

# Depression and Hand-Grip: Unraveling the Association

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Vijay Durga Pradeep Ganipineni <sup>1, 2</sup>, Ajay Sai Krishna Kumar Idavalapati <sup>3</sup>, Samuel Sowrab Tamalapakula <sup>4</sup>, Vagdevi Moparthi <sup>5</sup>, Monica Potru <sup>6</sup>, Oluwasayo J. Owolabi <sup>7</sup>

1. Department of General Medicine, SRM Medical College Hospital and Research Center, Chennai, IND 2. Department of General Medicine, Andhra Medical College/King George Hospital, Visakhapatnam, IND 3. Department of Medicine, Guntur Medical College, Guntur, IND 4. Department of Medicine, Katuri Medical College and Hospital, Guntur, IND 5. Department of Medicine, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Vijayawada, IND 6. Department of Medicine, Guntur Medical College, Guntur, IND 7. Department of Psychiatry, Lugansk State Medical University, Lugansk, UKR

**Corresponding author:** Vijay Durga Pradeep Ganipineni, pradeepganipineni94@gmail.com

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## Abstract

This review article explores the association between hand-grip strength and depression. A total of 14 studies were carefully considered to provide a comprehensive analysis of the topic. The studies reveal a consistent association between low hand-grip strength and depressive symptoms, independent of age, gender, and chronic disease status. The evidence suggests that hand-grip strength assessment could be a useful tool for identifying individuals at risk of depression, particularly older adults and those with chronic diseases. Incorporating physical activity and strength training into treatment plans can contribute to better mental health outcomes. Hand-grip strength assessment can also be used as a monitoring tool to track changes in physical and mental health over time in individuals with depression. Healthcare professionals should consider the relationship between hand-grip strength and depression when evaluating patients and developing treatment plans. The findings from this comprehensive clinical review have important clinical implications and highlight the importance of considering physical health factors in the context of mental health.

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**Categories:** Internal Medicine, Psychiatry, Geriatrics

**Keywords:** grip force, hospital anxiety depression scale (hads), : sarcopenia, muscle strength, hand grip dynamometer, hand grip, mdd, major depressive disorder, depression, mental health assessment

## Introduction And Background

Hand-grip strength, a simple yet powerful measure of overall muscular strength, has emerged as a topic of growing interest within the healthcare community [1]. As an easily accessible and reliable measure, it has garnered attention for its potential implications in a wide array of clinical domains. One of the most intriguing areas of investigation is the association between hand-grip strength and depression, a debilitating mental health disorder that affects millions of individuals worldwide [2].

Depression, characterized by persistent feelings of sadness, hopelessness, and a lack of interest or pleasure in activities, is a leading cause of disability and suffering across the globe [3]. The World Health Organization estimates that more than 280 million people of all ages suffer from depression, making it one of the most common mental health disorders [3]. The significant personal, societal, and economic impacts of depression cannot be overstated, highlighting the urgent need for effective prevention and treatment strategies [4].

One of the most challenging aspects of depression is its complex etiology, which involves a combination of genetic, environmental, and psychological factors [4]. This complexity necessitates a multifaceted approach to understanding and addressing the disorder, with a focus on identifying modifiable risk factors that can be targeted through preventive and therapeutic interventions [5]. Among the myriad factors implicated in the development and progression of depression, physical health indicators such as hand-grip strength have emerged as a promising area of research [5].

Hand-grip strength, which is strongly correlated with systemic muscle strength, is one of the promising candidates for the brief evaluation of physical function. Moreover, hand-grip strength is also used to predict future activities of daily life [6,7]. Hand-grip strength is an easily accessible, non-invasive, and cost-effective measure of muscular strength, making it an attractive candidate for clinical research and practice [6,7]. It has been shown to correlate with overall physical health, functional capacity, and even mortality, emphasizing its potential relevance to a broad spectrum of health outcomes [5]. Moreover, the assessment of hand-grip strength can be conducted with minimal equipment and training, making it an ideal tool for both research and clinical settings.

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Given the known benefits of physical activity and exercise in promoting mental health and well-being, it is perhaps unsurprising that a growing body of evidence has begun to explore the relationship between hand-grip strength and depression [8]. Several studies have reported associations between low hand-grip strength and increased depressive symptoms, suggesting that this simple measure may hold the key to understanding and addressing the complex interplay between physical and mental health [9].

However, the existing literature on the association between hand-grip strength and depression is characterized by a degree of heterogeneity in terms of study populations, methodologies, and outcomes. This diversity has generated both complementary and conflicting findings, underscoring the need for a comprehensive synthesis of the available evidence. By reviewing and integrating the findings from 14 key studies, this clinical review endeavors to provide a more coherent and nuanced understanding of the relationship between hand-grip strength and depression and elucidate the potential clinical implications of this association.

## Methods

A literature search was conducted to identify relevant studies investigating the association between hand-grip strength and depression from inception till date. Major databases, including PubMed, Google Scholar and Central, were diligently searched by including studies conducted on humans and published in English. The keywords used in the search included "hand grip strength," "muscle strength," "depression," "mdd," "mood disorder," "mental health," and "psychological well-being." The keywords were used in various combinations and searched using Boolean operators (AND, OR) to ensure a comprehensive search. Fourteen studies were carefully considered and analyzed in this review. These studies encompassed a range of study designs, including cross-sectional, longitudinal, and case-control studies, and were conducted in various countries and population groups.

Data were extracted from each study, including study design, sample characteristics (age distribution and population setting), depression assessment tools, and key findings. The extracted data were organized into a table, summarizing the essential features and results of each study. The study findings were synthesized to provide a comprehensive understanding of the association between hand-grip strength and depression.

The review focused on examining the consistency and variability of findings across studies, considering factors such as age, gender, and chronic disease status that may influence the relationship between hand-grip strength and depression. Additionally, the review assessed potential confounding factors and clinical implications of the study findings.

## Review

Fourteen studies were analyzed in this review, including Sternäng et al. 2016 [10], Ashdown-Franks et al. 2018 [11], Musalek et al. 2017 [12], Smith et al. 2022 [13], Mergl et al. 2007 [14], Zheng et al. 2022 [15], Kim et al. 2019 [2], Gu et al. 2021 [16], Phillips et al. 2011 [17], Marconcin et al. 2020 [18], McDowell et al. 2018 [19], Fukumori et al. 2015 [9], Smith et al. 2019 [20], Brook et al. 2018 [21], to provide a balanced synopsis of the contemporary literature.

The association between hand-grip strength and depression has been investigated in various populations, age groups, and settings. The 14 included studies reviewed here (Table 1) demonstrate that the relationship between hand-grip strength and depression is complex, with some studies showing a negative association between grip strength and depressive symptoms, while others have found no significant relationship or differential effects based on factors such as age, gender, or chronic disease status.

Study ID	Type of Study	Age	Handgrip Assessment	Depression Questionnaire	Conclusion
Sternäng et al. 2016 [10]	Longitudinal Cohort study	40-86	Collins hand grip dynamometer	N/A	Grip strength is inversely related to the risk of cognitive decline.
Ashdown-Franks. 2021 [11]	Cross-sectional study	>50		CIDI	Grip strength is negatively associated with depression severity.
Musalek et al. 2017 [12]	Cross-sectional study	18-30	Hand-held calibrated dynamometer (JAMAR, Hatfield, PA, USA)	BDI-II	No significant relationship between grip strength and depressive symptoms.
Smith et al. 2022 [13]	Longitudinal Cohort study	Adults (mean age: 63.7)	Dynamometer	PHQ-9	Greater handgrip strength is associated with lower risk of new-onset depressive symptoms.
Mergl et al. 2007 [14]	Longitudinal Cohort study. Two-part study.	Not specified	Digitizing graphic tablet and kinematic analysis of handwriting and rapid drawing movements.	HDR	Depressed patients show irregular hand-motor patterns; differential pharmaceutical effects on hand-motor function.
Zheng et al. 2022 [15]	Longitudinal cohort study	50+	Smedley handheld dynamometer (100 kg)	EURO-D	Interaction between grip strength and physical activity on depression; lower grip strength and inactivity worsen depression.
Kim et al. 2019 [2]	Longitudinal cohort study	Middle-aged and elderly	Handgrip dynamometer (Model number: NO6103, Manufacturer: TANITA, Japan)	MMSE, CES-D	Negative association between grip strength and cognitive decline and depressive symptoms.
Gu et al. 2021 [16]	Cross-sectional study	41.5 ± 11.9	Dynamometer	SDS	Inverse association between grip strength and depressive symptoms, stronger in females.
Phillips et al. 2011 [17]	Case-control study	Not specified	JAMAR 5-position grip strength dynamometer (Sammons Preston, Bolingbrook, IL)	DSM-IV	Clinically depressed individuals may produce results suggesting poor volitional effort in 5-position grip strength testing.
Marconcin et al. 2020 [18]	Cross-sectional study	Middle-aged and older adults	Smedley handgrip dynamometer	EURO-D	Association between grip strength and depressive symptoms depends on chronic conditions, age group, and gender.
McDowell et al. 2018 [19]	Cross-sectional and longitudinal cohort study	50+	Hand-held dynamometer	CESDS	Inverse association between grip strength and incident depression in older adults, stronger in females.
Fukumori et al. 2015 [9]	Longitudinal cohort study	40-79	Digital dynamometer	MHI-5	Lower hand-grip strength is both cross-sectionally and longitudinally associated with depressive symptoms.
Smith et al. 2019 [20]	Cross-sectional study	50+	Handheld dynamometer	CESDS	Grip strength was negatively associated with depressive symptoms in older adults in England.
Brooks et al. 2018 [21]	Cross-sectional study	60+	Handheld dynamometer	PHQ-9	Reduced levels of combined hand-grip strength are independently associated with greater depressive symptoms among U.S. adults aged 60 years and older.

TABLE 1: Summary of characteristics of included studies

CESDS: 8-item Center for Epidemiologic Studies Depression Scale, PHQ-9: Patient Health Questionnaire, BDI-II: Beckers Depression Inventory, HDR: Hamilton Depression Rating Scale, SDS: Self-Rated Depression Scale, MHI-5: Mental Health Inventory, EURO-D: European Depression Symptoms 12-item scale

A majority of the studies, including longitudinal and cross-sectional designs, found an inverse relationship between grip strength and depression, with greater grip strength associated with lower depression risk or severity (Ashdown-Franks et al. [11], Smith et al. [13], Zheng et al. [15], Kim et al. [2], Gu et al. [16], Marconcin et al. [18], McDowell et al. [19], Fukumori et al. [9]). This association was observed in various age groups, from middle-aged to elderly populations.

Some studies noted gender differences in the relationship between grip strength and depression (Gu et al. [16], McDowell et al. [19]). In these cases, stronger associations were observed among females compared to males. Additionally, Marconcin et al. [18] highlighted that the association between grip strength and depressive symptoms should consider factors such as chronic conditions, age group, and gender.

However, Musalek et al. [12] found no significant relationship between grip strength and depressive symptoms in a younger population aged 18-30. Furthermore, Mergl et al. [14] and Phillips et al. [17] focused on motor patterns and grip strength test interpretation in depressed patients, raising questions about the potential confounding effect of depression on the assessment of hand-grip strength.

In a groundbreaking study, Zhang et al. [22] explored the shared genetic variation between depression and grip strength using twin data from Qingdao, China. They discovered potential genetic correlations, Single Nucleotide Polymorphisms (SNPs), genes, and pathways common to both conditions [22]. The study revealed a moderate genetic correlation between grip strength and depression, with a genetic correlation coefficient of -0.41 (-0.96, -0.15), indicating a shared genetic basis [22]. Key findings in the SNP-based analysis included rs117744620, located in the LRR1 gene on chromosome 14, which exceeded the genome-wide significance level. LRR1 is involved in regulating 4-1BB-mediated signaling cascades that activate NF- $\kappa$ B [23], which could impact depression. LRR1 can also affect actin [24], thereby influencing muscle strength. Three SNPs (rs117546604, rs150220336, rs147079354) found in or near the ME2 gene also exceeded the genome-wide significance level. ME2, which encodes a mitochondrial NAD-dependent malic enzyme, has been linked to generalized epilepsy [25], psychosis, mania [26], and PI3K/AKT signaling [27], suggesting its association with both the nervous system and muscle strength as well as depression.

Among the top 60 SNPs with suggested levels of association, three SNPs (rs75534602, rs117533783, rs78161270) were located near the DDC gene [22]. The DDC gene has been linked to postpartum anxiety [28] and aromatic L-amino acid decarboxylase deficiency (AADCD), which include early-onset hypotonia [29] as a primary symptom. This suggests that the DDC gene might simultaneously affect grip strength and depression. Other notable genes include P2RX7, involved in inflammatory responses and neuroimmune mechanisms, and PRKD1, which regulates actin [30] and is associated with neurons [31], NF- $\kappa$ B [32], and the inflammatory response [33].

In gene-based analysis, two significant genes, GTF2H2C\_2 and GTF2H2C were identified, but their relationship with the phenotype remains unclear due to insufficient research [22]. Several genes with nominal significance levels were found to be associated with grip strength and depression, such as FNBPI, MOG, SACS, KMO, TECPR2, and MGTAS [22]. Additionally, expression levels of KCNN4, MOG, and SNHG12 genes can influence inflammatory factors [34-39], potentially impacting grip strength and depression through their effects on the inflammatory response [22].

Pathway enrichment analysis revealed numerous pathways related to hormone synthesis and neural signal transduction, such as those involving androgen biosynthesis, steroid hormones and potassium channels, a deficiency of which is known to cause both muscle weakness and depression [40-43]. Additionally, pathways, including RHO GTPases, fibroblast growth factors, and cytokine receptor interactions may collectively influence grip strength and depression through various mechanisms, actin regulation [44], neuronal development [45,46], skeletal muscle development [47], and inflammatory responses.

Brooks et al. [21] performed a cross-sectional study utilizing the NHANES 2011-2014 data and reported that reduced levels of combined handgrip strength are independently associated with greater depressive symptoms among U.S. adults aged 60 years and older. They found that this significance level is only found in the age group 60-69 years, owing to the difficulty in adjusting to senility.

## Clinical implications

The findings gleaned from this clinical review give rise to several vital clinical implications that warrant further discussion. It has been postulated that a biological connection, such as hormonal imbalances or changes in neurotransmitter levels in individuals with depression, might impact muscle function and consequently result in decreased handgrip strength [22]. Furthermore, chronic inflammation, which has been linked to both depression and reduced muscle strength, could play a role in the observed association between the two factors [48,49].

Another consideration is the influence of physical activity levels on the relationship between depression and handgrip strength. It is well-established that individuals with depression often experience reduced motivation and energy levels, leading to decreased physical activity, which may contribute to a decline in

muscle strength, including handgrip strength [21]. Likewise, poor nutrition or appetite changes common in people with depression could lead to muscle wasting and decreased handgrip strength [50].

Sleep disturbances, frequently observed in individuals with depression, can negatively impact muscle recovery and strength [51]. The association between handgrip strength and depression may indicate that people with depression have a lower overall health status, as handgrip strength has been considered a marker of overall health and physical fitness [52]. Additionally, depression's negative impact on cognitive function, including attention and concentration, may contribute to reduced handgrip strength [53].

The association between handgrip strength and depression could provide a simple, non-invasive tool for early detection and intervention in individuals at risk for depression. Handgrip strength measurement could be included in routine health assessments to identify those who may benefit from further mental health evaluation. Moreover, the findings could have implications for the development of new treatment approaches that target both depression and physical fitness, such as exercise-based interventions or combining psychotherapy with physical rehabilitation programs.

Public health campaigns and policies aimed at promoting mental and physical well-being could also be informed by these study results, emphasizing the importance of regular physical activity and mental health support for the general population. Furthermore, the study suggests potential shared genetic factors and pathways involved in both depression and handgrip strength [22], which could have implications for future research into the biological underpinnings of these conditions and potential treatment targets.

The interplay between physical and mental health is underscored by these findings, as depression is often associated with physical symptoms, such as fatigue and muscle weakness, and impaired handgrip strength could be a manifestation of these symptoms [54]. Alternatively, poor handgrip strength could contribute to a sense of physical limitation and low mood. Screening for depression and handgrip strength may be useful in identifying individuals at risk for these conditions, and interventions aimed at promoting physical activity and strength training could have potential benefits for both physical and mental health.

Finally, the study's findings could have implications for clinical practice, particularly in the context of geriatric care. Handgrip strength is often used as a measure of frailty in older adults and has been linked to a range of negative health outcomes [55]. The association between depression and grip strength could be an important consideration in the assessment and management of older adults' health.

## Future directions

The findings from the studies encompassed in this review consistently indicate a significant negative association between handgrip strength and depression. The groundbreaking research by Zhang et al. [22] uncovered shared genetic factors that may contribute to the association between grip strength and depression, providing valuable insight into the potential biological underpinnings of this relationship. Further research is warranted to deepen our understanding of the mechanisms underlying the association between grip strength and depression, including the potential role of genetics, the impact of confounding factors, and the influence of gender, age, and chronic disease status on this relationship. The results also pave the way for further exploration into the genetic and pathophysiological foundations of mental and physical health. We hope that such investigations will uncover innovative therapeutic targets for addressing both depression and physical performance, ultimately enhancing the overall well-being of individuals.

## Limitations

First, it is essential to recognize the methodological differences among the studies. The studies included a mix of cross-sectional, cohort, and case-control designs, which provide varying levels of evidence regarding causality. Longitudinal studies, such as those by Fukumori et al. [9] and McDowell et al. [19], offer stronger evidence for the potential causal relationship between hand-grip strength and depression. However, the majority of the studies included in this review were cross-sectional, limiting our ability to draw definitive conclusions about the directionality of the relationship between hand-grip strength and depression.

The studies also employed different measures of depression, such as the Center for Epidemiologic Studies Depression Scale (CESDS), the Mental Health Inventory (MHI-5), and the European Depression Symptoms 12-item scale (EURO-D). These variations in measurement may contribute to inconsistencies in the findings, making it challenging to compare results across studies directly.

Despite these methodological differences, several consistent findings emerged from the 14 studies. Most notably, a majority of the studies reported a significant association between lower hand-grip strength and increased depressive symptoms or depression risk, independent of age and gender. This association was observed in various populations, including older adults, individuals with chronic diseases, and community-dwelling adults.

However, it is crucial to consider the role of potential confounding factors in the relationship between

hand-grip strength and depression. For instance, Marconcin et al. [18] found that the association between grip strength and depressive symptoms varied based on the presence of chronic diseases. The study observed a significant relationship among participants with no chronic diseases and those with metabolic diseases but not among those with arthritis diseases [18]. This finding underscores the importance of considering the individual's specific health status when evaluating the association between hand-grip strength and depression.

Furthermore, some studies identified potential sex differences in the relationship between hand-grip strength and depression. For example, McDowell et al. [19] found that grip strength was inversely associated with incident depression in older adults, with stronger associations observed among females than males. This finding suggests that the relationship between hand-grip strength and depression may be influenced by sex-specific factors, which warrants further investigation.

In addition to these consistent findings, several studies also reported more nuanced results that could inform future research and clinical practice. For example, Phillips et al. [17] found that individuals with clinical depression were more likely to produce grip strength measures suggestive of poor volitional effort, which could be misinterpreted by clinicians as a lack of sincerity of effort. This finding highlights the importance of considering the potential impact of depression on grip strength testing and the need for healthcare professionals to be aware of this potential confounding factor.

In summary, these studies provide valuable insights into the association between hand-grip strength and depression. While the methodological differences and potential confounding factors limit our ability to draw definitive conclusions, the consistent findings across studies suggest that there is a significant relationship between lower hand-grip strength and increased depressive symptoms or depression risk. This relationship appears to be influenced by factors such as age, gender, and chronic disease status, highlighting the need for a personalized approach to understanding and addressing the complex interplay between hand-grip strength and depression.

Future research should focus on addressing the methodological limitations of the existing literature, including the need for more longitudinal studies to establish causality, as well as the need for standardized depression measurement tools to facilitate comparisons across studies. Moreover, additional research should investigate the underlying mechanisms that link hand-grip strength and depression, as well as the potential moderating factors, such as age, sex, and chronic disease status, which may influence this relationship.

## Conclusions

This review of literature on the association between hand-grip strength and depression offers valuable insights into the complex relationship between these factors. Although methodological differences and potential confounding factors limit our ability to draw definitive conclusions, the consistent findings across studies suggest a significant negative association between hand-grip strength and depression. This relationship appears to be influenced by factors such as age, gender, and chronic disease status, underlining the importance of a personalized approach to understanding and addressing this intricate interplay.

The interplay between physical and mental health is underscored by these findings, emphasizing the need for future research to investigate the underlying mechanisms linking hand-grip strength and depression and potential moderating factors. Longitudinal studies and standardized depression measurement tools are essential for facilitating comparisons across studies and establishing causality. Furthermore, these findings highlight the potential for hand-grip strength measurement to serve as a simple, non-invasive tool for early detection and intervention in individuals at risk for depression. The results of this review have significant implications for clinical practice, public health campaigns, and policies aimed at promoting mental and physical well-being. Interventions that target both depression and physical fitness, such as exercise-based interventions or combining psychotherapy with physical rehabilitation programs, could have potential benefits for both physical and mental health. Additionally, the findings could inform the development of new treatment approaches focusing on shared genetic factors and pathways involved in both depression and hand-grip strength.

## Additional Information

### Disclosures

**Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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## References

- Chon D, Shin J, Kim JH: Consideration of body mass index (BMI) in the association between hand grip strength and hypertension: Korean Longitudinal Study of Ageing (KLoSA). *PLoS One*. 2020, 15:e0241360. [10.1371/journal.pone.0241360](https://doi.org/10.1371/journal.pone.0241360)
- Kim JH: Effect of grip strength on mental health. *J Affect Disord*. 2019, 245:371-6. [10.1016/j.jad.2018.11.017](https://doi.org/10.1016/j.jad.2018.11.017)
- Institute for Health Metrics and Evaluation: GBD results. (2023). Accessed: April 4, 2023: <https://vizhub.healthdata.org/gbd-results>.
- World Health Organization: Depressive disorder (depression). (2023). Accessed: April 4: <https://www.who.int/news-room/fact-sheets/detail/depression>.
- Lewko J, Kochanowicz J, Zarzycki W, Mariak Z, Górka M, Krajewska-Kulak E: Poor hand function in diabetics. Its causes and effects on the quality of life. *Saudi Med J*. 2012, 33:429-35.
- Rantanen T, Guralnik JM, Foley D, Masaki K, Leveille S, Curb JD, White L: Midlife hand grip strength as a predictor of old age disability. *JAMA*. 1999, 281:558-60. [10.1001/jama.281.6.558](https://doi.org/10.1001/jama.281.6.558)
- Rantanen T, Harris T, Leveille SG, Visser M, Foley D, Masaki K, Guralnik JM: Muscle strength and body mass index as long-term predictors of mortality in initially healthy men. *J Gerontol A Biol Sci Med Sci*. 2000, 55:M168-73. [10.1093/gerona/55.3.m168](https://doi.org/10.1093/gerona/55.3.m168)
- Mahindru A, Patil P, Agrawal V: Role of physical activity on mental health and well-being: a review. *Cureus*. 2023, 15:e33475. [10.7759/cureus.33475](https://doi.org/10.7759/cureus.33475)
- Fukumori N, Yamamoto Y, Takegami M, et al.: Association between hand-grip strength and depressive symptoms: Locomotive Syndrome and Health Outcomes in Aizu Cohort Study (LOHAS). *Age Ageing*. 2015, 44:592-8. [10.1093/ageing/afv013](https://doi.org/10.1093/ageing/afv013)
- Sternäng O, Reynolds CA, Finkel D, Ernsth-Bravell M, Pedersen NL, Dahl Aslan AK: Grip strength and cognitive abilities: associations in old age. *J Gerontol B Psychol Sci Soc Sci*. 2016, 71:841-8. [10.1093/geronb/gbv017](https://doi.org/10.1093/geronb/gbv017)
- Ashdown-Franks G, Stubbs B, Koyanagi A, Schuch F, Firth J, Veronese N, Vancampfort D: Handgrip strength and depression among 34,129 adults aged 50 years and older in six low- and middle-income countries. *J Affect Disord*. 2019, 243:448-54. [10.1016/j.jad.2018.09.036](https://doi.org/10.1016/j.jad.2018.09.036)
- Musalek C, Kirchengast S: Grip strength as an indicator of health-related quality of life in old age-a pilot study. *Int J Environ Res Public Health*. 2017, 14: [10.3390/ijerph14121447](https://doi.org/10.3390/ijerph14121447)
- Smith CB, Rosenström T, Hagen EH: Strength is negatively associated with depression and accounts for some of the sex difference: A replication and extension. *Evol Med Public Health*. 2022, 10:130-41. [10.1093/emph/eoac007](https://doi.org/10.1093/emph/eoac007)
- Mergl R, Pogarell O, Juckel G, et al.: Hand-motor dysfunction in depression: characteristics and pharmacological effects. *Clin EEG Neurosci*. 2007, 38:82-8. [10.1177/155005940703800210](https://doi.org/10.1177/155005940703800210)
- Zheng H, He Q, Xu H, Zheng X, Gu Y: Lower grip strength and insufficient physical activity can increase depressive symptoms among middle-aged and older European adults: a longitudinal study. *BMC Geriatr*. 2022, 22:696. [10.1186/s12877-022-03392-x](https://doi.org/10.1186/s12877-022-03392-x)
- Gu Y, Li X, Zhang Q, et al.: Grip strength and depressive symptoms in a large-scale adult population: The TCLSIH cohort study. *J Affect Disord*. 2021, 279:222-8. [10.1016/j.jad.2020.08.023](https://doi.org/10.1016/j.jad.2020.08.023)
- Phillips HJ, Biland J, Costa R, Souverain R: Five-position grip strength measures in individuals with clinical depression. *J Orthop Sports Phys Ther*. 2011, 41:149-54. [10.2519/jospt.2011.3328](https://doi.org/10.2519/jospt.2011.3328)
- Marconcin P, Peralta M, Ferrari G, Gaspar de Matos M, Espanha M, Murawska-Ciałowicz E, Marques A: The association of grip strength with depressive symptoms among middle-aged and older adults with different chronic diseases. *Int J Environ Res Public Health*. 2020, 17: [10.3390/ijerph17196942](https://doi.org/10.3390/ijerph17196942)
- McDowell CP, Gordon BR, Herring MP: Sex-related differences in the association between grip strength and depression: Results from the Irish Longitudinal Study on Ageing. *Exp Gerontol*. 2018, 104:147-52. [10.1016/j.exger.2018.02.010](https://doi.org/10.1016/j.exger.2018.02.010)
- Smith L, Firth J, Grabovac I, et al.: The association of grip strength with depressive symptoms and cortisol in hair: A cross-sectional study of older adults. *Scand J Med Sci Sports*. 2019, 29:1604-9. [10.1111/sms.13497](https://doi.org/10.1111/sms.13497)
- Brooks JM, Titus AJ, Bruce ML, Orzechowski NM, Mackenzie TA, Bartels SJ, Batsis JA: Depression and handgrip strength among U.S. adults aged 60 years and older from NHANES 2011-2014. *J Nutr Health Aging*. 2018, 22:938-43. [10.1007/s12603-018-1041-5](https://doi.org/10.1007/s12603-018-1041-5)
- Zhang T, Ji L, Luo J, et al.: A genetic correlation and bivariate genome-wide association study of grip strength and depression. *PLoS One*. 2022, 17:e0278392. [10.1371/journal.pone.0278392](https://doi.org/10.1371/journal.pone.0278392)
- Jang LK, Lee ZH, Kim HH, Hill JM, Kim JD, Kwon BS: A novel leucine-rich repeat protein (LRR-1:304-312). *Starostina NG, Simpliciano JM, McGuirk MA, Kipreos ET: CRL2(LRR-1) targets a CDK inhibitor for cell cycle control in C. elegans and actin-based motility regulation in human cells. Dev Cell*. 2010, 19:753-64. [10.1016/j.devcel.2010.10.013](https://doi.org/10.1016/j.devcel.2010.10.013)
- Wang M, Greenberg DA, Stewart WC: Replication, reanalysis, and gene expression: ME2 and genetic generalized epilepsy. *Epilepsia*. 2019, 60:539-46. [10.1111/epi.14654](https://doi.org/10.1111/epi.14654)
- Lee BD, Walss-Bass C, Thompson PM, et al.: Malic enzyme 2 and susceptibility to psychosis and mania. *Psychiatry Res*. 2007, 150:1-11. [10.1016/j.psychres.2006.06.001](https://doi.org/10.1016/j.psychres.2006.06.001)
- Ren JG, Seth P, Clish CB, et al.: Knockdown of malic enzyme 2 suppresses lung tumor growth, induces differentiation and impacts PI3K/AKT signaling. *Sci Rep*. 2014, 4:5414. [10.1038/srep05414](https://doi.org/10.1038/srep05414)
- Costas J, Gratacòs M, Escaramís G, et al.: Association study of 44 candidate genes with depressive and anxiety symptoms in post-partum women. *J Psychiatr Res*. 2010, 44:717-24. [10.1016/j.jpsychires.2009.12.012](https://doi.org/10.1016/j.jpsychires.2009.12.012)
- Wen Y, Wang J, Zhang Q, Chen Y, Bao X: The genetic and clinical characteristics of aromatic L-amino acid decarboxylase deficiency in mainland China. *J Hum Genet*. 2020, 65:759-69. [10.1038/s10038-020-0770-6](https://doi.org/10.1038/s10038-020-0770-6)
- Olayioye MA, Barisic S, Hauser A: Multi-level control of actin dynamics by protein kinase D. *Cell Signal*.

- 2013, 25:1739-47. [10.1016/j.celsig.2013.04.010](https://doi.org/10.1016/j.celsig.2013.04.010)
31. Asaithambi A, Kanthasamy A, Saminathan H, Anantharam V, Kanthasamy AG: Protein kinase D1 (PKD1) activation mediates a compensatory protective response during early stages of oxidative stress-induced neuronal degeneration. *Mol Neurodegener.* 2011, 6:43. [10.1186/1750-1326-6-43](https://doi.org/10.1186/1750-1326-6-43)
32. Storz P, Tokar A: Protein kinase D mediates a stress-induced NF-kappaB activation and survival pathway . *EMBO J.* 2003, 22:109-20. [10.1093/emboj/cdg009](https://doi.org/10.1093/emboj/cdg009)
33. Wang P, Han L, Shen H, et al.: Protein kinase D1 is essential for Ras-induced senescence and tumor suppression by regulating senescence-associated inflammation. *Proc Natl Acad Sci U S A.* 2014, 111:7683-8. [10.1073/pnas.1310972111](https://doi.org/10.1073/pnas.1310972111)
34. Ohya S, Matsui M, Kajikuri J, Kito H, Endo K: Downregulation of IL-8 and IL-10 by the Activation of Ca(2+)-Activated K(+) Channel K(Ca)3.1 in THP-1-Derived M(2) Macrophages. *Int J Mol Sci.* 2022, 23:10.3390/ijms23158603
35. Hasso-Agopsowicz M, Scriba TJ, Hanekom WA, Dockrell HM, Smith SG: Differential DNA methylation of potassium channel KCa3.1 and immune signalling pathways is associated with infant immune responses following BCG vaccination. *Sci Rep.* 2018, 8:13086. [10.1038/s41598-018-31537-9](https://doi.org/10.1038/s41598-018-31537-9)
36. Schanda K, Peschl P, Lerch M, et al.: Differential binding of autoantibodies to MOG isoforms in inflammatory demyelinating diseases. *Neurol Neuroimmunol Neuroinflamm.* 2021, 8:10.1212/NXI.0000000000001027
37. Kinzel S, Lehmann-Horn K, Torke S, et al.: Myelin-reactive antibodies initiate T cell-mediated CNS autoimmune disease by opsonization of endogenous antigen. *Acta Neuropathol.* 2016, 132:43-58. [10.1007/s00401-016-1559-8](https://doi.org/10.1007/s00401-016-1559-8)
38. Yang X, Chen H, Zheng H, et al.: LncRNA SNHG12 promotes osteoarthritis progression through targeted down-regulation of miR-16-5p. *Clin Lab.* 2022, 68:10.7754/Clin.Lab.2021.210402
39. Yan L, Li L, Lei J: Long noncoding RNA small nucleolar RNA host gene 12/microRNA-138-5p/nuclear factor I/B regulates neuronal apoptosis, inflammatory response, and oxidative stress in Parkinson's disease. *Bioengineered.* 2021, 12:12867-79. [10.1080/21655979.2021.2005928](https://doi.org/10.1080/21655979.2021.2005928)
40. Nead KT: Androgens and depression: a review and update . *Curr Opin Endocrinol Diabetes Obes.* 2019, 26:175-9. [10.1097/MED.0000000000000477](https://doi.org/10.1097/MED.0000000000000477)
41. Gonzalez BD, Jim HS, Small BJ, et al.: Changes in physical functioning and muscle strength in men receiving androgen deprivation therapy for prostate cancer: a controlled comparison. *Support Care Cancer.* 2016, 24:2201-7. [10.1007/s00520-015-3016-y](https://doi.org/10.1007/s00520-015-3016-y)
42. McClain LL, Shaw P, Sabol R, et al.: Rare variants and biological pathways identified in treatment-refractory depression. *J Neurosci Res.* 2020, 98:1322-34. [10.1002/jnr.24609](https://doi.org/10.1002/jnr.24609)
43. Nishitani A, Yoshihara T, Tanaka M, Kuwamura M, Asano M, Tsubota Y, Kuramoto T: Muscle weakness and impaired motor coordination in hyperpolarization-activated cyclic nucleotide-gated potassium channel 1-deficient rats. *Exp Anim.* 2020, 69:11-7. [10.1558/expanim.19-0067](https://doi.org/10.1558/expanim.19-0067)
44. Aspenström P, Fransson A, Saras J: Rho GTPases have diverse effects on the organization of the actin filament system. *Biochem J.* 2004, 377:327-37. [10.1042/BJ20031041](https://doi.org/10.1042/BJ20031041)
45. Govek EE, Newey SE, Van Aelst L: The role of the Rho GTPases in neuronal development . *Genes Dev.* 2005, 19:1-49. [10.1101/gad.1256405](https://doi.org/10.1101/gad.1256405)
46. Fuchsova B, Alvarez Juliá A, Rizavi HS, Frasch AC, Pandey GN: Expression of p21-activated kinases 1 and 3 is altered in the brain of subjects with depression. *Neuroscience.* 2016, 333:331-44. [10.1016/j.neuroscience.2016.07.037](https://doi.org/10.1016/j.neuroscience.2016.07.037)
47. Olwin BB, Arthur K, Hannon K, et al.: Role of FGFs in skeletal muscle and limb development . *Mol Reprod Dev.* 1994, 39:90-100; discussion 100-1. [10.1002/mrd.1080390114](https://doi.org/10.1002/mrd.1080390114)
48. Beenakker KG, Ling CH, Meskers CG, de Craen AJ, Stijnen T, Westendorp RG, Maier AB: Patterns of muscle strength loss with age in the general population and patients with a chronic inflammatory state. *Ageing Res Rev.* 2010, 9:431-6. [10.1016/j.arr.2010.05.005](https://doi.org/10.1016/j.arr.2010.05.005)
49. Berk M, Williams LJ, Jacka FN, et al.: So depression is an inflammatory disease, but where does the inflammation come from?. *BMC Med.* 2013, 11:200. [10.1186/1741-7015-11-200](https://doi.org/10.1186/1741-7015-11-200)
50. Donini LM, Savina C, Cannella C: Eating habits and appetite control in the elderly: the anorexia of aging . *Int Psychogeriatr.* 2003, 15:73-87. [10.1017/s1041610203008779](https://doi.org/10.1017/s1041610203008779)
51. Piovezan RD, Abucham J, Dos Santos RV, Mello MT, Tufik S, Poyares D: The impact of sleep on age-related sarcopenia: Possible connections and clinical implications. *Ageing Res Rev.* 2015, 23:210-20. [10.1016/j.arr.2015.07.003](https://doi.org/10.1016/j.arr.2015.07.003)
52. Bohannon RW: Grip strength: an indispensable biomarker for older adults. *Clin Interv Aging.* 2019, 14:1681-91. [10.2147/CIA.S194543](https://doi.org/10.2147/CIA.S194543)
53. Lam RW, Kennedy SH, McIntyre RS, Khullar A: Cognitive dysfunction in major depressive disorder: Effects on psychosocial functioning and implications for treatment. *Can J Psychiatry.* 2014, 59:649-654. [10.1177%2F070674371405901206](https://doi.org/10.1177%2F070674371405901206)
54. Trivedi MH: The link between depression and physical symptoms . *Prim Care Companion J Clin Psychiatry.* 2004, 6:12-6.
55. Benton MJ, Spicher JM, Silva-Smith AL: Validity and reliability of handgrip dynamometry in older adults: A comparison of two widely used dynamometers. *PLoS One.* 2022, 17:e0270132. [10.1371/journal.pone.0270132](https://doi.org/10.1371/journal.pone.0270132)