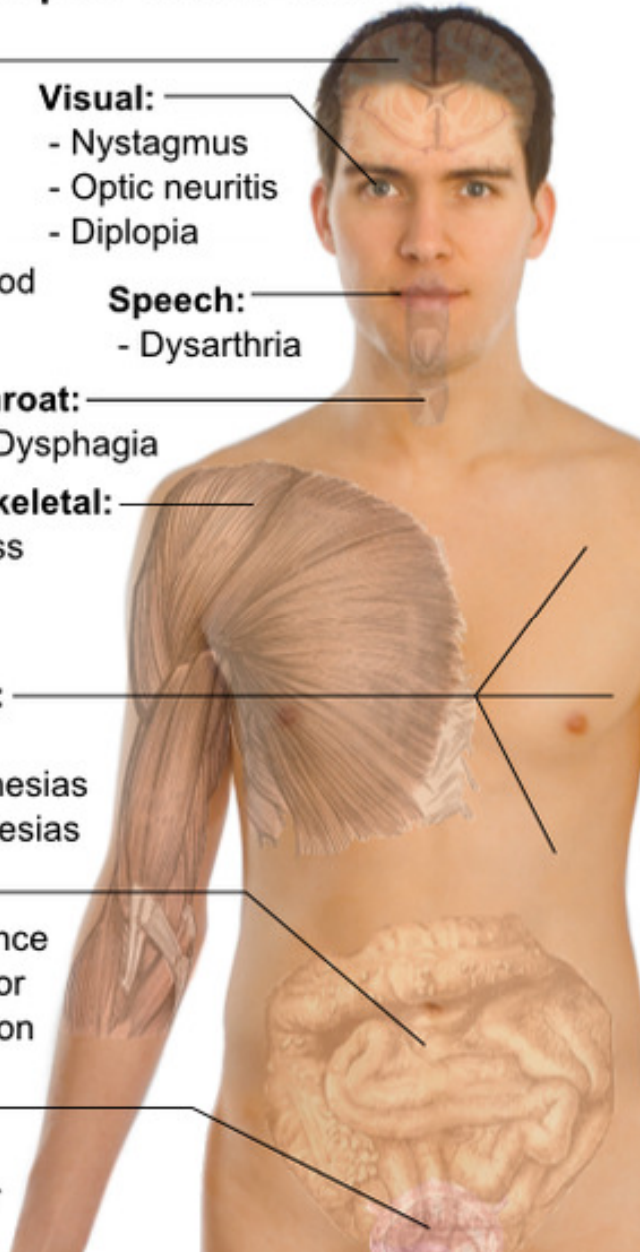
- Pain
- Hypoesthesias
- Paraesthesias

### Bowel:

- Incontinence
- Diarrhea or constipation

### Urinary:

- Incontinence
- Frequency or retention



# Symptoms And Signs

# Signs & Symptoms :

- The person with MS can suffer almost any neurological symptom or sign, including:
- changes in sensation,
- muscle weakness,
- spasm,
- or difficulty in moving;
- difficulties with coordination and balance;

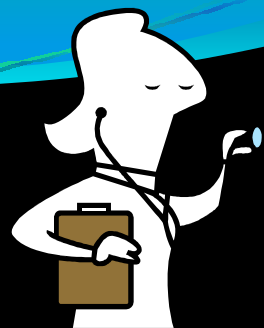
# Signs & Symptoms :

- problems in speech or swallowing,
- visual problems,
- fatigue,
- pain
- bladder and bowel difficulties.
- Cognitive impairment of varying degrees
- emotional symptoms of depression
- or unstable mood are also common.




# Symptoms of MS

- Fatigue
- Depression
- Memory change
- Pain
- Spasticity
- Vertigo
- Tremor
- Double Vision/Vision Loss

- 
- Weakness
  - Dizziness/Unsteadiness
  - Numbness/Tingling
  - Ataxia
  - Euphoria
  - Speech disturbance
  - Bladder/Bowel/Sexual dysfunction

# Causes Of MS :

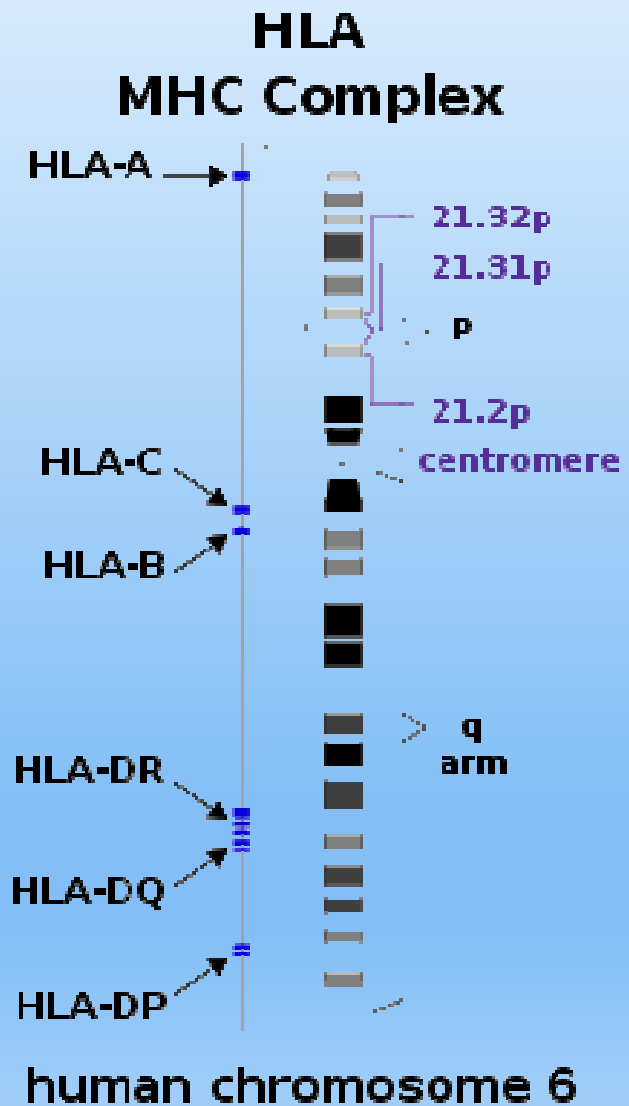
- Most likely MS occurs as a result of some combination of genetic, environmental and infectious factors.
- Epidemiological studies of MS have provided hints on possible causes for the disease.



**Theories try to combine the known data into plausible explanations, but none has proved definitive.**

- **Genetics:**
- **Environmental factors:**
- **Infections:**

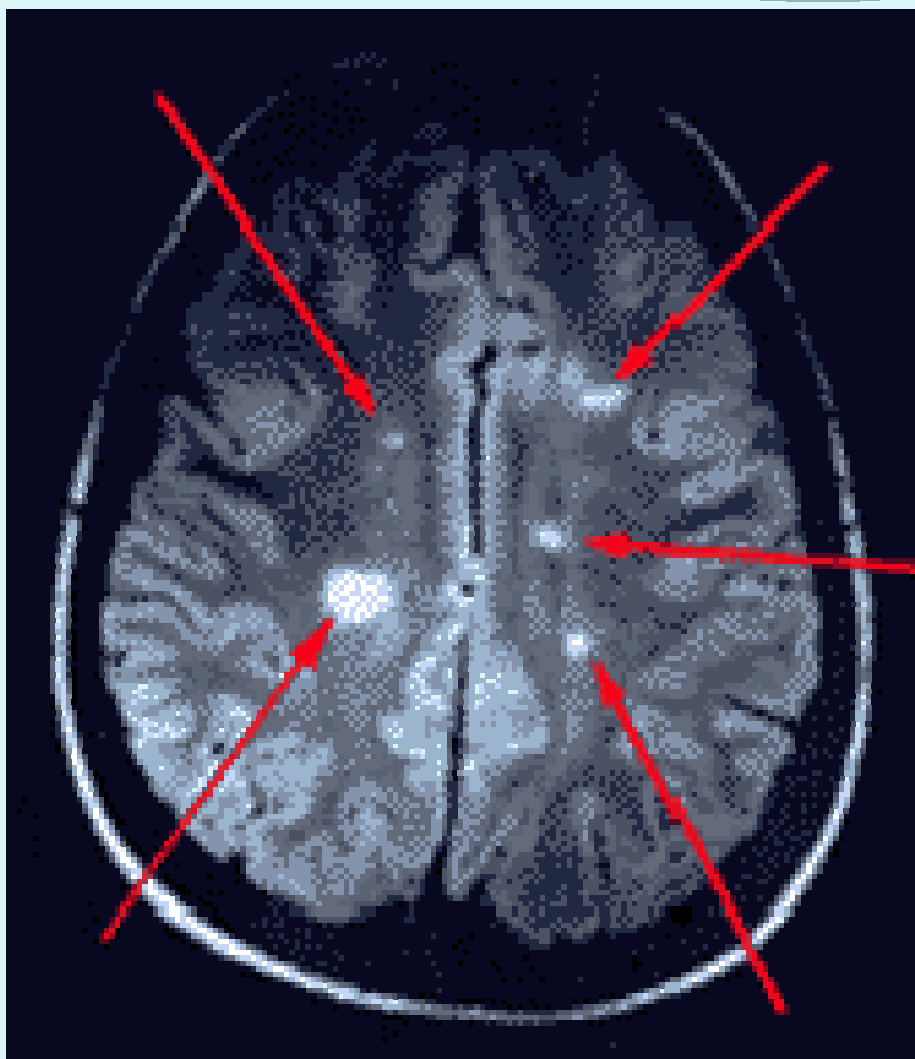
# Genetics Of MS



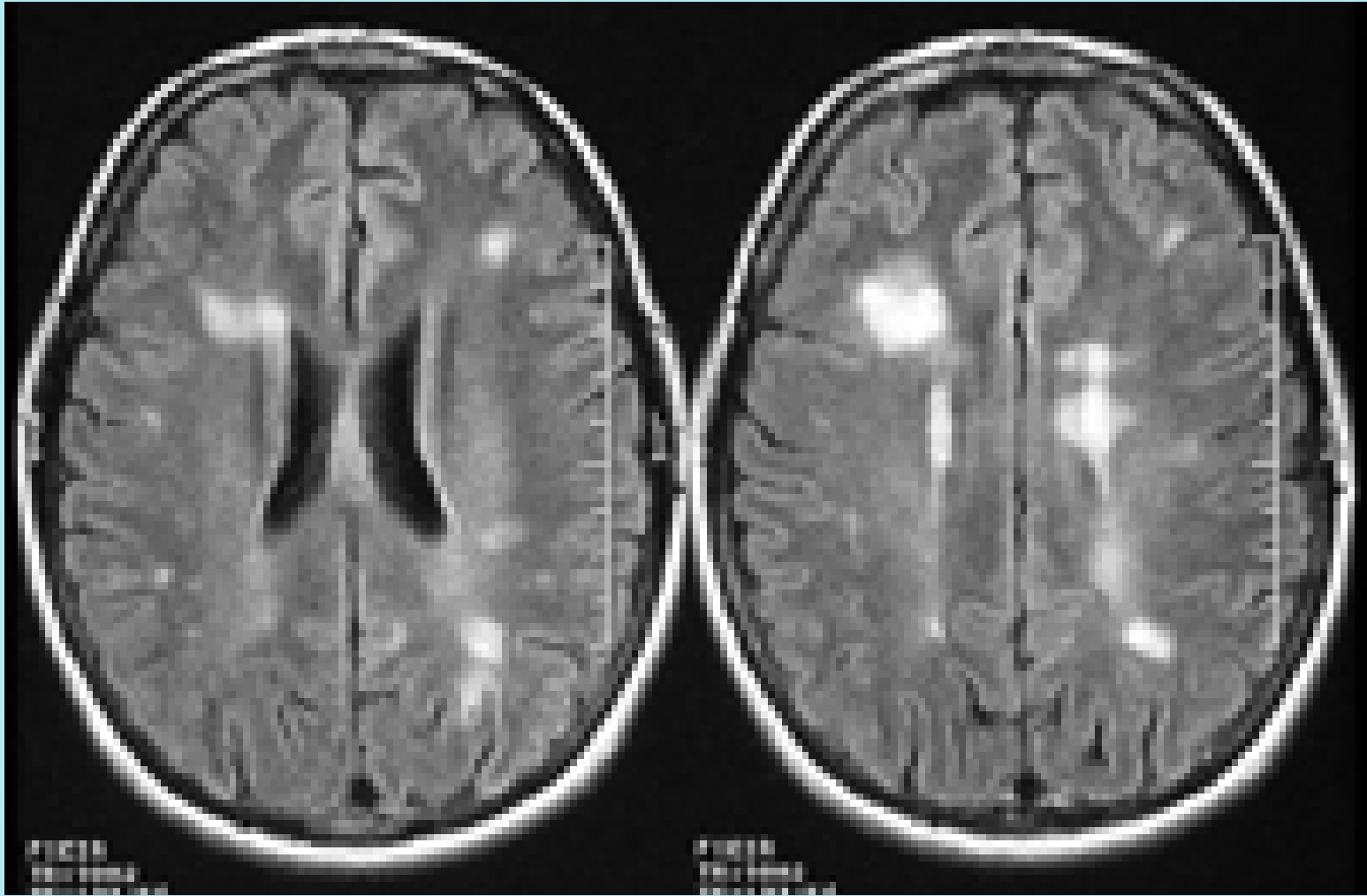




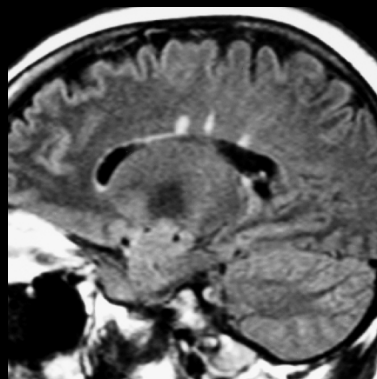
# Radiological Findings







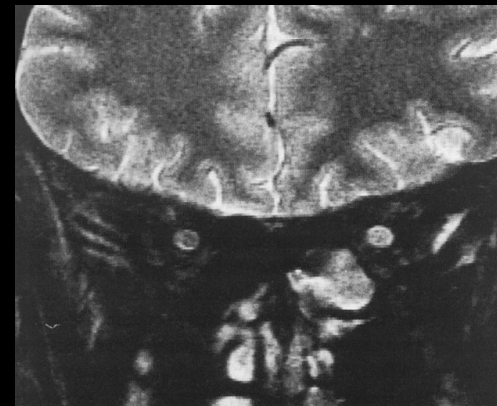
# Magnetic Resonance Imaging in MS



**Brain**

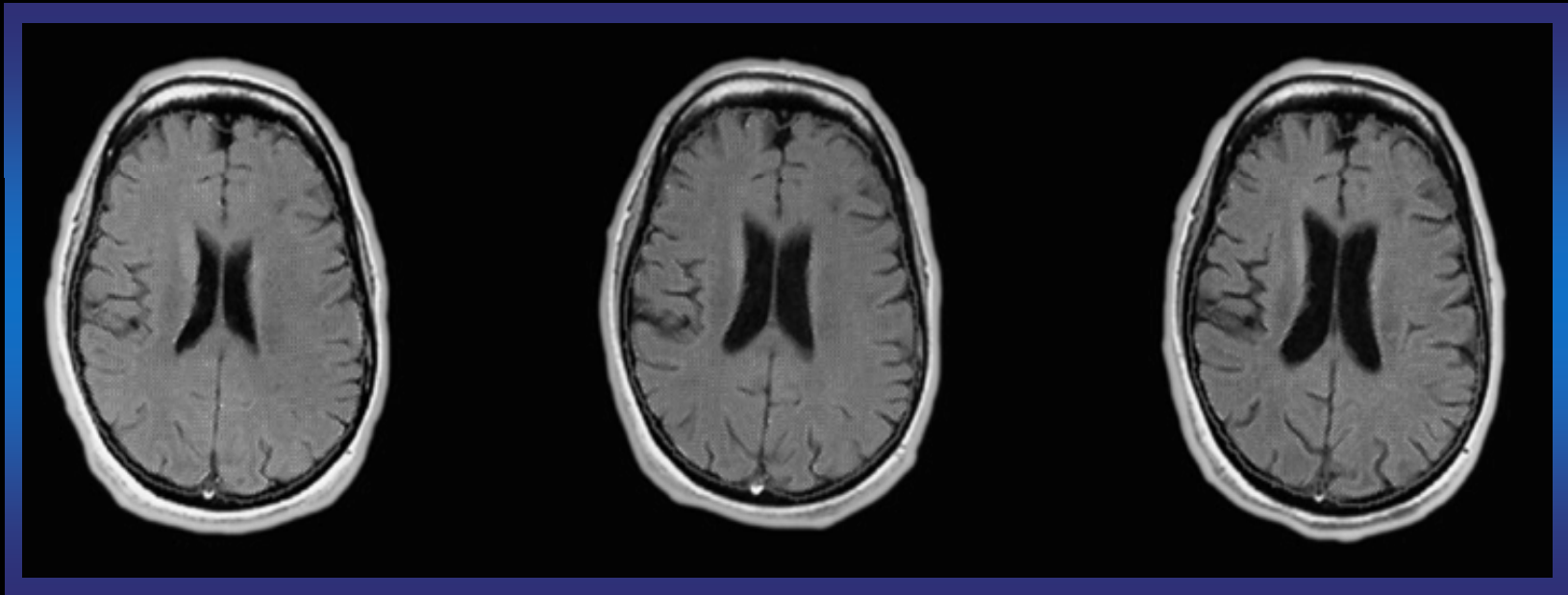


**Spinal cord**



**Optic nerve**

# Brain Atrophy (Shrinkage) in Untreated MS



Images acquired over the course of 7 years  
from a single person with untreated MS

# MRI: Spinal Imaging

A

A sagittal MRI scan of the spine, showing the vertebral column and surrounding soft tissue structures. The image is in grayscale, with the vertebrae appearing as dark, segmented blocks. The intervertebral discs are visible between the vertebrae. The spinal cord is visible within the vertebral canal. The surrounding soft tissue, including muscles and ligaments, is shown in various shades of gray. The image is labeled with a small white 'A' on the left side.



# Materials & Methods



- Eighty patients known to be with MS,
- Twenty four males
- and fifty six females,
  
- their ages ranged between 26-71 years, with a mean of  $38.7 \pm 4.8$  . 2 .

- All cases were subjected to
- complete clinical
- and neurological history
- and examination to confirm the diagnosis.

- There were 44 cases with quadriparesis,  
(12 males and 32 female)
- and 36 cases with paraparesis  
(12 males and 24 females).

- All cases were under their regular treatment either by corticosteroids, or interferon.
- These cases were divided into two main groups, each group consists of 40 cases (12 males and 28 females),

- Group I received
- honey, pollen, royal jelly and propolis and were treated with bee acupuncture 3 times weekly, for 12 months, started gradually by one sting then gradually increase up to 25 stings per session,
- in addition to their medical treatment

- while group II remains on their ordinary medical treatment only.

- Bee acupuncture done by bee stings for regulating the immune system in the following points Du 13, 14, Li 11, S6, S9, points for MS Pat Wagner Buttocks Jiagi points for cervical area and lumbar area and vision points GB2 and Li3.

- All patients were instructed to receive
- 2000-3000 mg Vitamin C,
- 15 mg Vit. B1,
- 3 mg Vit. B2,
- 2mg Vit. B6,
- 5 mg Vit. B12,



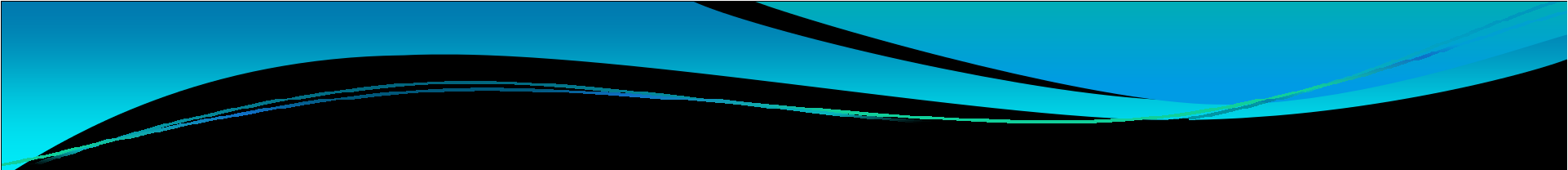
- 25 mg Folic acid,
- 3 mg Calcium pantothenate,
- 15mg Nicotinamide,
- 20 mg L- Arginine,
- 20 mg L- Lysine
- and 3 mcg Biotin / day.

- Serum samples were obtained from patients with clinically definite MS for estimation of serum levels of immunoglobulin E (Hirano et al., 1989)
- using commercially available ELISA kits according to the manufacturers' directions.

## cytokine levels

- IFN- $\gamma$ ,
- interleukin (IL) 1 $\beta$ ,
- IL-4,
- IL-6,
- IL-10,
- tumor necrosis factor alpha (TNF $\alpha$ )

were assessed using enzyme linked - immunosorbent assays (Abrams, 1995) using commercially available ELISA kits according to the manufacturers' directions (kits produced by Bender Med System, Vienna, Austria).

- 
- All these investigations were done at the beginning of the study and by the end of one year of supplementation and bee sting sessions



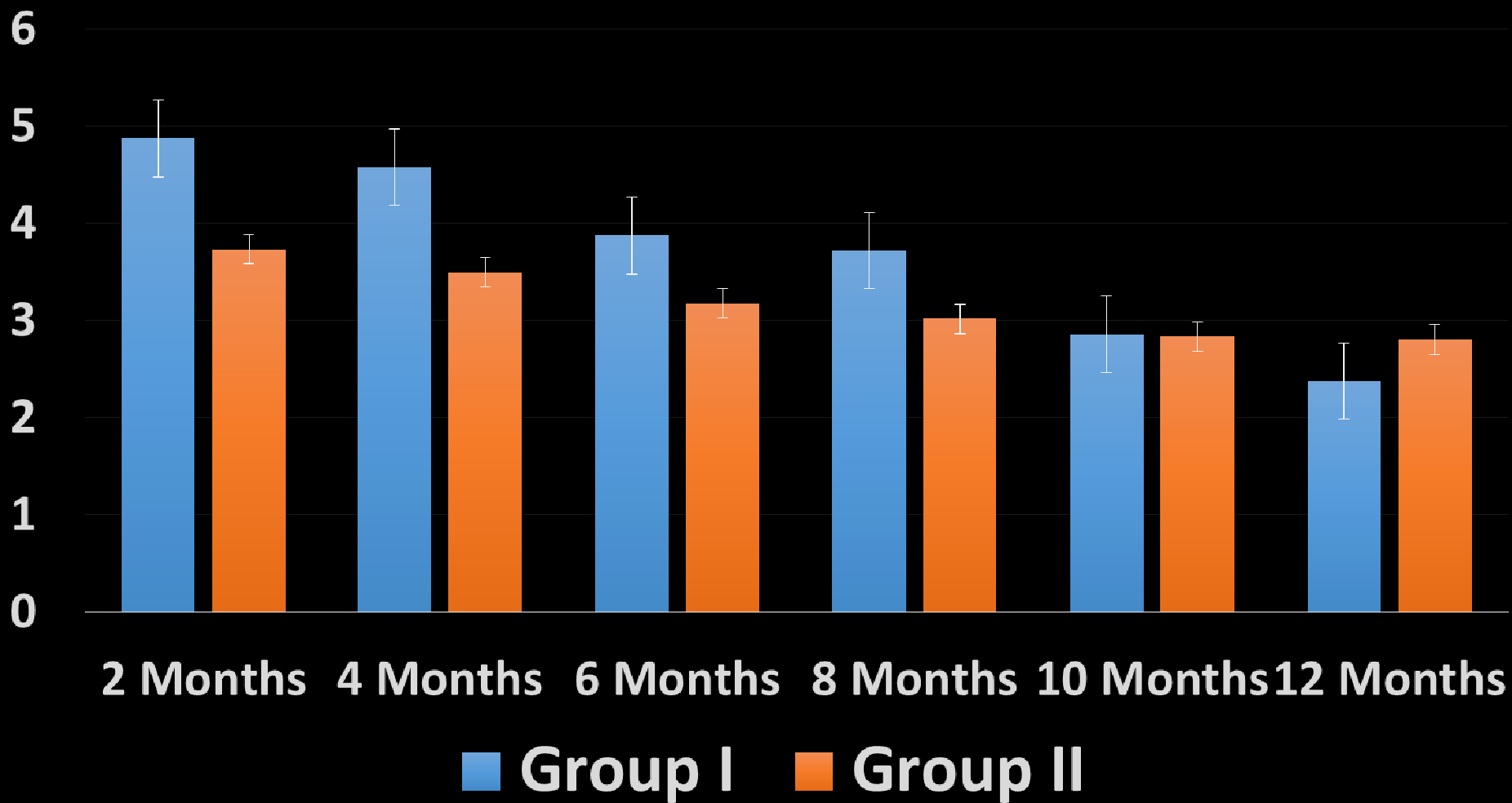
**RESULTS**

- We found that 8 patients out of 12 (66.6 % of paraparesis cases),
  - showed some improvement regarding
  - their defects in gait,
  - bowel control,
  - constipation
  - and urination,

- while 12 cases out of 16 cases (75% of quadriparesis cases),
- showed some mild improvement in their
  - movement in bed,
  - and better improvement in bed sores,
  - sensation,
  - and better motor power,
  - only two cases of them ( 12.5% ) were able to stand for few minutes with support.

# Symptoms Score Improvement Recorded Every Two Months (1-12):

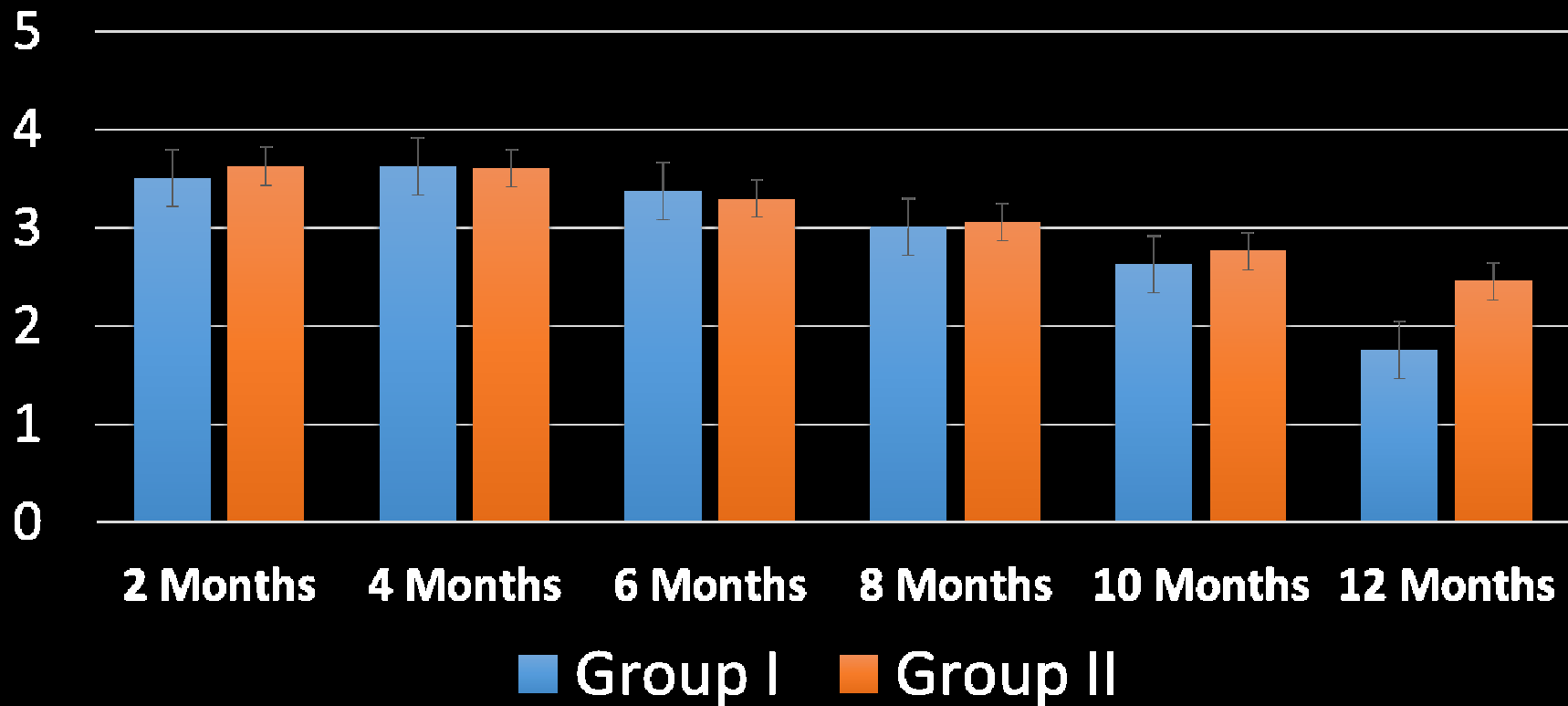
## General Condition





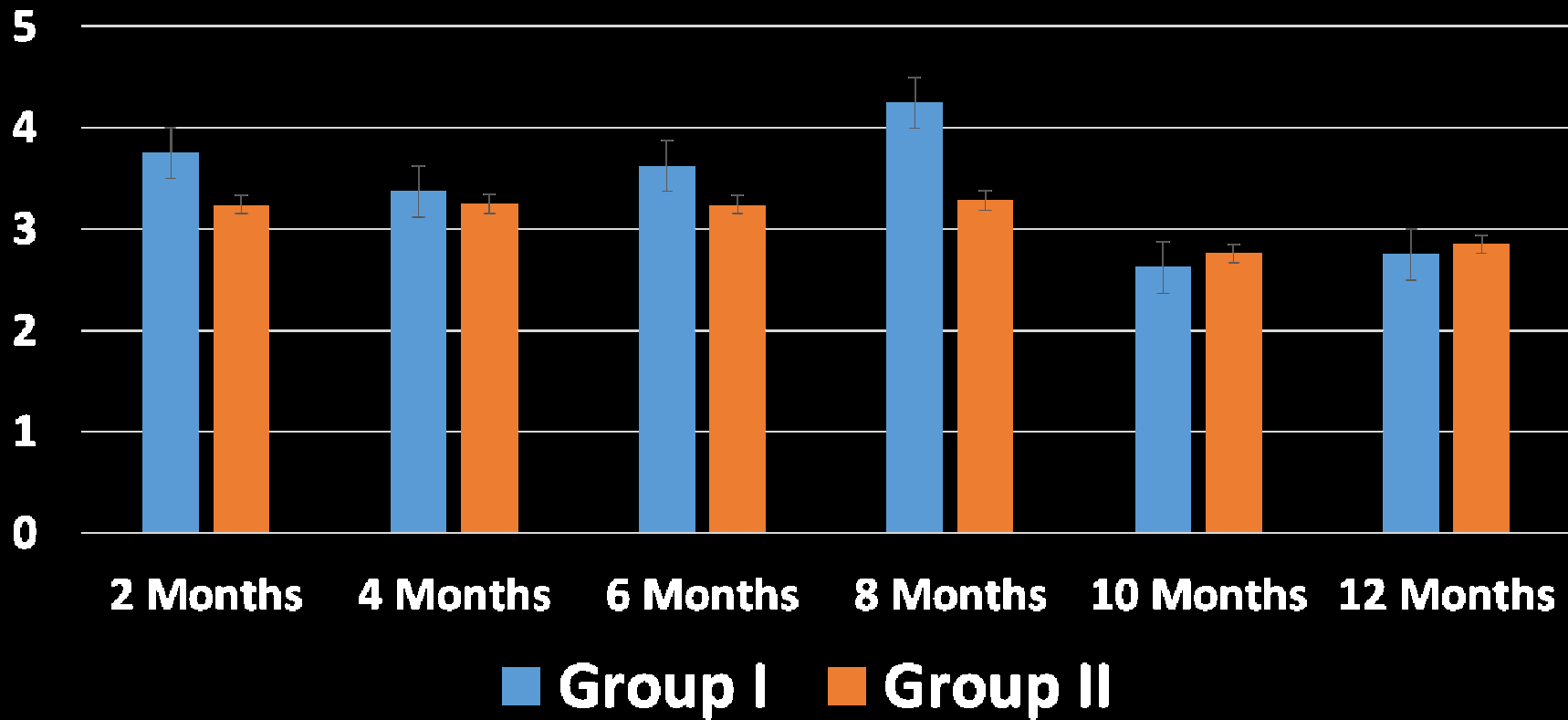
# Symptoms Score Improvement Recorded Every Two Months (1-12):

## Depression



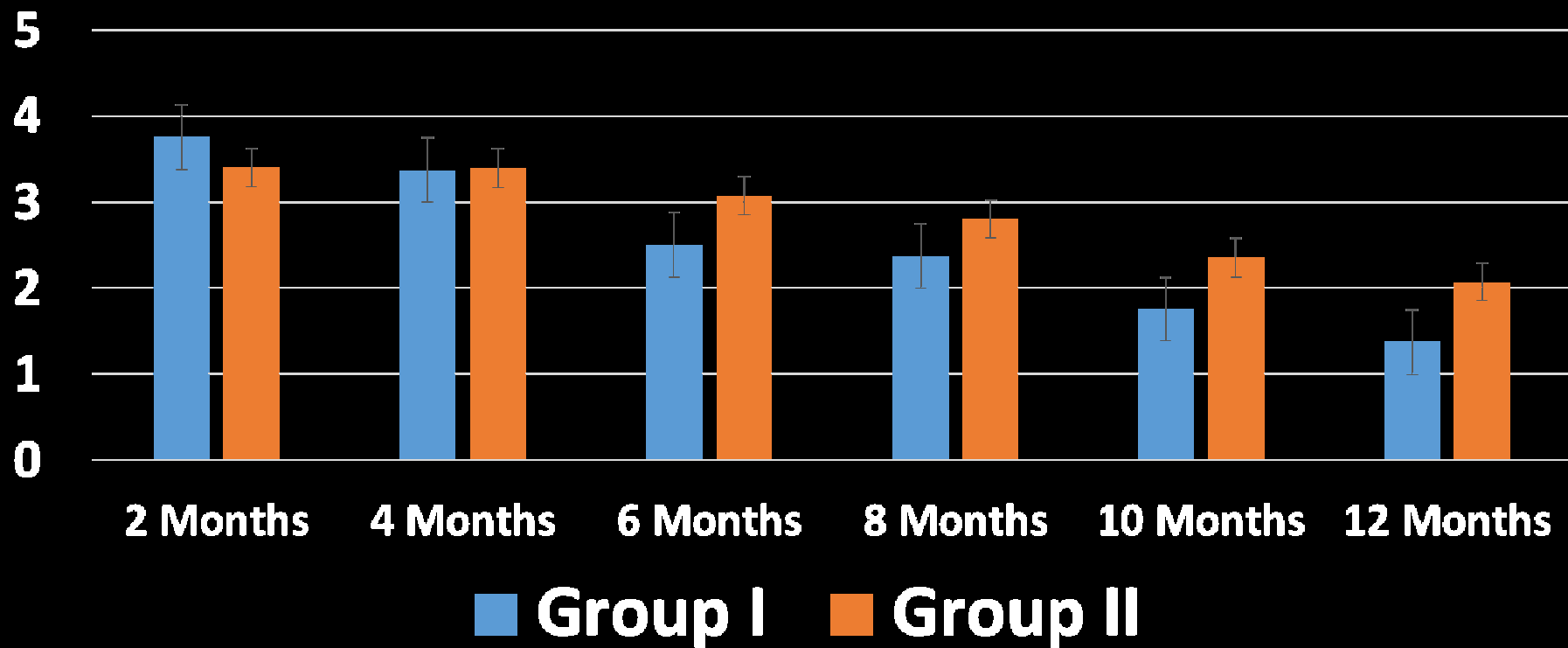
# Symptoms Score Improvement Recorded Every Two Months (1-12):

## No Energy Fatigue



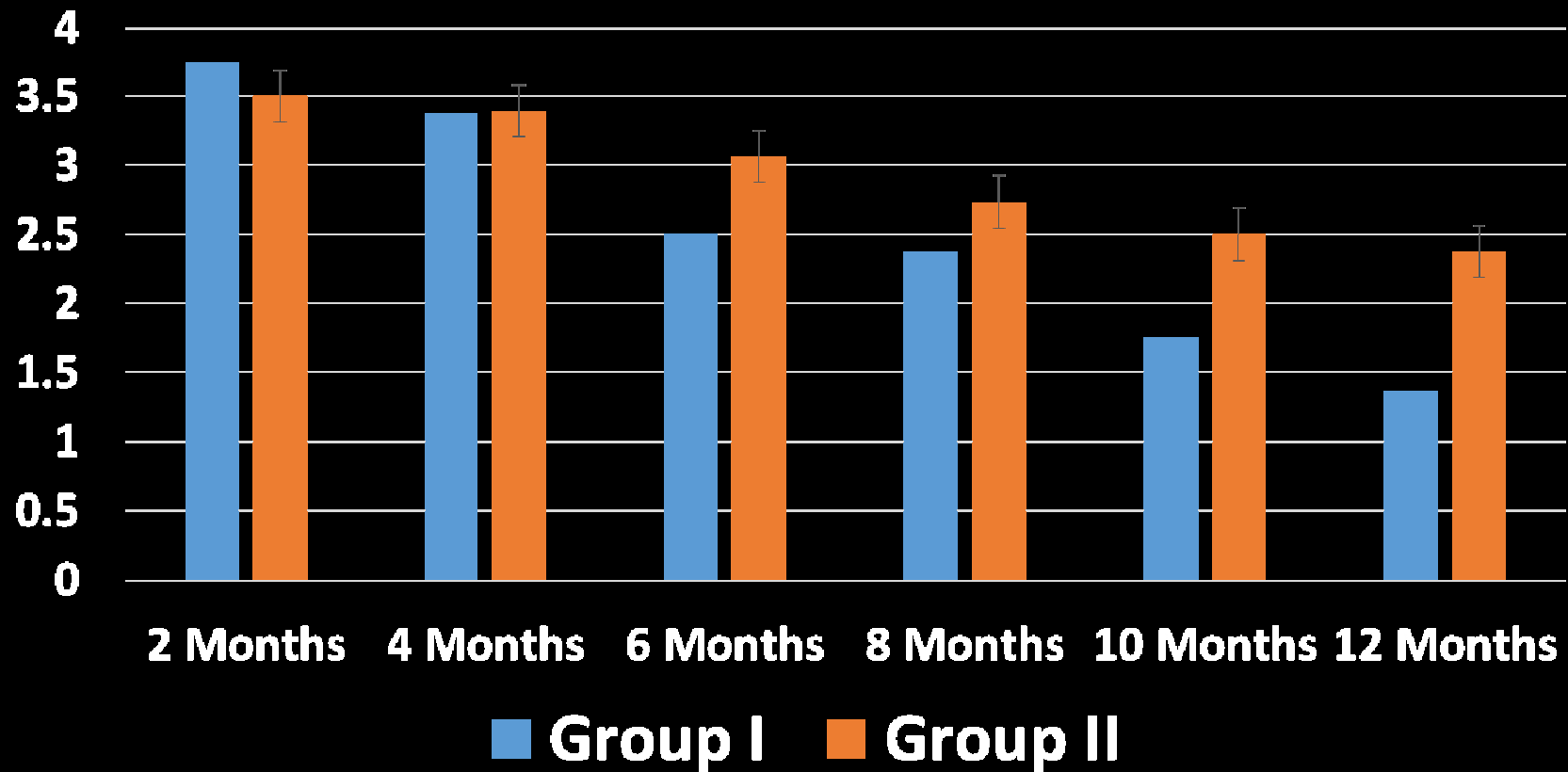
# Symptoms Score Improvement Recorded Every Two Months (1-12):

## Sleeping



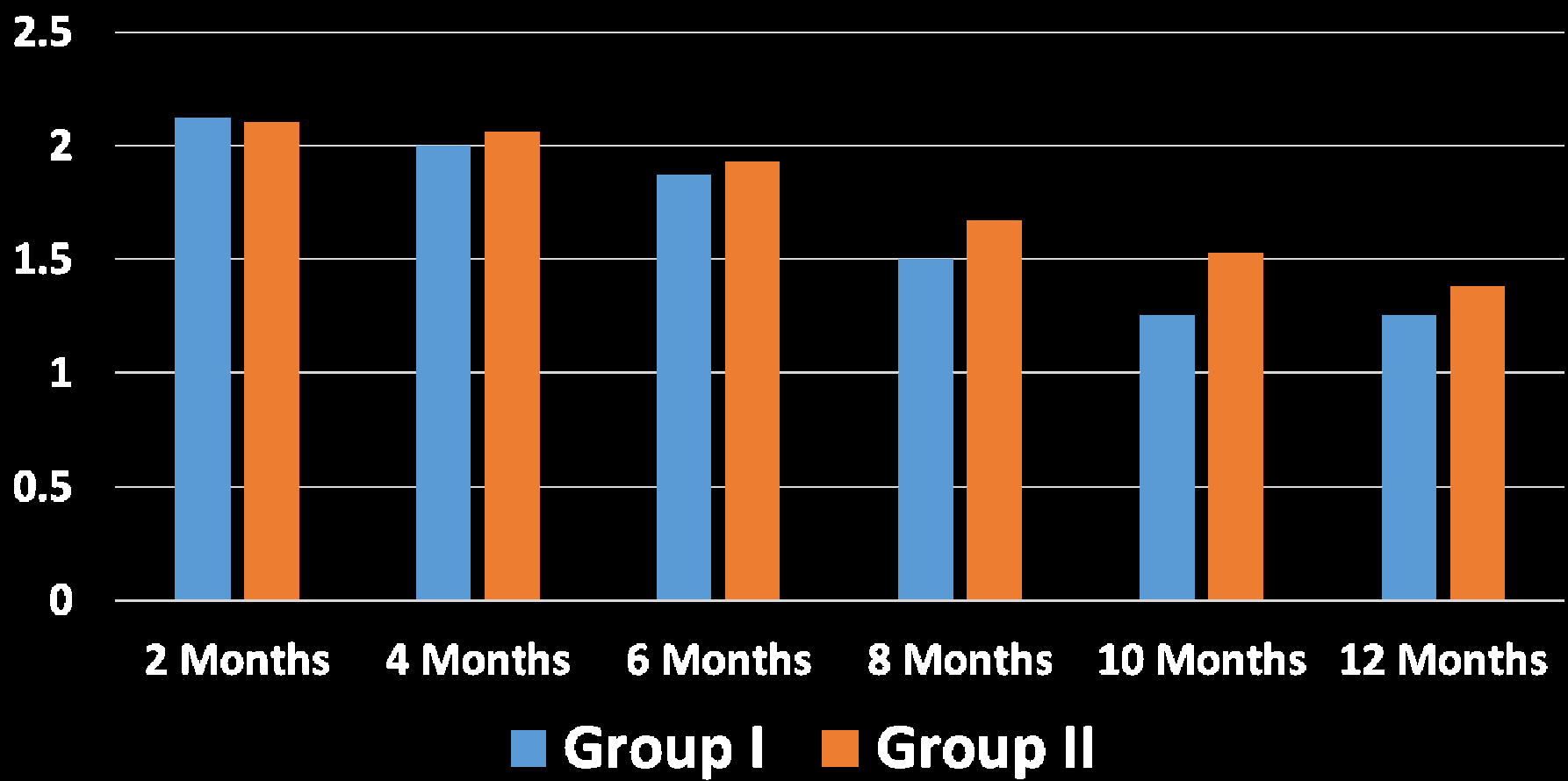
# Symptoms Score Improvement Recorded Every Two Months (1-12):

## Heat tolerance



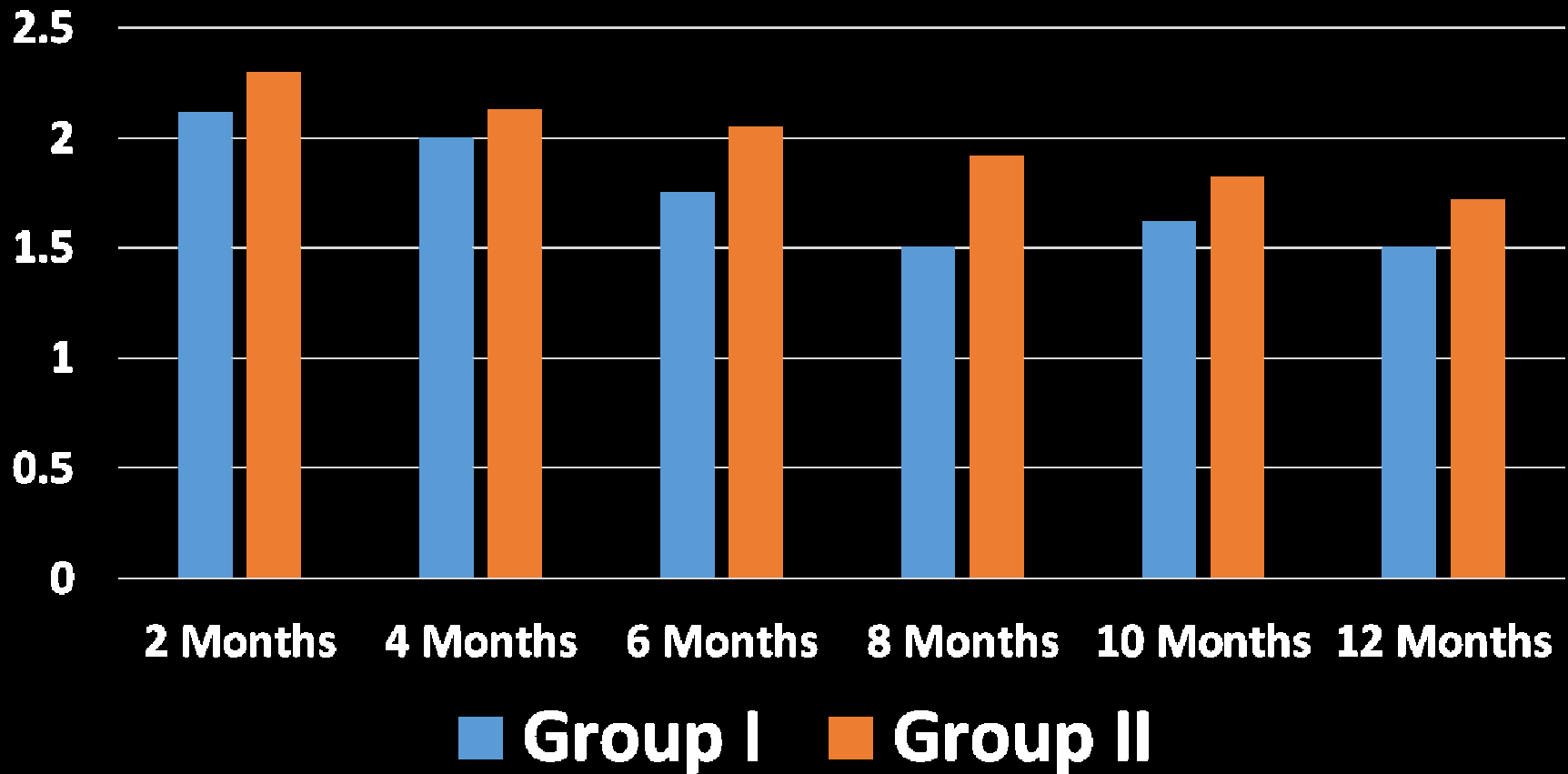
Symptoms Score Improvement Recorded Every Two Months (1-12):

### Attention span



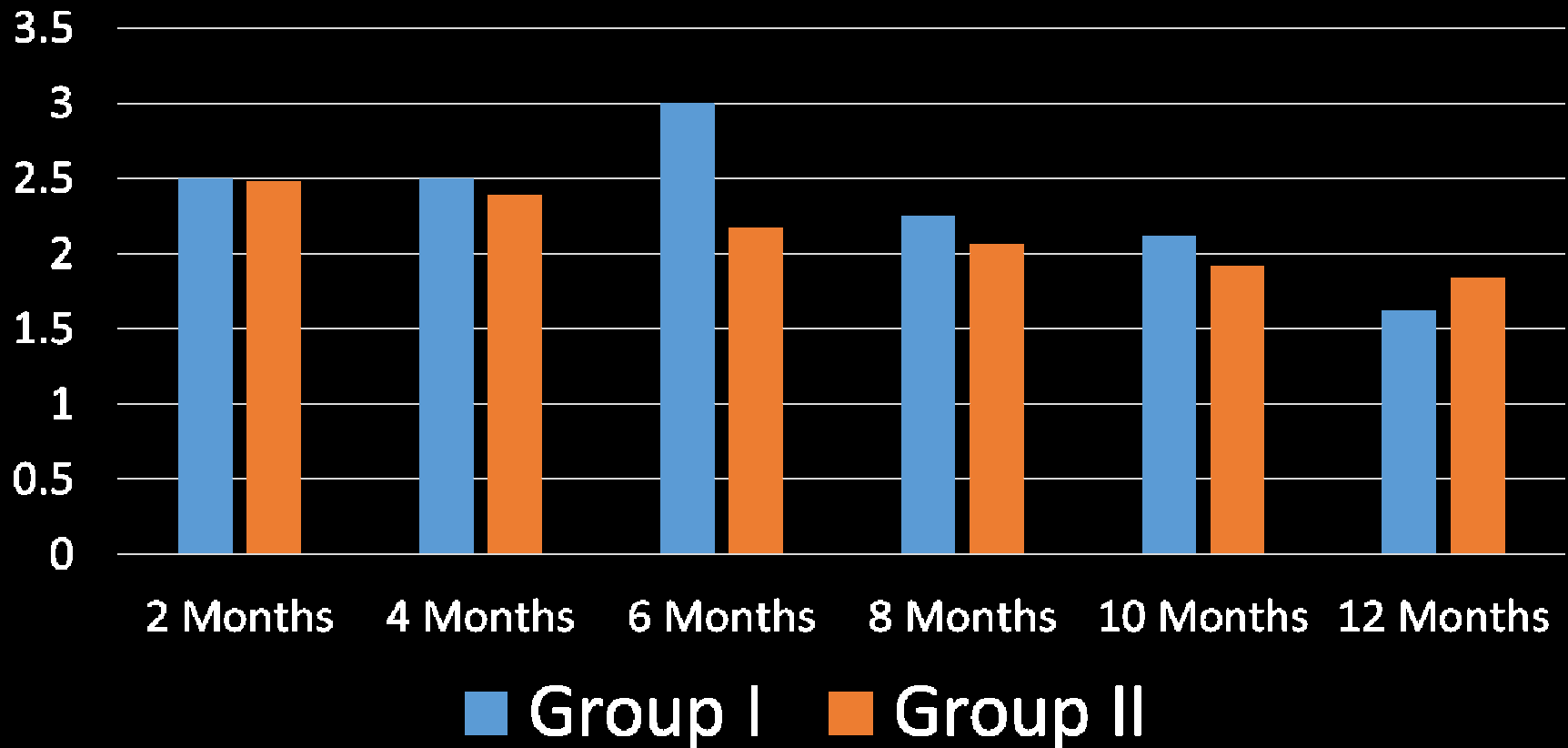
Symptoms Score Improvement Recorded Every Two Months (1-12):

## Memory



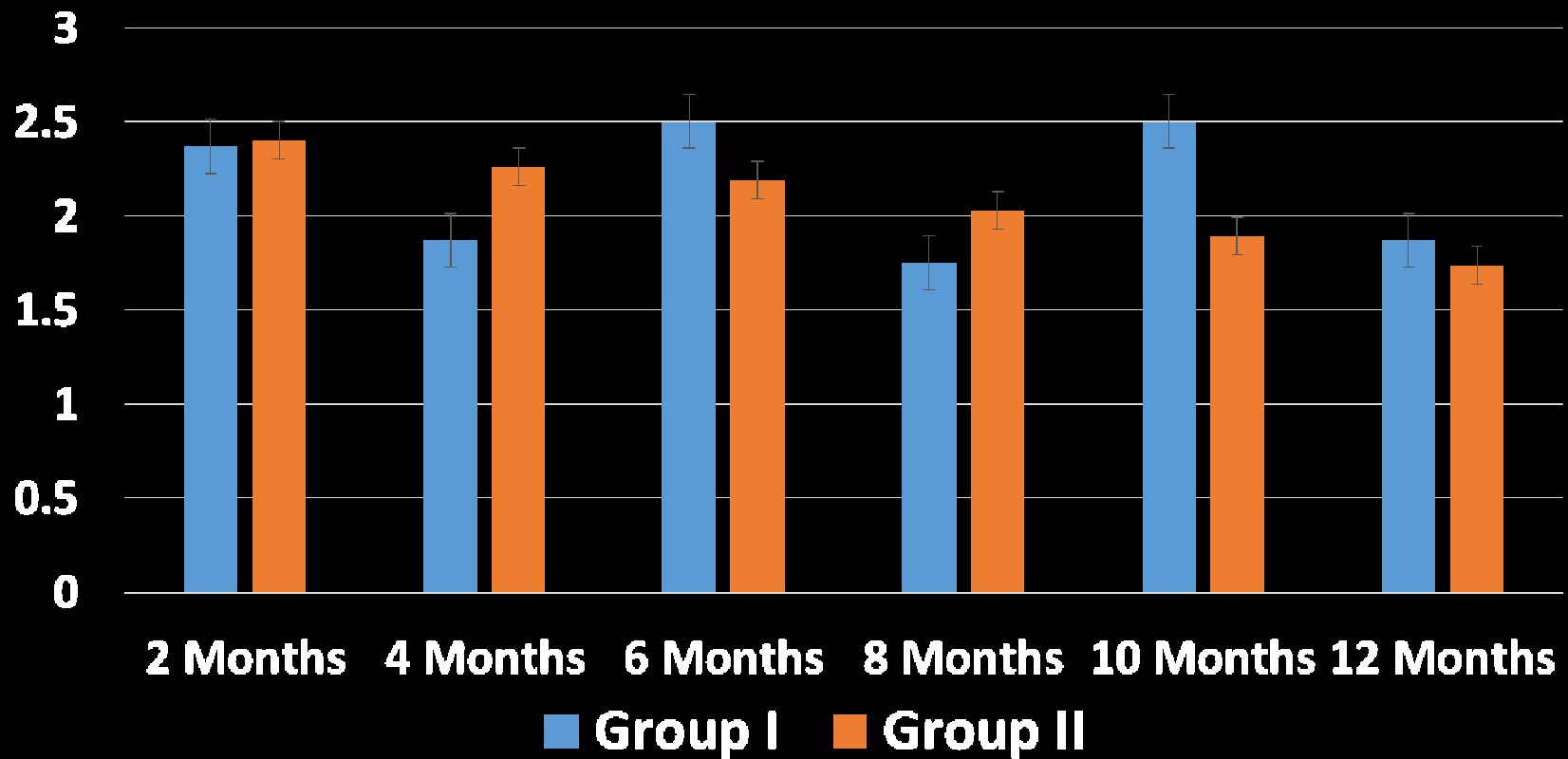
Symptoms Score Improvement Recorded Every Two Months (1-12):

# Rigidity



# Symptoms Score Improvement Recorded Every Two Months (1-12):

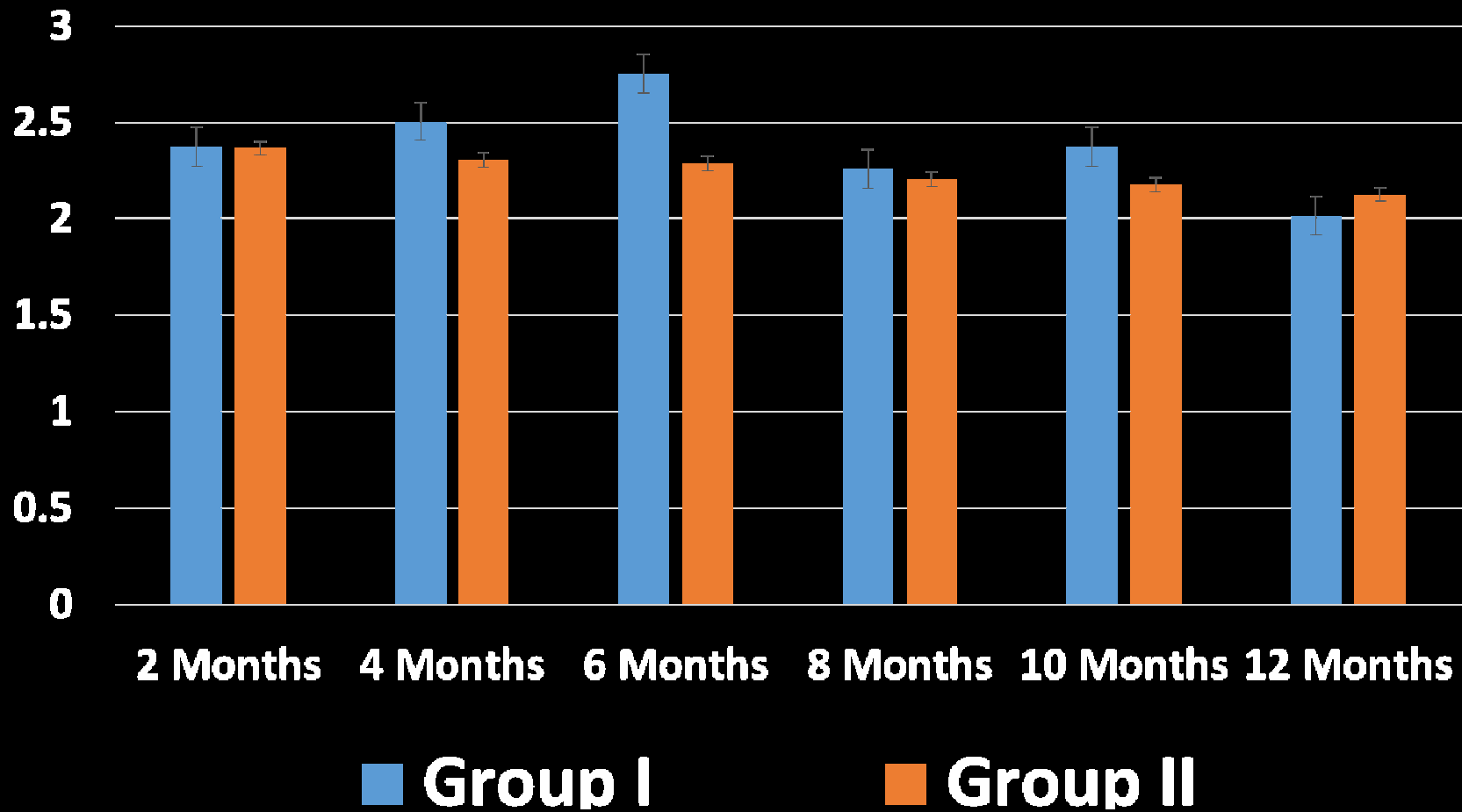
## Spasms





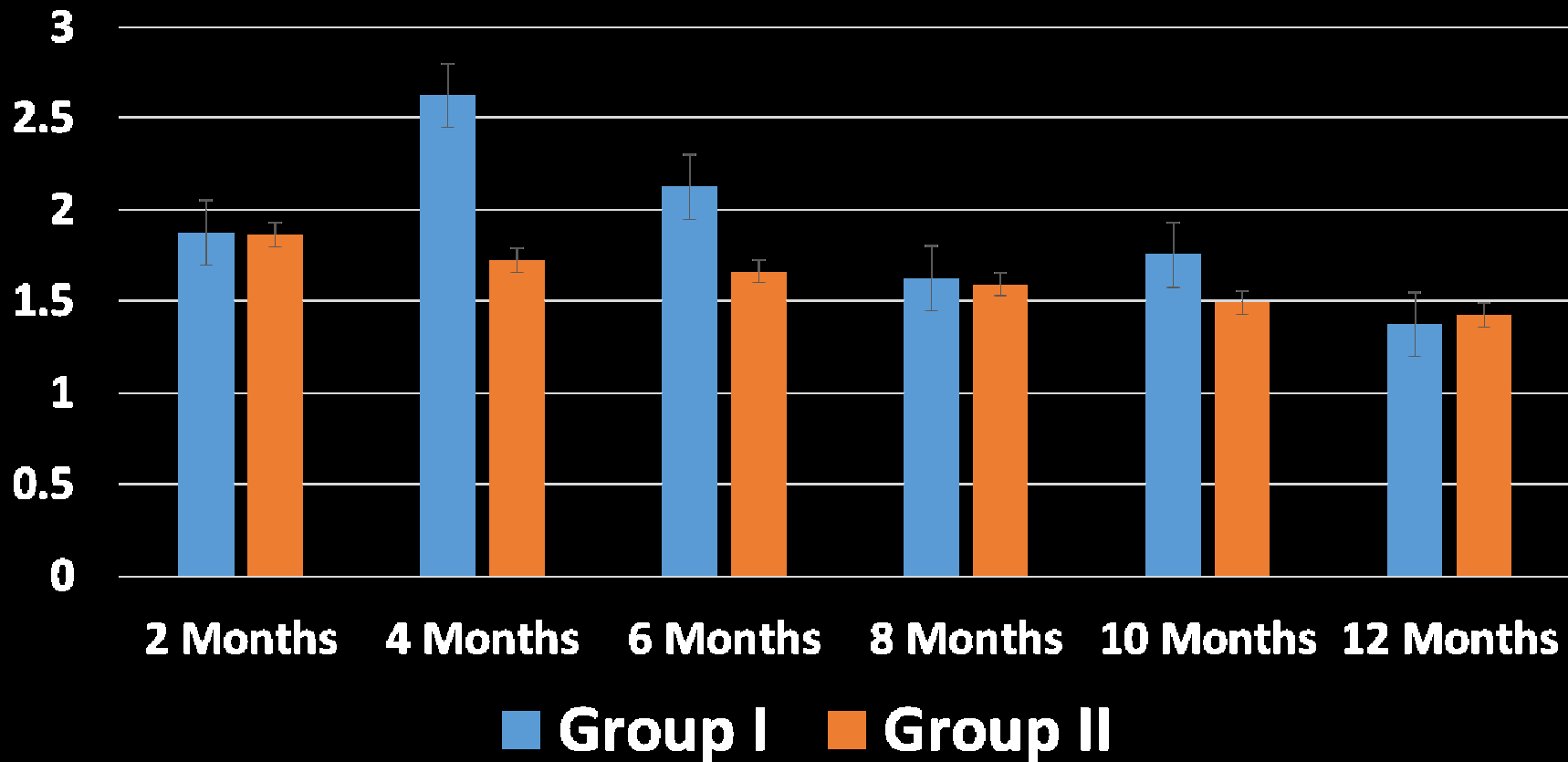
# Symptoms Score Improvement Recorded Every Two Months (1-12):

## Tremors



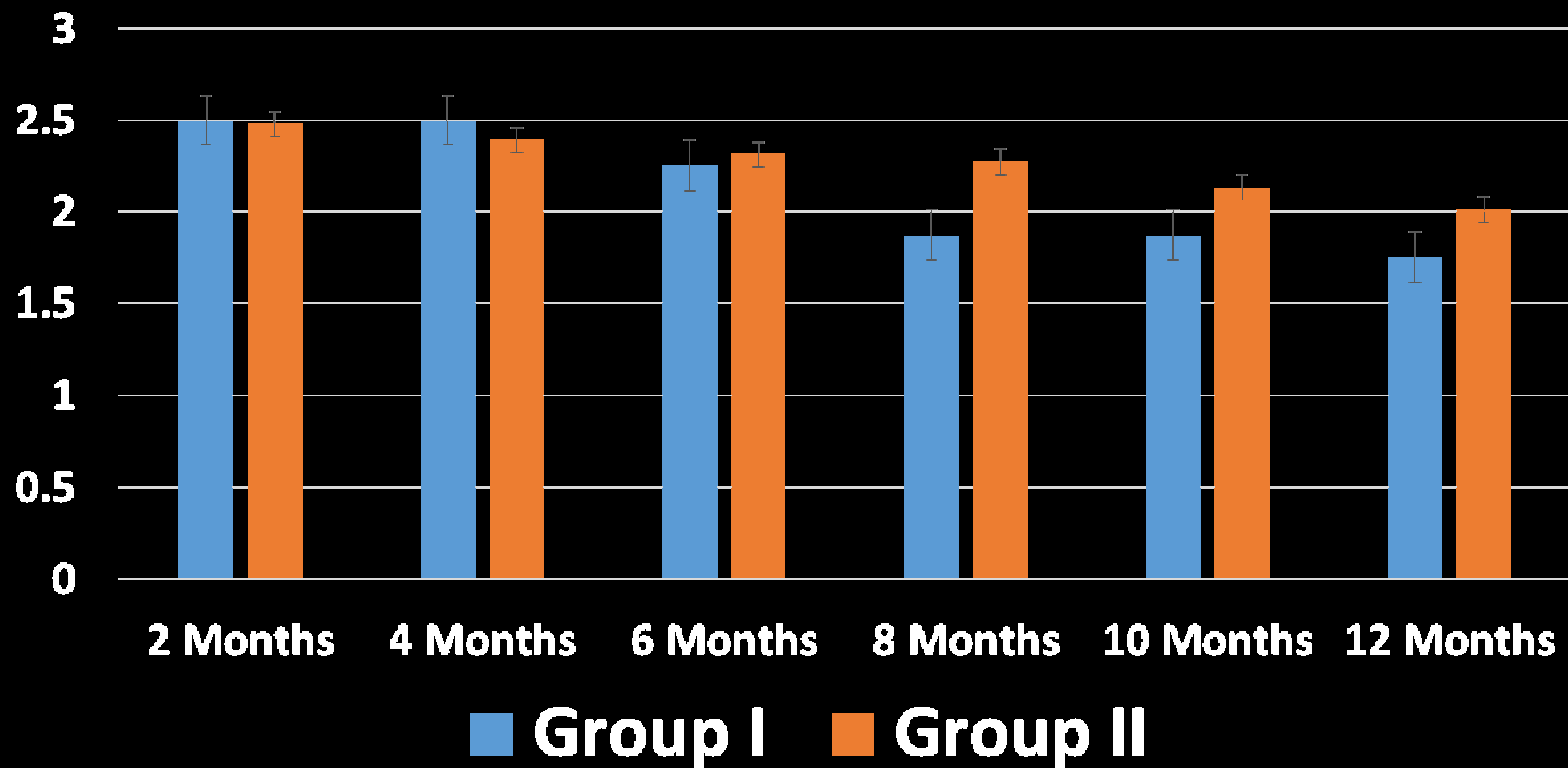
# Symptoms Score Improvement Recorded Every Two Months (1-12):

## Headaches



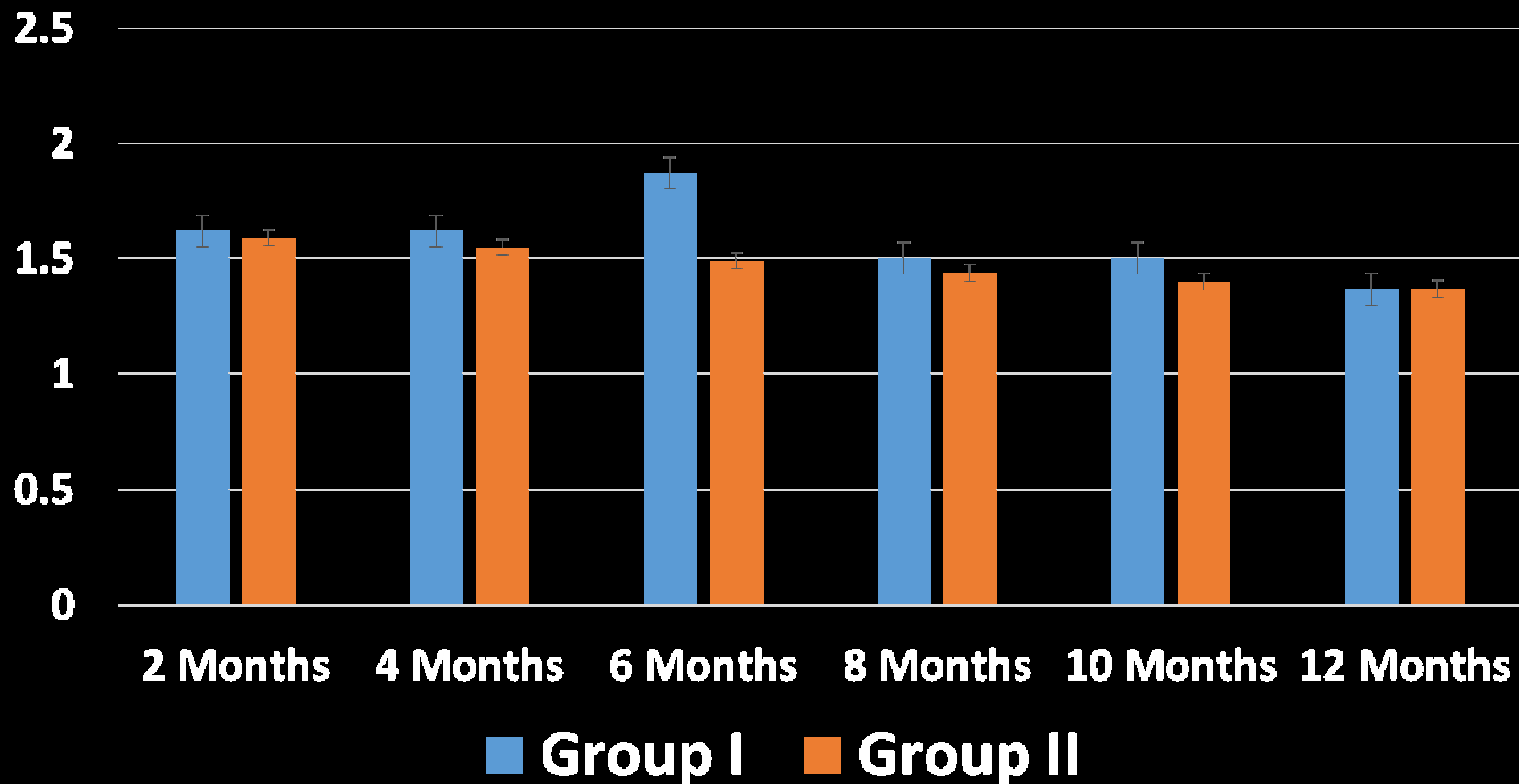
# Symptoms Score Improvement Recorded Every Two Months (1-12):

## Eye sight



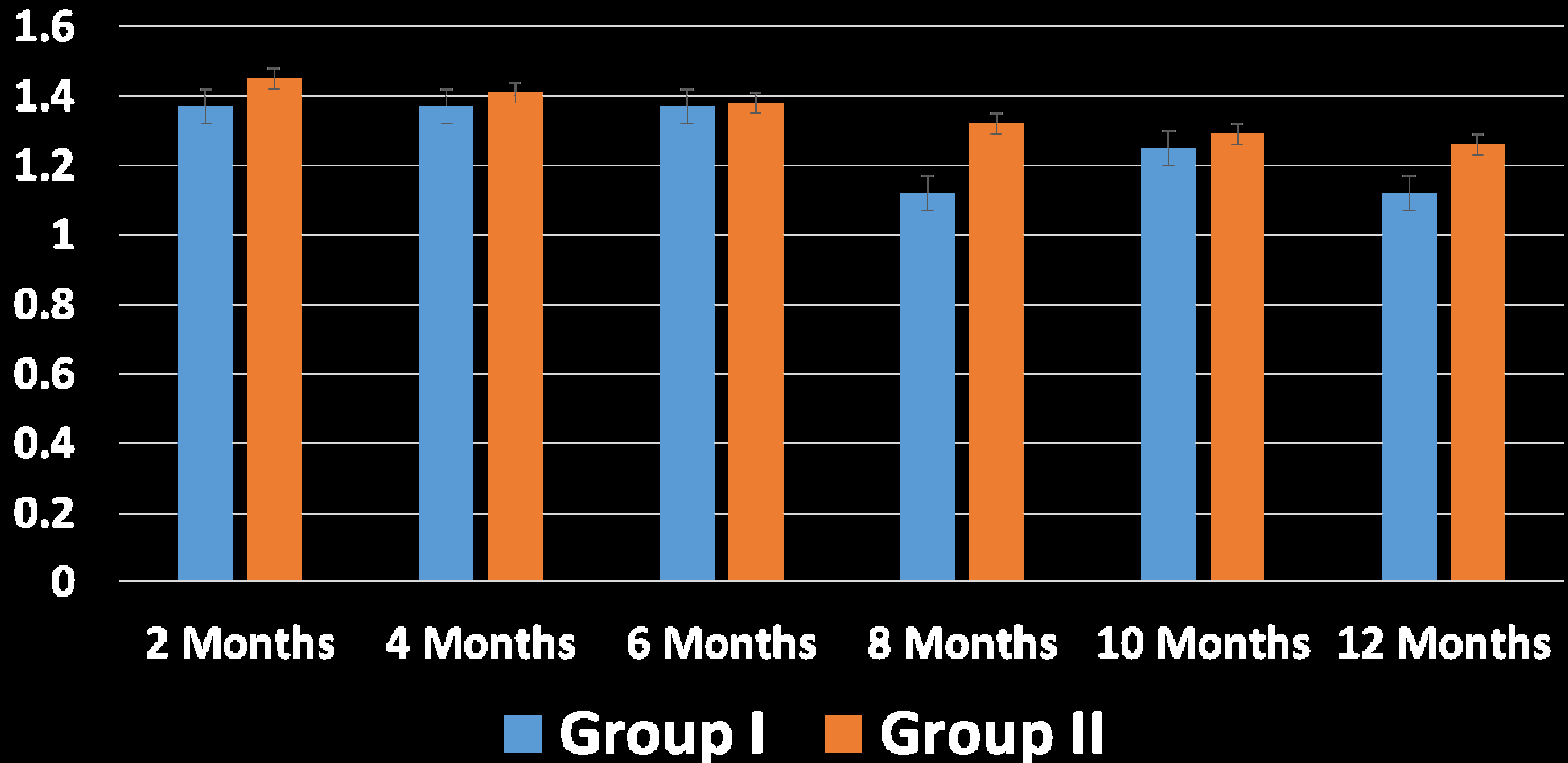
# Symptoms Score Improvement Recorded Every Two Months (1-12):

## Speech



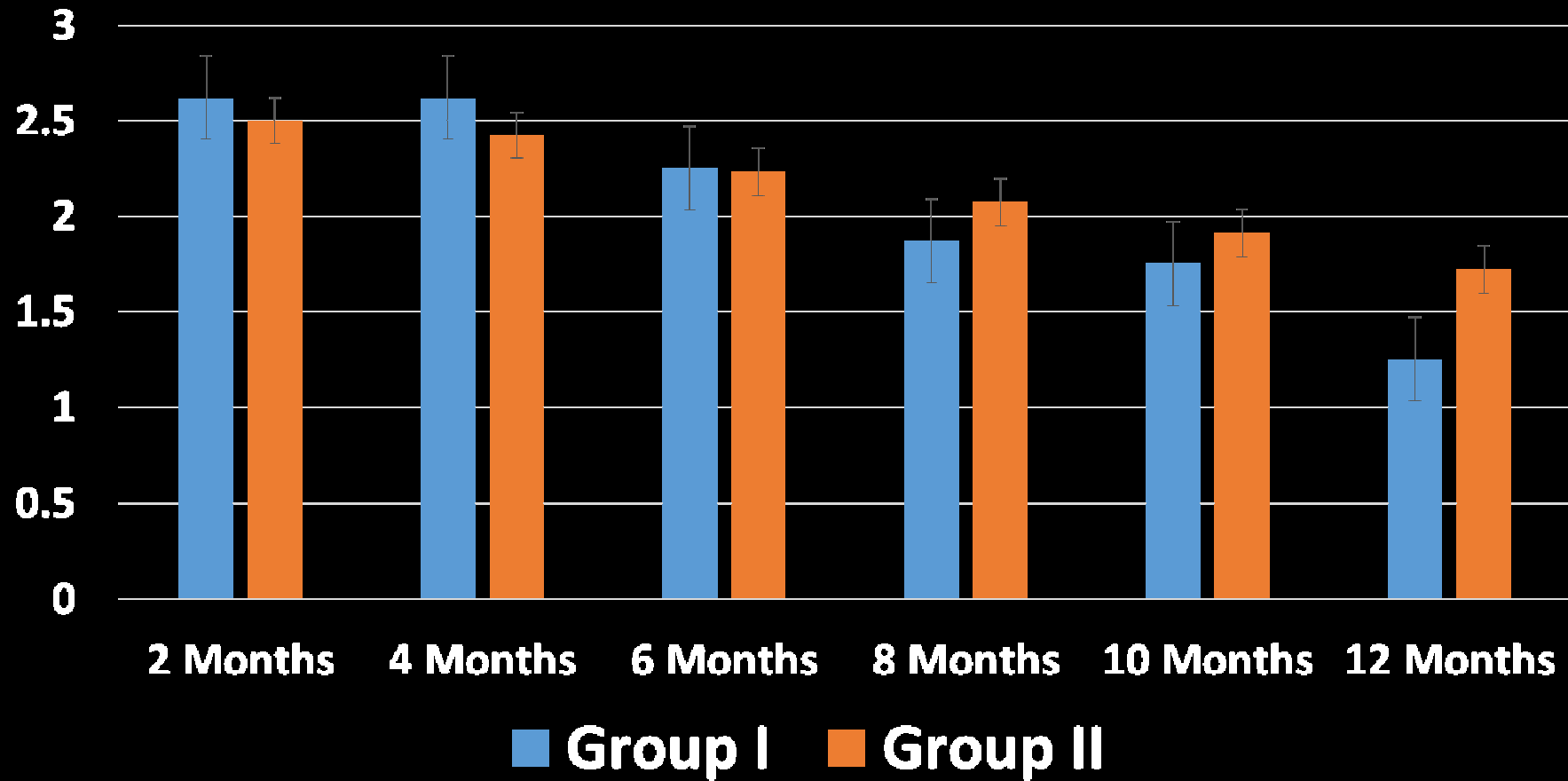
# Symptoms Score Improvement Recorded Every Two Months (1-12):

## Swallowing



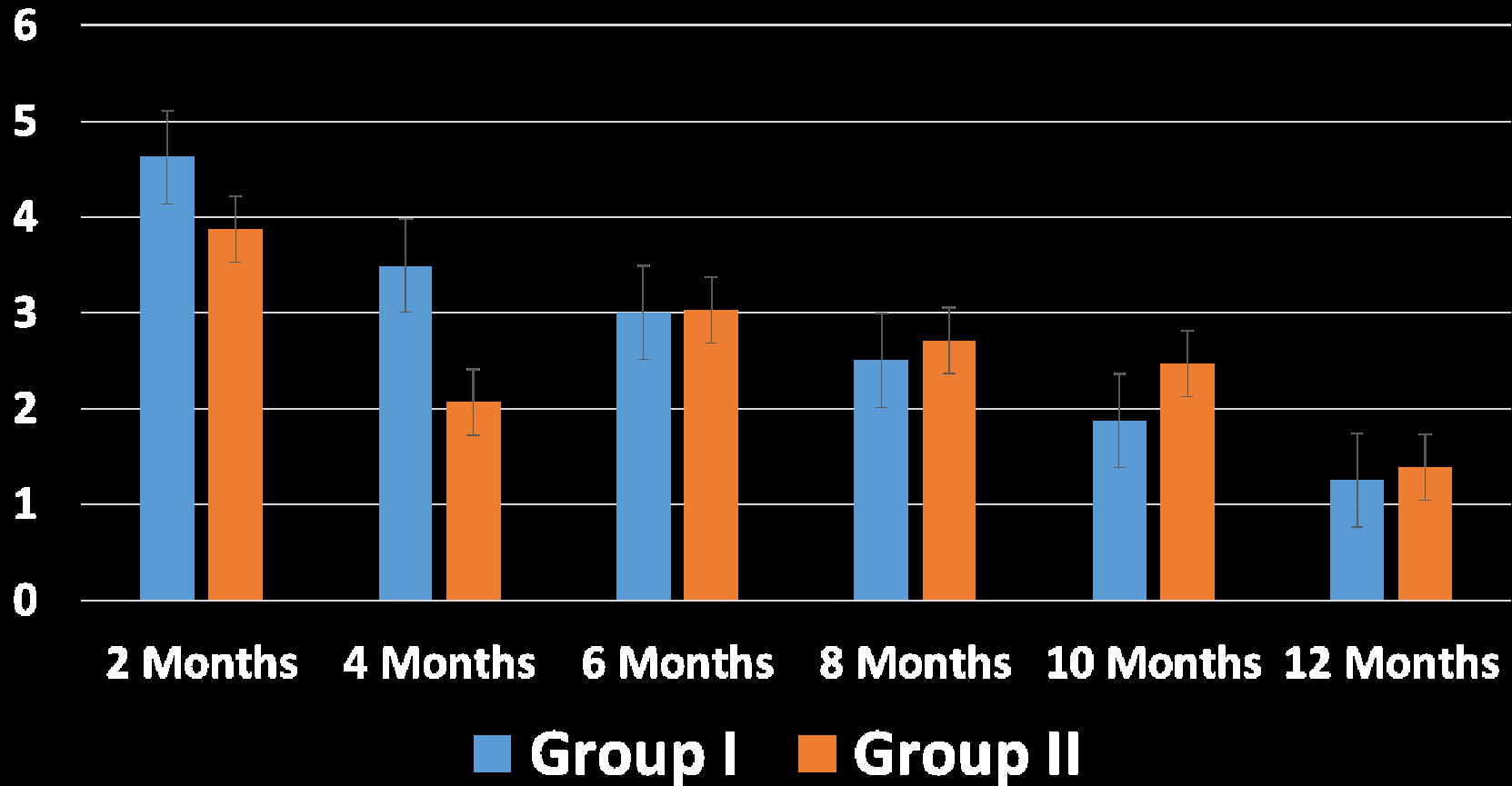
# Symptoms Score Improvement Recorded Every Two Months (1-12):

## Numbness



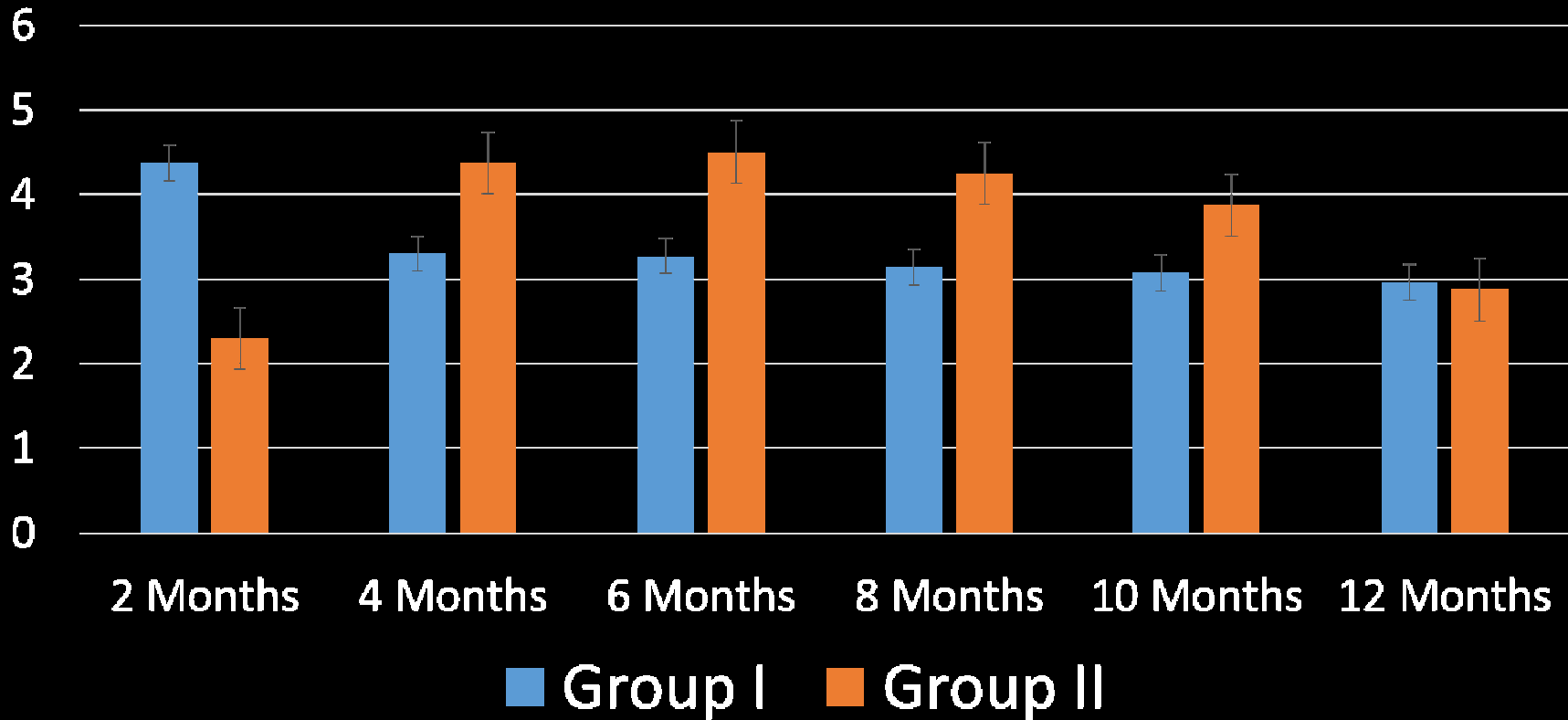
# Symptoms Score Improvement Recorded Every Two Months (1-12):

## Balance



# Symptoms Score Improvement Recorded Every Two Months (1-12):

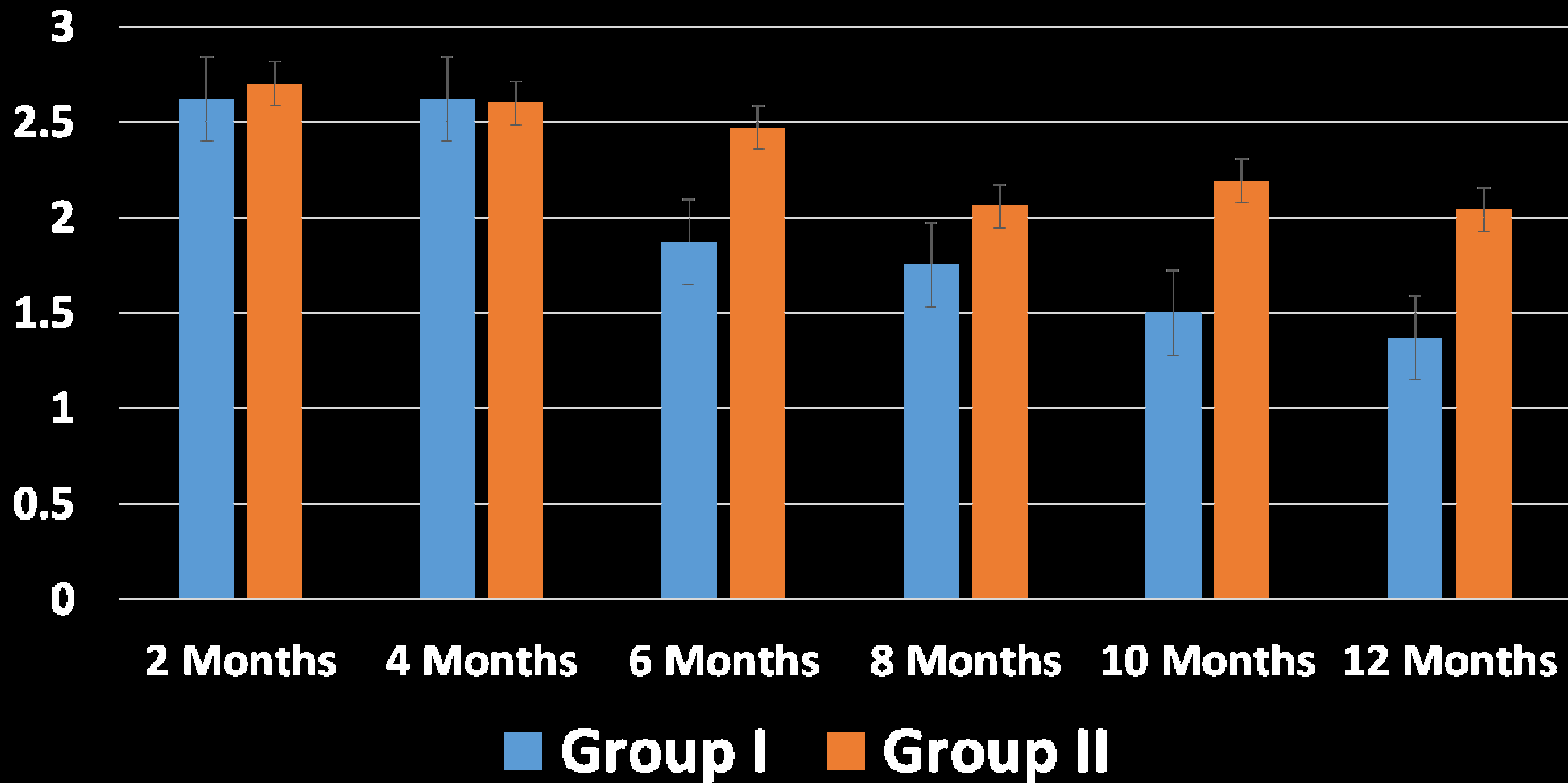
## Walking



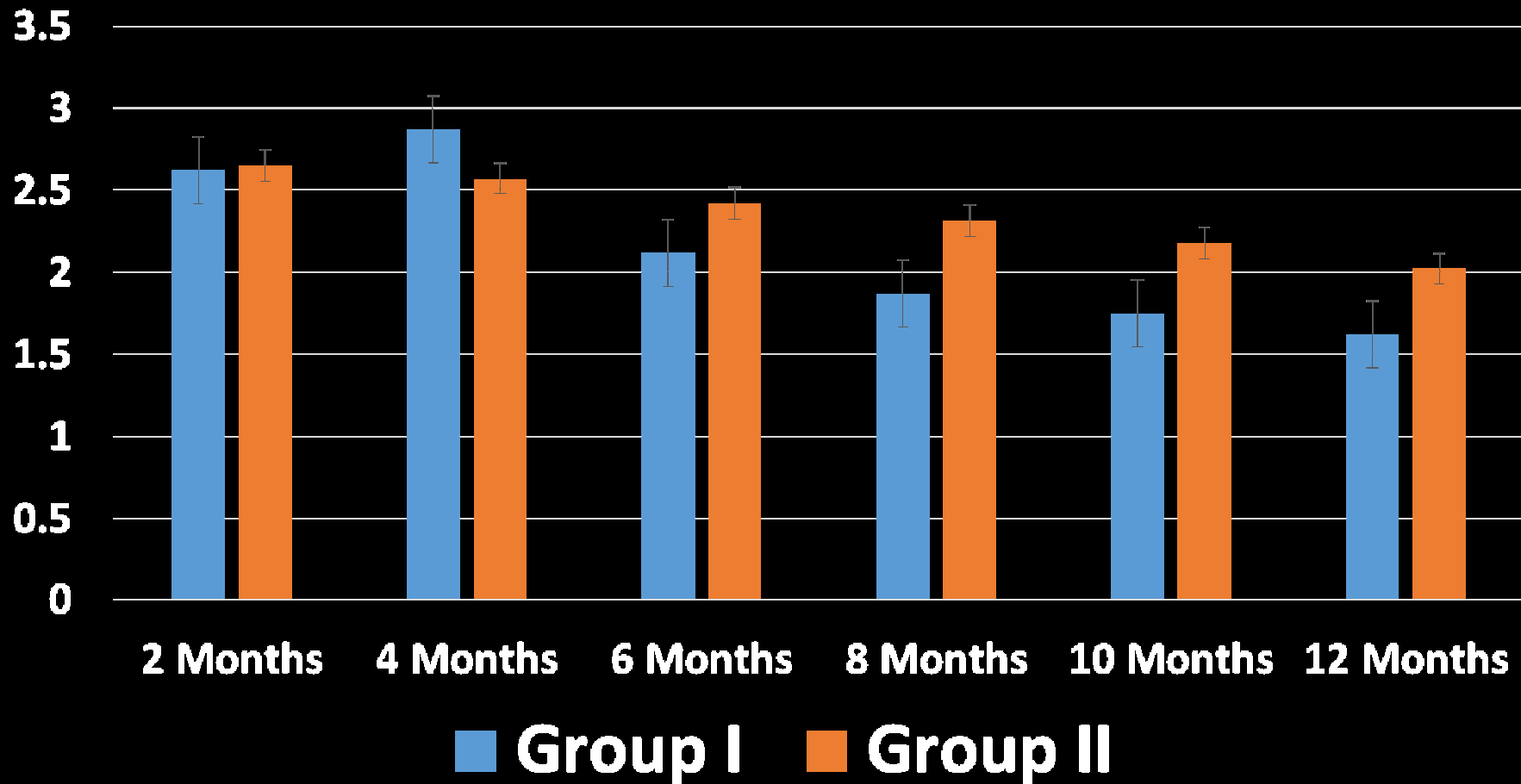


# Symptoms Score Improvement Recorded Every Two Months (1-12):

## Hand coordination

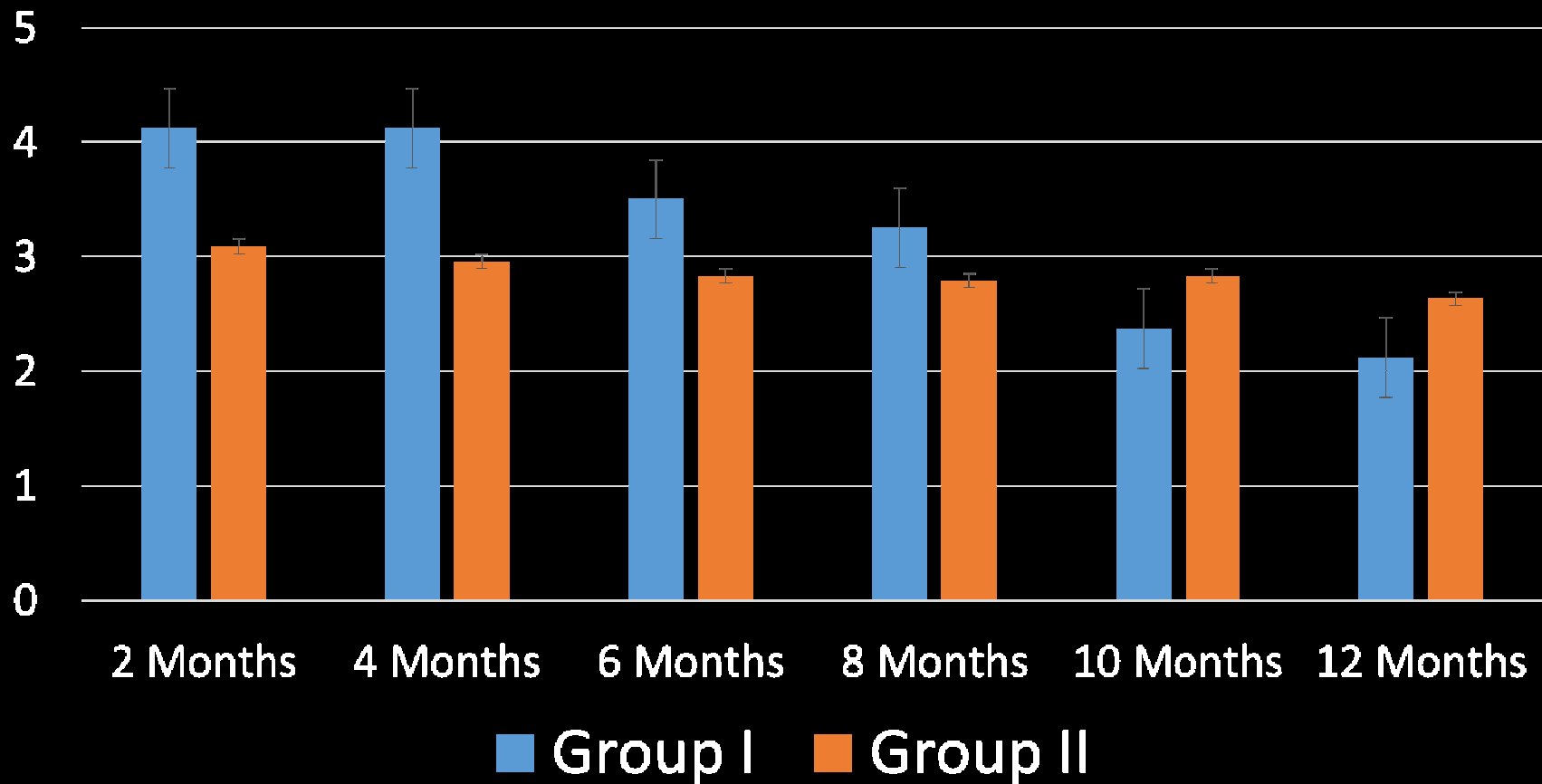


# Symptoms Score Improvement Recorded Every Two Months (1-12): Writing

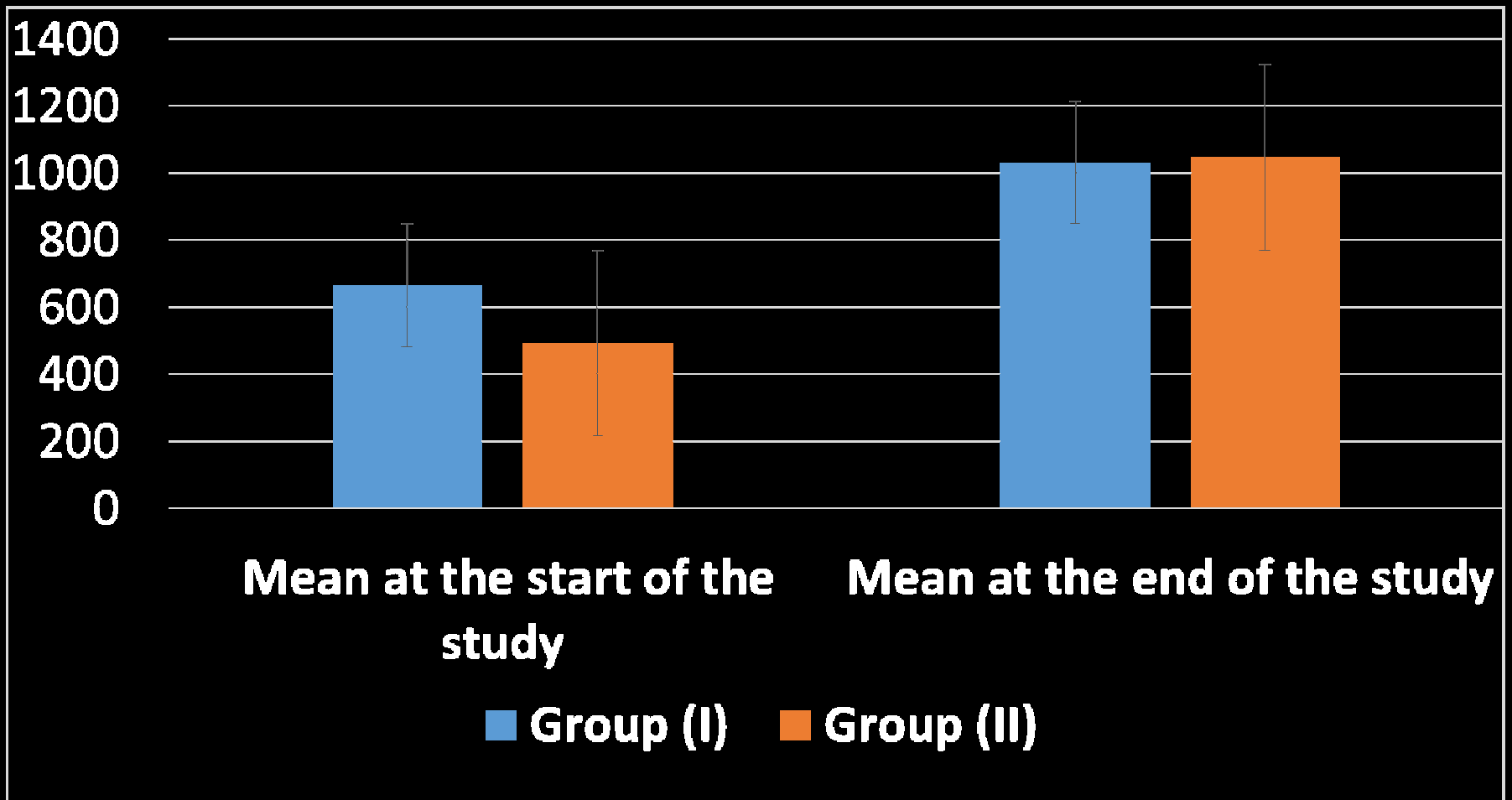


# Symptoms Score Improvement Recorded Every Two Months (1-12):

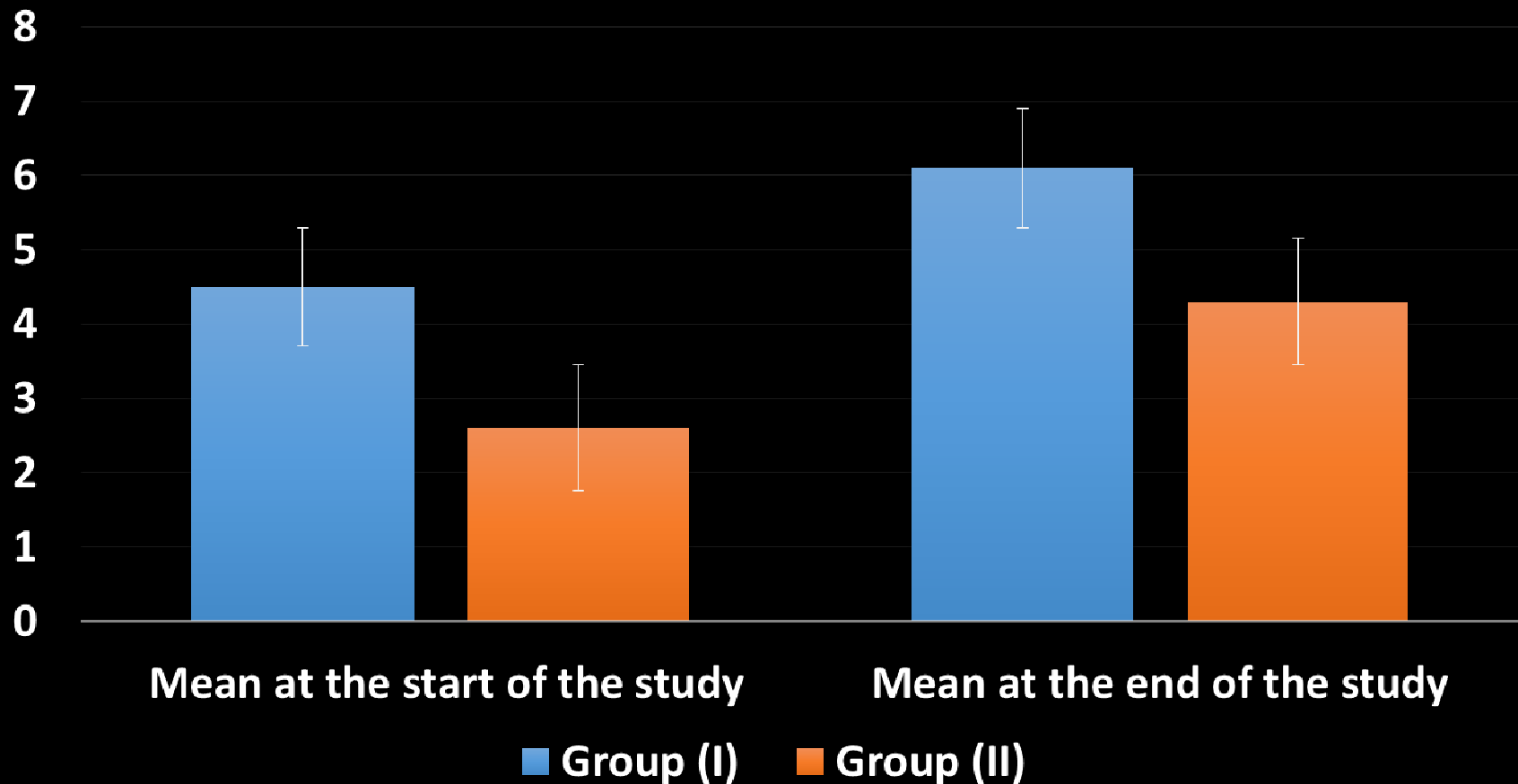
## Bladder & Bowel



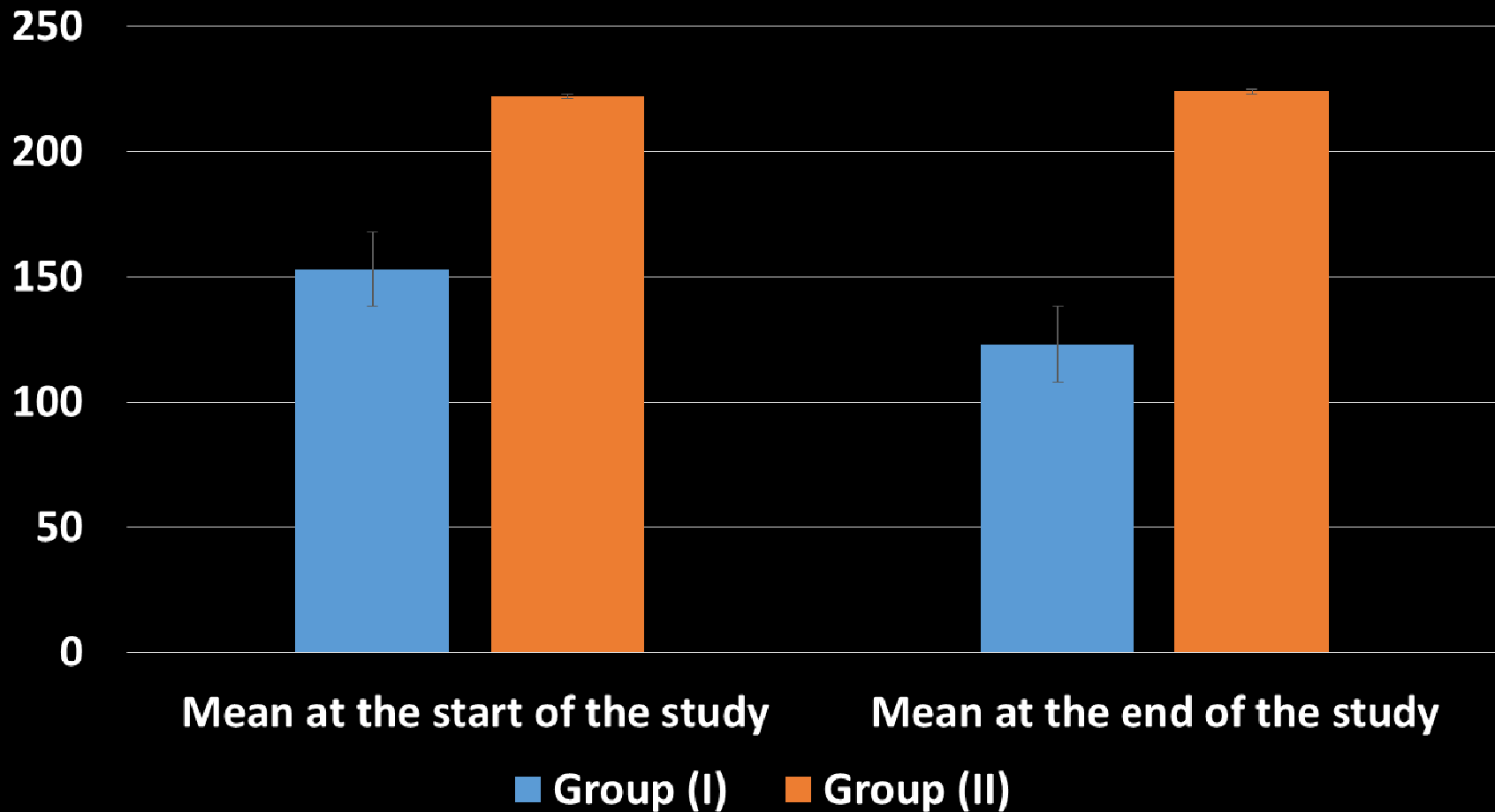
# Mean levels of IgE of both groups at the start and end of the study



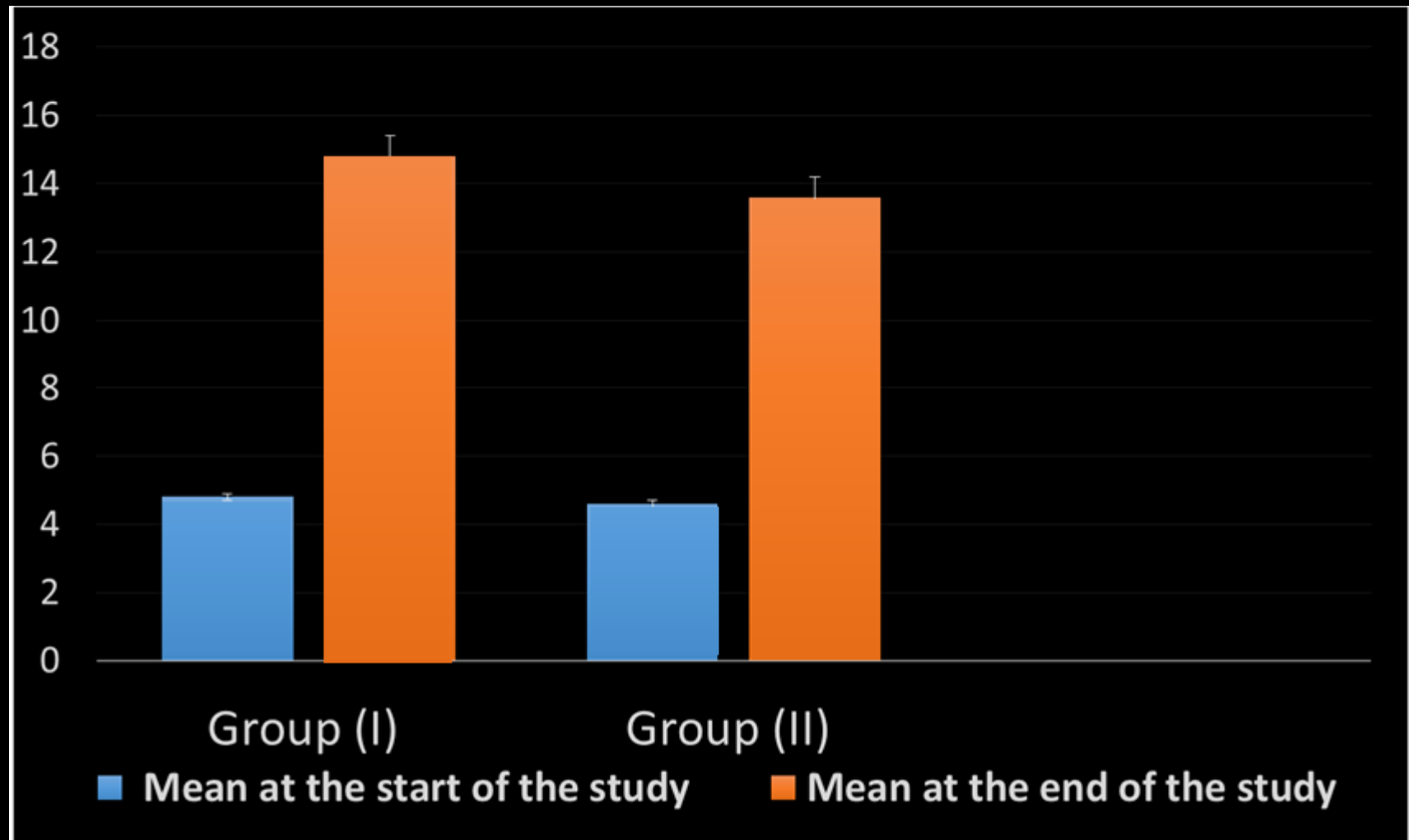
# Mean levels of (TNF) $\alpha$ of both groups at the start and end of the study



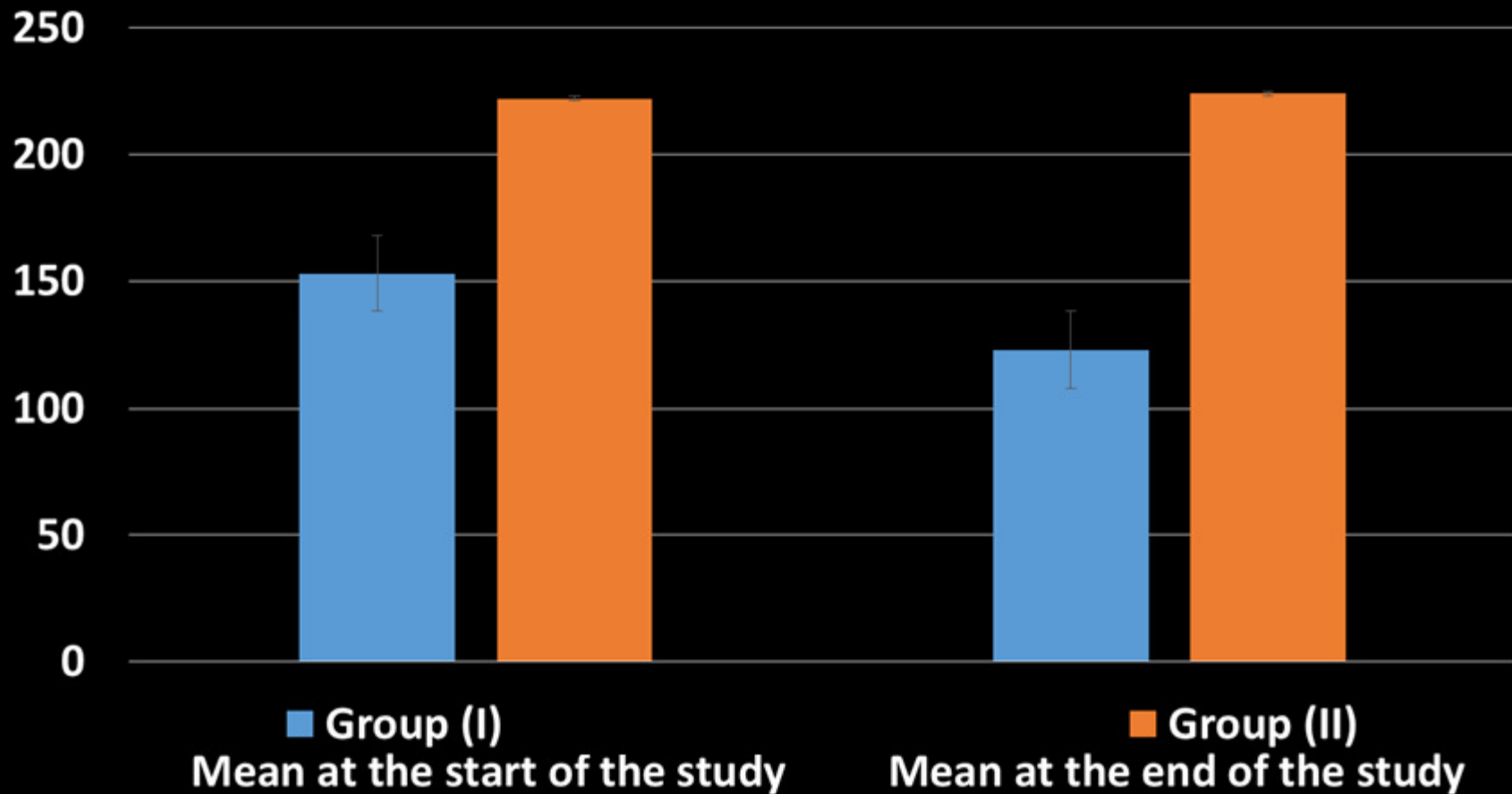
# Mean levels of (IL) $1\beta$ of both groups at the start and end of the study



# Mean levels of IL-6 of both groups at the start and end of the study

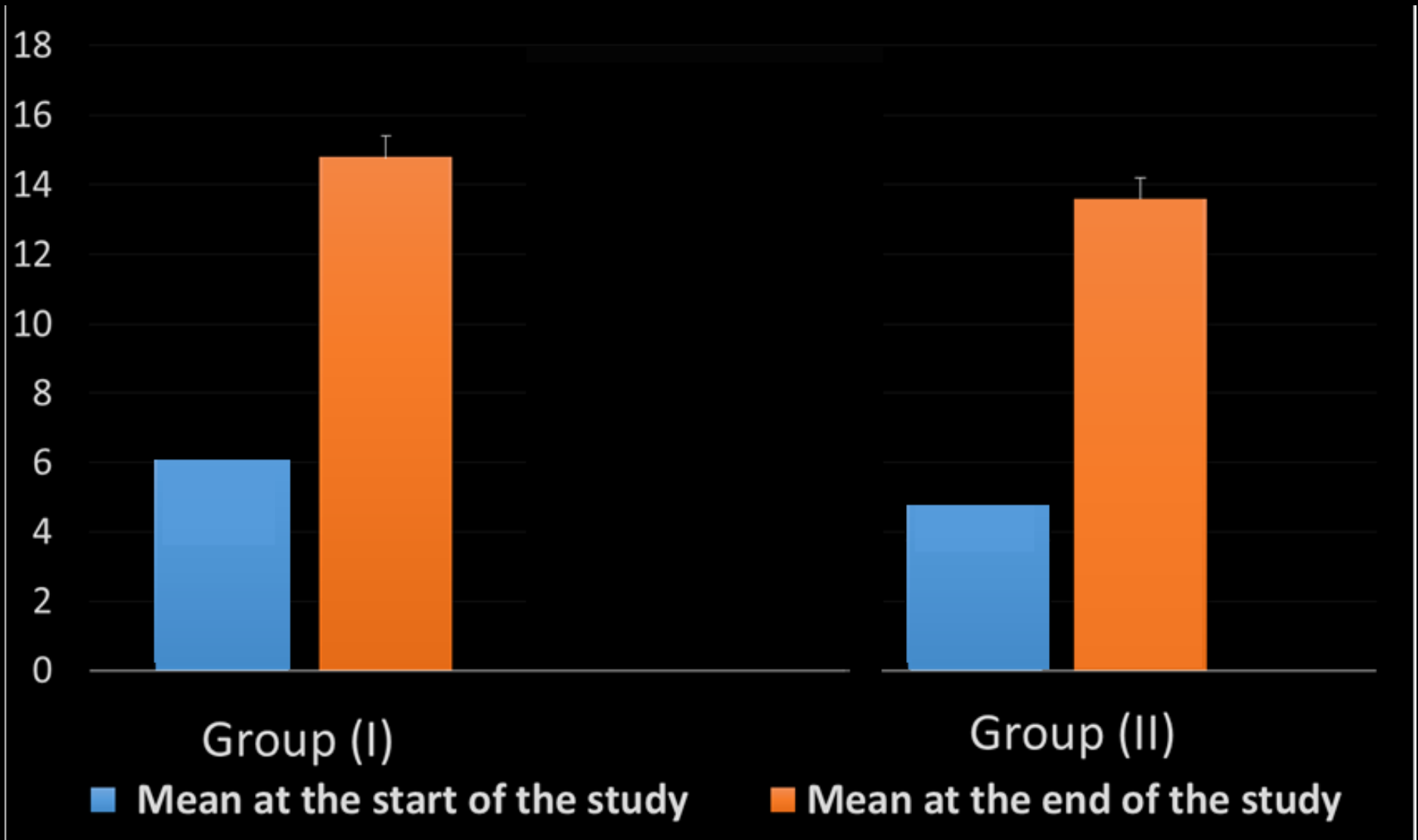


# Mean levels of (IL 4) of both groups at the start and end of the study





# Mean levels of IL-10 of both groups at the start and end of the study





CONCLUSION

- Although Apitherapy is not a curable therapy in MS, but it can be used to minimize some of the clinical symptoms of MS, and can be included among programs of MS therapy.

By By By By By By



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Thank you

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