BEZMİÂLEM VAKIF ÜNİVERSİTESİ 1845

THE ROLE OF THROMBOSPONDIN-2 IN REFRACTORY EPILEPSY

Serra SAĞLAM
Mentor: Şahabettin SELEK, MD
Türkan UYGUR ŞAHİN, MD

TÜBİTAK

Outline

Introduction

Aim of the Study

Material and Methods

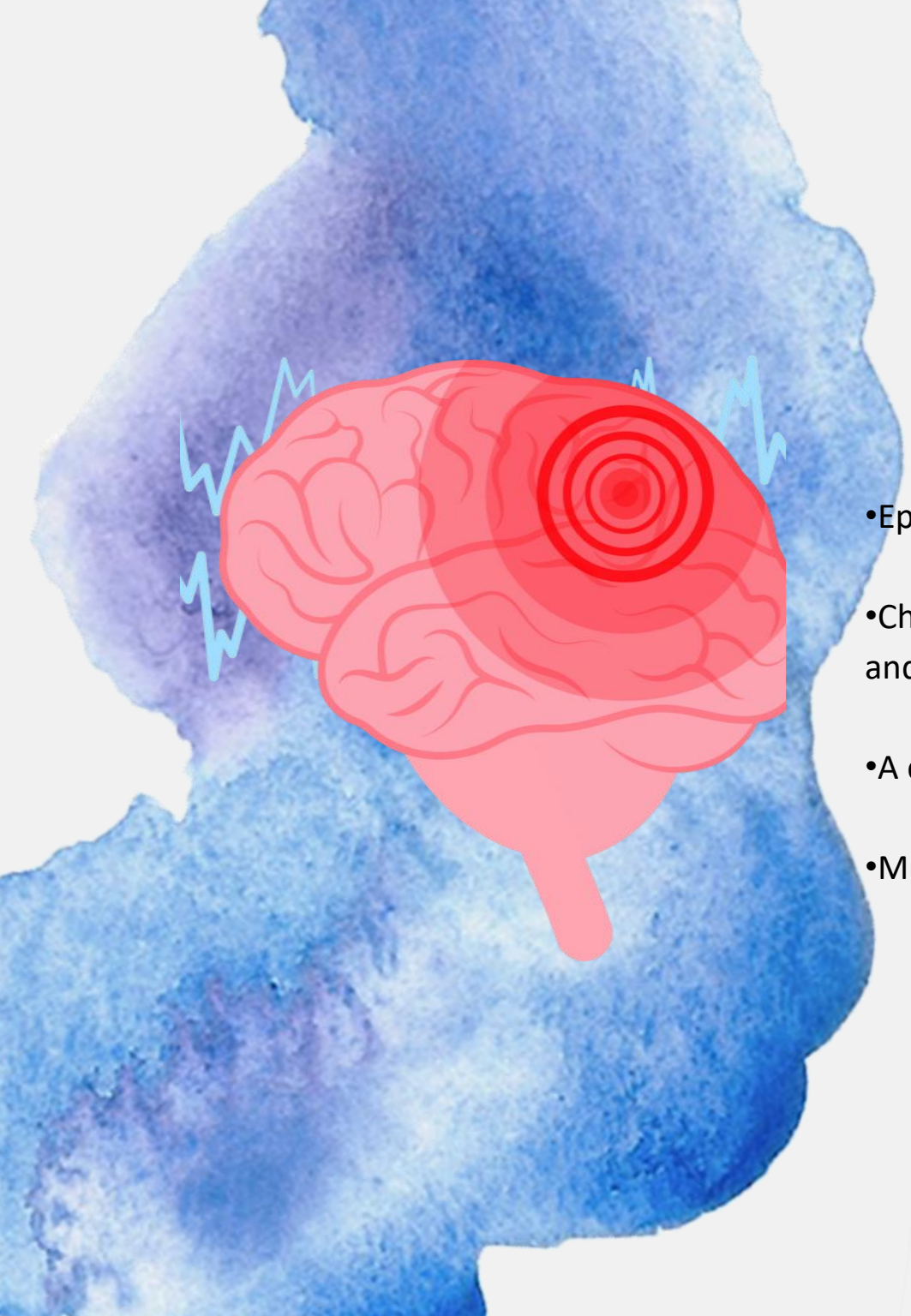
Results

Conclusion

Limitations

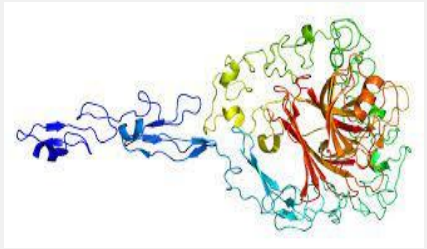
Discussion

References

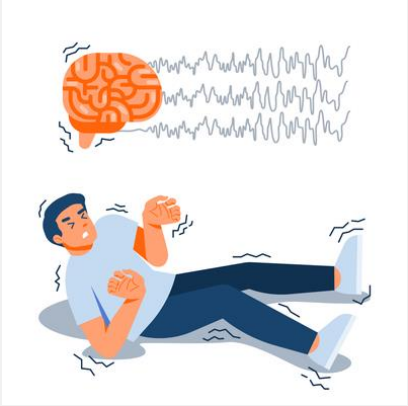


What is Epilepsy?

- Epilepsy is a common chronic neurological disease
- Characterized by repetitive seizures related to sudden and abnormal discharges of neurons
- A common disease that affects around 50 million people
- Multiple treatment approaches



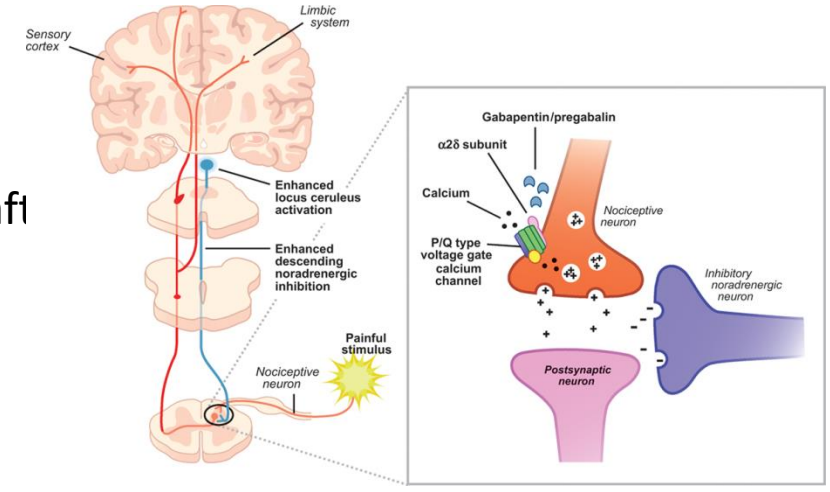
What is Thrombospondin-2?

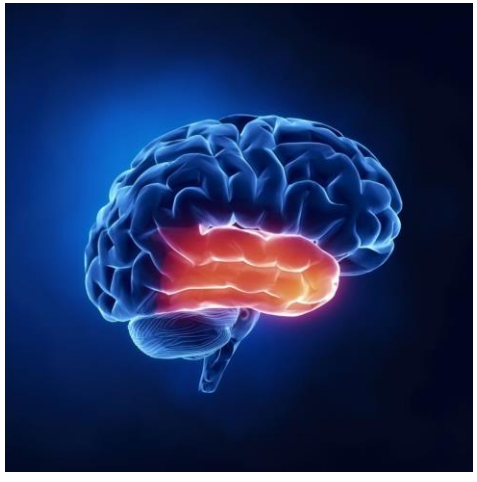


- One of 5 types of Thrombospondins
- A glycoprotein produced by astrocytes
- Promotes angiogenesis and synaptogenesis

Background

•In an animal study, seizures of rats stopped afı
Gabapentin treatment





•A clinical study showed that patients with temporal lobe epilepsy had higher levels than healthy controls

Aim of Study

The aim of this study is to investigate the role of TSP-2 in refractory epilepsy.

•This study was approved by the Bezmialem Vakıf University Ethics Committee in March 2023.

•A sample size and power calculation determined that sufficient statistical power required 18 people for each group(power=%80, $p<0.05$) based on a previous study(Naumnik W. et al,2015)

Material and Method

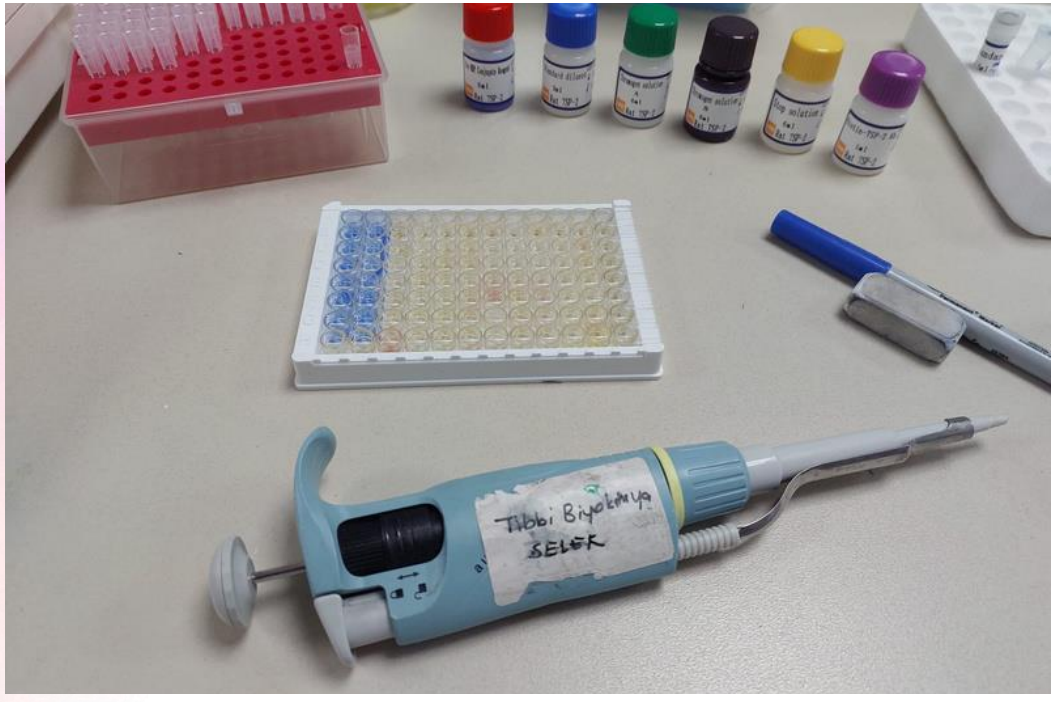
•82 children that attended Bezmialem Vakıf University Hospital Pediatrics Department between August 2023 and January 2024 were included

•Children that had any other chronic disease than epilepsy or that had any lesion detected in cranial MR were excluded.

•They were classified into three groups: an epilepsy group (n=33), a refractory epilepsy group (n=28) and a healthy group (n=20).

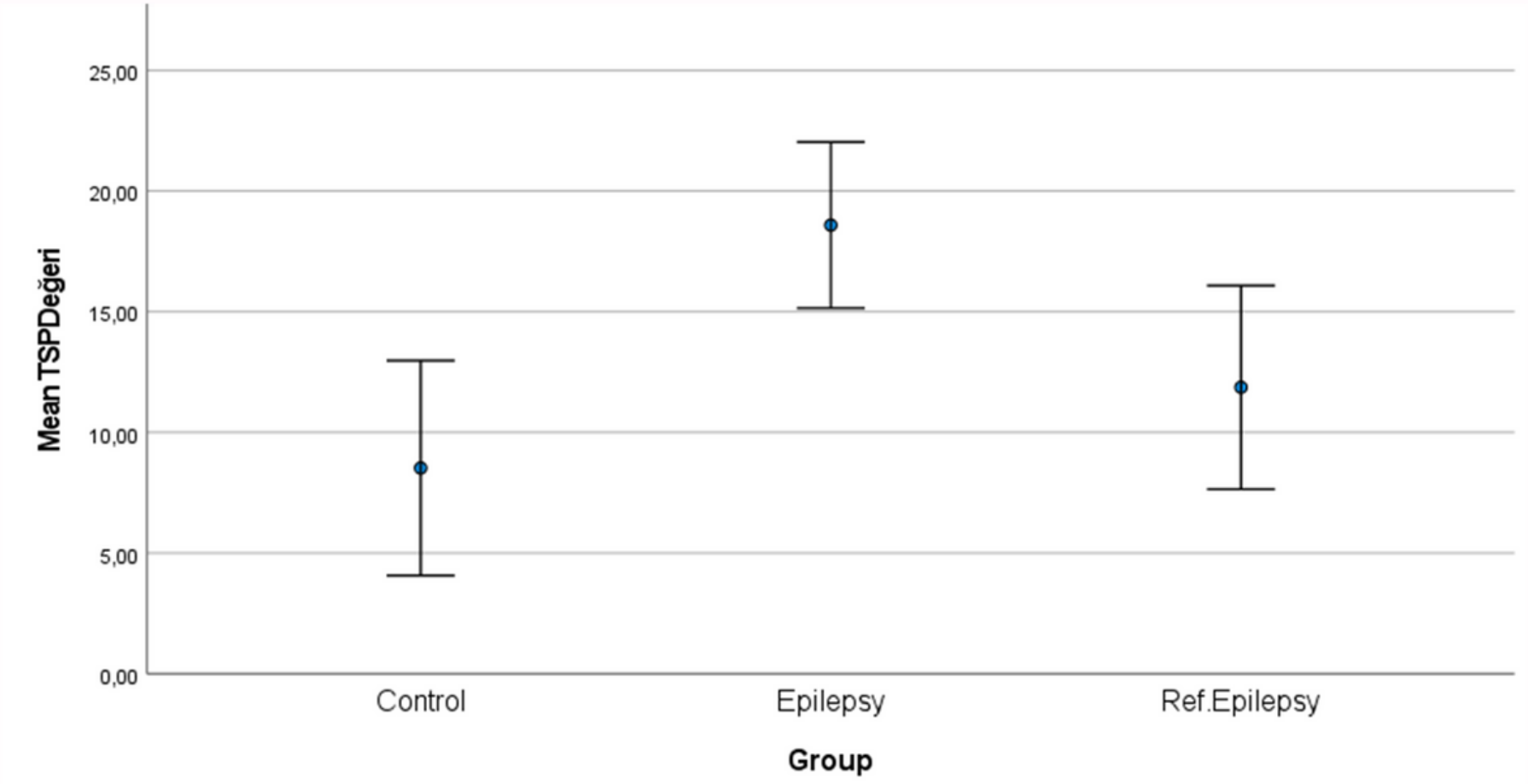
1.Epilepsy Group	Patients whose convulsions are under control by using 1 drug
2.Refractory Epilepsy Group	Patients that use 2 or more drugs and still have convulsions
3.Control Group	Children with no chronic disease

TSP-2 levels in serum samples were analyzed using a commercial Elisa kit in Bezmialem Vakıf University Biochemistry Laboratuary and compared between each group by using Kruskal Wallis H test.

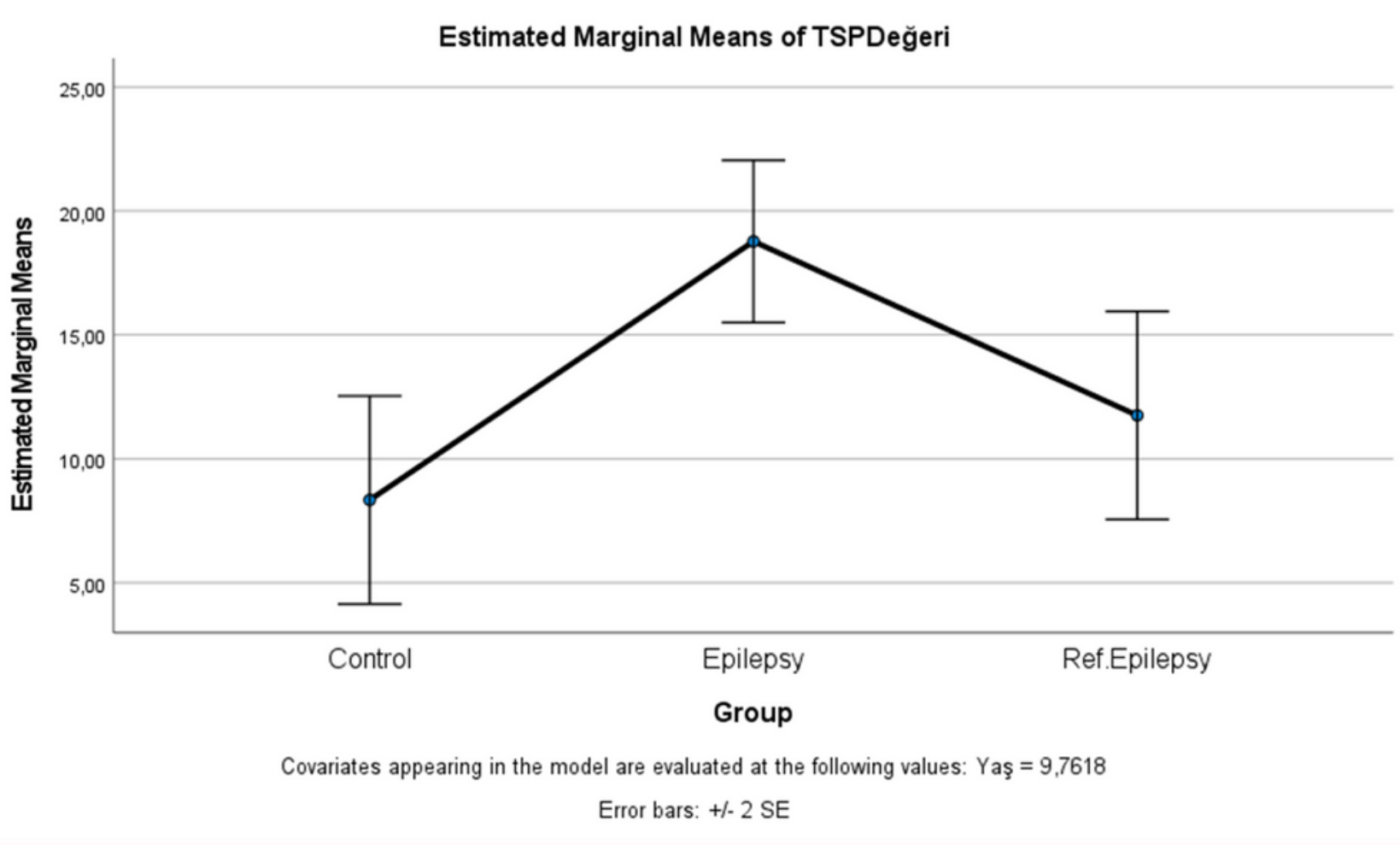


Results

Group	TSP-2
Epilepsy	2.73 ± 0.72
Refractory Epilepsy	2.31 ± 0.73
Control Group	1.77 ± 0.80
Kruskal-Wallis H-Statistics	17.17
Kruskal-Wallis P Value	<0.001


25,00
20,00
15,00
10,00
5,00
0,00
Mean TSPDeğeri
Control
Epilepsy
Ref.Epilepsy
Group

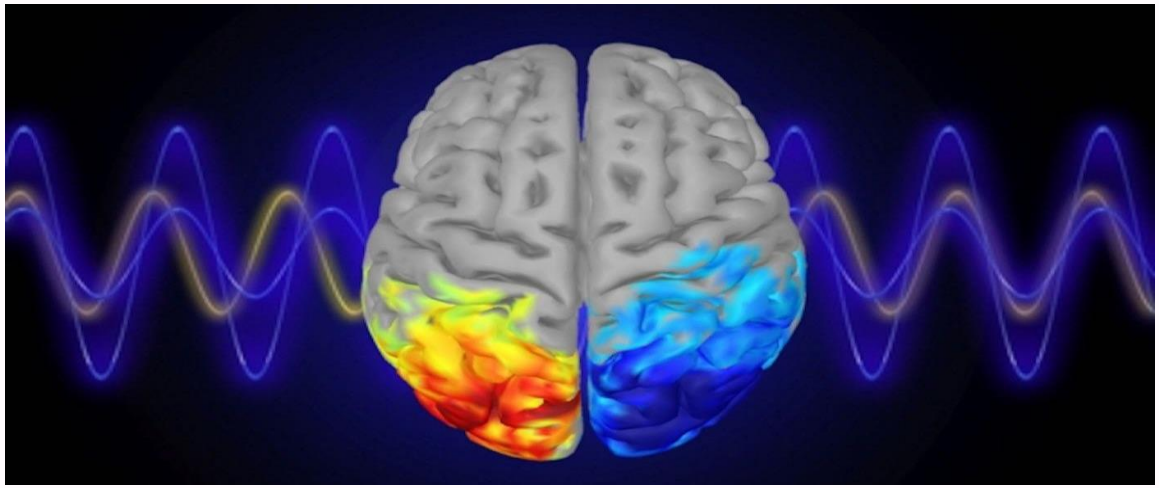
Epilepsy Group	• 10.24 ± 4.51
Refractory Epilepsy Group	• 9.40 ± 5.11
Control Group	• 9.28 ± 3.56


Estimated Marginal Means of TSPDeğeri
Estimated Marginal Means
25,00
20,00
15,00
10,00
5,00
Control
Epilepsy
Ref.Epilepsy
Group
Covariates appearing in the model are evaluated at the following values: Yaş = 9,7618
Error bars: +/- 2 SE

CONCLUSION

•TSP-2 levels in both epilepsy and refractory epilepsy patients were increased while the difference between refractory epilepsy group and control group was doubtful.

•There is no correlation between TSP-2 levels and age.



LIMITATIONS

A limited financial support, a time of study and a limited population

Study could have a more balanced distribution of gender and number of participants between the groups

No information about the types of seizures or which anti-epileptic drugs were used

DISCUSSION

Our study is one of a few studies that analyzes TSP-2 levels in patients with epilepsy.

New studies are essential to confirm our results

REFERENCES

1) Benini R, Roth R, Khoja Z, Avoli M, Wintermark P. Does angiogenesis play a role in the establishment of mesial temporal lobe epilepsy? Int J Dev Neurosci. 2016 Apr;49:31-6.
2) Morin-Brureau M, Rigau V, Lerner-Natoli M. Why and how to target angiogenesis in focal epilepsies. Epilepsia. 2012 Nov;53 Suppl 6:64-8.
3) Hayatdavoudi P, Hosseini M, Hajali V, Hosseini A, Rajabian A. The role of astrocytes in epileptic disorders. Physiol Rep. 2022 Mar;10(6):e15239.
4) Robel S, Sontheimer H. Glia as drivers of abnormal neuronal activity. Nat Neurosci. 2016 Jan;19(1):28-33.
5) Liauw J, Hoang S, Choi M, Eroglu C, Choi M, Sun GH, Percy M, Wildman-Tobriner B, Bliss T, Guzman RG, Barres BA, Steinberg GK. Thrombospondins 1 and 2 are necessary for synaptic plasticity and functional recovery after stroke. J Cereb Blood Flow Metab. 2008 Oct;28(10):1722-32.
6) Risher WC, Eroglu C. Thrombospondins as key regulators of synaptogenesis in the central nervous system. Matrix Biol. 2012 Apr;31(3):170-7.
7) Santolini I, Celli R, Cannella M, Imbriglio T, Guiducci M, Parisi P, Schubert J, Iacomino M, Zara F, Lerche H; EuroEPINOMICS CoGIE Consortium; Genetic Commission of Italian League Against Epilepsy (LICE); Moyanova S, Ngomba RT, van Luijtelaar G, Battaglia G, Bruno V, Striano P, Nicoletti F. Alterations in the α 2 δ ligand, thrombospondin-1, in a rat model of spontaneous absence epilepsy and in patients with idiopathic/genetic generalized epilepsies. Epilepsia. 2017 Nov;58(11):1993-2001.
8) Zhang Y, Zhang M, Zhu W, Pan X, Wang Q, Gao X, Wang C, Zhang X, Liu Y, Li S, Sun H. Role of Elevated Thrombospondin-1 in Kainic Acid-Induced Status Epilepticus. Neurosci Bull. 2020 Mar;36(3):263-276.
9) Andresen L, Hampton D, Taylor-Weiner A, Morel L, Yang Y, Maguire J, Dulla CG. Gabapentin attenuates hyperexcitability in the freeze-lesion model of developmental cortical malformation. Neurobiol Dis. 2014 Nov;71:305-16.
10) Li H, Graber KD, Jin S, McDonald W, Barres BA, Prince DA. Gabapentin decreases epileptiform discharges in a chronic model of neocortical trauma. Neurobiol Dis. 2012 Dec;48(3):429-38.
11) Alizada O, Akgun MY, Ozdemir AF, Toklu S, Kemerdere R, Orhan B, Inal BB, Yeni SN, Tanriverdi T. Circulating Levels of Thrombospondin-1 and Thrombospondin-2 in Patients with Temporal Lobe Epilepsy Before and After Surgery. Turk Neurosurg. 2021;31(2):228-232.
12) Wang YH, Huang TL, Chen X, Yu SX, Li W, Chen T, Li Y, Kuang YQ, Shu HF. Glioma-Derived TSP2 Promotes Excitatory Synapse Formation and Results in Hyperexcitability in the Peritumoral Cortex of Glioma. J Neuropathol Exp Neurol. 2021 Jan 20;80(2):137-149.
13) Kemerdere R, Akgun MY, Toklu S, Aydin S, Orhan B, Inal BB, Korkmaz TS, Aktas B, Kacira T, Tanriverdi T. Circulating Levels of Thrombospondin-1 and Thrombospondin-2 in Patients with Common Brain Tumors. Turk Neurosurg. 2021;31(3):399-403.
14) Naumnik W, Ossolińska M, Płońska I, Chyczewska E, Nikliński J. Circulating Thrombospondin-2 and FGF-2 in Patients with Advanced Non-small Cell Lung Cancer: Correlation with Survival. Adv Exp Med Biol. 2015;833:9-14.

ACKNOWLEDGEMENTS

Şahabettin SELEK, MD
Türkan UYGUR ŞAHİN, MD
Ufuk SARIKAYA, Phd

Thank You for Listening

serrasaglam9@gmail.com

+905323919061