

TÜRKİYE CUMHURİYETİ

MARMARA ÜNİVERSİTESİ

SAĞLIK BİLİMLERİ ENSTİTÜSÜ

**KRONİK ŞİZOFRENİ HASTALARINDA KANNABİDİOLÜN BİLİŞSEL FONKSİYONLAR ÜZERİNE ETKİLERİ**

AYŞE GÜLER

DOKTORA TEZİ

DANIŞMAN

PROF. DR. ZEYNEP GRIFFIN

FARMAKOLOJİ DOKTORA PROGRAMI

EŞ-DANIŞMAN

PROF. DR. ALİ KOÇAK

İSTANBUL- 2023



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| **İlk Yayın Tarihi: 18.01.2022** |
| **Revizyon Tarihi: 09.05.2022** |
| **Revizyon No: 01** |
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| Program türü : Doktora  |
| Anabilim Dalı :  |
| Tez Sahibi : |
| Sınav Tarihi ve Saati :  |
| Tez Başlığı :  |
| Bu çalışma, içerik ve kalite bakımından Doktora Tezi olarak kabul edilmiştir. |
| **JÜRİ ÜYELERİ** | **Unvan, Adı-Soyadı (Kurum adı)** | **İmza** |
| Danışman  |  |  |
| Üye |  |  |
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| **ONAY**Bu tez, yukarıda isimleri bulunan jüri üyeleri tarafından ”Marmara Üniversitesi Lisansüstü Eğitim Öğretim ve Sınav Yönetmeliği” nin ilgili maddeleri uyarınca kabul edilmiş ve Enstitü Yönetim Kurulu'nun ............................................tarih ve ...............................................sayılı kararı ile onaylanmıştır.Prof. Dr. Feyza ARICIOĞLU Sağlık Bilimleri Enstitüsü Müdürü |

**BEYAN**

Bu tez çalışmasının kendi çalışmam olduğunu, tezin planlanmasından yazımına kadar bütün safhalarda etik dışı davranışımın olmadığını, bu tezdeki bütün bilgileri akademik ve etik kurallar içinde elde ettiğimi, bu tez çalışması ile elde edilmemiş bütün bilgi ve yorumlara kaynak gösterdiğimi ve bu kaynakları da kaynaklar listesine aldığımı, yine bu tezin çalışılması ve yazımı sırasında patent ve telif haklarını ihlal edici bir davranışımın olmadığı beyan ederim.

Öğrenci Adı ve Soyadı

İmzası

**TEŞEKKÜR**

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**KISALTMALAR LİSTESİ**

|  |  |  |
| --- | --- | --- |
| ACTH | : | Adrenokortikotropik hormon (Adrenocorticotropic hormone) |
| BH4 | : | Tetrahidrobiopterin |
| BOS | : | Beyin omirilik sıvısı |
| CRP | : | C-reaktif protein |
| iNOS | : | İndüklenebilir nitrik oksit sentetaz |
| MSS | : | Merkezi sinir sistemi |
| NF-κB | : | Nükleer faktör kappa B |
| NLRP | : | NOD-benzeri reseptör proteini (NOD-like receptor protein) |
| NMDA | : | N-metil-D-aspartat |
| ODK | : | Ornitin dekarboksilaz |

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**1. ÖZET**

**Tezin başlığı :** Kronik Şizofreni Hastalarında Kannabidiolün Bilişsel Fonksiyonlar Üzerine Etkileri

**Öğrencinin Adı Soyadı :** Ayşe Güler

**Danışmanın Adı Soyadı :** Prof. Dr. Zeynep Griffin

**Programın Adı :** Farmakoloji Doktora Programı

**Amaç:**…………………………………………………………………………………………...

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**Anahtar Kelimeler:** Şizofreni, kannabidiol, bilişsel fonksiyon, hipokampus, BDNF

**2. SUMMARY**

**Title of Thesis:** Effects of Cannabidiol on Cognitive Functions in Patients with Chronic Schizophrenia

**Student Name, Surname:** Ayşe Güler

**Supervisor Name :** Prof. Zeynep Griffin

**Program Name :** Pharmacology PhD Program

**Objective:** ………………………………………………………………………………………

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**Conclusion:** …………………………………………………………………………………….

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**Keywords:** Schizophrenia, cannabidiol, cognitive function, hippocampus, BDNF

**3. GİRİŞ ve AMAÇ**

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**4. GENEL BİLGİLER**

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**5. GEREÇ ve YÖNTEM**

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**6. BULGULAR**

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**7. TARTIŞMA ve SONUÇ**

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**8. KAYNAKLAR**

**ÖRNEKLER**

**Makale**

Grady, J. S., Her, M., Moreno, G., Perez, C., & Yelinek, J. (2019). Emotions in storybooks: A comparison of storybooks that represent ethnic and racial groups in the United States. *Psychology of Popular Media Culture*, 8(3), 207–217. <https://doi.org/10.1037/ppm0000185>

Jackson, L. M. (2019). The psychology of prejudice: From attitudes to social action (2nd ed.). *American Psychological Association*. https://doi.org/10.1037/0000168-000

Sapolsky, R. M. (2017). Behave: The biology of humans at our best and worst. Penguin Books.

Svendsen, S., & Løber, L. (2020). The big picture/Academic writing: The one-hour guide (3rd digital ed.). *Hans Reitzel Forlag*. https://thebigpicture-academicwriting.digi.hansreitzel.dk/

**Kitap Bölümü**

Aron, L., Botella, M., & Lubart, T. (2019). Culinary arts: Talent and their development. In R. F. Subotnik, P. Olszewski-Kubilius, & F. C. Worrell (Eds.), *The psychology of high performance: Developing human potential into domain-specific talent* (pp. 345–359). American Psychological Association. https://doi.org/10.1037/0000120-016

Dillard, J. P. (2020). Currents in the study of persuasion. In M. B. Oliver, A. A. Raney, & J. Bryant (Eds.), *Media effects: Advances in theory and research* (4th ed., pp. 115–129). Routledge.

Thestrup, K. (2010). To transform, to communicate, to play—The experimenting community in action. In E. Hygum & P. M. Pedersen (Eds.), *Early childhood education: Values and practices in Denmark*. Hans Reitzels Forlag. https://earlychildhoodeducation.digi.hansreitzel.dk/?id=192

**Resmi Raporlar**

National Cancer Institute. (2019). *Taking time: Support for people with cancer* (NIH Publication No. 18-2059). U.S. Department of Health and Human Services, National Institutes of Health. https://www.cancer.gov/publications/patient-education/takingtime.pdf

**Yayınlanmamış Tez**

Harris, L. (2014). *Instructional leadership perceptions and practices of elementary school leaders* [Unpublished doctoral dissertation]. University of Virginia.

**Bir dergide basılmış genişletilmiş konferans özet metni (proceeding)**

Duckworth, A. L., Quirk, A., Gallop, R., Hoyle, R. H., Kelly, D. R., & Matthews, M. D. (2019). Cognitive and noncognitive predictors of success. *Proceedings of the National Academy of Sciences*, USA, 116(47), 23499–23504. https://doi.org/10.1073/pnas.1910510116

**Resmi bir kurumun web sitesi**

National Institute of Mental Health. (2018, July). *Anxiety disorders*. U.S. Department of Health and Human Services, National Institutes of Health. https://www.nimh.nih.gov/health/topics/anxiety-disorders/index.shtml

Ek örnekler için bu bağlantıyı takip ediniz<https://apastyle.apa.org/style-grammar-guidelines/references/examples>

**9. ÖZGEÇMİŞ**

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| Adı  |  | Soyadı  |  |
| Doğum Yeri  |  | Doğum Tarihi  |  |
| Uyruğu  |  | Tel |  |
| E-mail |  |  |  |

**Eğitim Düzeyi**

|  |  |  |
| --- | --- | --- |
|  | Mezun Olduğu Kurumun Adı | Mezuniyet Yılı |
| Doktora/Uzmanlık |  |  |
| Yüksek Lisans |  |  |
| Lisans |  |  |

**İş Deneyimi**

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| Görevi  | Kurum  | Süre (Yıl - Yıl) |
| 1 |  |  |  |
| 2 |  |  |  |
| 3 |  |  |  |

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| **Yabancı Dilleri** | **Okuduğunu Anlama\*** | **Konuşma\*** | **Yazma\*** |
|  |  |  |  |
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| **Yabancı Dil Sınav Notu #** |
| YDS | ÜDS | IELTS | TOEFL IBT | TOEFL PBT | TOEFL CBT | FCE | CAE | CPE |
|  |  |  |  |  |  |  |  |  |

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|  | **Sayısal** | **Eşit Ağırlık** | **Sözel** |
| ALES Puanı  |  |  |  |
| (Diğer) Puanı |  |  |  |

**Bilgisayar Bilgisi**

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| Program | Kullanma Becerisi |
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***\*****Çok iyi, iyi, orta, zayıf olarak değerlendiriniz.*

**10. BİLİMSEL FAALİYETLER**

**ÖRNEKLER**

**Makale**

Grady, J. S., Her, M., Moreno, G., Perez, C., & Yelinek, J. (2019). Emotions in storybooks: A comparison of storybooks that represent ethnic and racial groups in the United States. *Psychology of Popular Media Culture*, 8(3), 207–217. <https://doi.org/10.1037/ppm0000185>

**Kitap**

Jackson, L. M. (2019). *The psychology of prejudice: From attitudes to social action* (2nd ed.). American Psychological Association. https://doi.org/10.1037/0000168-000

Sapolsky, R. M. (2017). *Behave: The biology of humans at our best and worst*. Penguin Books.

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Aron, L., Botella, M., & Lubart, T. (2019). Culinary arts: Talent and their development. In R. F. Subotnik, P. Olszewski-Kubilius, & F. C. Worrell (Eds.), *The psychology of high performance: Developing human potential into domain-specific talent* (pp. 345–359). American Psychological Association. https://doi.org/10.1037/0000120-016

Dillard, J. P. (2020). Currents in the study of persuasion. In M. B. Oliver, A. A. Raney, & J. Bryant (Eds.), *Media effects: Advances in theory and research* (4th ed., pp. 115–129). Routledge.

Thestrup, K. (2010). To transform, to communicate, to play—The experimenting community in action. In E. Hygum & P. M. Pedersen (Eds.), *Early childhood education: Values and practices in Denmark.* Hans Reitzels Forlag. <https://earlychildhoodeducation.digi.hansreitzel.dk/?id=192>

**Proceeding**

Duckworth, A. L., Quirk, A., Gallop, R., Hoyle, R. H., Kelly, D. R., & Matthews, M. D. (2019). Cognitive and noncognitive predictors of success. *Proceedings of the National Academy of Sciences*, USA, 116(47), 23499–23504. <https://doi.org/10.1073/pnas.1910510116>

**Bildiri (Poster veya Sözel)**

Evans, A. C., Jr., Garbarino, J., Bocanegra, E., Kinscherff, R. T., & Márquez-Greene, N. (2019, August 8–11). *Gun violence: An event on the power of community* [Conference presentation]. APA 2019 Convention, Chicago, IL, United States. https://convention.apa.org/2019-video

**Proje**

Griffin, Z. & Güler, A. Kannabisin bilişsel fonksiyonlar üzerine etkisi. TÜBİTAK 1002 (SBAG-xxxxxxx), 2020-2022.

Griffin, Z. & Güler, A. Kannabisin bilişsel fonksiyonlar üzerine etkisi. Marmara Üniversitesi Bilimsel Araştırma Projeleri Koordinasyon Birimi (SAG-C-DRP-xxxxxx-xxxx), 2020-2022.

1. **EKLER**