Evaluation of thiol/disulfide homeostasis in patients with a first episode of major depressive disorder
Medical Science and Discovery (http://www.medscidiscovery.com) is an international open access, peer-reviewed scientific research journal that provides rapid publication of articles in all disciplines of human health, clinical and basic medical science such as Biophysics, Biochemistry, Histology, Physiology, Genetics, Pathology, Toxicology, Anatomical Sciences, Pharmacology, Embryology, Internal and Surgical Medicine.

The policy of top priority of MSD is to put forward and highlight medical innovations and inspiring patents.

MSD offers an exceptionally fast publication schedule including prompt peer-review by the experts in the field and immediate publication upon acceptance. The editorial board aims at reviewing the submitted articles as fast as possible and promptly including them in the forthcoming issues.

This journal is published under ethical publishing policy of international scientific Bioethics and publication rules.

MSD supports the Open Access Initiative. Abstracts and full texts (HTML and PDF format) of all articles published by MSD are freely accessible to everyone immediately upon publication.

Medical Science and Discovery has scientific affiliation with Lycia Clinics London UK

Indexed Databases: Chemical Abstracts (CAS), Index Copernicus, Open Air, ULRICHs Database, Proquest, Advanced Science Index, Turkish Citation Index, Research Bible, Scholar Google, NLM Catalog

Medical Science and Discovery is an international open access, peer-reviewed scientific research journal.

ISSN: 2148-6832 (Print) E-ISSN: 2148-6832 (Online)

Category: Multi Disciplinary Health Science Journal


Frequency: Monthly

Review System: Double Blind Peer Review

Circulation: Globally, Online, Printed

Article Processing Charge (APC): US$ 100

Licensing: CC-BY-NC 4.0 International License Environmental

Editor-in-Chief: Assoc. Prof. Dr. Ahmad Rajabzadeh, Anatomical Department of Lorestan, University of Medical Sciences, Tabriz, Iran

Established: 30.04.2014

Web address: www.medscidiscovery.com; http://dergipark.ulakbim.gov.tr/msd

E-mail: editor [at] medscidiscovery.com

Phone: +44 020 3289 9294

Design and preparation of PDFs, Language editing, Web site design, Graphical design Services of international Journal of Medical Science and Discovery has been contracted with Lycia Press LONDON, UK (as Publisher), by the MSD Board of Directors

Publisher: Lycia Press Inc.

Address: 3rd Floor 86 - 90 Paul Street, EC2A 4NE, London, UK

Web address: www.lycians.com

Phone: +44 020 3289 9294

E-mail: office [at] lycians.com

E-mail: info [at] lycians.com
Medical Science and Discovery (http://www.medscidiscovery.com) is an international open access, peer-reviewed scientific research journal that provides rapid publication of articles in all disciplines of human health, clinical and basic medical science such as Biophysics, Biochemistry, Histology, Physiology, Genetics, Pathology, Toxicology, Anatomical Sciences, Pharmacology, Embryology, Internal and Surgical Medicine.

The policy of top priority of MSD is to put forward and highlight medical innovations and inspiring patents.

MSD offers an exceptionally fast publication schedule including prompt peer-review by the experts in the field and immediate publication upon acceptance. The editorial board aims at reviewing the submitted articles as fast as possible and promptly including them in the forthcoming issues.

This journal is published under ethical publishing policy of international scientific Bioethics and publication rules.

MSD supports the Open Access Initiative. Abstracts and full texts (HTML and PDF format) of all articles published by MSD are freely accessible to everyone immediately upon publication.

Medical Science and Discovery has scientific affiliation with Lycia Clinics London UK

**Indexed Databases:** Chemical Abstracts (CAS), Index Copernicus, Open Air, ULRICHs Database, Proquest, Advanced Science Index, Turkish Citation Index, Research Bible, Scholar Google (www.medscidiscovery.com)

**Medical Science and Discovery is an international open access, peer-reviewed scientific research journal.**

**ISSN:** 2148-6832 (Print) **E-ISSN:** 2148-6832 (Online)

**Category:** Multi Disciplinary Health Science Journal

**Abbreviated key title:** Med. Sci. Discov.

**Frequency:** Monthly

**Review System:** Double Blind Peer Review

**Circulation:** Globally, Online, Printed

**Article Processing Charge (APC):** US$ 100

**Licensing:** CC-BY-NC 4.0 International License Environmental

**Editor-in-Chief:** Assoc. Prof. Dr. Dr. Ahmad Rajabzadeh, Anatomical Department of Lorestan, University of Medical Sciences, Tabriz, Iran

**Established:** 30.04.2014

**Web address:** www.medscidiscovery.com; http://dergipark.ulakbim.gov.tr/msd

**E-mail:** editor [at] medscidiscovery.com

**Phone:** +44 020 3289 9294

**Design and preparation of PDFs, Language editing, Web site design, Graphical design Services of international Journal of Medical Science and Discovery has been contracted with Lycia Press LONDON, UK (as Publisher), by the MSD Board of Directors**

**Publisher:** Lycia Press Inc.

**Address:** 3rd Floor 86 - 90 Paul Street, EC2A 4NE, London, UK

**Web address:** www.lycians.com

**Phone:** +44 020 3289 9294

**E-mail:** office [at] lycians.com

**E-mail:** info [at] lycians.com
<table>
<thead>
<tr>
<th>Title</th>
<th>Name</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prof. Dr.</td>
<td>Aziz Sancar</td>
<td>UNC, Faculty of Medicine, Dept. of Biochemistry-Biophysics, Chapel Hill, NC, USA</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Giancarlo BAROLAT</td>
<td>Barolat Institute, 1721 E 19th Ave #434, Denver, CO 80218, USA</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Joyce REARDON</td>
<td>UNC, Faculty of Medicine, Dept. of Biochemistry-Biophysics, Chapel Hill, NC, USA</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Metin TULGAR</td>
<td>Yuzuncu Yil University, School of Medicine, Dept. of Biophysics, Van, TR</td>
</tr>
<tr>
<td>Assoc. Prof. Dr.</td>
<td>Ahmad Rajabzadeh</td>
<td>Anatomical Department of Isfahan, University of Medical Sciences, Tabriz, Iran</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Michael George KEMP</td>
<td>UNC, 120 Mason Farm Road, Campus Box 7260, Genetic Medicine Bldg Room 3010 Chapel Hill, NC 27599 USA</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Abdullah BOYUK</td>
<td>Dicle University, Faculty of Medicine, Dept. of General Surgery, Diyarbakir, Turkey</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Ahmet YULMAZ</td>
<td>Dicle University, Faculty of Medicine, Dept. of Family Medicine, Diyarbakir, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Alev Meltem ERCAN</td>
<td>Istanbul University, Cerrahpasa Medical Faculty, Dept. of Biophysics, Istanbul, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Ali Riza Bilge</td>
<td>CBU, Faculty of Medicine, Dept. of Cardiology, Manisa, Turkey</td>
</tr>
<tr>
<td>Assoc. Prof. Dr.</td>
<td>Alparslan SAHIN</td>
<td>Dicle University, Faculty of Medicine, Dept. of Ophthalmology, Diyarbakir, Turkey</td>
</tr>
<tr>
<td>PhD</td>
<td>Alper Tunga OZDEMIR</td>
<td>Manisa ME State Hospital Dept. of Medical Biochemistry, Manisa, Turkey</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Anzel BAHADIR</td>
<td>Duzce University, Faculty of Medicine, Dept. of Biophysics, Bolu, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Arash KHAKI</td>
<td>Islamic Azad University, Tabriz branch, Dept. of Pathology, Tabriz Iran</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Ayse Inhan GARIP</td>
<td>Marmara University, Faculty of Medicine, Dept. of Biophysics, Istanbul, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Ayse YUKSEL</td>
<td>Arel University, Health Sciences Academy, Dept. of Healthcare Management, Istanbul, Turkey</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Bahriye SIRAV</td>
<td>Gazi University, Faculty of Medicine, Dept. of Biophysics, Ankara, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Beki KAN</td>
<td>Acibadem University, Faculty of Medicine, Dept. of Biophysics, Istanbul, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Cevval ULMAN</td>
<td>CBU, Faculty of Medicine, Dept. of Biophysics, Manisa, Turkey</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Christopher SCHMITT</td>
<td>University of California, San Francisco Cardiovascular Res. Inst. CA, USA</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Cuneyt TEMIZ</td>
<td>Celal Bayar University, Faculty of Medicine, Dept. of Neurosurgery, Manisa, Turkey</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Gokhan OTO</td>
<td>YYU, Faculty of Medicine, Dept. of Pharmacology, Van, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Gonul Tezcan KELES</td>
<td>CBU, Faculty of Medicine, Dept. of Anaesthesiology and Reanimation, Manisa, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Halit DEMIR</td>
<td>YYU Faculty of Science, Dept. of Biochemistry, Van, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Hasan YILMAZ</td>
<td>YYU Faculty of Medicine, Dept. of Parasitology, Van, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Hatice SINAU USLU</td>
<td>ISMU, Faculty of Medicine, Dept. of Nuclear Medicine, Istanbul, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Hikmet YILMAZ</td>
<td>CBU, Faculty of Medicine, Dept. of Neurology, Manisa, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Hulya OZDEMIR</td>
<td>YYU Faculty of Medicine, Dept. of pharmacology, Van, Turkey</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Huseyin GUDUCUOGLU</td>
<td>YYU Faculty of Medicine, Dept. of Microbiology, Van, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>M. Derya BALBAY</td>
<td>Memorial Hospital, Dept. of Uro-oncology, Istanbul, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Mehmet Ali KÖRPINAR</td>
<td>Istanbul University, Cerrahpasa Medical Faculty, Dept. of Biophysics, Istanbul, Turkey</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Murat OZSARAC</td>
<td>CBU, Faculty of Medicine, Dept. of Emergency Medicine, Manisa, Turkey</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Mustafa OZBEK</td>
<td>CBU, Faculty of Medicine, Dept. of Physiology, Manisa, Turkey</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Mustafas USLU</td>
<td>Duzce University, Faculty of Medicine, Dept. of Orthopedics, Bolu, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Muzaffer POLAT</td>
<td>CBU, Faculty of Medicine, Dept. of Paediatric Neurology, Manisa, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Nasuhi Engin AYDIN</td>
<td>Katip Celebi University, Faculty of Medicine, Dept. of Pathology, Izmir, Turkey</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Nesrin Ceylan</td>
<td>Ankara Children’s Health, Training and Research Hospital, Department of Hematology Oncology , Ankara, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Nobuo INOTSUME</td>
<td>Hokkaido Pharmaceutical University, Clinical Pharmacology, Hokkaido AC, JAPAN</td>
</tr>
<tr>
<td>Assist. Prof.</td>
<td>Ozdemirhan SERCIN</td>
<td>Interdisciplinary Research Institute, Université Libre de Bruxelles, Belgium</td>
</tr>
<tr>
<td>Assist. Prof.</td>
<td>Pinar Solmaj HASDEMIR</td>
<td>CBU, Faculty of Medicine, Dept. of Obstetrics and Gynecology, Manisa, Turkey</td>
</tr>
<tr>
<td>Assist. Prof.</td>
<td>Secil ILHAN YILMAZ</td>
<td>Erciyes University, Genom and Stem Cell Research Center, Kayseri, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Seda VATANSEVER</td>
<td>CBU, Faculty of Medicine, Dept. of Histology and Embryology, Manisa, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Sevinc INAN</td>
<td>Izmir Economy University, Faculty of Medicine, Dept. of Histology and Embryology, Izmir, Turkey</td>
</tr>
<tr>
<td>Assist. Prof.</td>
<td>Shobhan GADDAMEEDHI</td>
<td>Washington State University College of Pharmacy, Dept. of Experimental and Systems Pharmacology, Spokane, WA, USA</td>
</tr>
<tr>
<td>Assist. Prof.</td>
<td>Tahir CAKIR</td>
<td>Yuzuncu Yil University, Medical Faculty, Dept. of Biophysics, Van, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Talat ECEMIS</td>
<td>CBU, Faculty of Medicine, Dept. of Microbiology, Manisa, Turkey</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Tamer ZEREN</td>
<td>CBU, Faculty of Medicine, Dept. of Biophysics, Manisa, Turkey</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Tevfik GUNES</td>
<td>PAU, Faculty of Medicine, Dept. of Cardiovascular Surgery, Denizli, Turkey</td>
</tr>
<tr>
<td>Prof. Dr.</td>
<td>Tunaya KALKAN</td>
<td>Istanbul University, Cerrahpasa Medical Faculty, Dept. of Biophysics, Istanbul, Turkey</td>
</tr>
<tr>
<td>Assist. Prof.</td>
<td>Younes El Bouzekri EL IDRISSI</td>
<td>Place Aboubakr, Imm 22, App 6, Bd Fal oude meur, Agdal Rabat</td>
</tr>
<tr>
<td>Assoc. Prof.</td>
<td>Yuksel Kaya</td>
<td>YYU Faculty of Medicine, Dept. of Cardiology, Van, Turkey</td>
</tr>
<tr>
<td>Assist. Prof.</td>
<td>Yusuf Kemal DEMIR</td>
<td>Marmara University, Faculty of Pharmacy, Dept. of Pharmaceutical Tech. Istanbul TR</td>
</tr>
<tr>
<td>Role</td>
<td>Name</td>
<td>Institution and Address</td>
</tr>
<tr>
<td>----------------------</td>
<td>----------------</td>
<td>--------------------------------------------------------------</td>
</tr>
<tr>
<td>Statistical Editor</td>
<td>Sıddık KESKİN</td>
<td>YYU Faculty of Medicine, Dept. of Medical Statistics, Van, TR</td>
</tr>
<tr>
<td>Language Editors</td>
<td>Hakan ERGİN</td>
<td>Istanbul University, Dept. of Foreign Languages, Istanbul, TR</td>
</tr>
</tbody>
</table>
Important
MSD is committed to deterring plagiarism, including self-plagiarism. Your manuscript will screen to compare for similarity with published articles.
For research studies using human or animal subjects, the trial's design, conduct and reporting of results must conform to Good Clinical Practice guidelines (such as the Good Clinical Practice in Food and Drug Administration (FDA)-Regulated Clinical Trials (USA) or the Medical Research Council Guidelines for Good Clinical Practice in Clinical Trials (UK)) and/or to the World Medical Association (WMA) Declaration of Helsinki

Dear Authors, please upload just these three files to the manuscript submission system
Title Page Sample
Manuscript Sample
Copyright Transfer and Author Consent Form
Please select Keywords from the MESH source
Manuscripts should be prepared in accordance with the "Uniform Requirements for Manuscripts Submission to Biomedical Journals” proclaimed by the International Committee of Medical Journal Editors (www.icmje.org).
MSD uses Vancouver reference style, please prepare articles due to Vancouver reference style rules.

Manuscript Preparation Rules
1. Cover letter
   a- A statement that the manuscript has been read and approved by all the authors.
   b- That the requirements for authorship have been met for all the authors, based on the criteria stated by ICMJE.
   c- Approval of all the authors regarding the order in which their names have appeared.
   d- That each author confirms the manuscript represents honest work.
   e- The name, address, and telephone number of the corresponding author who is responsible for communicating with other authors about revisions and final approval.
   f- The letter should give any additional information that may be helpful to the editor, such as the type or format of the article. If the manuscript has been submitted previously to another journal or in another language, it is helpful to include the previous editor's and reviewers' comments with the submitted manuscript, along with the authors' responses to those comments. Submitting previous evaluatory review of another journal accelerates the review process.
   g- For accepted manuscripts, the authors are requested to fill and sign the journal's cover letter to express their consent for its publication.
   h- To reproduce published material, to use illustrations or tables or report information about identifiable people, the author should submit a copy of the permission with the manuscript to the journal.
2. Ethic Committee Approval
   Inclusion of the approval letter from the relevant Ethics Committee or Institution's Review Board regarding the research protocol and the rights of the subjects (if applicable to the study)
3. Consent Form
   Attach a copy of the consent form to the letter, if applicable. Consent forms would be evaluated by the Ethics Committee and then signed by the participant.
4. RCT or NCT Registration
   Emailing the letter denoting registration of RCTs or NCTs in domestic or international databases (The trial's registration number needs to be mentioned, too).
5. Manuscripts submitted in English, must be type written, double-spaced, on good quality A4 paper, or paper of similar format. Authors are requested to reserve margins of at least 2.5cm all around the paper. Original drawings of photos, tables and figures should be furnished together with the manuscripts.
6. Manuscripts should be kept to a minimum length and should be subdivided into labeled sections (Title page, Abstract, Keywords, Introduction, Materials and Methods, Results, Discussion, Conclusion, Acknowledgement, and References).
7. A title page is to be provided and should include the title of the article, authors' names with full first name (with degrees), authors' affiliation, suggested running title and corresponding author. The affiliation should comprise the department, institution (usually university or company), city and state (or nation). The suggested running title should be less than 50 characters (including spaces) and should comprise the article title or an abbreviated version thereof. For office purposes, the title page should include the name and complete mailing address, telephone and fax number, and email of the one author designated to review proofs.
8. An abstract no longer than 250 words for reviews and research articles is to be provided as the second page. Abstract should be structured as objective(s) (including purpose setting), materials and methods, results, and conclusion.
Instruction for Authors

- **Case Report**
  - A case report is a case study, case report, or other description of a case that should contain 1500 - 2000 words with a structured abstract of 200 words maximum. Case reports should comprise sections of Introduction, Case Presentation, and Conclusions in Abstract and Introduction, Case Presentation, and Discussion in full text with not more than 2 tables or figures and up to 20 references.

- **Brief Report**
  - Brief Reports should contain 1000 - 2000 words with a structured abstract of 200 words maximum. Short reports should comprise sections of Background, Objectives, Materials & Methods, Results and Discussion with not more than 2 tables or figures and up to 20 references.

- **Short Communication**
  - Short Communication, follow the instructions for original articles, except that the total word number of the main text (excluding references, tables and figure legends) is limited to 2000 with no more than 2 figures and/or tables and no more than 15 references. An abstract, not exceeding 150 words, should be presented at the beginning of the article.

- **News**
  - News should contain 1000 - 2000 words with a structured abstract of 200 words maximum. News should comprise sections of Background, Objectives, Materials & Methods, Results and Discussion with not more than 2 tables or figures and up to 20 references.

- **Publication Policies**
  - Manuscripts, or the essence of their content, must be previously unpublished and should not be under simultaneous consideration by another Journal. The authors should also declare if any similar work has been submitted to or published by another Journal. By virtue of the submitted manuscript, the corresponding author acknowledges that all the co-authors have seen and approved the final version of the manuscript. The corresponding author should provide all co-authors with information regarding the manuscript, and obtain their approval before submitting any revisions. Manuscripts are only accepted for publication on the understanding that the authors will permit editorial amendments, though proofs will always be submitted to the corresponding author before being sent finally to press. Prior to the initial submission of a new manuscript, please carefully consider that all authors’ names are included as no change to authors’ details will be permitted after the acceptance. The decision to accept a contribution rests with the Editorial Board of the MSD.

- **Peer review process**
  - All submissions will be reviewed anonymously by at least two independent referees. All manuscripts will be acknowledged upon presenting to the Journal office, provided that all stated requirements are met. Authors are encouraged to suggest names of three expert reviewers, but selection remains a prerogative of the Editor. The whole review process depends on receiving referees comments and revising the manuscripts based on these comments to the author. On receipt of the revised article from the author, and after final approving by referees, the letter of acceptance is issued to the author. Authors have the right to communicate to the editor if they do not wish their manuscript to be reviewed by a particular reviewer because of potential conflicts of interest. No article is rejected unless negative comments are received from at least two reviewers. **MSD employs double blind reviewing process, where both the referee and author remain anonymous throughout the process.**
Instruction for Authors

- **Ethical Rules and Rights**
- **Conflicts of interest**
  - Conflicts of interest arise when authors, reviewers, or editors have interests that are not fully apparent and that may influence their judgments on what is published. They have been described as those which, when revealed later, would make a reasonable reader feel misled or deceived. (The Committee on Publication Ethics (COPE) states in its Guidelines on Good Publication Practice 2003).
  - Authors should disclose, at the time of submission, information on financial conflicts of interest or other interests that may influence the manuscript. Authors should declare sources of funding for the work undertaken.
- **The Journal's Policy on Plagiarism**
  - Any practice of plagiarism will not be tolerated by the journal regarding submitted manuscripts. Non-identifiable quoted segments of articles or close paraphrases from other author/s or even submitting the author's previously published work are known as the act of plagiarism by this journal unless proper use of quotations or paraphrasing with decent citation or referencing are in place. Heavy use of one or a couple of articles is discouraged, even if paraphrased fully. Advertent practice of plagiarism will abort reviewing process or later submission to this journal. All submitted articles will evaluate by iThenticate software belonged to cross check for stop any plagiarism and improve publication quality.
- **Statement of Human and Animal Rights**
  - All submitted articles involving human experiments should be performed only in accordance with the ethical standards provided by the responsible committee of the institution in accordance with the Declaration of Helsinki (as revised in Edinburgh 2000), available at [http://www.wma.net/en/30publications/10policies/b3/index.html](http://www.wma.net/en/30publications/10policies/b3/index.html). Papers describing animal experiments can be accepted for publication only if the experiment conforms the National Institute of Health Guide (National Institute of Health Publications No. 80-23, Revised 1978) for the care and use of Laboratory Animals for experimental procedure. Authors must provide a full description of their anesthetics and surgical procedures. All manuscripts reporting the results of experimental investigations involving human subjects should include a statement confirming the informed consent was obtained from each subject or subject's guardian.
  - **Humans:** When reporting experiments on human subjects, authors should indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). If doubt exists whether the research was conducted in accordance with the Helsinki Declaration, the authors must explain the rationale for their approach and demonstrate that the institutional review body explicitly approved the doubtful aspects of the study.
  - **Animals:** When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.
  - All animal or human subjects should be used after approval of the experimental protocol by a local ethics committee.
- **Acknowledgements**
  - Contributors: In acknowledgement section, name people for their contributions or their permission to reproduce their published material, to use their illustrations or provide information about them- try to fully name people who have helped from the conception of the idea to adoption of the hypothesis, to finalization of the study, etc., earnestly. Statement of financial support: Aside from the title page, state any financial or other relationships that might lead to a conflict of interest.
- **Copyright**
  - After acceptance and publication; all ownership rights and Copyrights of the manuscript, passes to international journal of Medical Science and Discovery. Please complete copyright form and send via email to editor. [Download MSD Copyright Transfer and Author Consent Form](https://www.clockss.org/).

This work is licensed under a [Creative Commons Attribution-NonCommercial 4.0 International License](http://creativecommons.org/licenses/by-nc/4.0/).

- Copyright 2014: The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. All Rights reserved by international journal of Medical Science and Discovery.
- **Disposal of material**
  - Once published, all draft copies of the manuscript, correspondence and artwork will be held at least for 6 months before disposal. Authors and Readers may find original PDF file of article on backup servers such as CLOKKS (https://www.clockss.org/)
- **Digital Object Identifier DOI**
  - Once a manuscript is accepted for publication it will be provided with a registered DOI number following the acceptance decision. Manuscripts accepted for publication by the MSD will be published as ahead of print articles prior to the printing date of their scheduled issue. Corresponding author will be provided with a PDF Proof by the publisher once the production process of an accepted manuscript is over.
Instruction for Authors

- **Article Processing Charge**
- MSD is a non-profit Scientific Journal Platform; however, it uses professional services such as Language Editing, DOI, domain and hosting, iThenticate Plagiarism or similarity Detection Software. All of these professional services are used for all the article processes and an inevitable cost arises with this.
- Unfortunately, like most open journals, fees of the publication with MSD are charged to Authors. Payment is under the responsibilities of corresponding Author(s). MSD does not charge any fee during the submission period. However, after the peer-review process, a non-refundable charge (100 USD ) for each accepted manuscript must be paid by the author(s) via MSD's official PayPal account. An invoice will be sent for each accepted manuscript to corresponding author(s).
- **Following with completion of payment procedure, the galley proof and acceptance letter of article will be send to authors for last check**
- Preparation of articles in PDF and HTML format is covered by Lycia Press Inc. (press.lycians.com) and Article Processing Charges paid to Lycia Press London UK (www.lycians.com)
- **MSD revenue sources and Sponsorships**
- All costs arising from the publications are covered by the Sponsor Companies and Article Processing Charges. Sponsorship request evaluates by the MSD Journal Management Board and the sponsor company logos will be included on the back page of printed magazine and in the sponsor section of journal website

<table>
<thead>
<tr>
<th>Article Processing Charge (APC)</th>
<th>Discount %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular</td>
<td>100 USD</td>
</tr>
<tr>
<td>for Editorial Board Members</td>
<td>70 USD</td>
</tr>
<tr>
<td>for Affiliated Institution Members</td>
<td>80 USD</td>
</tr>
</tbody>
</table>

- **APC not includes Proofreading Services fee. Editor in Chief may direct the corresponding Author to Lycia Press, Language Office for Proofreading Service [www.lycians.com](http://www.lycians.com)

- **References**
Contents

Research Article

Evaluation of thiol/disulfide homeostasis in patients with a first episode of major depressive disorder / Pages: 1-7
Özgül Karaaslan, Yunus Hacimusalar, Ceylan Bal, Müjgan Ercan
Evaluation of thiol/disulfide homeostasis in patients with a first episode of major depressive disorder

Özgül Karaaslan¹*, Yunus Hacimusalar¹, Ceylan Bal², Müjgan Ercan³

Abstract

Objective: The aim of this study was to investigate the role of dynamic thiol-disulfide homeostasis as a new oxidative stress parameter in patients with major depressive disorder (MDD).

Material and Methods: Sixty-three patients with their first episode of untreated MDD, and 61 healthy volunteers were included in the study. Serum thiol/disulfide levels were measured in fasting blood samples. The data were compared between the two groups.

Results: No significant difference was observed between the two groups in terms of age, gender distribution, or body mass index. Plasma native and total thiol levels were lower in the MDD group compared to those in the controls (p=0.004, p=0.001). No significant differences were observed between the groups in terms of disulfide, the disulfide/native thiol, the disulfide/total thiol or the native thiol/total thiol ratio (p>0.05). No relationship was detected between these parameters.

Conclusion: As far as we know, this is the first study to evaluate changes in thiol/disulfide homeostasis in male and female patients with MDD. Our data show that thiol levels decrease during the first episode of untreated depression. Thiol/disulfide homeostasis may be useful as a biomarker for depression after long-term follow-up and treatment studies.

Keywords: major depressive disorder, oxidative stress, thiol/disulfide homeostasis.

Introduction

Major depressive disorder (MDD) is a recurrent and chronic disorder with a high mortality rate (1). The incidence rates of MDD in a lifetime are 10–25% in women and 5–12% in men. According to data of the World Health Organization, unipolar major depression constitutes 36% of all psychiatric disorders (2). It is predicted that depressive diseases will be the second major cause of labor-power loss in the entire world by the year 2020 (3), suggesting that MDD is a growing important public health issue (4).

Environmental and genetic factors as well as neurotransmitters and neuroendocrine system disorders play important roles in the pathogenesis of MDD (5).

Oxidative stress is defined as the altered balance between oxidant and antioxidant mechanisms. Oxidant end products generated by oxidative stress damage lipids, proteins, and nucleic acids (6). A number of studies have researched the role of oxidative metabolism in MDD (7,8).

Cumurcu et al. reported that serum total oxidant status (TOS) and the oxidative stress index (OSI) levels are high and total antioxidant capacity level is low in patients with MDD, whereas the total antioxidant level increases and TOS and OSI levels decrease after antidepressant treatment (9).

Thiols are a group of sulfur-containing organic compounds that combine with amino acids and proteins to play important roles in the pathogenesis of MDD (5).

Thiols are antioxidants that neutralize reactive oxygen types enzymatically and non-enzymatically. Major thiols in the plasma include albumin thiols, protein thiols, and thiols with low molecular weights, such as cysteine, homocysteine, and glutathione. Thiols react with oxidant molecules to form disulfide bonds. Therefore, active thiol/disulfide homeostasis (TDH) is necessary for regulating detoxification, apoptosis, and enzymatic reactions (11,12,13).
Previous studies have shown that TDH is related to the etiopathogenesis of diseases, such as Parkinson’s disease, diabetes, Alzheimer’s disease, cardiovascular disease, malignancy and multiple sclerosis (14,15,16,17).

The brain is sensitive to changes in oxidative mechanisms, and neurodegenerative changes have been detected in patients with neuropsychiatric diseases, suggesting that oxidative damage may be involved in the etiology of neuropsychiatric disorders (18,19). Oxidants interact with membrane-bound proteins and block neurotransmitter re-uptake causing psychiatric disorders (20). Thiol and disulfide take part in the dysregulation of the oxidative stress system, and their role has been reported in various neuropsychiatric disorders (21,22,23,24,25). The purpose of this study was to compare dynamic TDH in untreated patients with a first episode of MDD with healthy controls. This is the first study to consider TDH in male and female patients with MDD together.

Material and Methods

Subjects

Between April 2017 and February 2018, 66 patients who accepted the study were recruited from 74 patients with a first episode of untreated MDD aged 18–65 years and diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria who applied to the psychiatric outpatient clinic. Since the inadequate sample of 3 patients excluded from study. Sixty-three patients (34 women and 29 men) and 61 healthy volunteers (32 women, 29 men) were included. All 124 participants, who were admitted to the psychiatric clinic of Bozok University Medical School, were included in the study. This study was approved by the Bozok University Ethics Committee (2017-12/04), and written informed consent was obtained from all participants. Subjects with comorbid psychiatric disorders, systemic or metabolic disease, obesity, smokers, alcohol and substance use disorders, and pregnant and lactating women were excluded from the study. Severity of MDD in the patients was evaluated by the Hamilton Depression Rating Scale (HDRS). The patients were separated into three groups according to this scale as mild, moderate, and severe MDD (Table 1).

Hamilton Depression Rating Scale

The original version of the (Hamilton Depression Rating Scale) HDRS contains 17 items, designed by Hamilton (1960), each scored from 0 to 4 for a maximum total score of 53 (26). The Turkish version of the scale has been validated and is reliable (27). In our study, all patients were evaluated with the 17 item version.

Biochemical tests

Blood Samples were collected in 10 ml serum separator tubes and centrifuged at 1300g for 10 min and stored at –80°C until time of analysis. For serum thiol/ disulfide homeostasis measured by, a novel fully automated colorimetric method described by Erel and Neselioglu (28), (used modified Elman reagents for thiol measurement ). First, for total thiol determination, NaHB₄, a reducing agent was added into serum. This operation causes reduction of dynamic disulphide bonds and generates free thiol groups.

Remaining reductants were eliminated by extraction with 110 ml 6.715 mM formaldehyde and 10.0 mM EDTA in Tris buffer 100 mM (pH 8.2). For native thiol detection, 10 ml sample was treated with 10 ml 10 mM sodium chloride in 50% methanol– water solution (v/v; R10 ) and 110 ml 6.715 mM formaldehyde and 10.0 mM EDTA in Tris buffer 100 mM (pH 8.2) and DTNB solution was added. The primary wavelength is 415 nm, and the secondary wavelength is 700 nm (optionally bichromatic).

Statistical Analysis

The data were analyzed with SPSS v18 software (SPSS Inc., Chicago, IL, USA). Kolmogorov-Smirnov test was employed to check the compliance of the continuous variables to a normal distribution. Student’s t-test was applied because distribution of age, native thiol, total thiol and disulfide were normally. Correlations between the groups were identified by Pearson’s and Spearman’s rho tests. A p-value < 0.05 was deemed to be significant for all tests.

Results

A total of 63 patients (34 females and 29 males) and 61 healthy controls (32 females and 29 males) were evaluated in this study. The mean age of patients was 39.02 ± 12.11 years, and the mean age of the control group was 38.43 ± 9.84 years. No statistically significant differences were observed in terms of age or gender. The demographic characteristics of the patients with MDD and the control group are summarized in Table 1.

The median total thiol level was 378.76±64.45 mmol/l and that of native thiol was 342.98±59.14 mmol/l in the MDD group. The median total thiol level was 415.24±60.39 mmol/l and native thiol level was 373.24±54.71 mmol/l in the healthy control group . Plasma native thiol and total thiol levels were lower in patients than controls (p: 0.004, p: 0.001) (Figure 1, 2).

The median disulphide level was 17.88±8.47 mmol/l in the MDD group and 21.00±11.35 mmol/l in the healthy control group (Figure 3). The differences observed between the two groups in terms of disulfide, the disulfide/native thiol ratio, the disulfide/total thiol ratio, or the native thiol/total thiol ratio were insignificant. The serum TDH parameters of the MDD and control groups are summarized in Table 2.

The thiol/disulfide levels compared between male and female patient groups and also with healthy controls. No statistically significant differences were observed (p>0.05).

No statistically significant correlations were detected between the patient’s parameters and disease severity as determined by HDRS in the untreated patients with MDD.
Table 1. Demographic characteristics of the patients with MDD and the control.

<table>
<thead>
<tr>
<th></th>
<th>MDD (n=63)</th>
<th>Controls (n=61)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female/Male</td>
<td>34/29</td>
<td>32/29</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Age (Mean ± SD)</td>
<td>39.02 ± 12.11</td>
<td>38.43 ± 9.84</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>BMI (Mean ± SD)</td>
<td>25.4 ± 4.1</td>
<td>25.1 ± 3.9</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>HDRS mild</td>
<td>6 (9.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDRS moderate</td>
<td>25 (39.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDRS severe</td>
<td>32 (50.8%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BMI: body mass index; HDRS: Hamilton Depression Rating Scale; MDD: major depressive disorder; SD: standard deviation

Table 2. Serum thiol/disulfide homeostatic parameters in patients with major depressive disorder and healthy controls.

<table>
<thead>
<tr>
<th></th>
<th>MDD (n = 63)</th>
<th>Controls (n = 60)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Native thiol (μmol/l)</td>
<td>342.98 ± 59.14</td>
<td>373.24 ± 24</td>
<td>0.004*</td>
</tr>
<tr>
<td>Total thiol (μmol/l)</td>
<td>378.76 ± 76</td>
<td>415.24 ± 60.39</td>
<td>0.001*</td>
</tr>
<tr>
<td>Disulfide (μmol/l)</td>
<td>17.88 ± 8.47</td>
<td>21 ± 11.35</td>
<td>0.086</td>
</tr>
<tr>
<td>Disulfide/Native thiol</td>
<td>5.27 ± 2.53</td>
<td>5.71 ± 3.23</td>
<td>0.405</td>
</tr>
<tr>
<td>Disulfide/Total thiol</td>
<td>4.68 ± 2.09</td>
<td>4.98 ± 2.50</td>
<td>0.46</td>
</tr>
<tr>
<td>Native thiol/Total thiol</td>
<td>90.63 ± 4.18</td>
<td>90.02 ± 5.01</td>
<td>0.46</td>
</tr>
</tbody>
</table>

MDD: major depressive disorder; SD: standard deviation; *p<0.01; **p<0.001

Table 3. Correlations between HDRS and other parameters

<table>
<thead>
<tr>
<th></th>
<th>r</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Native thiol</td>
<td>−0.146</td>
<td>0.10</td>
</tr>
<tr>
<td>Total thiol</td>
<td>−0.172</td>
<td>0.057</td>
</tr>
<tr>
<td>Disulfide</td>
<td>−0.127</td>
<td>0.16</td>
</tr>
</tbody>
</table>

HDTRS: Hamilton Depression Rating Scale

**Figure 1:** Total thiol levels and 95% confidence intervals (CIs) in patients with major depressive disorder and controls.
Discussion

TDH in patients with a first episode of untreated MDD was evaluated in this study. Plasma native and total thiol levels of patients with MDD were lower than those in the control group.

No statistically significant differences were observed in disulfide levels, disulfide/native thiol, disulfide/total thiol or native thiol/total thiol ratios between the patient and control groups.

Figure 2: Native thiol levels and 95% confidence intervals (CIs) in patients with major depressive disorder and controls.

Figure 3: Disulfide levels and 95% confidence intervals (CIs) in patients with major depressive disorder and controls.
No statistical correlation was found between any of these parameters and the HDRS score, which evaluates disease severity (Table 3). Similar to many other psychiatric disorders, the etiology and pathogenesis of depression is not fully understood; however, environmental, genetic, and stress-related factors are known to take part in the etiology. Oxidative system deficits are also thought to be part of the etiology of depression and other psychiatric disorders (9,22,23,24,25). Meta-analysis results have shown that oxidative stress plays a role in depression, and that antidepressant treatment mediates the regulation of oxidative stress/antioxidant balance (29). Thiols are a relatively new parameter with antioxidant properties. Thiols have been used to evaluate balance in the oxidative system of patients with different psychiatric disorders. Thiols enter the oxidative reaction through oxidants and form a covalent disulfide bond. The disulfide bonds can be reduced to thiol groups; thus, maintaining dynamic TDH (30). Thiols play a major role in reactions against oxidative metabolism, apoptosis, signal transmission, protein synthesis, cell growth, and proliferation, immunoregulation, and metabolism of xenobiotics (31). Erel and Neselioglu (2014) reported that increases in thiol and decreases in disulfide levels are associated with a proliferative diseases such as malignancies and multiple myeloma, whereas lower thiol levels and higher disulfide levels are associated with degenerative diseases, such as obesity, diabetes and smoking-related diseases (28). Total and native thiol levels are significantly lower in patients with Parkinson’s disease (32). Once serum thiol levels decrease, their antioxidant power decreases as well. Oxidative stress is believed to take place in the pathiology of neuropsychiatric disorders (33). Unbalanced oxidative metabolism has been increasingly reported in patients with schizophrenia, bipolar disorders, MDD, and anxiety disorders (23,34,35,36).

All thiol levels are lower and disulfide levels are higher in patients with schizophrenia, which is a chronic psychiatric disease. This has been explained by a shift to the disulfide bond side of the equilibrium after reduction of thiols. Lower total thiol levels are also related to nutritional insufficiency. TDH parameters are correlated with disease severity (22). Changes in the oxidative system in patients with schizophrenia have also been reported previously (36). Total and native thiol levels are lower in patients with Parkinson’s disease, which is a chronic degenerative disorder. A negative correlation has been detected between these parameters and disease duration (32).

Oxidative stress is higher and antioxidant status is lowered in patients with generalized anxiety disorder (GAD) (37). Total and native thiol levels are similar to controls, while disulfide levels are higher in patients with GAD than those in controls. No correlation has been observed between these parameters and disease severity (23). Similarly, no correlation has been reported between oxidative stress parameters and the severity of panic disorder (38). Oxidative stress findings are controversial in patients with an anxiety disorder (39).

Serum thiol levels are higher during the period of mania in patients with bipolar disorder compared to those in remission and a control group. No statistically significant difference was found between serum disulfide, disulfide/total thiol, or native thiol/total thiol ratios in manic, remission, and control group subjects. The reduction in total thiol levels in the manic and remission periods, without a change in disulfide levels, is associated with a decrease in thiol levels. Disulfide levels do not increase despite a decrease in thiol levels associated with insufficient nutrient intake and increased consumption to synthesize substances, such as pheomelanin and neuromelanin, rather than converting thiol to disulfide (25).

It was shown in the previous studies that the oxidative stress system is impaired in patients with depression and is improved by antidepressant treatment (9). Baykan et al. (2018) showed that native thiol levels in female patients with MDD are elevated and disulfide levels are lower, whereas total thiol levels are not different. That study concluded that depression is related to an increase in oxidative stress but a shift occurs in the reductive side in female patients. This was explained by the possible involvement of TDH in compensatory mechanisms of oxidative stress, which caused an increase in thiol, but the mechanisms of action were not clarified (24). That study was the first to evaluate thiol and disulfide together but it was conducted only in female subjects. Our results revealed that plasma native and total thiol levels decreased and disulfide level increased in MDD compared to those in the control group. The reasons why our results are different from those of Baykan et al. can be summarized as follows. Thiol can be affected by nutrition, body mass index, smoking status, and sleep routine. Another reason may be disease duration; 38.9% of all subjects in the study of Baykan et al. were second episode patients. Our study group was composed solely of first episode patients. Recurrent attacks in depression are known to cause neurobiological changes. A first episode patient with a short duration of disease may have lower thiol levels but not higher disulfide levels. A relationship between disease duration and changes in the oxidative system has been shown in some disorders (22,40). However, few studies have shown a relationship between disease duration and changes in the oxidative system of patients with MDD. Another reason for the low thiol levels in our study may be changes in nutrition and appetite patterns of patients with MDD. Erzin et al. (2018) suggested that low thiol levels during mania and formal periods may be due to dietary habits (25).

No statistical correlation was found between the HDRS score and thiol and disulfide levels in our study. In concordance with our results, no correlations have been reported between disease severity and oxidative parameters in patients with bipolar affective disorder, GAD, or a panic disorder (23,25,38).

**Conclusion**

In summary, there is no clear evidence on whether oxidative stress causes psychiatric disorders or psychiatric disorders cause disruptions in the oxidative balance. Oxidative parameters are found in different systems and are released in the body from various organs. In addition, MDD cases generally present with co-morbidities, such as other
psychiatric disorders, including drug or alcohol abuse. Lifestyle, nutritional habits, smoking status and pre-disease antioxidant activities are known to affect these results. Oxidative parameters are affected by numerous factors but a deficit occurs in this system in patients with depression according to other studies. For a parameter to be used as a biomarker, the disease period must be routinely followed, parameters of treated and untreated patients should be compared, different phases of the disease must be evaluated (active, remission etc.), and differences in subtypes of the disease must be detected. However, like many other psychiatric disorders, no biological marker has been used routinely in patients with MDD in clinical practice. Although deficits of oxidative balance in patients with MDD are insufficient for identifying the etiopathology of the disease, data obtained from long-term follow-up studies of patients in different phases of the disease may bring us candidate biomarkers to be used in these patients.

Limitations of this study are the relatively small number of patients, the lack of a cross-sectional design, difficulties recording nutritional status, and the lack of information about MDD, such as the duration of disease and depressive symptomatology (e.g. suicidal ideation, lack of appetite, sleep disturbances).

Acknowledgements: Authors would like to thank Dr. Çiğdem Yücel for her efforts during the English translation of the present manuscript.

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author’s Contributions: ÖK, YH: Research concept and design; data collecting, CB, ME: Biochemical analysis and interpretation of data. ÖK: Preparation of article, and Revisions. All authors approved the final version of the manuscript

Ethical issues: All Authors declare, Originality and ethical approval of research. Responsibilities of research, responsibilities against local ethics commission are under the Authors responsibilities.

References


