ΠΛΗΡΩΜΕΝΟ ΤΕΛΟΣ
Ταχ. Γραφείο Κ.Ε.Μ.Π. ΚΡΥΟΝΕΡΙΟΥ
Αρ. Αδειας 4739

PRESS POST (Χ+7) PRESS POST

ΕΛΤΑ Hellenic Post

ΕΝΤΥΠΟ ΚΛΕΙΣΤΟ ΑΡ. ΑΔΕΙΑΣ 2931 ΚΕΜΠΑ
Κωδικός 016951
ΒΗΤΑ ΙΑΤΡΙΚΕΣ ΕΚΔΟΣΕΙΣ
Κατεχάκη & Αδριανείου 3 – 115 25 ΑΘΗΝΑ

Περιοδικό "Ψυχιατρική"
Διονυσίου Αιγινήτου 17, 3ος όροφος, 115 28 Αθήνα
Τηλ.: 210-77 58 410 • Fax: 210-77 09 044 • e-mail: editor@psychiatriki-journal.gr

The Journal "Psychiatriki"
17, Dionisiou Eginitou str., 3rd floor, 115 28 Athens, Greece
Tel.: (+30) 210-77 58 410 • Fax: (+30) 210-77 09 044 • e-mail: editor@psychiatriki-journal.gr

Ελληνική Ψυχιατρική Εταιρεία
Παπαδιαμαντοπούλου 11, 115 28 Αθήνα
Τηλ.: 210-72 14 184, Fax: 210-72 42 032 • e-mail: psych@psych.gr

Hellenic Psychiatric Association
11, Papadiamantopoulou str., 115 28 Athens, Greece
Tel.: (+30) 210-72 14 184, Fax: (+30) 210-72 42 032 • e-mail: psych@psych.gr

PSYCHIATRIKI Volume 33 (3) 169-252 July-September 2022

ΕΤΕ 1986

PSYCHIATRIKI

Quarterly journal published by the Hellenic Psychiatric Association, Volume 33, No 3, July-September 2022

βήτα medical arts

GR ISSN 1105-2333

Καταχωρείται και περιλαμβάνεται στα MEDLINE/PubMed, Index Copernicus, PsychINFO, Scopus, SCImago, Google Scholar, EMBASE/Excerpta Medica, EBSCOhost™ και στο Iatrotek, (Scopus CiteScore 2021=1,2)

Τριμηνιαία έκδοση της Ελληνικής Ψυχιατρικής Εταιρείας, Τόμος 33, Τεύχος 3, Ιούλιος-Σεπτέμβριος 2022

ΨΥΧΙΑΤΡΙΚΗ

ΕΤΕ 1986

Καταχωρείται και περιλαμβάνεται στα MEDLINE/PubMed, Index Copernicus, PsychINFO, Scopus, SCImago, Google Scholar, EMBASE/Excerpta Medica, EBSCOhost™ και στο Iatrotek

Οδηγίες προς τους συγγραφείς και το συνοδευτικό έντυπο είναι διαθέσιμα στην ιστοσελίδα: http://www.psychiatriki-journal.gr

Εργασίες για δημοσίευση υποβάλλονται μέσω του παραπάνω ιστότοπου ή εναλλακτικά μέσω ηλεκτρονικού ταχυδρομείου στην ηλεκτρονική διεύθυνση editor@psychiatriki-journal.gr

ΨΥΧΙΑΤΡΙΚΗ

Τριμηνιαία έκδοση
της Ελληνικής Ψυχιατρικής Εταιρείας
Διονυσίου Αιγινήτου 17, 115 28 Αθήνα
Τηλ.: 210-77 58 410, Fax: 210-77 09 044

Εκδότης:
Ελληνική Ψυχιατρική Εταιρεία
Παπαδιαμαντοπούλου 11, 115 28 Αθήνα
Τηλ.: 210-72 14 184

Indexed and included in MEDLINE/PubMed, Index Copernicus, PsychINFO, Scopus, SCImago, Google Scholar, EMBASE/Excerpta Medica, EBSCOhost™ and in Iatrotek

Instructions to contributors and the submission form are available at the webpage http://www.psychiatriki-journal.gr

Manuscripts should be submitted for publication through the above website or should be sent as an attachment by email to editor@psychiatriki-journal.gr

PSYCHIATRIKI

Quarterly journal published
by the Hellenic Psychiatric Association
17, Dionisiou Eginitou str., 115 28 Athens
Tel.: +30-210-77 58 410, Fax: +30-210-77 09 044

Publisher:
Hellenic Psychiatric Association
11, Papadiamantopoulou str., 115 28 Athens
Tel.: +30-210-72 14 184

Γραμματεία Ελληνικής Ψυχιατρικής Εταιρείας:
Υπεύθυνη: Ε. Γκρέτσα
Τηλ.: 210-72 14 184, Fax: 210-72 42 032
E-mail: psych@psych.gr, Ιστοσελίδα: www.psych.gr
FB: ΕΛΛΗΝΙΚΗ ΨΥΧΙΑΤΡΙΚΗ ΕΤΑΙΡΕΙΑ

Ετήσιες συνδρομές του Περιοδικού:
Εσωτερικού € 40,00
Εξωτερικού $ 80,00 + ταχυδρομικά
Μεμονωμένα τεύχη € 10,00
Καταβάλλονται με επιταγή στον ταμία της ΕΨΕ:
Παπαδιαμαντοπούλου 11, 115 28 Αθήνα
Τα ταμειακώς εντάξει μέλη της Εταιρείας δεν υποχρεούνται σε καταβολή συνδρομής

Secretariat of Hellenic Psychiatric Association:
Head: H. Gretsa
Tel.: (+30) 210-72 14 184, Fax: (+30) 210-72 42 032
E-mail: psych@psych.gr, Web-site: www.psych.gr

Annual subscriptions of the Journal:
€ 40.00 or $ 80.00 + postage – each separate issue € 10.00
are payable by check to the treasurer
of the Hellenic Psychiatric Association:
11, Papadiamantopoulou str., GR-115 28 Athens

For the members of the Association in good standing subscription is free

ΕΠΙΜΕΛΕΙΑ ΕΚΔΟΣΗΣ
EN ISO 9001:2000
ΒΗΤΑ Ιατρικές Εκδόσεις
ΜΟΝΟΠΡΟΣΩΠΗ ΕΠΕ
Αδριανείου 3 και Κατεχάκη, 115 25 Αθήνα (Ν. Ψυχικό)
Τηλ.: 210-67 14 371 – 210-67 14 340, Fax: 210-67 15 015
e-mail: betamedarts@otenet.gr
e-shop: www.betamedarts.gr
EN ISO 9001:2000

Υπεύθυνος τυπογραφείου
Α. Βασιλάκου, Αδριανείου 3 – 115 25 Αθήνα
Τηλ. 210-67 14 340

EDITING
EN ISO 9001:2000
BETA Medical Publications
3, Adrianiou str., GR-115 25 Athens-Greece
Tel.: (+30) 210-67 14 371 – (+30) 210-67 14 340,
Fax: (+30) 210-67 15 015
e-mail: betamedarts@otenet.gr, e-shop: www.betamedarts.gr
EN ISO 9001:2000

Printing supervision
A. Vassilakou, 3 Adrianiou str. – GR-115 25 Athens
Tel. (+30)-210-67 14 340

ΕΛΛΗΝΙΚΗ ΨΥΧΙΑΤΡΙΚΗ ΕΤΑΙΡΕΙΑ

ΔΙΟΙΚΗΤΙΚΟ ΣΥΜΒΟΥΛΙΟ

Πρόεδρος: Β.Π. Μποζίκας
Αντιπρόεδρος: Κ. Φουντουλάκης
Γεν. Γραμματέας: Δ. Τσακλακίδου
Ταμίας: Λ. Μαρκάκη
Σύμβουλοι: Χ. Τουλούμης
Ν. Γκούβας
Η. Τζαβέλλας

ΠΕΙΘΑΡΧΙΚΟ ΣΥΜΒΟΥΛΙΟ

Μέλη: Ι. Νηματούδης
Π. Φωτιάδης
Α. Σπυροπούλου

ΕΞΕΛΕΓΚΤΙΚΗ ΕΠΙΤΡΟΠΗ

Μέλη: Φ. Μωρόγιαννης
Ι. Λιάππας
Θ. Βορβολάκος

ΕΠΙΤΙΜΟΙ ΠΡΟΕΔΡΟΙ

Γ.Ν. Χριστοδούλου, †Α. Παράσχος,
Ν. Τζαβάρας, Ι. Γκιουζέπας, Δ. Πλουμπίδης

ΕΠΙΤΙΜΑ ΜΕΛΗ

†Σπ. Σκαρπαλέζος, Χ. Βαρουχάκης, †Ν. Ζαχαριάδης,
†Ι. Πιτταράς

ΠΕΡΙΦΕΡΕΙΑΚΑ ΤΜΗΜΑΤΑ

ΑΘΗΝΩΝ
Πρόεδρος: Κ. Κόντης
Γραμματέας: Σ. Θεοδωροπούλου
Ταμίας: Η. Τζαβέλλας

ΜΑΚΕΔΟΝΙΑΣ
Πρόεδρος: Ι. Νηματούδης
Γραμματέας: Ι. Διακογιάννης
Ταμίας: Π. Φωτιάδης

ΚΕΝΤΡΙΚΗΣ ΕΛΛΑΔΟΣ
Πρόεδρος: Π. Στοφόρος
Γραμματέας: Α. Θωμάς
Ταμίας: Μ. Παπαλιάγκα

ΒΟΡΕΙΟΔΥΤΙΚΗΣ ΕΛΛΑΔΟΣ & ΔΥΤΙΚΗΣ ΣΤΕΡΕΑΣ
Πρόεδρος: Α. Φωτιάδου
Γραμματέας: Λ. Ηλιοπούλου
Ταμίας: Π. Πετρίκης

ΠΕΛΟΠΟΝΝΗΣΟΥ
Πρόεδρος: Κ. Σωτηριάδου
Γραμματέας: Μ. Σκώκου
Ταμίας: Α. Κατριβάνου

ΜΕΓΑΛΗΣ ΒΡΕΤΤΑΝΙΑΣ
Πρόεδρος: Ε. Παλαζίδου
Γραμματέας: Κ. Κασιακόγια
Ταμίας: Π. Λέκκος

ΤΟΜΕΑΣ ΝΕΩΝ ΨΥΧΙΑΤΡΩΝ
Πρόεδρος: Κ. Προβή
Α΄ Γραμματέας: Θ. Γκέσογλου
Β΄ Γραμματέας: Θ. Κουτσομήτρος

ΕΝΩΣΗ ΕΛΛΗΝΩΝ ΕΙΔΙΚΕΥΟΜΕΝΩΝ ΨΥΧΙΑΤΡΩΝ
Πρόεδρος: Ι. Χατζηδάκης
Γραμματέας: Αθ. Πουλουτίδου
Ταμίας: Δ. Μπαλτζή

HELLENIC PSYCHIATRIC ASSOCIATION

EXECUTIVE COUNCIL

Chairman: V.P. Bozikas
Vice-Chairman: K. Fountoulakis
Secretary General: D. Tsaklakidou
Treasurer: L. Markaki
Consultants: C. Touloumis
N. Gouvas
E. Tzavellas

DISCIPLINARY COUNCIL

Members: I. Nimatoudis
P. Fotiadis
A. Spyropoulou

FINANCIAL CONTROL COMMITTEE

Members: F. Morogiannis
I. Liappas
T. Vorvolakos

HONORARY PRESIDENTS

G.N. Christodoulou, †A. Paraschos,
N. Tzavaras, J. Giouzepas, D. Ploumpidis

HONORARY MEMBERS

†S. Scarpalezos, Ch. Varouchakis, †N. Zachariadis,
†I. Pittaras

DIVISIONS

ATHENS
Chairman: C. Kontis
Secretary: S. Theodoropoulou
Treasurer: E. Tzavellas

MACEDONIA
Chairman: J. Nimatoudis
Secretary: J. Diakoyiannis
Treasurer: P. Fotiadis

CENTRAL GREECE
Chairman: P. Stoforos
Secretary: A. Thomas
Treasurer: M. Papaliagka

NORTHWESTERN GREECE
Chairman: A. Fotiadou
Secretary: L. Iliopoulou
Treasurer: P. Petrikis

PELOPONNESE
Chairman: K. Sotiriadou
Secretary: M. Skokou
Treasurer: A. Katrivanou

GREAT BRITAIN
Chairman: H. Palazidou
Secretary: K. Kasiakogia
Treasurer: P. Lekkos

SECTOR OF YOUNG PSYCHIATRISTS
Chairman: K. Provi
Secretary A΄: Th. Gkesoglou
Secretary B΄: Th. Koutsomitros

UNION OF GREEK PSYCHIATRIC TRAINEES
Chairman: I. Chatzidakis
Secretary: Ath. Pouloutidou
Treasurer: D. Baltzi

ΚΛΑΔΟΙ

ΑΥΤΟΚΑΤΑΣΤΡΟΦΙΚΩΝ ΣΥΜΠΕΡΙΦΟΡΩΝ
Πρόεδρος: Ηλ. Τζαβέλλας
Γραμματείς: Δ. Καραϊσκος, Θ. Παπασλάνης

ΒΙΑΙΩΝ ΣΥΜΠΕΡΙΦΟΡΩΝ
Πρόεδρος: Χ. Τσόπελας
Γραμματείς: Μ. Δημητρακά, Δ. Πέτσας

ΒΙΟΛΟΓΙΚΗΣ ΨΥΧΙΑΤΡΙΚΗΣ
Πρόεδρος: Π. Σακκάς
Γραμματείς: Α. Μπότσης, Κ. Ψάρρος

ΔΙΑΠΟΛΙΤΙΣΜΙΚΗΣ ΨΥΧΙΑΤΡΙΚΗΣ
Πρόεδρος: Σ. Καπρίνης
Γραμματείς: Σ. Μπουφίδης, Ε. Παρλαπάνη

ΔΙΑΤΑΡΑΧΕΣ ΠΡΟΣΛΗΨΗΣ ΤΡΟΦΗΣ
Πρόεδρος: Φ. Γονιδάκης
Γραμματείς: Ι. Μιχόπουλος, Γ. Γεωργαντόπουλος

ΔΙΠΛΗ ΔΙΑΓΝΩΣΗ
Πρόεδρος: Γ. Τζεφεράκος
Γραμματείς: Αθ. Αποστολόπουλος, Κ. Κοκκώλης

ΕΓΚΑΙΡΗ ΠΑΡΕΜΒΑΣΗ ΣΤΗΝ ΨΥΧΩΣΗ
Πρόεδρος: Ν. Στεφανής
Γραμματείς: Β.Π. Μποζίκας, Κ. Κόλλιας

ΙΔΙΩΤΙΚΗΣ ΨΥΧΙΑΤΡΙΚΗΣ
Πρόεδρος: Λ. Μαρκάκη
Γραμματείς: Φ. Μωρόγιαννης, Π. Γκίκας

ΙΣΤΟΡΙΑΣ ΤΗΣ ΨΥΧΙΑΤΡΙΚΗΣ
Πρόεδρος: Δ. Πλουμπίδης
Γραμματείς: Αθ. Καράβατος, Ι. Πολυχρονίδης

ΚΛΙΝΙΚΗΣ ΨΥΧΟΦΑΡΜΑΚΟΛΟΓΙΑΣ
Πρόεδρος: Χ. Τουλούμης
Γραμματείς: Χ. Τσόπελας, Ν. Χριστοδούλου

ΚΟΙΝΩΝΙΚΗΣ ΨΥΧΙΑΤΡΙΚΗΣ
Πρόεδρος: Α. Μιχοπούλου
Γραμματείς: Γ. Γαρυφαλλος, Μ. Οικονόμου

ΜΕΛΕΤΗΣ ΤΗΣ ΕΠΑΓΓΕΛΜΑΤΙΚΗΣ ΠΡΟΑΣΠΙΣΗΣ ΤΟΥ ΨΥΧΙΑΤΡΟΥ
Πρόεδρος: Γ. Αλεβιζόπουλος
Γραμματείς: Μ. Σκόνδρας, Γ. Καραμπουτάκης

ΝΕΥΡΟΑΝΑΠΤΥΞΙΑΚΕΣ ΔΙΑΤΑΡΑΧΕΣ ΔΙΑ ΒΙΟΥ
Πρόεδρος: Α. Πεχλιβανίδης
Γραμματείς Ε. Καλαντζή, Κ. Κορομπίλη

ΟΥΣΙΟΕΞΑΡΤΗΣΕΩΝ
Πρόεδρος: Θ. Παπαρρηγόπουλος
Γραμματείς: Ι. Διακογιάννης, Ελ. Μέλλος

ΠΑΙΔΟΨΥΧΙΑΤΡΙΚΗΣ
Πρόεδρος: Δ. Αναστασόπουλος
Γραμματείς: Δ. Αναγνωστόπουλος, Κ. Κανελλέα

ΠΛΗΡΟΦΟΡΙΚΗ & ΚΑΙΝΟΤΟΜΕΣ ΤΕΧΝΟΛΟΓΙΕΣ ΣΤΗΝ ΨΥΧΙΑΤΡΙΚΗ
Πρόεδρος: Ν. Γκούβας
Γραμματείς: Α. Δουζένης, Π. Φωτιάδης

ΠΡΟΛΗΠΤΙΚΗΣ ΨΥΧΙΑΤΡΙΚΗΣ
Πρόεδρος: Η. Τζαβέλλας
Γραμματείς: Δ. Κόντης, Δ. Καραϊσκος

ΣΕΞΟΥΑΛΙΚΟΤΗΤΑΣ ΚΑΙ ΔΙΑΠΡΟΣΩΠΙΚΩΝ ΣΧΕΣΕΩΝ
Πρόεδρος: Λ. Αθανασιάδης
Γραμματείς: Κ. Παπασταμάτης, Η. Μουρίκης

ΣΤΡΑΤΙΩΤΙΚΗΣ ΨΥΧΙΑΤΡΙΚΗΣ
Πρόεδρος: Π. Φωτιάδης
Γραμματείς: Ι. Νηματούδης, Δ. Μοσχονάς

ΣΥΜΒΟΥΛΕΥΤΙΚΗΣ - ΔΙΑΣΥΝΔΕΤΙΚΗΣ ΨΥΧΙΑΤΡΙΚΗΣ & ΨΥΧΟΣΩΜΑΤΙΚΗΣ
Πρόεδρος: Θ. Υφαντής
Γραμματείς: Α. Καρκανιάς, Μ. Διαλλινά

ΤΕΧΝΗΣ & ΨΥΧΙΑΤΡΙΚΗΣ
Πρόεδρος: Σ. Κρασανάκης
Γραμματείς: Η. Βλάχος, Χ. Γιαννουλάκη

ΤΗΛΕΨΥΧΙΑΤΡΙΚΗΣ
Πρόεδρος: Κ. Κατσαδώρος
Γραμματείς: Ι. Χατζιδάκης, Ι. Αποστολόπουλος

ΦΙΛΟΣΟΦΙΑΣ & ΨΥΧΙΑΤΡΙΚΗΣ
Πρόεδρος: Ι. Ηλιόπουλος
Γραμματείς: Γ. Νικολαΐδης, Α. Κομπορόζος

ΨΥΧΙΑΤΡΙΚΗΣ ΗΘΙΚΗΣ & ΔΕΟΝΤΟΛΟΠΑΣ
Πρόεδρος: Γ. Χριστοδούλου
Γραμματείς: Ι. Γκιουζέπας, Β. Αλεβίζος

ΨΥΧΙΑΤΡΙΚΗΣ & ΘΡΗΣΚΕΙΑΣ
Πρόεδρος: Στ. Κούλης
Γραμματείς: Κ. Εμμανουηλίδης, Αθ. Καρκανιάς

ΨΥΧΙΚΗΣ ΥΓΕΙΑΣ ΓΥΝΑΙΚΩΝ & ΨΥΧΙΑΤΡΙΚΗΣ ΤΗΣ ΑΝΑΠΑΡΑΓΩΓΗΣ
Πρόεδρος: Α. Λεονάρδου
Γραμματείς: Α. Σπυροπούλου, Κ. Αρβανίτη

ΨΥΧΙΑΤΡΟΔΙΚΑΣΤΙΚΗΣ
Πρόεδρος: Α. Δουζένης
Γραμματείς: Δ. Τσακλακίδου, Ι. Γιαννοπούλου

ΨΥΧΟΘΕΡΑΠΕΙΑΣ
Πρόεδρος: Ρ. Γουρνέλλης
Γραμματείς: Φ. Γονιδάκης, Ι. Μαλογιάννης

ΨΥΧΟΓΗΡΙΑΤΡΙΚΗΣ
Πρόεδρος: Α. Πολίτης
Γραμματείς: Α. Κώνστα, Θ. Βορβολάκος

ΨΥΧΟΜΕΤΡΙΚΩΝ & ΝΕΥΡΟΨΥΧΟΛΟΓΙΚΩΝ ΜΕΤΡΗΣΕΩΝ
Πρόεδρος: Κ. Κόλλιας
Γραμματείς: Β. Π. Μποζίκας, Ζ. Νασίκα

ΨΥΧΟΟΓΚΟΛΟΓΙΑΣ
Πρόεδρος: Αθ. Καρκανιάς
Γραμματείς: Μ. Συγγελάκης, Ζ. Σαντά

ΨΥΧΟΠΑΘΟΛΟΓΙΑΣ
Πρόεδρος: Ν. Τζαβάρας
Γραμματείς: [1]Γ. Καπρίνης, Μ. Διαλλινά

ΨΥΧΟΦΥΣΙΟΛΟΓΙΑΣ
Πρόεδρος: Ι. Λιάππας
Γραμματείς: Ι. Νηματούδης, Χ. Παπαγεωργίου

SECTIONS

SELF-DESTRUCTIVE BEHAVIORS
Chairman: E. Tzavellas
Secretaries: D. Karaiskos, Th. Papaslanis

VIOLENT BEHAVIORS
Chairman: Ch. Tsopelas
Secretaries: M. Dimitraka, D. Petsas

BIOLOGICAL PSYCHIATRY
Chairman: P. Sakkas
Secretaries: A. Botsis, C. Psarros

CROSS-CULTURAL PSYCHIATRY
Chairman: S. Kaprinis
Secretaries: S. Boufidis, H. Parlapani

EATING DISORDERS
Chairman: F. Gonidakis
Secretaries: J. Michopoulos, G. Georgantopoulos

DUAL DIAGNOSIS
Chairman: G. Tzeferakos
Secretaries: Ath. Apostolopoulos, K. Kokkolis

EARLY INTERVENTION IN PSYCHOSIS
Chairman: N. Stefanis
Secretaries: V.P. Bozikas, K. Kollias

PRIVATE PRACTICE PSYCHIATRY
Chairman: L. Markaki
Secretaries: F. Morogiannis, P. Gkikas

HISTORY OF PSYCHIATRY
Chairman: D. Ploumpidis
Secretaries: Ath. Karavatos, J. Polyhronidis

PSYCHOPHARMACOLOGY
Chairman: C. Touloumis
Secretaries: C. Tsopelas, N. Christodoulou

SOCIAL PSYCHIATRY
Chairman: A. Michopoulou
Secretaries: G. Garyfallos, M. Economou

ADVOCACY OF PSYCHIATRIC PRACTICE
Chairman: G. Alevizopoulos
Secretaries: M. Skondras, G. Karampoutakis

NEURODEVELOPMENTAL DISORDERS ACROSS THE LIFESPAN
Chairman: A. Pechlivanidis
Secretaries: E. Kalantzi, K. Korompili

SUBSTANCE ABUSE
Chairman: T. Paparrigopoulos
Secretaries: J. Diakoyiannis, El. Mellos

CHILD PSYCHIATRY
Chairman: D. Anastasopoulos
Secretaries: D. Anagnostopoulos, K. Kanellea

INFORMATICS & INNOVATIVE TECHNOLOGIES IN PSYCHIATRY
Chairman: N. Gouvas
Secretaries: A. Douzenis, P. Fotiadis

PREVENTIVE PSYCHIATRY
Chairman: E. Tzavellas
Secretaries: D. Kontis, D. Karaiskos

SEXUALITY AND INTERPERSONAL RELATIONSHIPS
Chairman: L. Athanasiadis
Secretaries: K. Papastamatis, H. Mourikis

MILITARY PSYCHIATRY
Chairman: P. Fotiadis
Secretaries: J. Nimatoudis, D. Moschonas

CONSULTATION-LIAISON PSYCHIATRY & PSYCHOSOMATICS
Chairman: T. Hyphantis
Secretaries: A. Karkanias, M. Diallina

ART & PSYCHIATRY
Chairman: S. Krasanakis
Secretaries: E. Vlachos, C. Giannoulaki

TELEPSYCHIATRY
Chairman: K. Katsadoros
Secretaries: J. Chatzidakis, J. Apostolopoulos

PHILOSOPHY & PSYCHIATRY
Chairman: J. Iliopoulos
Secretaries: G. Nikolaidis, A. Komborozos

PSYCHIATRY & ETHICS
Chairman: G. Christodoulou
Secretaries: J. Giouzepas, V. Alevizos

PSYCHIATRY & RELIGION
Chairman: S. Koulis
Secretaries: K. Emmanouilidis, A. Karkanias

WOMEN'S MENTAL HEALTH & REPRODUCTIVE PSYCHIATRY
Chairman: A. Leonardou
Secretaries: A. Spyropoulou, K. Arvaniti

FORENSIC PSYCHIATRY
Chairman: A. Douzenis
Secretaries: D. Tsaklakidou, J. Giannopoulou

PSYCHOTHERAPY
Chairman: R. Gournellis
Secretaries: F. Gonidakis, J. Malogiannis

PSYCHOGERIATRICS
Chairman: A. Politis
Secretaries: A. Konsta, Th. Vorvolakos

PSYCHOMETRIC & NEUROPSYCHOLOGICAL MEASUREMENTS
Chairman: K. Kollias
Secretaries: V.P. Bozikas, Z. Nasika

PSYCHO-ONCOLOGY
Chairman: A. Karkanias
Secretaries: M. Syngelakis, Z. Santa

PSYCHOPATHOLOGY
Chairman: N. Tzavaras
Secretaries: [1]G. Kaprinis, M. Diallina

PSYCHOPHYSIOLOGY
Chairman: J. Liappas
Secretaries: J. Nimatoudis, C. Papageorgiou

PSYCHIATRIKI

Quarterly journal published by the Hellenic Psychiatric Association

CONTENTS

ΨΥΧΙΑΤΡΙΚΗ

Τριμηνιαία έκδοση της Ελληνικής Ψυχιατρικής Εταιρείας

ΠΕΡΙΕΧΟΜΕΝΑ

https://doi.org/10.22365/jpsych.2022.087 / Psychiatriki 2022, 33:183–186

Editorial

Fake news in the age of COVID-19: Evolutional and psychobiological considerations

ARTICLE HISTORY: Received 10 July 2022/Published Online 19 July 2022

The COVID-19 outbreak has been accompanied by a massive infodemic: an overabundance of information, some accurate and some not. At this pandemic we have seen a large scale of fake news and misinformation, leading to anti-vaccine, anti-mask and anti-5G protests.[1] Fake news is intentionally misleading and deceptive news that is written and published with the intent to damage an entity or a person. They may contain false, misleading, imposter, manipulated or fabricated content. Much of the discourse on fake news conflates three notions, named "information disorders": (a) Misinformation: false information someone shares without knowing it's untrue, (b) Disinformation: false information that's shared with the intention to harm or mislead, and (c) Malinformation: true information that's used to harm others.[2]

False beliefs generally arise through the same mechanisms that establish accurate beliefs. People appear to encode all new information as if it were true and later tag the information as being either true or false. Different cognitive, social and affective factors lead people to form or endorse misinformed views. The emotional content of the information shared also affects false-belief formation. An angry mood can boost misinformation sharing, while social exclusion, which is likely to induce a negative mood, can increase susceptibility to conspiratorial content.[3] As shown by the Illusory Truth Effect, repeated exposure to an article, whether real or fake, increases people's perceptions of its accuracy. In social media, falsehood seems to diffuse significantly farther, faster, deeper and more broadly than the truth in all categories of information, while the effects are more pronounced for false political news than for false news about terrorism, natural disasters and science. Moreover, although prior knowledge of a statement leads people to confirm the statement the next time they see it (confirmation bias), novelty facilitates decision making since it updates our understanding of the world.[4]

The fitness value of accurate information seems so obvious, while self-deception seems to threaten such hard-won informational gains. Then, why has not it selected out? The American evolutionary biologist and sociobiologist Robert Trivers[5] suggested that although our senses have evolved to give us an exquisitely detailed perception of the outside world, as soon as that information hits our brains, it often becomes biased and distorted, usually without conscious effort. Why should this be so? For Trivers, the evolutionary origins of the human propensity for self-deception lie in the adaptive benefits of deceiving others. An animal becomes a better liar when it believes its own lies, or we deceive ourselves the better to deceive others. Deception in animals is the transmission of misinformation by one animal to another and natural selection favors deceptive signaling when aggression either confers a great benefit to signalers or imposes a great cost to receivers.[6] In humans, self-deception process may have a protective role against depression, while depression on its own may reduce mechanisms of self-deception.[7,8]

Humans are biased information-seekers that prefer to receive information that confirms their values and worldviews. Maybe, this is why myths and conspiracy theories around COVID-19 and vaccines exist. We may suggest that underlined neuropsychological processes, probably based on biologically determined self- or other-deceptive mechanisms, may serve in the development, and even the conservation, of at least some of the social behaviors related to the fake news phenomenon. These mechanisms may support the human tendency for biased information-seeking and even the evolutionary persistence of the fake news phenomenon.[9]

However, in cases such as of COVID-19 pandemic, the native urge to deceive ourselves and others is not without risk. Beliefs in COVID-19-related conspiracy narratives and fake news are negatively associated with vaccination willingness and infection-preventive behavior.[1] The COVID-19 pandemic and associated infodemic have magnified the underlying problem of trust. The vaccine hesitancy is primarily a trust issue rather than an informational problem. Fake news, rumors and conspiracy theories about COVID-19 and vaccines should not be understood only as false beliefs, but also as indicators of popular anxieties and fears. Stress inoculation treatment can help people prepare for subsequent misinformation exposure and to increase misinformation detection.[10] Finally, policymakers are advised to build information literacy skills for different levels and environments and to move away from polarization attitudes and behaviors.

Orestis Giotakos
Psychiatrist, MD, MSc, PhD, Editor Dialogues in Clinical Neuroscience & Mental Health",
Founder of the npo obrela and "I Care for my Brain",
President of the Hellenic Association of Sexology & Inter-Gender Relationships

References

1. Ripp T, Röer JP. Systematic review on the association of COVID-19-related conspiracy belief with infection-preventive behavior and vaccination willingness. *BMC Psychol* 2022, 10:66, doi: 10.1186/s40359-022-00771-2
2. Wardle C, Derakhshan H. *Information Disorder Toward an interdisciplinary framework for research and policymaking*. Council of Europe, October, 2017. Available from: https://rm.coe.int/information-disorder-toward-an-interdisciplinary-framework-for-researc/168076277c
3. Ecker UH, Lewandowsky S, Cook J, Schmid P, Fazio LK, Brashier N, et al. The psychological drivers of misinformation belief and its resistance to correction. *Nat Rev Psychol* 2022, 1:13–29, doi: 10.1038/ s44159-021-00006-y
4. Vosoughi S, Roy D, Aral S. The spread of true and false news online. *Science* 2018, 359 (6380):1146-1151, doi: 10.1126/science.aap9559.
5. Trivers R. *The folly of fools: The logic of deceit and self-deception in human life*. Basic Books/Hachette Book Group, 2011
6. Angilletta MJ, Kubitz G, Wilson RS. Self-deception in nonhuman animals: weak crayfish escalated aggression as if they were strong. *Behav Ecol* 2019, 30:1469–1476, doi.org/10.1093/beheco/arz103
7. Sackeim HA. Self-deception: A synthesis. In Lockard JS, Paulhus DL (eds) *Self-deception: An adaptive mechanism*. Prentice Hall, New Jersey, 1988
8. Giotakos O. Fake news: is it a social phenomenon based on neuropsychologically determined self- or other-deceptive mechanisms? Some thoughts based on insight and self-awareness' areas. *Ann Gen Psychiatry* 2018, 17(Suppl 1):A24, doi: 10.1186/s12991-018-0206-2
9. Giotakos O. Fake news and underlined neurocognitive mechanism. *Dialogues in Clinical Neuroscience & Mental Health* 2018, 1(Suppl 3):20, doi: 10.26386/obrela.v1is3.75
10. Pertwee P, Simas C, Larson HJ. An epidemic of uncertainty: rumors, conspiracy theories and vaccine hesitancy. *Nat Med* 2022, 28:456–459, doi: 10.1038/s41591-022-01728z

Άρθρο σύνταξης

Ψευδείς ειδήσεις στην εποχή του COVID-19: Εξελικτικές και ψυχοβιολογικές συσχετίσεις

ΙΣΤΟΡΙΚΟ ΑΡΘΡΟΥ: Παραλήφθηκε 10 Ιουλίου 2022/Δημοσιεύθηκε Διαδικτυακά 19 Ιουλίου 2022

Το ξέσπασμα της πανδημίας COVID-19 συνοδεύτηκε από μία μαζική παραγωγή πληροφοριών, άλλοτε ακριβείς, άλλοτε όμως όχι. Στην πανδημία αυτή ζήσαμε μια μεγάλης κλίμακας παραπληροφόρηση και ψευδείς ειδήσεις, οι οποίες οδήγησαν σε κινήματα έναντι του εμβολίου, της μάσκας, ακόμη και του 5G.[1] Ψευδείς ειδήσεις είναι οι με πρόθεση απατηλές και παραπλανητικές ειδήσεις που γράφονται και δημοσιεύονται με σκοπό να πλήξουν ένα άτομο ή έναν οργανισμό. Μπορεί να περιέχουν ψευδές, παραπλανητικό, απατηλό, χειραγωγημένο ή κατασκευασμένο περιεχόμενο. Το μεγαλύτερο μέρος της συζήτησης σχετικά με τις ψευδείς ειδήσεις περιέχεται σε τρεις έννοιες, που συνολικά έχουν ονομασθεί «διαταραχές της πληροφορίας»: (α) Misinformation: ψευδής πληροφορία που μοιράζεται κάποιος χωρίς να γνωρίζει ότι είναι αναληθής, (β) Disinformation: ψευδής πληροφορία που μοιράζεται κάποιος με σκοπό να παραπλανήσει ή να βλάψει κάποιον, (γ) Malinformation: αληθής πληροφορία που χρησιμοποιείται για να βλάψει κάποιον.[2]

Οι ψευδείς πεποιθήσεις παράγονται από τους ίδιους μηχανισμούς που παράγονται και οι ακριβείς πεποιθήσεις. Ο άνθρωπος φαίνεται να κωδικοποιεί όλες τις νέες πληροφορίες σαν να ήταν αληθείς και αργότερα οριστικοποιεί την πληροφορία είτε ως ψευδή ή ως αληθή. Διάφοροι γνωσιακοί, κοινωνικοί και συναισθηματικοί παράγοντες οδηγούν το άτομο να σχηματοποιήσει ή να εγκρίνει την ψευδή είδηση. Το συναισθηματικό περιεχόμενο της επινεμόμενης πληροφορίας μπορεί να επηρεάσει τον σχηματισμό ψευδούς πεποίθησης. Το συναίσθημα του θυμού μπορεί να ωθήσει στο μοίρασμα ψευδούς πληροφόρησης, ενώ ο κοινωνικός αποκλεισμός, που συνήθως περιέχει αρνητικό συναίσθημα, μπορεί να αυξήσει την προδιάθεση για αποδοχή ενός συνωμοσιολογικού περιεχομένου.[3] Όπως έδειξε το φαινόμενο του Illusory Truth Effect, η επαναλαμβανόμενη έκθεση σε κάποιο άρθρο, είτε αληθές ή ψευδές, αυξάνει την αντίληψη του ατόμου ότι αυτό είναι αληθές. Στα κοινωνικά δίκτυα οι ψευδείς ειδήσεις φαίνεται να διαχέονται σημαντικά πιο μακριά, γρήγορα και βαθιά, σε σύγκριση με τις αληθείς ειδήσεις, όλων των κατηγοριών ειδήσεων. Οι επιδράσεις είναι σημαντικότερες για την περίπτωση των ψευδών πολιτικών ειδήσεων, σε σύγκριση με τις ψευδείς ειδήσεις για την τρομοκρατία, τις φυσικές καταστροφές ή την επιστήμη. Επίσης, αν και η προηγούμενη γνώση κάποιας δήλωσης ωθεί το άτομο ώστε να την επιβεβαιώσει όταν την ξαναδεί (προκατάληψη επιβεβαίωσης), η νέα πληροφορία θα διευκολύνει τη λήψη απόφασης, αφού αυτή θα επικαιροποιήσει την κατανόηση όλων αυτών που συμβαίνουν.[4]

Η αξία της ακριβούς πληροφορίας για την υγεία και ευρωστία είναι προφανής, ενώ η αυτο-εξαπάτηση δείχνει να απειλεί την με τόσο κόπο κερδισμένη πληροφορία. Τότε, γιατί άραγε δεν έχει εξαλειφθεί μέσω της φυσικής επιλογής; Ο Αμερικανός εξελικτικός βιολόγος και κοινωνιολόγος Robert Trivers[5] υποστήριξε ότι αν και τα αισθητήρια όργανα έχουν εξελιχθεί ώστε να δίνουν μια εξαίσια λεπτομερή αντίληψη του εξωτερικού κόσμου, αμέσως μόλις η πληροφορία φτάσει στον εγκέφαλο, αυτή διαστρεβλώνεται χωρίς κάποια συνειδητή προσπάθεια. Γιατί άραγε θα πρέπει να γίνεται έτσι; Για τον Trivers, η εξελικτική αρχή της τάσης του ανθρώπου για αυτο-εξαπάτηση σχετίζεται με τα προσαρμοστικά οφέλη να εξαπατούμε τους άλλους. Ένα ζώο γίνεται καλύτερος ψεύτης όταν μπορεί πρώτα να πιστεύει τα δικά του ψεύδη ή, όσο καλύτερα μπορούμε να εξαπατούμε τον εαυτό μας, τόσο καλύτερα μπορούμε να εξαπατήσουμε τους άλλους. Εξαπάτηση στα ζώα λοιπόν είναι η μετάδοση της ψευδούς πληροφορίας από το ένα ζώο στο άλλο και η φυσική επιλογή ευνοεί τη διάδοση της εξαπάτησης, όταν είτε η επιθετικότητα προσφέρει ένα ισχυρό όφελος στον αποστολέα ή επιβάλλει ένα μεγάλο κόστος στον παραλήπτη της πληροφορίας.[6] Στον άνθρωπο, η διαδικασία της αυτο-εξαπάτησης μπορεί να έχει προστατευτικό ρόλο έναντι της κατάθλιψης, ενώ η κατάθλιψη από μόνη της μπορεί να μειώνει τη διαδικασία και μηχανισμό αυτο-εξαπάτησης.[7,8]

Ο άνθρωπος τείνει να αναζητά πληροφορίες μεροληπτικά προτιμώντας εκείνες τις πληροφορίες που ταιριάζουν με τις αξίες της ζωής του. Ίσως για τον λόγο αυτόν υπάρχουν οι μύθοι και οι θεωρίες συνωμοσίας σχετικά με τον COVID-19 και τον εμβολιασμό. Μπορούμε να υποθέσουμε λοιπόν ότι υποκείμενες νευροψυχολογικές διαδικασίες, βασισμένες πιθανόν σε βιολογικά καθορισμένους μηχανισμούς αυτο- ή ετερο-εξαπάτησης, μπορεί να βοηθούν στην ανάπτυξη ή ακόμη και τη διατήρηση τουλάχιστον κάποιων από τις κοινωνικές συμπεριφορές που σχετίζονται με το φαινόμενο της διάδοσης ψευδών ειδήσεων. Αυτοί οι μηχανισμοί ενδέχεται να στηρίζουν την τάση του ανθρώπου για αναζήτηση πληροφοριών με μεροληπτικό τρόπο, ακόμη μάλιστα και την εξελικτική διατήρηση του φαινομένου της διάδοσης ψευδών ειδήσεων.[9]

Όμως, σε περιπτώσεις όπως αυτή της πανδημίας COVID-19, η εγγενής τάση της αυτο- ή ετερο-εξαπάτησης δεν είναι άμοιρη κινδύνων. Οι πίστη σε σχετικές με τον COVID-19 θεωρίες συνωμοσίας και ψευδείς ειδήσεις βρέθηκε να σχετίζεται αρνητικά με την επιθυμία για εμβολιασμό και με συμπεριφορές πρόληψης της λοίμωξης.[1] Η επιδημία COVID-19 και η συνοδός πανδημία σχετικών πληροφοριών έχει διογκώσει το επικείμενο πρόβλημα εμπιστοσύνης. Το πρόβλημα διστακτικότητας απέναντι στον εμβολιασμό είναι περισσότερο πρόβλημα εμπιστοσύνης, παρά πρόβλημα πληροφόρησης. Οι ψευδείς ειδήσεις, οι φήμες και οι θεωρίες συνωμοσίας δεν θα πρέπει να νοηθούν μόνο ως ψευδείς πεποιθήσεις, αλλά και ως δημόσιες εκφράσεις φόβων και άγχους. Θεραπείες ανοσοποίησης άγχους μπορούν να βοηθήσουν τα άτομα στην αντιμετώπιση και επεξεργασία των ψευδών ειδήσεων, καθώς και στην έγκαιρη αναγνώρισή τους.[10] Τέλος, οι φορείς χάραξης πολιτικής συμβουλεύονται να κτίσουν ένα δίκτυο γνώσεων δεξιοτήτων για διάφορα επίπεδα και περιβάλλοντα, καθώς και να κινηθούν μακριά από στάσεις και συμπεριφορές πόλωσης.

Ορέστης Γιωτάκος
Editor του περιοδικού Dialogues in Clinical Neuroscience & Mental Health,
Ιδρυτής της ΑΜΚΕ Ομπρέλα - Νευροεπιστήμες & Ψυχική Υγεία και της καμπάνιας "I Care for my Brain",
Πρόεδρος της Ελληνικής Εταιρείας Σεξολογίας και Διαφυλικών Σχέσεων

Βιβλιογραφία

1. Ripp T, Röer JP. Systematic review on the association of COVID-19-related conspiracy belief with infection-preventive behavior and vaccination willingness. *BMC Psychol* 2022, 10:66, doi: 10.1186/s40359-022-00771-2
2. Wardle C, Derakhshan H. *Information Disorder Toward an interdisciplinary framework for research and policymaking*. Council of Europe, October, 2017. Available from: https://rm.coe.int/information-disorder-toward-an-interdisciplinary-framework-for-researc/168076277c
3. Ecker UH, Lewandowsky S, Cook J, Schmid P, Fazio LK, Brashier N, et al. The psychological drivers of misinformation belief and its resistance to correction. *Nat Rev Psychol* 2022, 1:13–29, doi: 10.1038/ s44159-021-00006-y
4. Vosoughi S, Roy D, Aral S. The spread of true and false news online. *Science* 2018, 359 (6380):1146-1151, doi: 10.1126/science.aap9559.
5. Trivers R. *The folly of fools: The logic of deceit and self-deception in human life*. Basic Books/Hachette Book Group, 2011
6. Angilletta MJ, Kubitz G, Wilson RS. Self-deception in nonhuman animals: weak crayfish escalated aggression as if they were strong. *Behav Ecol* 2019, 30:1469–1476, doi.org/10.1093/beheco/arz103
7. Sackeim HA. Self-deception: A synthesis. In Lockard JS, Paulhus DL (eds) *Self-deception: An adaptive mechanism*. Prentice Hall, New Jersey, 1988
8. Giotakos O. Fake news: is it a social phenomenon based on neuropsychologically determined self- or other-deceptive mechanisms? Some thoughts based on insight and self-awareness' areas. *Ann Gen Psychiatry* 2018, 17(Suppl 1):A24, doi: 10.1186/s12991-018-0206-2
9. Giotakos O. Fake news and underlined neurocognitive mechanism. *Dialogues in Clinical Neuroscience & Mental Health* 2018, 1(Suppl 3):20, doi: 10.26386/obrela.v1is3.75
10. Pertwee P, Simas C, Larson HJ. An epidemic of uncertainty: rumors, conspiracy theories and vaccine hesitancy. *Nat Med* 2022, 28:456–459, doi: 10.1038/s41591-022-01728z

https://doi.org/10.22365/jpsych.2022.064 / Psychiatriki 2022, 33:187–199

Research article

Effectiveness of a hybrid arts-based Cognitive Behavioral Therapy intervention for patients with non-malignant chronic pain

Asimina Kalmanti,[1,3] Chrysanthi Batistaki,[2] Christos Christodoulou,[1] Georgia Gerolouka-Kostopanagiotou,[2] Athanassios Douzenis,[1] Ioannis Michopoulos[1,4]

[1]*Second Department of Psychiatry, Medical School, National and Kapodistrian University of Athens, "Attikon" University Hospital, Athens,*

[2]*Second Department of Anaesthesiology-Pain Management Unit, Medical School, National and Kapodistrian University of Athens, "Attikon" University Hospital, Athens,*

[3]*Department of Occupational Therapy, School of Health and Care Sciences, University of West Attica, Athens,*

[4]*Hellenic Society for Cognitive Psychotherapies*

ARTICLE HISTORY: Received 10 June 2021/Revised 20 July 2021/Published Online 21 February 2022

ABSTRACT

Chronic Pain (CP) is defined as pain that persists or recurs for more than 3 to 6 months and may be conceived as a health condition in its own right. CP is a frequent condition, affecting an estimated 20% of people worldwide and requires special treatment and care. CP can contribute to depression, anxiety, sleep disturbances, poor quality of life and increased health care costs. Psychosocial approaches based on a cognitive conceptualization of pain can provide a solid foundation for research and clinical work. The development of a 10 week-session group treatment was based on key principles from the literature on Cognitive Behavioral Therapy for Chronic Pain (CBT-CP) and Creative Arts Therapy, integrated with advances in research on CP management framework. The aim of this study was to evaluate a CBT-CP arts-based group intervention for patients with non-malignant CP addressing the biopsychosocial factors that influence pain perception. A total of 100 University Pain Management Unit outpatients participated, 50 in the intervention group and 50 in the control group (treatment as usual). In analyses of the pretest-posttest research design intervention including all participants, treatment gains were observed in almost all domains examined: severity of pain measured by the Brief Pain Inventory, conceptualization of mental pain measured by the Orbach and Mikulincer Mental Pain Scale, tolerance for psychological pain measured by the Tolerance for Mental Pain Scale, anxiety and depression levels measured by the Hospital Anxiety and Depression Scale and quality of life measured by the WHO Quality of Life-BREF Questionnaire. The participants' mean age was 52.3 years and most were female (84%). Findings revealed that post-program there was significant reduction in pain intensity ($p<0.001$), depressive symptoms ($p<0.001$), confusion about pain ($p=0.037$) and improvement of emotional distress tolerance ($p=0.012$) and global health-related quality of life ($p<0.001$) in the intervention group. Beneficial effects can be expected from the implementation of an integrated CP intervention (includingcreative and CBT techniques) reappraising some of the coping responses defined as adaptive within current psychosocial non-malignant CP regimens.

KEYWORDS: Chronic pain, Cognitive Behavioral Therapy for Chronic Pain (CBT-CP), Creative Arts Therapy, mental pain, quality of life.

Corresponding author: Asimina Kalmanti, National and Kapodistrian University of Athens, Medical School, Second Department of Psychiatry, "Attikon" University Hospital, 1 Rimini street, 124 62 Athens, Greece • e-mail: minakalm@gmail.com

Introduction

Chronic pain (CP) is defined as pain that persists past normal healing time and hence lacks the acute warning function of physiological nociception.[1] Pain is regarded as chronic when it lasts or recurs for more than 3 to 6 months.[2] Chronic and recurrent pain should be viewed as diseases in their own right and pose a specific healthcare burden.[3] CP is a frequent condition, affecting an estimated 20% of people worldwide and accounting for 15–20% of physician visits.[4] Many non-physiologic factors (psychological, familial and societal attitudes, life stressors, cultural and spiritual) contribute to the experience of and response to pain.[5] CP can contribute to disability, depression and anxiety, sleep disturbances, poor quality of life and increased healthcare costs.[6] Adequate treatment and alleviation of pain is a human right and it is the duty of any healthcare system to provide it.[7] The World Health Organization identified a need for improved, standardized management of CP (both malignant and non-malignant) developed on the basis of good health professional-patient communication and jointly agreed goals that take account of the patient's pain characteristics, as well as their physical and psychosocial needs.[8]

Because of its clear research support Cognitive Behavioral Therapy (CBT), as the gold-standard evolving psychological treatment dominates the international guidelines for psychosocial treatments, making it a first-line treatment for many disorders.[9] Although CBT is effective, there is still room for improvement, as in many situations there are patients who do not respond to CBT and/or relapse. CBT for managing CP (CBT-CP) is based on the principle that the experience of pain results in a complex interaction among biological, cognitive, affective and behavioral factors and that changing these factors should positively affect the painful experience.[10]

Creative Arts Therapies (CATS) are a valuable psychosocial treatment option, which allow people to experience and express themselves through the arts. They foster exploration of creativity in a supportive environment anchored by a therapeutic relationship. Clinicians use evidence-based methods in the application of the art form and a variety of techniques and arts media.[11] There is a large body of research showing how arts engagement can enhance multidimensional subjective individual and social well-being, through effects on modifying cognitions and emotions and building socialization and resilience.[12,13] There is also a growing literature on the preventive benefits of arts engagement in relation to mental health.[14,15] Creativity is noted as a significant protective factor when facing life difficulties and trauma.[16]

However, CATS and CP remain an under-researched area indicating a growing need for quality exploratory studies to enrich our understanding of the mechanisms of therapy and to enable further assessment of effectiveness.[17,18] Most of the relevant literature addresses psychosomatic forms of pain and most studies describe how therapeutic arts experience was used in long-term treatment.[19,20] More quantitative studies need to be carried out to test the efficacy of brief forms of creative therapies in order to gain a better understanding of how many patients find CATS beneficial to their CP treatment, making the findings more generalizable.[21] Finally, there is relatively little information regarding how creative therapies operate in conjunction with other CP treatments.[22]

Therefore, we developed a hybrid intervention integrating CATS and CBT-CP components as a complementary CP treatment approach, that could be used in traditional pain management regimens. While a CATS perspective inspired arts-based methods and techniques (i.e., visualization, externalizing of inner processes), CBT-CP guided the rationale (i.e., psychoeducation, cognitive restructuring, problem solving, positive affirmation, relaxation training, relapse prevention) for using these methods and techniques to address CP and helped to explain why they were effective.[23–25]

The aim of this study was to evaluate a brief multicomponent arts-based CBT-CP group intervention for adults suffering from non-malignant CP of any aetiology. Our hypothesis was that the arts-based intervention would improve pain intensity, emotional distress, pain disability and health-related quality of life.

Material and Method

Participants

The sample consisted of one hundred adult patients. Inclusion criteria were: (a) aged between 18 and 60, (b) suffering from non-malignant CP of any aetiology, and (c) willing not to engage in any other group counseling treatment during the course of the study. Exclusion criteria applied to those (a) who were not able to give informed consent, (b) whose Greek was not fluent enough to communicate meaningfully, (c) who suffered from any mental health condition (based on self-disclosure and psychiatric interview).

Measures

According to the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT),[26] the following scales were used:

Brief Pain Inventory (BPI)

The BPI evaluates a patient's pain experience through a number of different scales. The benefits of the BPI are that it has shown to be reliable in a number of different pain states and is an excellent tool to use for monitoring the effect of pain or treatment of pain or both, in terms of a patient's functional ability or disability over time.[27] It has been translated and validated in Greek.[28]

Orbach and Mikulincer Mental Pain Scale (MPS)

The MPS consists of 45 self-rated items and draws on a conceptualization of mental pain as a perception of negative feelings. The items of the MPS are divided into nine factors: irreversibility, loss of control, narcissistic wounds, emotional flooding, freezing, self-estrangement, confusion, social distancing and emptiness. Subjects rate each item on a 5-point Likert scale, with higher values reflecting greater mental pain.[29] It has been translated and validated in Greek.[30]

Tolerance for Mental Pain Scale (TMPS)

The 20-item TMPS was developed, and is, as far as we know, the only questionnaire available to assess tolerance for psychological pain. The TMPS measures three facets of tolerance for psychological pain that reflect existing theoretical perspectives in the literature: surfeit of the pain, belief in the ability to cope with the pain and containing the pain.[31] It has been translated and validated in Greek.[30]

Hospital Anxiety and Depression Scale (HADS)

The HADS is a self-report rating scale of 14 items on a 4-point Likert scale (range 0–3) and provides clinicians with an acceptable, reliable, valid and easy to use practical tool for identifying and quantifying depression and anxiety in general hospital patients.[32] It has been translated and validated in Greek.[33]

WHO Quality of Life-BREF (WHOQoL-BREF) Questionnaire

The WHOQoL-BREF evaluates perceptions of health and assess interventions aimed at improving health-related QoL in patients with chronic medical conditions. This questionnaire consists of 4 broad domains, physical health, psychological, social relationships and environment. In addition to the four domains, the WHOQoL-BREF includes two stand-alone questions to assess rated QoL and satisfaction with health.[34] Finally, this instrument has been standardized for use within the Greek population.[35]

Procedure

The study protocol was approved in December 2016 (RN#EBD2106/6-2-2017) by the Research Ethics Board at "Attikon" University Hospital, Athens, Greece.[36] The participants' response to therapy was evaluated using a battery of questionnaires as well as interviews and observation. Pain Management Unit's outpatients with CP complaints were referred by their physician to the group program (max. 10 patients per group). The study was conducted from February 2017 to November 2019. The intervention was proposed to 160 outpatients. From 115 patients who accepted, 15 quit before the intervention. A total of 100 patients participated from which 50 accepted and formed the intervention group and 50 declined and formed the treatment as usual (TAU) control group. TAU included pharmacological pain management, case-by-case supportive psychotherapy and acupuncture. Every experimental group consisted of 4–10 participants, who attended 10 weekly structured 2-hour sessions. Pre- andpost-measurement took place at the start of the course (baseline, T0) and directly after the 10-week course (T1). All participants signed an informed consent form (see figure 1).

The goal of the treatment was described to patients as such: "to regain control over daily functioning by learning to accept limitations and start focusing on abilities; finding new pain coping waysand reflect on quality of life options for the future".

Intervention: key constructs

The development of the present intervention is based on key principles from the literature on CATS, and CBT-CP, integrated with advances in research on CP management and comorbid psychosocial symptoms. With this conceptual background, ten arts-based treatment group sessions were created and applied within the multicomponent CP management framework including psychoeducation and arts engagement (including drawing and expressive writing) addressing the psychological, cognitive, behavioral, social and physiological factors that influence pain perception through visual and creative expression. The decision to limit the intervention to ten sessions was based on: (a) the frequency of patient attrition due to CP-related issues and (b) the typical structure of brief CBT which reduces the average 12–20 therapy sessions into 4–8 sessions.[37] The ten sessions were organized into three stages: the Initial treatment phase (Sessions 1 and 2), the CBT skills building phase (Sessions 3–8) and the Discharge phase (Sessions 9 and 10) (presented in the Supplementary material). The emerging treatment manual of the actual intervention

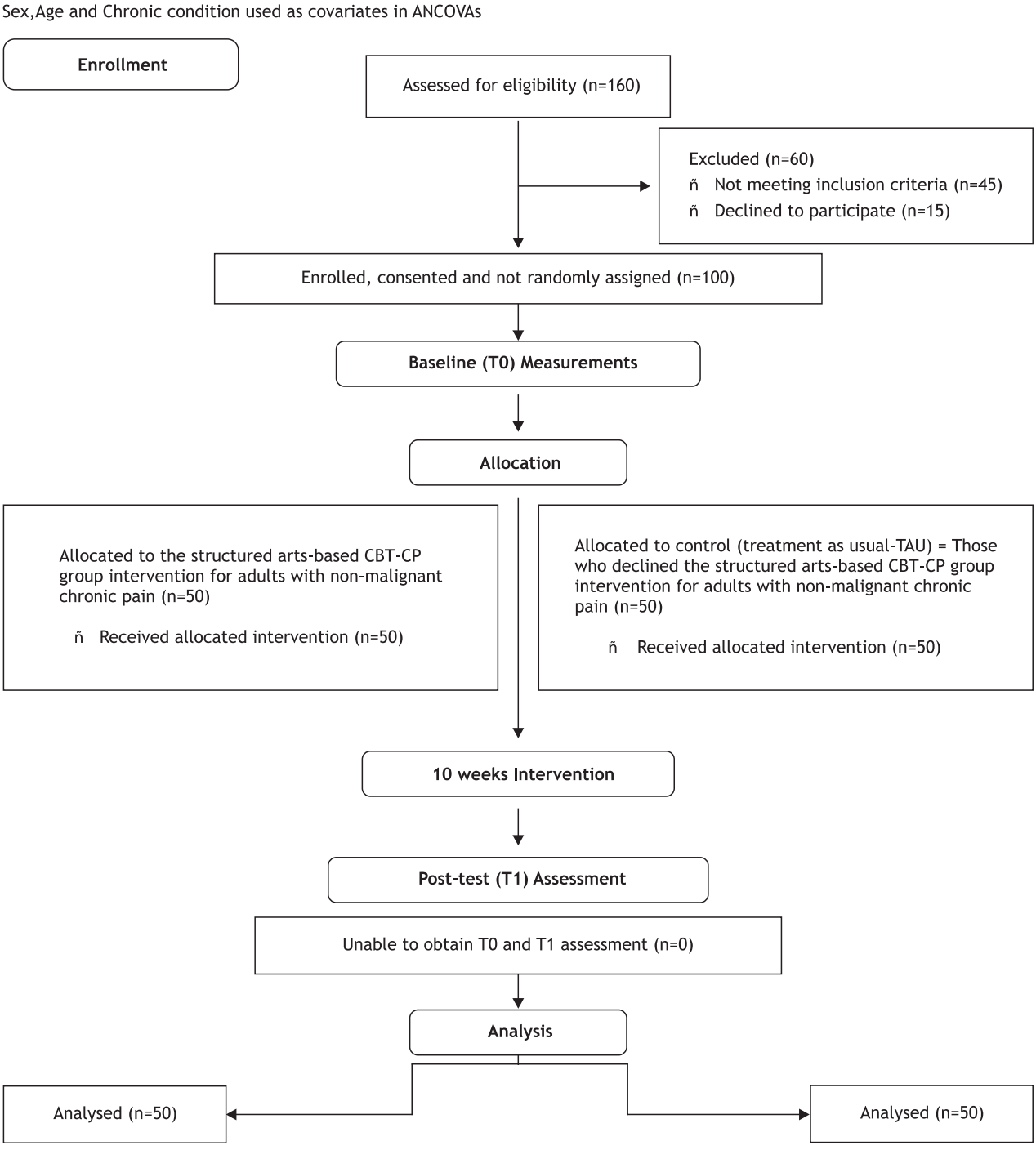

Figure 1. Participant flow through treatment as usual and arts-based CBT-Chronic Pain group intervention.

was the extensive modification of the treatment manual of Thorn on CP.[38]

The standard session structure

To enhance replication, we provide instructions and steps to use in each session. All group sessions (~2 h) offered general structure and flexibility at the same time. Structure is considered important in the context of CP, providing a safe space that does not affect the creative and therapeutic process and patients are invited to change the structure and make choices at all times. No drop-in participants are permitted and participants are given a program manual of notes and information about the different aspects of the program that highlights the main theoretical underpinnings of the planned intervention, discusses the aims of the therapy in the specific context of non-malignant CP, pictures the general structure of each session and suggests exemplary activ-

ities. The point is to keep the patient working on pain self-management in spite of the pain experience (see Supplementary material).

We focus on positive group affective tone as an energizing mechanism for team proactivity because positive affect increases cognitive and behavioral resources for participants to set future-focused and change-oriented goals and to persistently engage in coping activities to achieve anticipated outcomes.[39,40]

Therapist

The therapist was an occupational therapist, also trained on CBT. Supervision by an experienced CBT therapist was provided throughout the intervention procedure.

Statistical analysis

Quantitative variables were presented as mean values (SD) and minimum, maximum values across the total population and between groups. Qualitative variables were expressed as absolute and relative frequencies (N, %). Patient characteristics on baseline were compared using the non-parametric Mann–Whitney-U test and Chi-square or Fisher's exact test. Pearson and Spearman correlation coefficients were also used. A mixed model ANOVA was used to investigate the effect of time (time; within-subject variable), intervention (2 groups; between-subject variable) and their interaction term, after adjusting participants' age, sex and chronic condition on mental pain, mental pain tolerance and quality of life. Overall, all statistical analyses were performed with SPSS Version 25.0.[41] All the aforementioned statistical tests were two-sided and were performed at a 0.05 significance level.

Results

Patient characteristics

One hundred participants with non-malignant CP were recruited in the study. Patients' demographic characteristics such as age, gender, marital status, education level, CP classification[42] and coping strategies are presented in table 1. No significant baseline differences were found between the two groups, except for the participants' age. As shown in table 1, the vast majority were females (84%) in both groups, with younger participants being included in the intervention group (48.9±9.29 years vs

Table 1. Demographic characteristics across sample.

	Intervention group (N=50)	Control group (N=50)	Total sample (N=100)	p
Sex (female)	42 (84%)	42 (84%)	84 (84%)	1.000
Age	48.9±9.29 (22–60)	55.8±3.67 (40–60)	52.35±7.83 (22–60)	<0.001[b]
Education(years)	12.1±4.35 (6–18)	11.8±3.53 (6–18)	11.9±3.94 (6–18)	0.889[b]
Marital status				0.068[a]
Married	29 (64.4%)	39 (81.3%)	68 (73.1%)	
Living alone	16 (35.6%)	9 (18.7%)	25 (26.9%)	
Non–malignant chronic pain classification (ICD–11)				0.320[a]
Headache/ Orofacial pain	5 (10%)	2 (4%)	7 (7%)	
Musculosceletal pain	16 (32%)	19 (38%)	35 (35%)	
Neuropathic pain	9 (18%)	11 (22%)	20 (20%)	
Chronic posttraumatic/postsurgical pain	0 (0%)	3 (6%)	3 (3%)	
Visceral pain	1 (2%)	0 (0%)	1 (1%)	
Mixed pain	19 (38%)	15 (30%)	34 (34%)	
Selected coping mechanisms				0.109[a]
Newspaper / TV	20 (40%)	24 (48%)	44 (44%)	
PC activities	19 (38%)	23 (46%)	42 (42%)	
Exercise	2 (4%)	2 (4%)	4 (4%)	
Household / Children	7 (14%)	1 (2%)	8 (8%)	
Books / Music	2 (4%)	0 (0%)	2 (2%)	

M±SD (range) or N (%) are displayed, as appropriate; a: x^2 or Fisher's exact test; b: Mann–Whitney.

55.8±3.67 years, p<0.001). The mean years of education was 11.9 years in the total sample, similar results were found in both groups. There were no differences on pain classification or selected coping mechanisms.

Treatment effects: mixed model analysis

The complexity of objectives of this research study required flexible approaches to the research design, data collection and analysis methods. In analyses of the pre-test-posttest research design intervention including all participants, treatment gains were observed in almost all domains examined: severity of pain measured by the Brief Pain Inventory, conceptualization of mental pain measured by the Orbach and Mikulincer Mental Pain Scale, tolerance for psychological pain measured by the Tolerance for Mental Pain Scale, anxiety and depression levels measured by the Hospital Anxiety and Depression Scale, and quality of life measured by the WHO Quality of Life-BREF Questionnaire. The participants' mean age was 52.3 years and most were female (84%). The two groups showed statistically significant differences between T0 and T1 for most of the variables used to assess pain (severity; pain-related interference with functioning), mental pain, mental pain tolerance, anxiety and depression levels, and health-related quality of life (see table 2). Findings revealed that post-program, there

Table 2. Paired sample t-tests comparing changes in outcomes pre- and post-program.

	Intervention group (N=50)			Control group (N=50)		
	T0	T1	p	T0	T1	p
	Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	
Average pain (BPI)	6.3±1.89	4.7±2.27	<0.001[b*]	3.9±1.49	3.7±1.47	0.002[b*]
Relief pain medication provided (BPI)	54.4±19.29	68.8±17.92	<0.001[b*]	71.6±11.67	76±9.69	<0.001[b*]
Total pain-related interference with functioning (BPI)	6.5±2.45	4.7±2.47	<0.001[b*]	5.2±1.5	5.6±1.32	<0.001[b*]
a) General activity (BPI)	6.6±2.52	4.8±2.46	<0.001[b*]	5.1±1.98	5±1.68	0.397[b]
b) Mood (BPI)	6.8±2.69	4.8±2.71	<0.001[b*]	5.7±1.36	6.8±1.18	<0.001[b*]
c)Walking ability (BPI)	5.6±3.28	4.8±2.71	0.014[b*]	4.2±2.17	4.1±2	0.132[b]
d)Normal work (BPI)	6.5±2.54	4.7±2.54	<0.001[b*]	4.7±1.82	4.7±1.7	0.705[b]
e) Relations with other people (BPI)	6±2.77	4.4±2.5	<0.001[b*]	5.7±1.69	6.6±1.64	<0.001[b*]
f) Sleep (BPI)	6.7±3.55	5.1±3.19	<0.001[b*]	4.1±2.27	4.1±2.17	0.808[b]
g) Enjoyment of life (BPI)	7±2.58	4.4±2.8	<0.001[b*]	6.8±1.23	7.5±1.13	<0.001[b*]
Anxiety (HADS)	10.3±4.19	7.6±4.21	<0.001[b*]	7.4±3.8	8.6±3.96	<0.001[b*]
Depression (HADS)	9.1±4.45	6.7±3.93	<0.001[b*]	6.8±3.64	8.6±3.09	<0.001[b*]
Irreversibility (MPS)	32±8.54	24.4±7.53	<0.001[b*]	34±7.26	38.7±4.21	<0.001[b*]
Loss of control (MPS)	28.7±6.92	22.9±6.7	<0.001[b*]	31.4±6.61	37.9±4.41	<0.001[b*]
Narcissistic wounds (MPS)	10.3±3.91	8.9±3.63	<0.001[b*]	12.1±4.35	17.1±2.56	<0.001[b*]
Emotional flooding (MPS)	14.6±4.53	11.4±4.17	<0.001[b*]	10.7±3.86	11.8±3.97	0.018[b*]
Freezing (MPS)	8.3±3.19	5.9±2.88	<0.001[b*]	6.9±2.8	7.3±2.75	0.118[b]
Self-estrangement (MPS)	8.1±3.21	6.8±3.3	<0.001[b*]	7.3±3.25	8.8±3.09	<0.001[b*]
Confusion (MPS)	9.9±3.65	6.2±2.58	<0.001[b*]	7.7±2.08	11.8±2.17	<0.001[b*]
Emptiness (MPS)	11.9±4.27	8.5±3.48	<0.001[b*]	8.9±4.26	9.7±3.95	0.001[b*]
Social distancing (MPS)	13.8±3.22	10.8±3.02	<0.001[b*]	10.8±3.41	13.1±2	<0.001[b*]
Surfeit of the pain (TMPS)	26.7±8.07	30.7±8.5	<0.001[a*]	30.6±9.3	20.7±5.74	<0.001[b*]
Belief in the ability to cope with the pain (TMPS)	19.1±4.06	21.1±3.76	0.010[b*]	20.5±8.14	13.7±5.31	<0.001[b*]
Physical health (WHOQol-Bref)	11.2±2.19	12.8±2.88	<0.001[b*]	12.3±2.38	12.5±2.29	0.066[b]
Environment (WHOQol-Bref)	11.9±1.73	12.9±1.71	<0.001[b*]	12.7±1.68	12.7±1.52	0.593[b]

* indicates p<0.05. a: Paired samples t-test, b: Wilcoxon signed-rank test
Brief Pain Inventory (BPI) - Hospital Anxiety and Depression Scale (HADS) - Orbach and Mikulincer Mental Pain Scale (MPS) - Tolerance for Mental Pain Scale (TMPS) -WHO Quality of Life-BREF Questionnaire (WHOQoL-BREF)

was significant reduction in pain intensity (p<0.001), depressive symptoms (p<0.001), confusion about pain (p=0.037), and improvement of emotional distress tolerance (p=0.012) and global health-related quality of life (p<0.001) in the intervention group. A mixed model ANOVA was performed to evaluate the main effects of time and group (controlling for age), as well as group by time interaction on the impact of all variables examined (see table 3). A representation of the outcome data is graphically illustrated in figures 2 and 3.

Discussion

We examined the efficacy of a structured arts-based CBT-CP group intervention for adults with non-malignant CP. Compared to TAU, intensity of mental pain in the intervention group, which was assessed through nine factors, showed a significant reduction. Tolerance for mental pain was significantly higher for participants in the intervention group. Furthermore, severity of pain was reduced in the intervention group, as well as levels

Table 3. Analyses of Covariance (ANCOVAs).

	Fixed effect				Interaction term	
	Time		Group		Time*Group	
	F	p	F	p	F	p
Brief Pain Inventory (BPI) subscales						
Average pain	9.66	0.003	19.66	<0.001	17.51	<0.001
Relief pain medication provided	0.00	0.953	23.7	<0.001	18.86	<0.001
Total pain-related interference with functioning	4.85	0.030	0.17	0.685	101.10	<0.001
a) General activity	5.95	0.017	0.92	0.340	43.6	<0.001
b) Mood	1.59	0.211	0.72	0.398	107.13	<0.001
c) Walking ability	1.01	0.318	3.52	0.064	2.66	0.107
d) Normal work	1.56	0.214	2.46	0.121	57.57	<0.001
e) Relations with other people	5.13	0.026	5.67	0.019	47.98	<0.001
f) Sleep	0.13	0.724	11.57	0.001	27.08	<0.001
g) Enjoyment of life	7.73	0.007	12.42	0.001	96.04	<0.001
Hospital Anxiety and Depression Scale (HADS) subscales						
Anxiety	2.11	0.150	0.74	0.393	57.24	<0.001
Depression	0.97	0.326	1.37	0.246	49.68	<0.001
Orbach and Mikulincer Mental Pain Scale (MPS) subscales						
Irreversibility	3.64	0.060	30.86	<0.001	79.18	<0.001
Loss of control	0.22	0.638	48.46	<0.001	83.25	<0.001
Narcissistic wounds	3.37	0.070	37.12	<0.001	96.69	<0.001
Emotional flooding	4.02	0.048	5.77	0.018	25.25	<0.001
Freezing	0.44	0.510	0.68	0.412	30.85	<0.001
Self-estrangement	0.16	0.694	0.00	0.973	31.13	<0.001
Confusion	4.49	0.037	12.82	0.001	215.33	<0.001
Emptiness	6.27	0.014	1.03	0.312	74.91	<0.001
Social distancing	2.03	0.158	0.57	0.452	82.76	<0.001
Tolerance for Mental Pain Scale (TMPS) subscales						
Surfeit of the pain	4.02	0.048	1.02	0.314	73.10	<0.001
Belief in the ability to cope with the pain	0.02	0.883	13.12	<0.001	45.28	<0.001
WHO Quality of Life-BREF Questionnaire (WHOQoL-BREF) subscales						
Physical health	11.39	0.001	1.21	0.274	30.36	<0.001
Environment	3.03	0.085	5.95	0.017	19.98	<0.001

Sex, Age and Chronic condition used as covariates in ANCOVAs

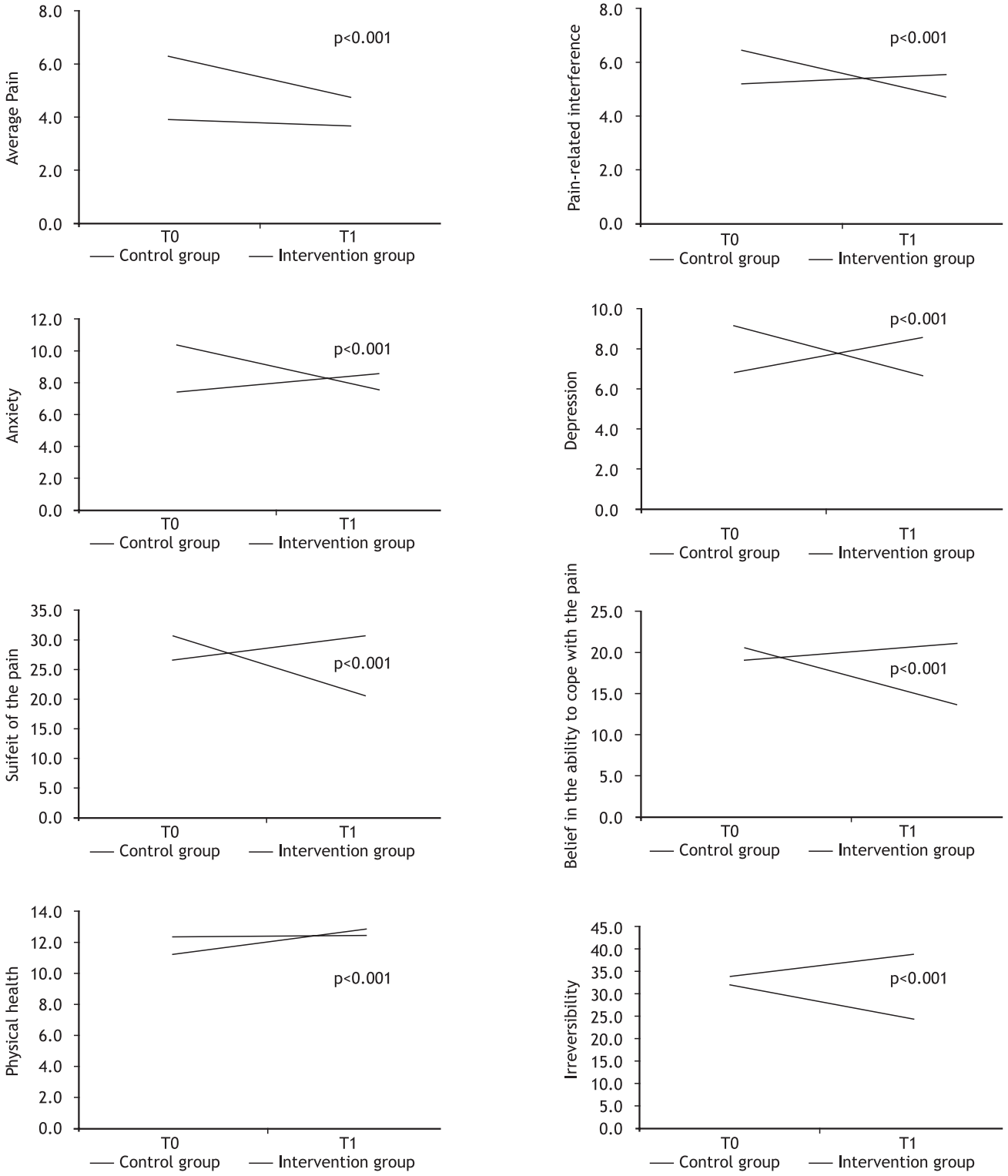

Figure 2. Estimated marginal means on the Brief Pain Inventory (BPI) - the Hospital Anxiety and Depression Scale (HADS) - the Orbach and Mikulincer Mental Pain Scale (MPS) - the Tolerance for Mental Pain Scale (TMPS) - the WHO Quality of Life-BREF Questionnaire (WHOQoL-BREF) in each time period and for each group over the course of the study.

of anxiety and depression. Finally, health-related quality of life of patients in the intervention group was also improved after the intervention. In contrast, the control group generally showed very little improvement in dealing with pain. The treatment benefited neuropathic and mixed pain patients more in mental pain variables, whilein terms of mental pain tolerance variables musculoskeletal pain patients seem to benefit more.

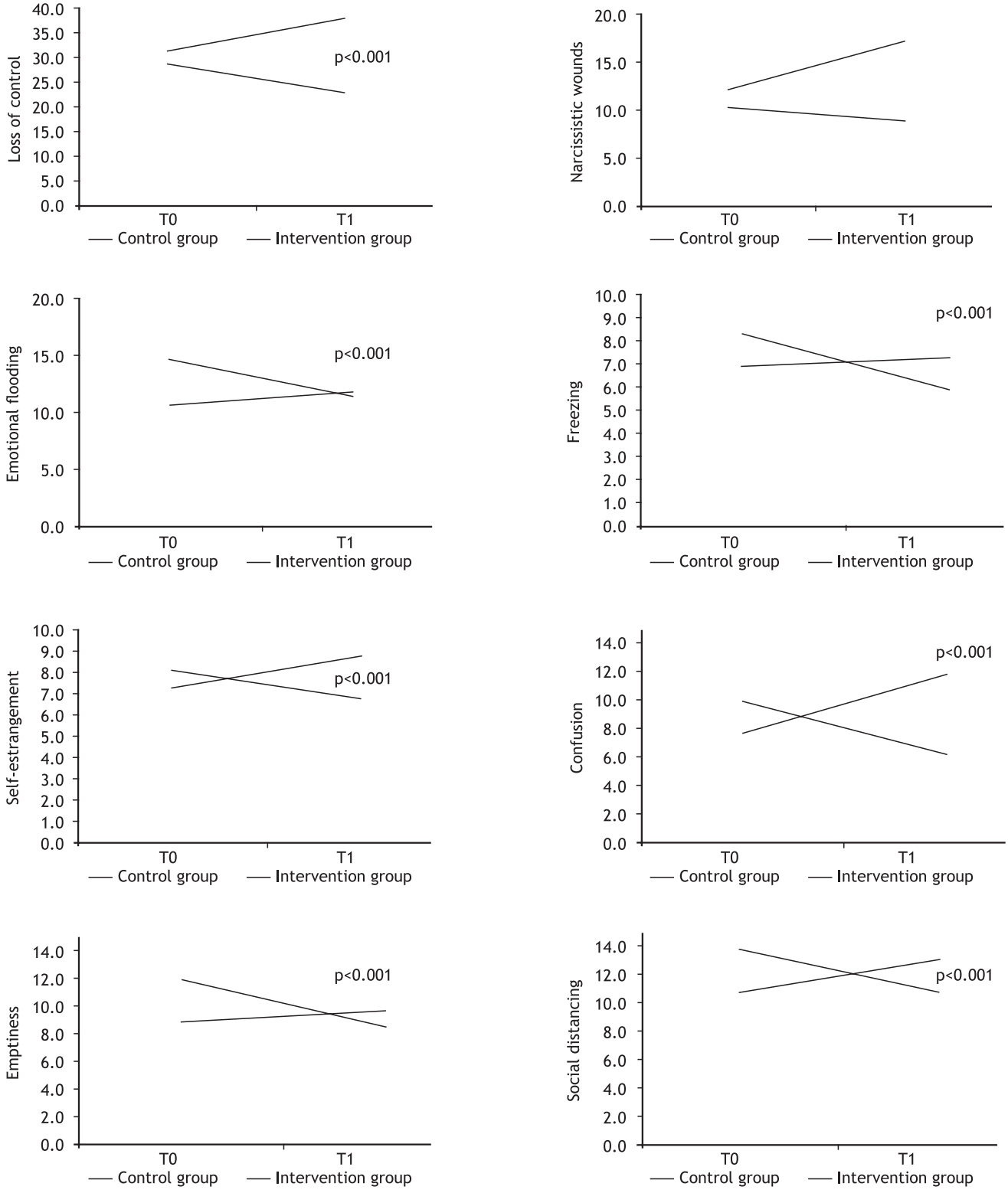

Figure 3. Estimated marginal means on the Orbach and Mikulincer Mental Pain Scale (MPS) in each time period and for each group over the course of the study.

The findings of this study offer new and supporting information regarding several therapeutic aspects of arts engagement. These include (a) evidence for the effectiveness of an arts-based psychoeducational program and (b) potential positive impact on pain intensity, pain disability and quality of life improvement and specifically examining factors associated with pain-related distress, since the positive impact of arts therapies on gen-

eral well-being has been widely recognized but, to the authors' knowledge, has not yet been documented in the treatment of non-malignant CP. An observation that continues to be true to this day, is that the dearth of outcome research regarding the effectiveness of CATS on the CP experience has resulted in an underrepresentation of creative therapies in the pain management literature.[23] Self-management refers to the patients' ability to recognize the factors that cause their pain to flare up and the techniques that can be used to avoid those flare-ups. The ability to recognize these factors hap¬pens during the creative process by allowing patients to draw metaphors for their art and applying them to their past and present experiences. Teaching self-management is currently regarded as one of the most important components of CP treatment. [43,44]

In respect to physical symptoms, distraction from pain during the art-making process is observed from reports of the patients.[45] Although there is no discussion in any articles regarding the potential reasons underlying this phenomenon, patients observed typically perceived more pain at times when they had little to do or were unoccupied. This might indicate that therapeutic art-making may redirect patients' attention away from pain into other activities.[46]

Saunders emphasized the connection between physical pain and mental suffering.[47] Suffering can be defined as a state of severe distress associated with events that threaten the intactness of the person, that occurs when an impending destruction of the person is perceived. Suffering alienates the sufferer from self and society and may engender a 'crisis of meaning' and a disintegration of hope.[48] The term 'suffering' contains nonphysical dimensions--social, psychological, cultural, spiritual and may mean different things to different people.[49] CP in most patients with little resources in terms of resilience should receive targeted psychosocial support to minimize mental distress and the risk of depression or anxiety disorders through a comprehensive workup and thoughtful treatment plan, which balances comfort with function and rehabilitation.[50] Recently, CBT has included a more trans-diagnostic/process-based and personalized approach, with the ultimate goal of linking the therapeutic technique to the process and the individual patient.[51]

Importantly, findings suggest that the negative emotion-pain cycle may be counteracted by this intervention as the people affected by non-malignant CP could focus on increasing their quality of life through establishing positive well-being instead of emphasizing the CP symptoms.[52] Function, in particular, performance of 'Valued life activities' (VLAS) which are the wide range of activities that individuals find meaningful or pleasurable, above and beyond activities that are necessary for survival or self-sufficiency, is associated with psychological well-being.[53,54] Change in psychological well-being is used as a marker for successful therapy.22 Factors such as generally improved affect, decreased anxiety or depression, improved emotional coping, expression of grief and ability to project oneself into the future, all appear to be associated with the patients' improved ability to cope with pain.[23,25,55,56]

The strengths of the study were the application of a novel brief integrative pain program using multiple treatment modalities implementing CBT-CP and mind-body treatments such as CATS and the comparatively big sample size. It also employed systematic research methods carried out with rigour to ensure validity and trustworthiness, multiple measures of treatment physical, social and emotional effectiveness and a comprehensive analysis of all case variables.

The current study also comes with various limitations. First, the sample of this study was primarily female and Caucasian, which might lead to issues with generalizability and highlight potential issues of program accessibility and barriers to participation. Second, the study was not fully randomized, as the control group constituted of those who declined the intervention. There was not a follow-up design or formal feedback designed to determine any changes to multimodal analgesia provided and our findings are based on self-reported information of individuals' beliefs about their way of thinking, feeling and behaving which have formed through different experiences over time.

Of note, the improvement can be attributed to the effects of "due care" of the intervention, which provides an opportunity to discuss concerns, hopes and fears. As an experimental study, we need to be aware of the Hawthorne effect, which is an inevitable bias that poses a threat to validity and should try to take into account when analysing the results, as individuals are always subject to behaviour modification once they know they are part of an experiment.[57]

Conclusion

This study demonstrated that a 10-week multicomponent arts-based CBT-CP program is associated with improvements in patient-related outcomes. The evidence synthesized in this study provides suggestions for integrating creative interventions for CP management as a new approach to providing more holistic treatment. A brief arts-based group therapy treatment may be safe, acceptable and valuable establishing the unique role that arts engagement might play in a global challenge

to tackle CP as an adjunctive treatment to CP management regimens.

Recognizing the added health value of engagement with the arts, further research should attempt (a) to determine the contribution that mental pain can provide towards an understanding of non-malignant CP dynamics and thereby contribute to the development of effective treatment programs, tailored for psychological aspects of CP and (b) to provide a larger sample size in order to be able to investigate which patients benefit most from the intervention.

Acknowledgements

Asimina Kalmanti would like to express sincere thanks to the Medical School of the National and Kapodistrian University of Athens, Greece for allowing her to conduct PhD research into the links between creative counseling interventions and non-malignant chronic pain. We acknowledge all the physicians who contributed their time to diligently helping this program and study run. Special thanks go to all of the patients who participated in our program and took the time to complete our questionnaires.

References

1. Bonica JJ. Basic principles in managing chronic pain. *Arch Surg* 1977, 112:783–788, doi: 10.1001/archsurg.1977.01370060115017
2. Merskey H, Bogduk N. *Classification of chronic pain*. 2nd ed. IASP Press, Seattle, WA,1994
3. Lynch ME, Schopflocher D, Taenzer P, Sinclair C. Research funding for pain in Canada. *Pain Res Manag* 2009, 14:113–115, doi: 10.1155/2009/746828
4. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol Bull* 2007, 133:581–624, doi: 10.1037/0033-2909.133.4.581
5. Diatchenko L, Nackley AG, Slade GD, Fillingim RB, Maixner W. Idiopathic pain disorders – pathways of vulnerability. *Pain* 2006, 123:226–230, doi: 10.1016/j.pain.2006.04.015
6. Osborn M, Smith JA. The personal experience of chronic benign lower back pain: an interpretative phenomenological analysis. *Br J Health Psychol* 1998, 3:65–83, doi: 10.1111/j.2044-8287.1998.tb00556.x
7. Brennan F, Carr D, Cousins M. Access to pain management-still very much a human right. *Pain Med* 2016, 17:1785–1789, doi: 10.1093/pm/pnw222
8. World Health Organization. *Normative guidelines on pain management. Report of a Delphi Study to determine the need for guidelines and to identify the number and topics of guidelines that should be developed by WHO*. World Health Organization, Geneva, 2007
9. Hofmann SG, Asnaani A, Vonk IJJ, Sawyer AT, Fang A. The efficacy of cognitive behavioral therapy: a review of meta-analyses. *Cognit Ther Res* 2012, 36:427–440, doi: 10.1007/s10608-012-9476-1
10. Thieme K, Gracely RH. Are psychological treatments effective for fibromyalgia pain? *Curr Rheumatol Rep* 2009, 11:443–450, doi: 10.1007/s11926-009-0065-6
11. National Collaborating Centre for Mental Health. *Schizophrenia. The Nice guideline on core interventions in the treatment and management of schizophrenia in adults in primary and secondary care*. National Institute for Health and Clinical Excellence, Leicester, UK, 2010. Available from: www.nice.org.uk/nicemedia/pdf/CG82FullGuideline
12. Grossi E, Tavano Blessi G, Sacco PL. Magic moments: determinants of stress relief and subjective well-being from visiting a cultural heritage site. *Cult Med Psychiatry* 2019, 43:4–24, doi: 10.1007/s11013-018-9593-8
13. Papinczak ZE, Dingle GA, Stoyanov SR, Hides L, Zelenko O. Young people's uses of music for well-being. *J Youth Stud* 2015, 18:1119–1134, doi: 10.1080/13676261.2015.1020935
14. Fancourt D, Finn S. *What is the evidence on the role of the arts in improving health and well-being*?: A scoping review. World Health Organization, Regional Office for Europe, & Health Evidence Network, 2019
15. Stevens K, McGrath R, Ward E. Identifying the influence of leisure-based social circus on the health and well-being of young people in Australia. *Ann Leis Res* 2019, 22:305–322, doi: 10.1080/11745398.2018.1537854
16. Wolin SJ, Wolin S. *The resilient self: how survivors of troubled families rise above adversity*. Villard Books, NY, 1993
17. Lancaster GA, Dodd S, Williamson PR. Design and analysis of pilot studies: recommendations for good practice. *J Eval Clin Pract* 2004, 10:307–312, doi: 10.1111/j..2002.384.doc.x
18. Thabane L, Ma J, Chu R, Cheng J, Ismaila A, Rios LP et al. A tutorial on pilot studies: the what, why and how. *BMC Medical Res Methodol* 2010, 6:1, doi: 10.1186/1471-2288-10-1
19. Bullington J, Nordemar K, Nordemar R, Sjöström-Flanagan C. From pain through chaos to new meaning: Two cases studies. *Arts Psychother* 2005, 32:261–274, doi: 10.1016/j.aip.2005.04.007
20. Long JK. Medical art therapy: Using imagery and visual expression in healing. In Camic P, Knight S (eds) *Clinical handbook of health psychology: A practical guide to effective interventions*. Hogrefe & Huber, TOR, 2004
21. Pavlek M. Paining out: An integrative pain therapy model. *Clin Soc Work J* 2008, 36:385–393, doi: 10.1007/s10615-007-0136-y
22. Theorell T, Konarski K, Westerlund H, Burell AM, Engström R, Lagercrantz AM et al. Treatment of patients with chronic somatic symptoms by means of art psychotherapy: A process description. *Psychother Psychosom* 1998, 67:50–56, doi: 10.1159/000012259
23. Camic P. Expanding treatment possibilities for chronic pain through the expressive arts. In: Malchiodi CA (ed) *Medical art therapy with adults*. Jessica Kingsley, PHL, 1999
24. McGuire SR, Strober L, Chiaravalloti ND, DeLuca J. Development and effectiveness of a psychoeducational wellness program for people with multiple sclerosis description and outcomes. *Int J MS Care* 2015, 17:1–8, doi: 10.7224/1537-2073.2013-045
25. Mantoudi A, Parpa E, Tsilika E, Batistaki C, Nikoloudi M, Kouloulias VJ et al. Complementary therapies for patients with cancer: reflexology and relaxation in integrative palliative care. A randomized controlled comparative study. *J Altern Complement Med* 2020, 26:794–800, doi: 10.1089/acm.2019.0402
26. Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations: *Pain* 2005, 113:9–19, doi: 10.1016/j.pain.2004.09.012

27. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singapore* 1994, 23:129–138, PMID: 8080219

28. Mystakidou K, Mendoza T, Tsilika E, Befon S, Parpa E, Bellos G et al. Greek Brief Pain Inventory: validation and utility in cancer pain. *Oncology* 2001, 60:35–42, doi: 10.1159/000055294

29. Guimarães R, Fleming M, Cardoso MF. Validation of the Orbach & Mikulincer Mental Pain Scale (OMMP) on a drug addicted population. *Soc Psychiatry Psychiatr Epidemiol* 2014, 49:405–415, doi: 10.1007/s00127-013-0751-6

30. Soumani A, Damigos D, Oulis P, Masdrakis V, Ploumpidis D, Mavreas V et al. Mental pain and suicide risk: application of the Greek version of the Mental Pain and the Tolerance of Mental Pain scale. *Psychiatriki* 2011, 22:330–340, PMID: 22271846

31. Orbach I, Gilboa-Schechtman E, Johan M, Mikulincer M. *Tolerance for Mental Pain Scale*. Bar Ilan University, Ramat-Gan, IL, 2004

32. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983, 67:361–370, doi: 10.1111/j.1600-0447.1983.tb09716.x

33. Michopoulos I, Douzenis A, Kalkavoura C, Christodoulou C, Michalopoulou P, Kalemi G et al. Hospital Anxiety and Depression Scale (HADS): Validation in a Greek general hospital sample. *Arch Gen Psychiatry* 2008, 7, doi: 10.1186/1744-859X-7-4

34. Group W. Development of the WHOQOL: rationale and current status. *Int J Ment Health* 1994, 23:24–56, doi: 10.1080/00207411.1994.11449286

35. Ginieri-Cocossis M, Triantafillou E, Tomaras V, Soldatos C, Mavreas V, Christodoulou G. Psychometric properties of WHOQOL-BREF in clinical and health Greek populations: incorporating new culture-relevant items. *Psychiatriki* 2012, 23:130–142, PMID: 22796911

36. World Medical Association. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. *Bull World Health Organ* 2001, 79:373–374

37. Cully J, Teten A. *A therapist's guide to brief cognitive behavioral therapy*. Department of Veterans Affairs, South Central MIRECC, Houston, TX, 2008

38. Thorn BE. *Cognitive therapy for chronic pain: a step-by-step approach*. Guilford Publications, NY, 2004

39. Aspinwall LG, Taylor SE. A stitch in time: self-regulation and proactive coping. *Psychol Bull* 1997, 121:417–436, doi: 10.1037/0033-2909.121.3.417

40. Hobfoll SE. Conservation of resources: A new attempt at conceptualizing stress. *Am Psychol* 1989, 44:513–524, doi: 10.1037/0003-066X.44.3.513

41. IBM SPSS Statistics for Windows, Version 25.0. IBM Corp. Armonk, NY

42. World Health Organization. *International statistical classification of diseases and related health problems* (*ICD-11*). World Health Organization, Geneva, 2019. Available from: http://icd.who.int/browse11/l-m/en

43. Butler D, Moseley L. *Explain pain*. NOI Group, Adelaide, SA,2008

44. Caudill MA. Managing pain before it manages you. Guilford Publications, NY, 2002

45. Reynolds F, Prior S. "A lifestyle coat-hanger": A phenomenological study of the meanings of artwork for women coping with chronic illness and disability. *Disabil Rehabil* 2003, 25:785–794, doi: 10.1080/0963828031000093486

46. Shapiro B. All I have is pain: Art therapy in an inpatient chronic pain relief unit. *Am J Art Ther* 1985, 24:44–48

47. Saunders C, Clark D. *Cicely Saunders*. Oxford University Press, 2006, doi: 10.1093/acprof:oso/9780198570530.001.0001

48. Kearsley JH. The therapeutic use of self and the relief of suffering. *Cancer Forum* 2010, 34:98–101

49. Sensky T. Suffering. *Int J Integr Care* 2010, 10, doi: 10.5334/ijic.494

50. Sturgeon JA, Zautra AJ. State and trait pain catastrophizing and emotional health in rheumatoid arthritis. *Ann Behav Med* 2013, 45:69–77, doi: 10.1007/s12160-012-9408-z

51. Hayes SC, Hofmann SG. The third wave of CBT and the rise of process-based care. *World Psychiatry* 2017, 16:245–246, doi: 10.102/wps.20442

52. Keyes CLM. Promoting and protecting mental health as flourishing: a complementary strategy for improving national mental health. *Am Psychol* 2007, 62:95–108, doi: 10.1037/0003-066X.62.2.95

53. Katz PP, Neugebauer A. Does satisfaction with abilities mediate the relationship between the impact of rheumatoid arthritis on valued activities and depressive symptoms? *Arthritis Care Res* 2001, 45:263–269, doi: 10.1002/1529-0131(200106)45:3

54. Ditto PH, Druley JA, Moore KA, Danks JH, Smucker WD. Fates worse than death: the role of valued life activities in health-state evaluations. *Health Psychol* 1996, 15:332–343, doi: 10.1037/0278-6133.15.5.332

55. Sivik T, Schoenfeld R. Psychosomatic integrated treatment and rehabilitation. *Adv Mind Body Med* 2005, 21:55–58, PMID: 20671349

56. Henare D, Hocking C, Smythe L. Chronic pain: Gaining understanding through the use of art. *Br J Occup Ther* 2003, 66:511–518, doi: 10.1177%2F030802260306601104

57. Oswald D, Sherratt F, Smith S. Handling the Hawthorne effect: the challenges surrounding a participant observer. *Rev Soc Sci* 2014, 1:53–73, doi: 10.21586/ROSS0000004

Ερευνητική εργασία

Αποτελεσματικότητα μιας συνδυασμένης Γνωσιακής-Εικαστικής Παρέμβασης σε ασθενείς με χρόνιο πόνο καλοήθους αιτιολογίας

Ασημίνα Καλμαντή,[1,3] Χρυσάνθη Μπατιστάκη,[2] Χρήστος Χριστοδούλου,[1] Γεωργία Γερολουκά-Κωστοπαναγιώτου,[2] Αθανάσιος Δουζένης,[1] Ιωάννης Μιχόπουλος[1,4]

[1]*Β΄ Ψυχιατρική Κλινική, Ιατρική Σχολή, Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών, ΠΓΝ «ΑΤΤΙΚΟΝ», Αθήνα*

[2]*Β΄ Κλινική Αναισθησιολογίας-Μονάδα Διαχείρισης Πόνου, Ιατρική Σχολή, Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών, ΠΓΝ «ΑΤΤΙΚΟΝ», Αθήνα*

[3]*Τμήμα Εργοθεραπείας, Σχολή Επιστημών Υγείας και Πρόνοιας, Πανεπιστήμιο Δυτικής Αττικής, Αθήνα*

[4]*Ελληνική Εταιρεία Γνωσιακών Ψυχοθεραπειών*

ΙΣΤΟΡΙΚΟ ΑΡΘΡΟΥ: Παραλήφθηκε 10 Ιουνίου 2021/Αναθεωρήθηκε 20 Ιουλίου 2021/Δημοσιεύθηκε Διαδικτυακά 21 Φεβρουαρίου 2022

ΠΕΡΙΛΗΨΗ

Ως Χρόνιος Πόνος (ΧΠ) ορίζεται αυτός, που έχει διάρκεια μεγαλύτερη των 3–6 μηνών ή ο πόνος που επανεμφανίζεται ανά τακτά χρονικά διαστήματα και αποτελεί από μόνος του μία ξεχωριστή νόσο. Σύμφωνα με μελέτες εμφανίζεται στο 20% του γενικού πληθυσμού παγκοσμίως και μπορεί να οδηγεί σε κατάθλιψη, άγχος, προβλήματα ύπνου, κακή ποιότητα ζωής και δαπανηρές θεραπείες. Σήμερα, η Γνωσιακή Συμπεριφορική Θεραπεία (ΓΣΘ), ως η πιο καλά τεκμηριωμένη ψυχοθεραπευτική παρέμβαση αποτελεί βάση για ερευνητικό και κλινικό έργο, ωθώντας το άτομο σε πιο λειτουργικά μοντέλα σκέψεων και συμπεριφορών. Σχεδιάστηκε μία δομημένη ομαδική παρέμβαση 10 εβδομαδιαίων συνεδριών, με ενισχυμένη ΓΣΘ για ΧΠ και την Εικαστική θεραπεία ως συμπληρωματικές, με προσανατολισμό στις ψυχοκοινωνικές διαστάσεις του ΧΠ, υιοθετώντας σύγχρονα δεδομένα διαχείρισης του πόνου. Ο σκοπός της μελέτης είναι να διερευνηθεί η επίδραση αυτής της παρέμβασης στη θετική διαχείριση του ΧΠ καλοήθους αιτιολογίας. Συμμετείχαν 100 εξωτερικοί ασθενείς, οι οποίοι παρακολουθούνται στη Μονάδα Πόνου της Β΄ Πανεπιστημιακής Κλινικής Αναισθησιολογίας στο ΠΓΝ «ΑΤΤΙΚΟΝ», οι οποίοι χωρίστηκαν σε 50 άτομα στην ομάδα παρέμβασης και 50 άτομα στην ομάδα ελέγχου (συνήθης θεραπεία). Η ανάλυση της κλινικής μελέτης παρέμβασης με προέλεγχο - μετέλεγχο ανέδειξε οφέλη σε πολλές διαστάσεις που αξιολογήθηκαν με κλίμακες, όπως η επίπτωση του πόνου στη λειτουργικότητα (Ελληνικό Συνοπτικό Ερωτηματολόγιο Πόνου-BPI), η υποκειμενική αντίληψη του ψυχικού πόνου (Κλίμακα ψυχικού πόνου Orbach και Mikulincer), η ανοχή του ψυχικού πόνου (Ερωτηματολόγιο ανοχής του ψυχικού πόνου Orbach και Mikulincer), τα επίπεδα του άγχους και της κατάθλιψης (Νοσοκομειακή Κλίμακα Άγχους και Κατάθλιψης-HADS) και η συνολική εκτίμηση της ποιότητας ζωής (Ερωτηματολόγιο Ποιότητας Ζωής του Παγκόσμιου Οργανισμού Υγείας-WHOQOL-BREF). Η μέση ηλικία των συμμετεχόντων ήταν τα 52,3 έτη και οι γυναίκες ήταν περισσότερες (84%). Τα ευρήματα της μελέτης δείχνουν στατιστικά σημαντική μείωση στην ένταση του σωματικού πόνου ($p<0,001$), στα καταθλιπτικά συμπτώματα ($p<0,001$), στη σύγχυση σχετικά με τον πόνο ($p=0,037$), καθώς και βελτίωση στην ανοχή του ψυχικού πόνου ($p=0,012$) και την αντιλαμβανόμενη ποιότητα ζωής ($p<0,001$) στην ομάδα παρέμβασης. Η παρούσα μελέτη ενισχύει την κλινική χρησιμότητα μίας ψυχοκοινωνικής θεραπευτικής παρέμβασης που περιλαμβάνει δημιουργικές και γνωσιακές τεχνικές, με στόχο την ολιστική διαχείριση του ΧΠ καλοήθους αιτιολογίας με καινοτόμες προσαρμοστικές και λειτουργικές στρατηγικές.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: Χρόνιος πόνος, Γνωσιακή Συμπεριφορική Θεραπεία για Χρόνιο Πόνο, εικαστική θεραπεία, ψυχικός πόνος, ποιότητα ζωής.

Συγγραφέας επικοινωνίας: Ασημίνα Καλμαντή, Β΄ Ψυχιατρική Κλινική, Ιατρική Σχολή, Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών, ΠΓΝ «ΑΤΤΙΚΟΝ», Ρίμινι 1, GR-124 62 Αθήνα, Διεύθυνση e-mail: minakalm@gmail.com

https://doi.org/10.22365/jpsych.2022.063 / Psychiatriki 2022, 33:200–209

Research article

Psychometric properties of the Greek version of Affective Lability Scale - Short Form (ALS-18) in a sample of adults with neurodevelopmental disorders

Eva Kalantzi, Artemios Pehlivanidis, Kalliopi Korobili, Vasilis Mantas, Charalabos Papageorgiou

Unit for Adult Neurodevelopmental Disorders, First Department of Psychiatry, National and Kapodistrian University of Athens, Eginition Hospital, Athens, Greece

ARTICLE HISTORY: Received 12 July 2021/Revised 15 September 2021/Published Online 21 February 2022

ABSTRACT

Affective dysregulation refers to maladaptive patterns of emotional regulation that impair daily life functioning, common in many psychiatric disorders. It is expressed with the form of affective lability, an emotional construct composed of frequent and intense fluctuations in emotion in response to both pleasant and unpleasant events or the interpretations of events. The Affective Lability Scale (ALS) is a widely used self-reporting questionnaire, that measures the tendency of emotions to shift from one to another, as well as their tendency to oscillate between depression and elation and between depression and anxiety. The original scale had 54 items, but a shorter form of 18-items (ALS-18) was created, with three domains: anxiety–depression shift, depression–elation shift and anger shift. The aim of the present study was to evaluate the psychometric properties of the ALS-18 Greek version. The translation was conducted by two of the authors. The study took place in the 1st Department of Psychiatry of the National and Kapodistrian University of Athens at Eginition hospital. A sample of 108 adults was included in the survey divided into two groups, neurodevelopmental disorder group (NDD: attention deficit hyperactivity disorder or autism spectrum disorder) and control group. They all completed ALS-18, The State – Trait Anxiety Inventory (STAIT), Difficulties in Emotion Regulation Scale (DERS), The Hospital Anxiety and Depression Scale (HADS). The ALS-18 had satisfactory internal consistency; Cronbach's α value was 0.91 for the total scale and 0.89 for Anxiety/Depression, 0.86 for Depression/Elation and 0.85 for Anger. The three-factor structure was replicated in our data. The internal consistency and reliability of all the ALS-18 factors in our study could be considered satisfactory with a Cronbach's alpha coefficient of 0.85 or above for all factors. Significantly higher mean values were found for all the subscales, Anxiety/Depression, Depression/Elation and Anger, in NDD subjects as compared to controls, showing good discriminative ability. The ALS factors discriminated well between clinical and non-clinical samples. The present study reveals that the Greek version of ALS-18 presents good psychometric properties, showing good internal consistency and reliability, as well as concurrent and discriminative validity. It has an elevated score in NDD and thus, our results indicate that affective lability could and maybe should, be a target integrated in therapeutic strategies.

KEYWORDS: Affective Lability Scale, ALS-18, affective lability, Greek, psychometric properties, neurodevelopmental disorders.

Introduction

Affective dysregulation refers to maladaptive patterns of emotional regulation that impair daily life functioning.[1] It is common in many psychiatric disorders – namely, depression,[2] anxiety disorders,[3] attention deficit hyperactivity disorder (ADHD),[4] autism spectrum disorder (ASD),[5] borderline personality disorder[6] – with the form of affective instability. That is an emotional feature that can be expressed with affective lability (AL), a construct composed of frequent and intense fluctuations in emotion in response to both pleasant and unpleasant events or the interpretations of events.[7] It is associated with poorer clinical outcomes and increased use of antipsychotic and

Corresponding author: Eva Kalantzi, First Department of Psychiatry, National and Kapodistrian University of Athens, Eginition Hospital, 72–74 Vas. Sophias Ave., GR-115 26 Athnes, Greece • e-mail: kalantzieva@yahoo.gr

non-antipsychotic mood stabilizer therapy, regardless of the mental disorder with which an individual initially presents.[8] Although frequent, it is measured in several ways that may lead to confusion. It is not always found as a core symptom, but it is often met as a "component" that plays a significant role in the clinical expression of many psychiatric disorders. The National Institute of Mental Health has proposed a dimensional framework for research, the Research Domain Criteria (RDoC)[9] and Affective Lability is proposed as the sixth domain of the matrix, being a regulatory factor for the expression of the initial five.[10]

In order to measure AL, Harvey et al[11] developed the Affective Lability Scale (ALS). It is a 54-item scale in which people rate their agreement with statements regarding the tendency of their mood to shift between what they consider normal mood to the affective domains of anger, depression, elation, and anxiety as well as their tendency to oscillate between depression and elation and between depression and anxiety. Items were created to tap into subjective experiences, physiological perceptions and behaviors, using six subscales.[11] Recognizing that this self-report measure is lengthy, Oliver and Simons[12] created an 18-item short form (ALS-18) of the 54 item ALS. Factor analysis has confirmed good fit in a non-clinical sample for three domains in the ALS-18: anxiety–depression shift (AD, five items), depression–elation shift (DE, eight items), and anger shift (Ang, five items).

Neurodevelopmental disorders (NDD) are a group of conditions with onset in the developmental period. The disorders typically manifest early in development, often before the child enters grade school and are characterized by developmental deficits that produce impairments of personal, social, academic, or occupational functioning. The two most common neurodevelopmental disorders are attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). ADHD and ASD often co-occur.[13,14] Schizophrenia and bipolar disorder are not included in NDD.[15,16]

The emotional dimension in ADHD, although recognized for years,[17] is still not considered in the core diagnostic criteria for the disorder.[15] AL is considered as an important associate feature of ADHD.[18,19] ADHD is a common example of developmental psychopathology that, although typically studied through the lens of cognitive control, might be better understood by taking an emotion regulation perspective.[20] Samson et al[21] support that there is a relationship between all the core features of autism and emotion dysregulation.

Given that the ALS-18 was created using responses from a non-clinical sample of undergraduate students, Look et al,[22] aimed to evaluate the structure and construct validity of the ALS-18 in a sample that included people with DSM-IV Axis II personality disorders and healthy control participants, by comparing them in clusters and not by differentiating them according to specific diagnosis. They evaluated and showed the utility of this short form in a clinical sample that included people with impairment associated with AL. Weibel et al[23] demonstrated a good validity of ALS-18 in measuring affective lability in adult ADHD patients, a clinical group defined by attentional and hyperactive symptoms, but in which emotional dysregulation is also an important feature. Aas et al[24] found differentiation in ALS scores between bipolar patients from relatives and healthy controls. These three studies, showed that ALS has a good discriminant validity in differentiating clinical sample groups and healthy controls, making it a useful tool. The ALS has good internal consistency and is also the most frequently used measure having been used in almost all clinical diagnostic groups.[25]

Based on the existing studies, as well as on the fact that there is no proposed threshold or cut-off point that AL becomes pathological, it is possible that it exists as a continuum from normal to pathological.[24] The above mentioned good discriminant validity of ALS remains even when healthy controls are compared to a group of conditions and not only to a single disorder, such as the psychosis spectrum disorders.[26] According to Thomson emotion dysregulation is a transdiagnostic element of affective psychopathology.[27] Emotion regulation deficits are found in children with ASD and ADHD, suggesting that emotion regulation may be a transdiagnostic feature in neurodevelopmental disorders. Waddington[28] compared emotion regulation in ASD+ADHD, ASD-only, and ADHD-only groups and they did not significantly differ from each other on emotion recognition factors. The ASD+ADHD more strongly deviated from the controls than the non-comorbid groups. These findings suggest that emotion recognition is an overlapping feature for ASD and ADHD. In a recent review Mason[29] also found evidence that emotion regulation constitutes a transdiagnostic feature in the two common neurodevelopmental disorders, ADHD and ASD.[30] The purpose of this study was to evaluate, for the first time, the psychometric properties of the Greek version of ALS-18, when used in a clinical sample of adult normal intelligent, neurodevelopmental population, so as to provide a useful tool for clinical and research purposes in assessing affective lability in this population, in comparison to healthy controls.

Material and Method

Participants

A sample of 108 adults was included in the survey divided in two groups: one consisting of 91 adults with neurodevelopmental disorder (NDD), ADHD or ASD, with 61.5% being men and 38.5% women and mean age 28.8 years and another group consisting of 17 controls with 29.4% being men and 70.6% women and mean age 41.5 years (table 1).

The study was part of a larger research project on de novo diagnosed adults with ADHD and ASD.[13] The multi-disciplinary team that carries out all assessments consists of psychiatrists who have extended experience in the diagnosis and treatment of NDD in adults and are trained in Autism Diagnostic Observation Schedule (ADOS),[31,32] Autism Diagnostic Interview-Revised (ADI-R)[32,33] and Diagnostic Interview for ADHD in Adults (DIVA)[34] and clinical psychologists. In order to be included in the study subjects had to be adults with normal intelligence and fluent phrase/speech and to be assessed for the first time in their life for a possible ADHD and/or ASD diagnosis. Exclusion criteria were a previous ADHD and/or ASD diagnosis, the presence of acute psychopathology requiring urgent psychiatric treatment, current substance abuse disorder, IQ<70 according to WAIS and a known genetic cause. Diagnosis regarding the presence of ADHD and/or ASD is given during a consensus meeting of the multidisciplinary team and is based on DSM-5 criteria, while taking into consideration all available information. Written informed consent was obtained from all participants and the study was approved by the scientific and ethics committee of the University of Athens.

Measurements

The ALS was administered along with other measures, which are reported in detail below.

ALS-18

The Affective Lability Scale - Short Form (ALS-18) comprises a three-factor model of affective lability, measuring rapid changes from euthymic mood to other emotional states including elation, depression, and anger. It is generally assumed to measure aspects of temperament. Participants are asked to indicate how well each item describes their feelings over the past week on a scale of very undescriptive of me, rather undescriptive, rather descriptive, very descriptive of me (scored 0 to 3). In addition to having a total score (ranging from 0–54), the ALS-18 has three subscale scores: Anxiety/Depression (ranging from 0–15), Depression/Elation (ranging from 0–24) and Anger (ranging from 0–15), with each factor retaining at least two items from each of the original six scales of the ALS and it has been shown to correlate highly with the original ALS total score. Two fluent English-speaking researchers adapted the present version of the questionnaire from the original English version using the back-translation procedure. A written permission to adapt ALS-18 to the Greek language was given by the authors of the original scale.

The following scales were also administered in order to examine the validity of the Greek version of ALS-18.

The State – Trait Anxiety Inventory (STAIT)[35]

STAI-X2 is a self-report measure assessing anxiety as a state condition and anxiety as a trait characteristic, that consists of 40 questions on a 4-point Likert Scale. In our

Table 1. Sample characteristics.

	Total	NDD (N=91, 84.3%)	Control (N=17, 15.7%)		
	N (%)	N (%)	N (%)	Test statistic (df)	p
Gender					
Males	61 (56.5)	56 (61.5)	5 (29.4)	6.02 (1)	0.014[+]
Females	47 (43.5)	35 (38.5)	12 (70.6)		
Age (years), mean (SD)	31.1 (10.3)	28.8 (8.1)	41.5 (12.8)	–5.22 (93)	0.001[‡]
Educational status					
High school	20 (20.2)	18 (22)	2 (11.8)	5.97 (3)	0.104[++]
Technical college	14 (14.1)	11 (13.4)	3 (17.6)		
University	45 (45.5)	40 (48.8)	5 (29.4)		
Other	20 (20.2)	13 (15.9)	7 (41.2)		

[+]Pearson's chi-square; [++]Fisher's exact test; [‡]Student's t-test

study we used the second part of the inventory, regarding the trait characteristics. The STAI Greek version has good psychometric qualities and is widely used.[36]

Difficulties in Emotion Regulation Scale (DERS)[37]

DERS was designed to assess emotion dysregulation multi-dimensionally. Six dimensions were created that underline the DERS: Difficulty accepting emotion responses (Acceptance), lack of emotional awareness (Awareness), limited access to emotion regulation strategies (Strategies), difficulties engaging in goal directed behavior when emotionally aroused (Goals), impulse control difficulties (Impulse) and lack of emotional clarity (Clarity). The Greek version of the DERS, which demonstrated adequate reliability as evidenced in both internal consistency and test-retest stability comparable to the original scale, was used.[38]

The Hospital Anxiety and Depression Scale (HADS)[39]

HADS is widely used in several countries to assess anxiety and depression. It consists of 14 questions, with four possible answers (0–3) and a total score 0–42. The Greek version of HADS shows good psychometric properties in assessing anxiety and depression in general hospital patients.[40]

Statistical analysis

The statistical analysis was conducted using SPSS and AMOS (SPSS, Chicago, IL, USA) Statistical Software programs and statistically significant level was set at 0.05.

A confirmatory factor analysis (CFA) with maximum likelihood procedure was performed in order to confirm the model of ALS. The variance of the latent constructs was fixed at one during parameter estimation. The fit of the CFA model was assessed using the comparative fit index (CFI), the goodness of fit index (GFI) and the root mean square error of approximation (RMSEA). For the CFI and GFI indices, values close to or greater than 0.95 were taken to reflect a good fit to the data. RMSEA values of less than 0.05 indicate a good fit and values as high as 0.08 indicate a reasonable fit. The internal consistency of the questionnaire was analyzed with Cronbach's alpha. Reliability equal to or greater than 0.70 was considered acceptable. Pearson correlations coefficients were used to explore the association among the ALS subscales. Correlation coefficient between 0.1 and 0.3 were considered low, between 0.31 and 0.5 moderate and those over 0.5 were considered high. For the comparison of proportions chi-square and Fisher's exact tests were used. Independent samples Student's t-tests were used for the comparison of mean values between the two groups. P values reported are two-tailed.

Results

Participant characteristics

Females were 56 (61.5%) among the 91 participants of the NDD group and 5 (29.4%) among the 17 participants who constituted the control group (p= 0.014). The mean age of the NDD group was 31,3 years while for the controls was 41.5 years (p=0.001). The two groups showed no difference in the educational level (p=0.104) (table 1).

Psychometric properties of ALS

Internal consistency

Corrected item-total correlations and Cronbach's alpha if an item was deleted per factor are presented in table 2. All corrected item-total correlations were high, between 0.70–0.75 for Anxiety/Depression, between 0.49–0.74 for Depression/Elation and between 0.53–0.73 for Anger. Internal consistency reliability was accepted with Cronbach's alpha equal to 0.89 for Anxiety/Depression, 0.86 for Depression/Elation and 0.85 for Anger. Cronbach's alpha for the whole questionnaire was equal to 0.91. The alpha, if item deleted, was also computed for each item and there was no item that reduced the reliabilitythat was between 0.86–0.87 for Anxiety/Depression, between 0.83–0.86 for Depression/Elation and between 0.80–0.85 for Anger. Therefore, there were no problematic items with respect to internal consistency and the scale can be considered sufficiently reliable.

Factor analysis

A CFA was conducted to estimate if the model fitted the data well. The CFA indicated an adequate fit of the three-factor model (RMSEA=0.079, CFI=0.969 and GFI=0.958). None of the item cross loadings exceeded the item loadings on the intended latent construct.

The intercorrelations of the ALS subscales were Anxiety/Depression - Depression/Elation: 0.67, Anxiety/Depression – Anger: 0.83, Depression/Elation – Anger: 0.60. All subscales were significantly and positively correlated with each other and the correlations were above 0.6 and higher.

Concurrent validity

Association of ALS subscales with DERS dimensions are presented in table 3. Anxiety/Depression, Depression/Elation and Anger were positively correlated with all DERS subscales, except for lack of emotional awareness. The correlation coefficients ranged from low to high.

Table 2. Corrected Item-Total Correlations, internal consistency reliability and means of the ALS factors.

	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted	Cronbach's Alpha	Mean (SD)
Anxiety/depression			0.89	6.93 (4.26)
Item 1	0.70	0.87		
Item 3	0.75	0.86		
Item 5	0.73	0.86		
Item 6	0.71	0.87		
Item 7	0.75	0.86		
Depression/elation			0.86	9.84 (5.76)
Item 2	0.53	0.86		
Item 10	0.64	0.84		
Item 12	0.74	0.83		
Item 13	0.49	0.86		
Item 15	0.65	0.84		
Item 16	0.69	0.84		
Item 17	0.63	0.85		
Item 18	0.52	0.86		
Anger			0.85	5.10 (3.95)
Item 4	0.67	0.82		
Item 8	0.71	0.81		
Item 9	0.73	0.80		
Item 11	0.67	0.82		
Item 14	0.53	0.85		

ALS: Affective Lability Scale

Table 3. Pearson's correlation coefficients of ALS subscales with DERS questionnaire.

	Anxiety/depression	Depression/elation	Anger
Nonacceptance of emotional responses	0.54***	0.48***	0.44***
Difficulty engaging in goal-directed behavior	0.56***	0.540***	0.53***
Impulse control difficulties	0.63***	0.40***	0.66***
Lack of emotional awareness	–0.09	–0.03	0.058
Limited access to emotion regulation strategies	0.63***	0.46***	0.57***
Lack of emotional clarity	0.27**	0.30**	0.37***
Total DERS score	0.68***	0.52***	0.68***

*p<0.05, **p<0.01, ***p<0.001, ALS: Affective Lability Scale, DERS: Difficulties in Emotion Regulation Scale

Convergent validity

Higher values in HADS subscales or in STAI were significantly associated with higher values in all ALS subscales (table 4).

Discriminative validity

Table 5 shows a comparison of all ALS subscales between subjects with NDD and controls. Significantly higher mean values were found for all the subscales, Anxiety/Depression, Depression/Elation and Anger, in NDD subjects as compared to controls, showing good discriminative ability.

Discussion

The study included adult patients with NDD (ADHD and high functioning ASD) and normal controls, in order to assess the usefulness of the Greek translation of the ALS-18. The ALS-18 had satisfactory internal consistency;

Table 4. Pearson's correlation coefficients of ALS subscales with HADS and STAI questionnaires.

	Anxiety/depression (ALS-18)	Depression/elation (ALS-18)	Anger (ALS-18)
Depression (HADS-14)	0.47	0.35	0.40
Anxiety (HADS-14)	0.50	0.38	0.42
STAI	0.69	0.60	0.59

All correlation coefficients were significant with p<0.001, ALS: Affective Lability Scale, HADS: The Hospital Anxiety and Depression Scale, STAI: The State – Trait Anxiety Inventory

Table 5. Comparison of ALS subscales between subjects with NDD and controls.

	Group					
	NDD		Control			
	Mean	SD	Mean	SD	t (df)	p
Anxiety/depression	7.54	4.27	3.65	2.23	3.65 (106)	<0.001
Depression/elation	11.04	5.41	3.41	2.18	5.71 (106)	<0.001
Anger	5.54	4.08	2.76	1.99	2.74 (106)	0.007

ALS: Affective Lability Scale, NDD: Neurodevelopmental Disorder

Cronbach's alpha value was 0.91 for the total scale and 0.89 for Anxiety/Depression, 0.86 for Depression/Elation and 0.85 for Anger. The three-factor structure was replicated in our data. The internal consistency and reliability of all the ALS-18 factors in our study could be considered satisfactory with a Cronbach's alpha coefficient of 0.85 or above for all factors. In the original ALS-18 the average alpha coefficient for the three factors was 0.83 while the overall total scale alpha coefficient was 0.90.[12]

The item-subscale correlations were moderate to high; from 0.49 to 0.75, with the majority being above 0.6, results that are consisted to previous literature. All subscales were significantly and positively correlated with each other and the correlations were above 0.6 and higher. In the original scale the factors were moderately correlated (from 0.49 [depression/elation–anger] to 0.59 [depression/anxiety–depression/elation]).[12]

Correlations with the DERS subscales were positive except for lack of emotional awareness subscale, whose correlations with the ALS-18 were weak. The correlation coefficients ranged from low (lack of emotional clarity) to high. This indicates that ALS and DERS are probably dependent, but in a complex way. This is similar to the findings of the Italian version of the scale, where the weakest correlation was with awareness, followed by clarity.[41]

The correlations of ALS with STAI and HADS scores were positive (moderate to high), with anxiety having slightly higher correlation than depression. Co-occurring anxiety and/or depression is a normal finding among both patients asking for an NDD diagnosis[14] and among depressive and/or anxious psychiatric outpatients diagnosed with ADHD.[42]

To evaluate the utility of the ALS-18 in a clinical sample, the ALS-18 total and subscales scores were compared across the two groups (NDD, HC). Results indicated that the groups differed on the total score and on each subscale. The ALS factors discriminated well between non-clinical and clinical sample, as shown before by Look[22] and Weibel.[23]

Our study has strengths and limitations. We cannot make causal attributions about the associations between the clinical variables and elevated AL due to the mixed population (ADHD and ASD) of the study group, although the NDD group was homogenous in many aspects like intellectual ability, functionality and years of education, with the vast majority having over 15 years of education. An investigation of potential differences in AL between the different diagnoses of ADHD and ASD groups would have been informative, but this was not possible due to the small sample group sizes. There is a need for the results to be replicated in larger samples. The small number of healthy controls, resulting in heterogeneity in demographics between the two study groups, should be considered as a limitation of the study. Future study aiming to assess the utility of the Greek of ALS-18 translation among different diagnostic categories should have a larger number of participants. Nevertheless, although the number of healthy controls was low, our results indicate that there is statistically significant difference between the scores of the two groups in all subscales (as in the aforementioned studies).

Conclusion

The present study reveals that the Greek version of ALS-18 exhibits good psychometric properties, showing good internal consistency and reliability as well as concurrent and discriminative validity. It has an elevated score in NDD and thus, our results indicate that affective lability could and maybe should, be a target integrated in therapeutic strategies (pharmacological or psychotherapeutic) in ADHD or ASD patients. Symptoms of ADHD and ASD often overlap. It is important to have trait-based dimensions when trying to discriminate adults with ADHD, ASD, or co-occurring ADHD/ASD.[13] In future research the possible differences in ALS scores between ADHD and ASD patients should be studied. The use of ALS may constitute another useful tool and facilitate differential diagnosis in the NDD population.

References

1. Carver CS, Lawerence JW, Scheier MF. A control-process perspective on the origins of affect. In L.L. Martin & A. Tesser (ed) *Striving and feeling: Interactions among goals, affect, and self-regulation*. Lawrence Erlbaum Associates, New Jersey, 1996.
2. Bowen RC, Mahmood J, Milani A, Baetz M. Treatment for depression and change in mood instability. *J Affect Disord* 2011, 128:171–174, doi: 10.1016/j.jad.2010.06.040
3. Bowen RC, Clark M, Baetz M. Mood swings in patients with anxiety disorders compared with normal controls. *J Affect Disord* 2004, 78:185–192, doi: 10.1016/S0165-0327(02)00304-X
4. Skirrow C, McLoughlin G, Kuntsi J, Asherson P. Behavioral, neurocognitive and treatment overlap between attention-deficit/hyperactivity disorder and mood instability. *Expert Rev Neurother* 2009, 9:489–503, doi: 10.1586/ern.09.2
5. Simonoff E, Jones CR, Pickles A, Happé F, Baird G, Charman T. Severe mood problems in adolescents with autism spectrum disorder. *J Child Psychol Psychiatry* 2012, 53:1157-1166, doi: 10.1111/j.1469-7610.2012.02600.x
6. Silvers J, Hubbard A, Biggs E, Shu J, Fertuck E, Chaudhury S et al. Affective lability and difficulties with regulation are differentially associated with amygdala and prefrontal response in women with Borderline Personality Disorder. *Psychiatry Res Neuroimaging* 2016, 254:74-82, doi: 10.1016/j.pscychresns.2016.06.009
7. Thompson RJ, Berenbaum H, Bredemeier K. Cross-sectional and longitudinal relations between affective instability and depression. *J Affect Disord* 2011, 130:53–59, doi: 10.1016/j.jad.2010.09.021
8. Patel R, Lloyd T, Jackson R, Ball M, Shetty H, Broadbent M et al. Mood instability is a common feature of mental health disorders and is associated with poor clinical outcomes. *BMJ Open* 2015, 5:e007504, doi: 10.1136/bmjopen-2014-007504
9. Insel T, Cuthbert B, Garvey M, Heinssen R, Kozak M, Pine DS et al. Research Domain Criteria (RDoC): Toward a new classification framework for research on mental disorders. *Am J Psychiatry* 2010, 167:748-751, doi: 10.1176/appi.ajp.2010.09091379
10. Fernandez KC, Jazaieri H, Gross JJ. Emotion Regulation: A Transdiagnostic Perspective on a New RDoC Domain. *Cognit Ther Res* 2016, 40:426–440, doi: 10.1007/s10608-016-9772-2
11. Harvey PD, Greenberg BR, Serper MR. The affective lability scales: development, reliability, and validity. *J Clin Psychol* 1989, 45:786-793, doi: 10.1002/1097-4679(198909)45:5<786:aid-jclp2270450515>3.0.co;2-p
12. Oliver M, Simons J. The affective lability scales: Development of a short-form measure. *Pers Individ Dif* 2004, 37:1279–1288, doi: 10.1016/j.paid.2003.12.013
13. Pehlivanidis A, Papanikolaou K, Korobili K, Kalantzi E, Mantas V, Pappa D et al. Trait-Based Dimensions Discriminating Adults with Attention Deficit Hyperactivity Disorder (ADHD), Autism Spectrum Disorder (ASD) and Co-occurring ADHD/ASD. *Brain Sci* 2020, 11:18, doi:10.3390/brainsci11010018
14. Pehlivanidis A, Papanikolaou K, Mantas V, Kalantzi E, Korobili K, Xenaki LA et al. Lifetime co-occurring psychiatric disorders in newly diagnosed adults with attention deficit hyperactivity disorder (ADHD) or/and autism spectrum disorder (ASD). *BMC Psychiatry* 2020, 20:423, doi: 10.1186/s12888-020-02828-1
15. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 5th ed. American Psychiatric Publishing, Arlington, VA, 2013
16. World Health Organization. *International statistical classification of diseases and related health problems*. 11th ed. World Health Organization, Geneva, 2020. Available from https://icd.who.int/en
17. Wender PH, Reimherr FW, Wood DR. Attention deficit disorder (minimal brain dysfunction) in adults. A replication study of diagnosis and drug treatment. *Arch Gen Psychiatry* 1981, 38:449–456, doi: 10.1001/archpsyc.1981.01780290083009
18. Skirrow C, Ebner-Priemer U, Reinhard I, Malliaris Y, Kuntsi J, Asherson P. Everyday emotional experience of adults with attention deficit hyperactivity disorder: evidence for reactive and endogenous emotional lability. *Psychol Med* 2014, 44:3571–3583, doi: 10.1017/S0033291714001032
19. Shaw P, Stringaris A, Nigg J, Leibenluft E. Emotion dysregulation in attention deficit hyperactivity disorder. *Am J Psychiatry* 2014, 171:276–293, doi: 10.1176/appi.ajp.2013.13070966
20. Martel MM. Research review: a new perspective on attention-deficit/hyperactivity disorder: emotion dysregulation and trait models. *J Child Psychol Psychiatry* 2009, 50:1042–1051, doi: 10.1111/j.1469-7610.2009.02105.x
21. Samson AC, Phillips JM, Parker KJ, Shah S, Gross JJ, Hardan AY. Emotion dysregulation and the core features of autism spectrum disorder. *J Autism Dev Disord* 2014, 44:1766–1772, doi: 10.1007/s10803-013-2022-5
22. Look AE, Flory JD, Harvey PD, Siever LJ. Psychometric properties of a short form of the Affective Lability Scale (ALS-18). *Pers Individ Dif* 2010, 49:187–191 doi: 10.1016/j.paid.2010.03.030
23. Weibel S, Micoulaud-Franchi JA, Brandejsky L, Lopez R, Prada P, Nicastro R et al. Psychometric Properties and Factor Structure of the Short Form of the Affective Lability Scale in Adult Patients With ADHD. *J Atten Disord* 2019, 23:1079–1089, doi: 10.1177/1087054717690808
24. Aas M, Pedersen G, Henry C, Bjella T, Bellivier F, Leboyer M et al. Psychometric properties of the Affective Lability Scale (54 and 18-item version) in patients with bipolar disorder, first-degree relatives, and healthy controls. *J Affect Disord* 2015, 172:375–380, doi: 10.1016/j.jad.2014.10.028
25. Marwaha S, He Z, Broome M, Singh SP, Scott J, Eyden J et al. How is affective instability defined and measured? A systematic review. *Psychol Med* 2014, 44:1793–1808, doi: 10.1017/S0033291713002407

26. Høegh MC, Melle I, Aminoff SR, Laskemoen JF, Büchmann CB, Ueland T et al. Affective lability across psychosis spectrum disorders. *Eur Psychiatry* 2020, 63:e53, doi: 10.1192/j.eurpsy.2020.44

27. Thompson RA. Emotion dysregulation: A theme in search of definition. *Dev Psychopathol* 2019, 31:805-815, doi: 10.1017/S0954579419000282.

28. Ros R, Graziano PA. A Transdiagnostic Examination of Self-Regulation: Comparisons Across Preschoolers with ASD, ADHD, and Typically Developing Children. *J Clin Child Adolesc Psychol* 2020, 49:493–508, doi: 10.1080/15374416.2019.1591280.

29. Waddington F, Hartman C, de Bruijn Y, Lappenschaar M, Oerlemans A, Buitelaar J et al. Visual and auditory emotion recognition problems as familial cross-disorder phenomenon in ASD and ADHD. *Eur Neuropsychopharmacol* 2018, 28:994–1005, doi: 10.1016/j.euroneuro.2018.06.009.

30. England-Mason G. Emotion Regulation as a Transdiagnostic Feature in Children with Neurodevelopmental Disorders. *Curr Dev Disord Rep* 2020, 7:130–138, doi: 10.1007/s40474-020-00200-2.

31. Lord C, Rutter M, DiLavore PC, Risi S, Gotham K, Bishop SL. *Autism diagnostic observation schedule*. 2nd ed. Western Psychological Services, Torrance, CA, 2012

32. Papanikolaou K, Paliokosta E, Houliaras G, Vgenopoulou S, Giouroukou E, Pehlivanidis A et al. Using the Autism Diagnostic Interview-Revised and the Autism Diagnostic Observation Schedule-Generic for the diagnosis of autism spectrum disorders in a Greek sample with a wide range of intellectual abilities. *J Autism Dev Disord* 2009, 39:414–420, doi: 10.1007/s10803-008-0639-6

33. Le Couteur A, Lord C, Rutter M. *The autism diagnostic interview – revised (ADI-R).* Western Psychological Services, Los Angeles, CA, 2003

34. Kooij SJ, Francken MH, Bron TI. *Diagnostic Interview for ADHD in Adults (DIVA).* Greek Version (Pehlivanidis A & Papanikolaou K) DIVA Foundation, The Hague, the Netherlands, 2019

35. Spielberger CD, Gorsuch RL, Lushene RE, Vagg PR, Jacobs GA. *The State-Trait Anxiety Inventory of Adults (STAIT).* Manual. Mind Garden, Palo Alto, CA, 1983

36. Fountoulakis KN, Papadopoulou M, Kleanthous S, Papadopoulou A, Bizeli V, Nimatoudis I et al. Reliability and psychometric properties of the Greek translation of the State-Trait Anxiety Inventory Form Y: Preliminary data. *Ann Gen Psychiatry* 2006, 5:2, doi: 10.1186/1744-859X-5-2

37. Gratz KL, Roemer L. Multidimensional assessment of emotion regulation and dysregulation: Development, factor structure, and initial validation of the Difficulties in Emotion Regulation Scale. *J Psychopathol Behav Assess* 2004, 26:41–54, doi: 10.1023/B:JOBA.0000007455.08539.94

38. Mitsopoulou E, Kafetsios, Karademas E, Papastefanakis E, Simos P. The Greek Version of the Difficulties in Emotion Regulation Scale: Testing the Factor Structure, Reliability and Validity in an Adult Community Sample. *J Psychopathol Behav Assess* 2013, 35:123–131, doi: 10.1007/s10862-012-9321-6

39. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983, 67:361–370, doi: 10.1111/j.1600-0447.1983.tb09716.x

40. Michopoulos I, Douzenis A, Kalkavoura C, Christodoulou C, Michalopoulou P, Kalemi G et al. Hospital Anxiety and Depression Scale (HADS): validation in a Greek general hospital sample. *Ann Gen Psychiatry* 2008, 7:4, doi: 10.1186/1744-859X-7-4

41. Contardi A, Imperatori C, Amati I, Balsamo M, Innamorati M. Assessment of Affect Lability: Psychometric Properties of the ALS-18. *Front Psychol* 2018, 9:427, doi: 10.3389/fpsyg.2018.00427

42. Pehlivanidis A. Awareness of adult attention-deficit/hyperactivity disorder (ADHD) in Greece. *Psychiatriki* 2012, 23(Suppl 1):60–65, PMID: 22796974

APPENDIX
Κλίμακα Συναισθηματικής Ευμεταβλητότητας
Affective Lability Scale - Short Form (ALS-18)

Κατάσταση	Δεν με χαρακτηρίζει καθόλου	Με χαρακτηρίζει μερικές φορές	Με χαρακτηρίζει τις περισσότερες φορές	Με χαρακτηρίζει απόλυτα
1. Κάποιες φορές νιώθω όπως όλοι και μέσα σε λίγα λεπτά μπορεί να εκνευριστώ τόσο πολύ ώστε να έχω σωματικά ενοχλήματα	0	1	2	3
2. Υπάρχουν φορές που έχω πολύ λίγη ενέργεια και σε μικρό χρονικό διάστημα έχω την ίδια ενέργεια με τους περισσότερους	0	1	2	3
3. Τη μία στιγμή μπορεί να νιώθω εντάξει και την επόμενη να είμαι εκνευρισμένος/η και σε ένταση	0	1	2	3
4. Συχνά υπάρχει εναλλαγή ανάμεσα στην ικανότητά μου να ελέγχω τα νεύρα μου και στην αδυναμία μου να το κάνω	0	1	2	3
5. Πολλές φορές ο εκνευρισμός και η ένταση που νιώθω μετατρέπονται ξαφνικά σε στεναχώρια και πτώση τις διάθεσης	0	1	2	3
6. Μερικές φορές το έντονο άγχος μου για κάτι μετατρέπεται σε άσχημο συναίσθημα γι' αυτό	0	1	2	3
7. Έχω εναλλαγές από την απόλυτη ηρεμία στην υπερένταση και τον εκνευρισμό	0	1	2	3
8. Υπάρχουν φορές που ενώ νιώθω ήρεμος/η, την επόμενη στιγμή μπορεί να εκνευριστώ από κάτι μικρό ή ασήμαντο	0	1	2	3
9. Συχνά νιώθω καλά και μετά ξαφνικά μπορεί να θυμώσω τόσο που να θέλω να χτυπήσω ή να σπάσω κάτι	0	1	2	3
10. Κάποιες φορές μπορεί να σκέφτομαι καθαρά και να είμαι συγκεντρωμένος/η και την επόμενη στιγμή να έχω μεγάλη δυσκολία να το κάνω	0	1	2	3
11. Υπάρχουν φορές που είμαι τόσο θυμωμένος/η που δεν μπορώ να σταματήσω να φωνάζω και σύντομα μετά δεν έχω διάθεση να το κάνω	0	1	2	3
12. Η ενεργητικότητά μου εναλλάσσεται: άλλες φορές είναι πολύ υψηλή και κάποιες άλλες η παραμικρή προσπάθεια μου φαίνεται «βουνό»	0	1	2	3
13. Υπάρχουν στιγμές που ενώ αισθάνομαι πολύ καλά για τον εαυτό μου σύντομα νιώθω πως δεν διαφέρω από τους υπόλοιπους	0	1	2	3
14. Υπάρχουν φορές που είμαι τόσο θυμωμένος/η που νιώθω την καρδιά μου να σφυροκοπά και μπορεί να αρχίσω να τρέμω, σύντομα όμως ηρεμώ	0	1	2	3
15. Η παραγωγικότητά μου άλλοτε μπορεί να είναι πολύ χαμηλή και άλλοτε σαν όλων των υπολοίπων	0	1	2	3
16. Κάποιες φορές νιώθω πολύ ενεργητικός/η τη μία στιγμή και την επόμενη μπορεί να έχω τόσο λίγη ενέργεια που με δυσκολία να κάνω οτιδήποτε	0	1	2	3
17. Υπάρχουν στιγμές που έχω περισσότερη ενέργεια από ό,τι συνήθως και περισσότερη από τους περισσότερους ανθρώπους, σύντομα όμως έχω την ίδια ενέργεια με τους υπόλοιπους	0	1	2	3
18. Κάποιες φορές νιώθω πως τα κάνω όλα με αργό ρυθμό, αλλά σύντομα νιώθω πως δεν είμαι πιο αργός/ή από τους υπόλοιπους	0	1	2	3

Ερευνητική εργασία

Ψυχομετρικές ιδιότητες της ελληνικής έκδοσης της Κλίμακας Συναισθηματικής Ευμεταβλητότητας (ALS-18) σε δείγμα ενηλίκων με νευροαναπτυξιακές διαταραχές

Εύα Καλαντζή, Αρτέμιος Πεχλιβανίδης, Καλλιόπη Κορομπίλη, Βασίλειος Μαντάς, Χαράλαμπος Παπαγεωργίου

Ειδικό Ιατρείο Νευροαναπτυξιακών Διαταραχών Ενηλίκων, Α΄ Ψυχιατρική Κλινική, Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών, Αιγινήτειο Νοσοκομείο, Αθήνα

ΙΣΤΟΡΙΚΟ ΑΡΘΡΟΥ: Παραλήφθηκε 12 Ιουλίου 2021/Αναθεωρήθηκε 15 Σεπτεμβρίου 2021/Δημοσιεύθηκε Διαδικτυακά 21 Φεβρουαρίου 2022

ΠΕΡΙΛΗΨΗ

Η συναισθηματική αστάθεια αναφέρεται σε δυσπροσαρμοστικά πρότυπα συναισθηματικής ρύθμισης, τα οποία επηρεάζουν τη λειτουργικότητα στην καθημερινή ζωή και εμφανίζεται συχνά σε πολλές ψυχιατρικές διαταραχές. Συναντάται με τη μορφή της συναισθηματικής ευμεταβλητότητας, μια συναισθηματική «κατασκευή» που εκφράζεται με συχνές και έντονες διακυμάνσεις του συναισθήματος ως απάντηση τόσο σε ευχάριστα όσο και σε δυσάρεστα γεγονότα ή σε ερμηνείες των γεγονότων. Η Κλίμακα Συναισθηματικής Ευμεταβλητότητας (ALS) είναι ένα ευρέως χρησιμοποιούμενο ερωτηματολόγιο αυτοαναφοράς, που μετρά την τάση των συναισθημάτων να αλλάζουν από το ένα στο άλλο, καθώς και τις διακυμάνσεις μεταξύ κατάθλιψης και ενθουσιασμού και μεταξύ κατάθλιψης-άγχους. Η αρχική κλίμακα είχε 54 λήμματα, αλλά δημιουργήθηκε μια μικρότερη μορφή 18 λημμάτων (ALS-18), με τρεις υποκλίμακες: εναλλαγή άγχους-κατάθλιψης, εναλλαγή κατάθλιψης-ενθουσιασμού και εμφάνιση θυμού. Σκοπός της παρούσας μελέτης ήταν η αξιολόγηση των ψυχομετρικών ιδιοτήτων της ελληνικής μετάφρασης της ALS-18. Η μετάφραση πραγματοποιήθηκε από δύο από τους συγγραφείς. Η μελέτη έλαβε χώρα στην Α΄ Ψυχιατρική Κλινική ΕΚΠΑ, στο Αιγινήτειο Νοσοκομείο, στα πλαίσια της μονάδας νευροαναπτυξιακών διαταραχών (ΝΑΔ). Δείγμα 108 ενηλίκων συμπεριλήφθηκε στην έρευνα χωρισμένο σε δύο ομάδες, ΝΑΔ (διαταραχή ελλειμματικής προσοχής - υπερκινητικότητας και διαταραχή αυτιστικού φάσματος) και μάρτυρες. Όλοι συμπλήρωσαν τις ALS-18, State – Trait Anxiety Inventory (STAIT), Difficulties in Emotion Regulation Scale (DERS) και Hospital Anxiety and Depression Scale (HADS). Η στατιστική ανάλυση έδειξε ικανοποιητική εσωτερική συνέπεια. Το Cronbach α ήταν 0,91 συνολικά και 0,89 για την υποκλίμακα Άγχος/Κατάθλιψη, 0,86 για την υποκλίμακα Κατάθλιψης/Ενθουσιασμού και 0,85 για την υποκλίμακα του Θυμού. Η δομή των τριών παραγόντων αναπαράχθηκε στα δεδομένα μας. Η αξιοπιστία εσωτερικής συνέπειας όλων των παραγόντων ALS-18 στη μελέτη μας θα μπορούσε να θεωρηθεί ικανοποιητική με συντελεστή Cronbach α τουλάχιστον 0,85 για όλους τους παράγοντες. Σημαντικά υψηλότερες μέσες τιμές βρέθηκαν για όλες τις υποκλίμακες, Άγχος/Κατάθλιψη, Κατάθλιψη/Ενθουσιασμός και Θυμός σε άτομα με ΝΑΔ, σε σύγκριση με τους υγιείς μάρτυρες, εμφανίζοντας έτσι μια καλή ικανότητα διάκρισης. Η ALS δείχνει καλή διακριτική ικανότητα μεταξύ κλινικού και μη κλινικού δείγματος. Η ελληνική έκδοση του ALS-18 παρουσιάζει καλές ψυχομετρικές ιδιότητες και αποτελεί ένα εύχρηστο εργαλείο στα χέρια των κλινικών, ώστε να μελετάται καλύτερα η διάσταση της συναισθηματικής αστάθειας, η οποία είναι παρούσα σε μεγάλο ποσοστό ψυχιατρικών διαταραχών, με στόχο την εξατομικευμένη θεραπευτική παρέμβαση.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: Affective Lability Scale, ALS-18, συναισθηματική αστάθεια, Ελληνικά, ψυχομετρικές ιδιότητες, νευροαναπτυξιακές διαταραχές.

Συγγραφέας επικοινωνίας: Εύα Καλαντζή, Α΄ Ψυχιατρική Κλινική, Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών, Αιγινήτειο Νοσοκομείο, Λεωφ. Βασιλίσσης Σοφίας 72–74, 115 26 Αθήνα, Διεύθυνση e-mail: kalantzieva@yahoo.gr

https://doi.org/10.22365/jpsych.2022.068 / Psychiatriki 2022, 33:210–218

Research article

Coping strategies in mothers of children with autism spectrum disorder and their relation to maternal stress and depression

Vassiliki Ntre,[1] Katerina Papanikolaou,[2] Eirini Amanaki,[3] Kalliopi Triantafyllou,[4] Chara Tzavara,[4] Gerasimos Kolaitis[2]

[1]*Cardiology and Cardiac Surgery Unit "Aghia Sophia" Children's Hospital, Athens,*

[2]*Department of Child Psychiatry, Faculty of Medicine, National and Kapodistrian University of Athens, "Aghia Sophia" Children's Hospital, Athens,*

[3]*Master of Education Program School of Humanities, Hellenic Open University, Patra,*

[4]*Medical School, National and Kapodistrian University of Athens, Greece*

ARTICLE HISTORY: Received 11 June 2021/Revised 11 October 2021/Published Online 21 February 2022

ABSTRACT

Having a child with autism may have a strong impact on the family, especially on mothers, who are usually the primary caregivers of children with autism. Parents of children with autism report more mental health problems compared to parents of children with normal development or other developmental disabilities. Parental copying strategies may play a significant role when parents have to overcome stressful situations during the child's development. The present study aimed to investigate the coping strategies used by mothers of children with autism spectrum disorder (ASD) and their relation to maternal stress and depression. One hundred and forty-three (143) mothers (mean age 42.7 years) of children with ASD (6-17years), who attended the ASD Outpatient Clinic of the Department of Child Psychiatry, at a Children's Hospital, participated in the current study. Mothers completed a series of questionnaires: a demographic characteristics questionnaire, the Center for Epidemiologic Studies Depression Scale (CES-D), the Family Crisis Oriented Personal Scales (F-COPES) and the Parenting Stress Index Short-Form (PSI-SF). Mothers with higher educational level scored significantly lower in total F-COPES and its subscale "reframing". Increased daily hours related to child care and the child's medication schedule were additional factors significantly associated with lower scores on "reframing". Reframing subscale was also negatively correlated with "parental distress", whereas "passive appraisal" was positively correlated with depressive symptoms. Lower scores on "mobilizing family to acquire" and "accept help" were associated with family life being more seriously affected. Coping strategies of mothers of children with ASD are associated with a number of factors related to personal characteristics of caregivers, child treatment and family characteristics. Mental health professionals should examine factors that may strengthen coping strategies that handle the challenges of having a child with ASD.

KEYWORDS: Autism spectrum disorders, coping strategies, depression, parental stress.

Introduction

Autism Spectrum Disorder (ASD) refers to a range of complex developmental and neurological disorders that include deficits in social communication, as well as stereotyped, restricted and repetitive behaviors and interests.[1] Individuals with autism do not constitute a homogenous population but they vary in terms of onset, symptoms, and severity.[2]

Having a child with autism has an impact on the family.[3–8] Upon receiving the diagnosis of their child's

Corresponding author: Vassiliki Ntre, "Aghia Sophia" Children's Hospital, Thivon & Papadiamantopoulou street, GR-115 27 Athens, Greece • e-mail: vassilikintre@yahoo.gr

disorder, it is possible for the parents to experience frustration due to their expectations for a normally developing child.[9,10] In the existing literature it has been clearly demonstrated that parents of children with autism report more mental health problems than parents of children with normal development or other developmental disabilities.[11] As Sharpley et al noted,[12] the three more powerful stressors arising from raising a child with ASD were (1) the permanent nature of the disorder, (2) the dearth of acceptance of autistic behavior by family members and society and (3) the lack of sufficient support supplied by health care services and other social services. Also, it became clear that autism affected the family organization in dramatic ways. Parents describe feelings of loss and desperationfollowing their child's diagnosis; however, they are willing to activate every possible resource to assist their child.[13]

Parents vary considerably in their ability to adequately meet the challenges posed by their child's autism, with some of them experiencing little difficulty and others developing serious mental health problems.[14,15] A qualitative study, identified nine positive themes and 15 negative themes, that were subsumed into five clusters: (1) child's behavior, (2) social isolation, (3) impact on the whole family, (4) stress and (5) parents' personal well-being, work and marital relationship. According to the researchers, the mix of both positive and negative themes could be interpreted as a dialectical standpoint of finding positive meaning to life, although having a child with autism was acknowledged as a source of stress and obstacles.[16]

It should not be overlooked that high levels of stress, when left unmanaged, can lead to the development of depressive symptoms,[17–21] a finding that further underscores the importance of coping supports. In addition to the aforementioned finding, it has been shown that the risk for poor mental health and high stress levels can be reduced by the presence of strong maternal coping skills and coping strategies, in the form of emotional and neighborhood social supports.[21] Especially mothers of an autistic child, as the primary caregivers, have higher stress levels and are more likely to report mental health problems, compared to mothers in the general population.[22–24] In particular, a study showed that mothers of children with ASD reported higher levels of negative affectivity, anxiety, parental stress and social inhibition, as well as higher levels of avoidance coping, compared to those of normally developing children.[21] Another study also found increased levels of parental anxiety and depression and impaired quality of life, mainly in mental health and social functioning. This psychosocial burden was related to female gender, increased number of children and higher child's age.[23–25]

A review of coping strategies of parents of children with ASD[26] indicated that parental strategies were influenced by (1) demographic characteristics, (2) psychological attributes (e.g., personality, coping styles, emotional health etc.), (3) child characteristics and (4) situational variables (e.g., family function, treatment availability etc.). Parents of children with ASD use several coping strategies that include: (1) seeking treatment or intervention and information, (2) seeking social support, (3) reappraisal and reframing, (4) adjusting to child's needs, (5) spirituality and (6) seeking respite. Based on the findings of their review, the authors stressed that parents of children with ASD used both problem-focused (e.g., treatments/interventions for child, reappraisal, and reframing) and emotion-focused (e.g., social support, spirituality, and respite) coping strategies. Additionally, a recent study with parents of children with ASD, mainly mothers, found that social support was reported as one of the most beneficial coping strategies.[27]

In light of the above mentioned studies, the present work examines the coping strategies used by mothers of children with ASD in relation to maternal stress and depressive symptoms. The associations between child characteristics, demographic factors and mothers' coping strategies are also explored.

Hence, our research hypotheses were as follows: (1) maternal coping strategies will be related to child age, daily hours for child care and treatment, (2) family demographic characteristics will be related to maternal coping strategies and (3) maternal coping strategies will be related to maternal distress and depression.

Material and Method

Participants

One hundred forty-three (143) mothers (mean age: 42.7, SD: 7.0 years; husbands mean age=47.2, SD=6.4years) with a child (6–17years, mean age: 10.0, SD=3.0 years, 79% boys) with ASD, who attended the ASD Outpatient Clinic of University Department of Child Psychiatry, in "Aghia Sophia" Children's Hospital participated in the study. The majority of the participants were married (70.0%) and 55.2% of them had high educational level (University/or post-graduate studies). The participation criterion was the ability to speak and write fluently in Greek.

Procedure

The researcher initially informed parents who were coming for a prearranged follow-up appointment to the ASD Outpatient Clinic about the study and scheduled home visits. During the home visits the participants signed the consent forms and completed the questionnaires. Ethical approval of the study was obtained by

the scientific committee of the "Aghia Sophia" Children's Hospital, Athens, Greece.

Measures

Child Diagnosis and Clinical Characteristics

All children had been diagnosed with ASD based on ICD-10 criteria for Pervasive Developmental Disorders. They all underwent a standard psychometric evaluation and were tested for fragile X and other chromosomal abnormalities.

Demographic Characteristics Questionnaire

This questionnaire, which was developed for the purpose of the current study, includes questions about the child's gender and age, the parents' age, nationality, marital status, educational/ occupational status, the number of children in the family and social support (e.g., partner, family, friends and therapeutic specialists).

Center for Epidemiologic Studies Depression Scale[28]

It is a self-reported questionnaire that consists of 20 items, measuring the presence of depressive symptoms in the past week, on a 4-point scale ranging from 0 (rarely) to 3 (most of the time). It has good psychometric properties[29] (Cronbach alpha for the present study was 0.74).

Family Crisis Oriented Personal Scales (F-COPES)[30]

It consists of 30 coping behavior items, evaluating the family's coping style. It includes two types of interaction: (a) the way a family internally handles difficult situations and problems and (b) the way that the family interacts with the social environment, when asking for help in order to find solutions. The responses ranging from 1 (strongly agree) to 5 (strongly disagree) explore internal and external family-coping patterns It includes five subscales: (a) acquiring social support, (b) reframing, (c) seeking spiritual support, (d) mobilizing family to acquire and accept help and (e) passive appraisal. The total score shows the degree to which the family uses a specific coping strategy. It is a reliable and valid tool, that measures coping strategies and level of adaptation. The Greek version has satisfactory psychometric properties[31] (Cronbach alpha for this study was 0.83).

Parenting Stress Index Short-Form (PSI-SF)32

It consists of 36 items and comprises three subscales, namely the Parental Distress (PD), Parent-Child Dysfunctional Interaction (PCDI) and Difficult Child (DC) subscales. The PD subscale measures anxiety due to personal factors related to parenting; the PCDI subscale assesses how parents perceive their interactions with their children and the DC subscale measures the characteristics of child behavior and how difficult it can be to deal with such behavior. Child and Parent domains combine to form the total parental stress. Participants answer according to a 5-point Likert scale ranging from 1 (strongly agree) to 5 (strongly disagree).[33] Reliability and validity of the test supports that parenting stress is a useful measure across diverse populations.[34] Studies with Greek population have shown high internal consistency.[35] In our study Cronbach alpha was 0.82, 0.86 and 0.88 for the PCDI, PD and DC, respectively.

Statistical analysis

Pearson correlations coefficients were used to explore the association of F-COPES with PSI dimensions and CES-D. Also, partial correlation coefficients were computed to explore the association of F-COPES with PSI dimensions and CES-D controlling for child and parent characteristics. The normality assumption was evaluated using the Kolmogorov-Smirnov criterion. Multiple linear regression analyses were conducted in order to find independently associated factors with F-COPES dimensions. The regression equation included terms of child and parent demographic and clinical characteristics. Adjusted regression coefficients (β) with standard errors (SE), were computed from the results of the linear regression analyses. Also, coefficients of determination (R2) of the regression models were reported. All reported p values are two-tailed. Statistical significance was set at $p<0.05$ and analyses were conducted using SPSS statistical software (version 22.0).

Results

Demographic and family characteristics of the sample are displayed in table 1. The mean age of the mothers was 42.7 years (SD=7.0 years) and the mean age of the husbands was 47.2 years (SD=6.4 years). Concerning children, 79% were boys and 21% girls and their mean age was 10.0 years (SD=3.0 years). The majority of the participants were married (70.0%) and 55.2% of them had high educational level (University/or post-graduate studies). The majority of mothers (71.3%) declared that the presence of the child with autism affects family's social life and 34.3% reported more than five hours of daily care of the child. The mean number of stressful events reported for the last year was 1.8 (SD=1.6). 49% of the children were under pharmacological treatment and more than half of the mothers (58%) reported having a health problem.

Results from multiple linear regression analyses with dependent variables Reframing, Mobilizing Family to acquire and Accept Help and Seeking Spiritual Support are shown in tables 2 and 3. Concerning Reframing, it was

Table 1. Sample characteristics.

	N (%)
Mothers with a child with ASD	143 (100)
Child's gender	
Boys	113 (79.0)
Girls	30 (21.0)
Child's age (years), mean (SD)	10.0 (3.0)
Mother's age (years), mean (SD)	42.7 (7.0)
Father's age (years), mean (SD)	47.2 (6.4)
Educational status of them others	
Primary/Middle/High school or 2-year college	64 (44.8)
University/ Post-graduate studies	79 (55.2)
Married	100 (70.0)
Number of children in the family	
1	36 (25.2)
2	84 (58.7)
>2	23 (16.1)
The presence of the child affects family's social life	
Not at all	41 (28.7)
A little	44 (30.8)
Some	30 (21.0)
Very	14 (9.8)
Very much	14 (9.8)
Daily hours for taking care of the child	
Less than 2,5 hours	43 (30.1)
2,6-5 hours	51 (35.7)
5,1-7,5 hours	24 (16.8)
7,6 -10 hours	10 (7.0)
More than 10 hours	15 (10.5)
Social support scale, mean (SD)	2.30 (0.69)
Child under treatment with medicine	70 (49.0)
Mother with health problem	83 (58.0)

found that mothers with higher educational level had lower scores on Reframing. Also, increased daily hours for taking care of the child and the children's treatment were associated with lower scores on Reframing. The R^2 of the model was 0.13. Higher affection of family's social life due to the children was associated with lower scores on Mobilizing Family to Acquire and Accept Help in multiple analyses. Furthermore, increased social support was found to be associated with greater scores on Mobilizing Family to Acquire and Accept Help and the R2 of the model was 0.11. Increased age of the child and increased number of children in the family were found to be associated with greater scores on Seeking Spiritual Support. Additionally, married mothers had higher score on Seeking Spiritual Support and the R^2 of the model was 0.15. Regarding Acquiring Social Support, increased social support was found to be associated with greater scores (R^2=0.08) and it was also found to be associated with greater scores on Passive Appraisal dimension (R^2=0.09). Mothers with higher educational level had lower scores overall on F-COPES dimension, while increased age of the child was found to be associated with greater scores on overall F-COPES and the R2 of the model was 0.16.

Correlation analysis between F-COPES and PSI dimensions and CES-D (table 4) revealed that Reframing was significantly negatively correlated with Parental Distress, while Parent-Child Dysfunctional Interaction was significantly positively correlated with Passive Appraisal. Passive Appraisal was the only F-COPES dimension that was found to be significantly positively correlated with depression. The aforementioned correlations were significant but low. Adjusting the analysis for demographic factors the partial correlations between Passive Appraisal and depression (r=0.19, p=0.038), between Reframing and Parental Distress (r=–0.20, p=0.031) and between Passive Appraisal and Parent-Child Dysfunctional Interaction (r=–0.25, p=0.005), remained significant.

Discussion

The present study examined the coping strategies used by mothers of children with ASD, as well as the associations between maternal stress, depressive symptoms and coping strategies. Coping strategies were related to family demographic characteristics maternal stress, depressive symptoms, as well as characteristics specific to child age and to the disorder.

Examining the relationship between coping strategies and marital status, seeking spiritual support was significantly associated with marital status, that is married mothers scored higher in the aforementioned subscale, while increased number of children in the family predicted higher maternal spiritual support. Also, older child's age was found to be associated with a greater search for spiritual support. As both children and mothers get older it is more likely for mothers to experience an existential crisis and anxiety about their child's future, that would lead them to seek spiritual support.

An interesting finding of the present study was that mothers of higher education level used the coping strategy of reframing less often and had a lower score on overall F-COPES. It seems that higher educated parents may have higher expectations for their child's development and at the same time be aware of the nature of the disorder and the related difficulties, leading to higher levels of frustration.[36]

Table 2. Linear regression analyses results for the dependent variables Reframing, Mobilizing Family to acquire and Accept Help and Seeking Spiritual Support.

	Reframing		Mobilizing Family to Acquire and Accept Help		Seeking Spiritual Support	
	β (SE)[+]	p	β (SE)[+]	p	β (SE)[+]	p
Child's gender						
Boys (reference)						
Girls	0.60 (1.99)	0.767	–0.35 (1.47)	0.817	0.37 (1.36)	0.788
Child's age (years)	0.09 (0.26)	0.720	0.16 (0.19)	0.410	1.00 (0.18)	<0.001
Mother's age (years)	–0.11 (0.19)	0.569	0.10 (0.15)	0.514	–0.09 (0.15)	0.579
Father's age (years)	0.11 (0.15)	0.482	–0.11 (0.11)	0.338	–0.02 (0.11)	0.849
Educational status						
Primary/ Middle/ High school or 2–year college						
University/ Post–graduate studies	–2.02 (0.77)	0.010	0.50 (1.41)	0.727	–0.50 (1.44)	0.731
Married						
No (reference)						
Yes	–1.77 (2.49)	0.487	0.09 (1.91)	0.962	3.80 (1.69)	0.036
Number of children in the family	1.03 (1.15)	0.381	–0.83 (0.86)	0.348	2.71 (0.91)	0.008
Number of stressful events	–0.29 (0.37)	0.441	–0.20 (0.29)	0.489	0.33 (0.30)	0.282
The presence of the child affects family's social life	0.17 (0.76)	0.825	–0.22 (0.11)	0.048	0.83 (0.59)	0.177
Daily hours for taking care the child	–0.65 (0.30)	0.029	–0.68 (0.61)	0.281	–0.98 (0.56)	0.096
Social support scale	–0.89 (1.39)	0.533	1.19 (0.39)	0.003	0.12 (1.00)	0.905
Child under treatment with medicine						
No (reference)						
Yes	–1.87 (0.86)	0.035	–0.05 (1.07)	0.963	1.16 (1.12)	0.311
Mother with health problem						
No (reference)						
Yes	2.19 (1.32)	0.115	–0.17 (1.02)	0.870	–1.14 (1.08)	0.305

[+]regression coefficient (Standard Error)

Increased daily hours for taking care of the child with autism, as well as child's pharmacological treatment were associated with lower scores on reframing. These two conditions might reflect a higher severity of the disorder. In line with the notion that parental stress is positively correlated with their children's behavioral problems and the severity of ASD symptoms,[27] it might be that the severity of child's ASD symptoms and the obligations arising from it do not leave much room for mothers to use reframing as an effective coping strategy. On the other hand, a recent report highlighted the usefulness of reframing for all levels of child behavior problems as an effective strategy, even in families with a child with severe symptomatology.[37]

Higher affection of family's social life due to the children was associated with lower levels of mobilizing family to acquire and accept help. At the same time, increased social support was found to be associated with greater scores on mobilizing family to acquire and accept help and acquiring social support. In cases where the social life of the family is strongly influenced by the child with autism, it is possible that the mothers have experienced stigma and rejection from the wider society.[38] Perhaps the fear of social stigma and impending frustration prevents mothers of children with autism from accepting the help of others. On the other hand, when they have the positive social experience of receiving social support it is probably easier for them to seek and receive it again.

Table3. Linear regression analyses with dependent variables Acquiring Social Support, Passive Appraisal and Overall F Copes

	Acquiring Social Support		Passive Appraisal		Overall F Copes	
	β (SE)+	p	β (SE)+	p	β (SE)+	p
Child's gender						
Boys (reference)						
Girls	–0.14 (3.05)	0.963	–0.02 (1.73)	0.992	5.66 (6.89)	0.423
Child's age (years)	0.50 (0.40)	0.227	0.17 (0.23)	0.473	0.20 (0.09)	0.026
Mother's age (years)	0.34 (0.34)	0.324	–0.03 (0.19)	0.874	–0.10 (0.67)	0.880
Father's age (years)	0.04 (0.26)	0.872	0.07 (0.15)	0.648	–0.02 (0.51)	0.970
Educational status						
Primary/ Middle/ High school or2–year college						
University/ Post–graduate studies	0.46 (3.21)	0.888	–1.16 (1.83)	0.535	–5.50 (2.46)	0.028
Married						
No (reference)						
Yes	2.28 (3.78)	0.553	1.60 (2.15)	0.466	3.01 (8.60)	0.731
Number of children in the family	0.66 (2.04)	0.752	–0.08 (1.16)	0.945	5.47 (3.94)	0.184
Number of stressful events	0.26 (0.67)	0.708	0.13 (0.38)	0.744	0.51 (1.28)	0.695
The presence of the child affects family's social life	–2.58 (1.34)	0.070	–0.31 (0.75)	0.687	0.09 (2.65)	0.974
Daily hours for taking care the child	1.02 (1.25)	0.427	0.01 (0.71)	0.984	–2.79 (2.74)	0.324
Social support scale	2.15 (0.89)	0.017	–1.00 (0.43)	0.029	2.82 (1.81)	0.124
Child under treatment with medicine						
No (reference)						
Yes	0.68 (2.50)	0.790	0.65 (1.43)	0.653	2.88 (4.83)	0.560
Mother with health problem						
No (reference)						
Yes	0.97 (2.45)	0.696	0.55 (1.37)	0.693	2.12 (4.62)	0.652

+regression coefficient (Standard Error); F–COPES: Family Crisis Oriented Personal Scales

Table 4. Correlation coefficients between F-COPES and PSI-SF dimensions, CES-D.

	PSI				CES-D
	Defensive Responding	Parental Distress	Parent-Child Dysfunctional Interaction	Difficult Child	
F-COPES					
Reframing	–.15	–.23*	–.11	–.01	–.16
Mobilizing Family to Acquire and Accept Help	.03	–.02	–.13	.02	–.11
Seeking Spiritual Support	–.05	–.03	–.04	.06	–.14
Acquiring Social Support	.02	–.02	.07	.03	–.11
Passive Appraisal	.11	.07	.21*	.17	.20*
Overall F Copes	.00	–.06	.04	.11	–.13

*p<.05; **p<.01; ***p<.001; F-COPES: Family Crisis Oriented Personal Scales; PSI-SF: Parenting Stress Index Short-Form; CES-D: Center for Epidemiologic Studies Depression Scale

Examining the relationship between coping strategies and parental distress, reframing was found to be negatively correlated with parental distress. This is in accordance with findings from previous studies,[39,40] which have shown that positive reframing of potentially traumatic and stressful events could be an effective coping strategy under extreme conditions, where direct actions for stress reduction cannot be applied.[34] In addition, in a recent study[37] reframing was one of the coping strategies associated with lower parental stress.

We also found that parent-child dysfunctional interaction was positively correlated with passive appraisal. It is possible for mothers of children with autism who have difficulty interacting with them, to resort to a passive assessment strategy in order to avoid overreacting to their child's problem behavior, which could further complicate the interaction between each other. In addition, it was found that increased social support was associated with lower levels of passive appraisal as a coping strategy. Perhaps, mothers who receive increased social support are more likely to receive the psychological and emotional help they need, in order to take a more proactive approach to the problems arising from their child's disorder. Moreover, the present study showed that passive appraisal was positively correlated with depression. Dunn and his colleagues[40] examined moderators of stress on parents of children with autism and found that increased use of avoidance and escape as coping methods corresponded to increased depression. Also, increased use of avoidance and escape corresponded to increased social isolation, while increased use of positive reappraisals corresponded to decreased social isolation.

To our knowledge, the present study is the first to explore coping strategies in Greek families having a child with ASD; nonetheless, it has a number of limitations. First, the sample was composed exclusively by mothers and the paternal coping strategies have not been explored. However, mothers are usually the primary caregivers of children in Greek culture and seem to be the ones that shoulder a heavy burden when rising a child with ASD.24 Second, the majority of children were boys. The 3.5:1 male: female ratio, though is the usual ratio reported for children with ASD.[41] Third, maternal emotional state was measured only by a self-report questionnaire, the CES-D. Nevertheless, this is a highly sensitive tool, and has been used to detect depression in the general population and has been used in Greek populations.[29] In the future multi-informant assessments could also be used in order to obtain more measures of the predictor variables. Finally, the study has a cross-sectional design meaning that we cannot draw conclusions about causality.

To conclude, our findings illustrate the coping strategies implemented by mothers of children with ASD and the importance of the available social support. Interventions based on a Cognitive-Behavior Therapy approach help parents of children with ASD develop reframing strategies, dispirit them from using avoidance and escape coping styles and encourage them to use a more proactive, problem-focused coping strategies. Also, increasing the quality of social support networks in the environment of the family with a child with an ASD diagnosis, could help mothers to effectively cope with the distress arising from their child's disorder.

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. American Psychiatric Publishing, Arlington, VA, 2013, doi:10.1176/appi.books.9780890425596
2. Ooi KL, Ong YS, Jacob SA, Khan, TM. A meta-synthesis on parenting a child with autism. *Neuropsychiatr Dis Treat* 2016, 12: 745–762, doi: 10.2147/NDT.S100634
3. Benevides TW, Lee J, Nwosu NAO, Franks J. Understanding the family impact of autism spectrum disorder in a racially and ethnically diverse sample: findings from the national survey of children with special health care needs. *Matern Child Health J* 2019, 23:951–960, doi: 10.1007/s10995-018-02724-x
4. Chan KKS, Lam CB, Law NCW, Cheung RYM. From child autistic symptoms to parental affective symptoms: A family process model. *Res Dev Disabil* 2018, 75:22–31, doi: 0.1016/j.ridd.2018.02.005
5. Dovgan K, Mazurek MO. Impact of multiple co-occurring emotional and behavioural conditions on children with autism and their families. *J Appl Res Intellect Disabi*l 2019, 32: 967–980, doi: 10.1111/jar.12590
6. Karst JS, Van Hecke AV. Parent and family impact of autism spectrum disorders: A review and proposed model for intervention evaluation. *Clin Child Fam Psychol Rev* 2012, 15: 247-277, doi:10.1007/s10567-012-0119-6
7. Kogan MD, Strickland BB, Blumberg SJ, Singh GK, Perrin GM, Van Dyck PCA. A national profile of the health care experiences and family impact of autism spectrum disorder among children in United States. *Pediatrics* 2008, 122: e1149-1158, doi:10.1542/peds.2008-1057
8. Petrou MA, Soul A, Koshy B, McConachie H, Parr R J. The impact on the family of the co-existing conditions of children with autism spectrum disorder: Impact of co-existing conditions in ASD. *Autism Res* 2018, 11: 776-787, doi: 10.1002/aur.1932
9. Dale E, Jahoda A, Knott F. Mothers' attributions following their child's diagnosis of autistic spectrum disorder: Exploring links with maternal levels of stress, depression and expectations about their child's future. *Autism* 2006, 10: 463-479, doi: 10.1177/1362361306066600
10. Poslawsky EI, Naber F, Daalen VE, Engeland VH. Parental reaction to early diagnosis of their children's autism spectrum disorder: An exploratory study. *Child Psychiatry Hum Dev* 2014, 45:294–305, doi: 10.1007/s10578-013-0400-z
11. Estes A, Olson E, Sullivan K, Greenson J, Winter J, Dawson G, et al. Parenting-related stress and psychological distress in mothers of toddlers with autism spectrum disorders. *Brain Dev* 2013, 35:133–138, doi: 10.1016/j.braindev.2012.10.004

12. Sharpley C, Bitsika V, Efremidis B. Influence of gender, parental health, and perceived expertise of assistance upon stress, anxiety, and depression among parents of children with autism. *J Intellect Dev Disabil* 1997, 22:19–28, doi: 10.1080/13668259700033261

13. Altiere J, Von Kluge S. Family functioning and coping behaviors in parents of children with autism. *J Child Fam Stud* 2009, 18:83–92, doi: 10.1007/s10826-008-9209-y

14. Benson PR. Coping, distress, and well-being in mothers of children with autism. *Res Autism Spectr Disord* 2010, 4: 217-228, doi: 10.1016/j.rasd.2009.09.008

15. Benson PR, Karlof KL. Anger, stress proliferation, and depressed mood among parents of children with ASD: A longitudinal replication. *J Autism Dev Disord* 2009, 39: 350-362, doi: 10.1007/s10803-008-0632-0

16. Schlebusch L, Dada S. Positive and negative cognitive appraisal of the impact of children with autism spectrum disorder. *Res Autism Spectr Disord* 2018, 51: 86–93, doi: 10.1016/j.rasd.2018.04.005

17. Barker ET, Hartley SL, Seltzer MM, Floyd F J, Greenberg JS, Orsmond GI. Trajectories of emotional well-being in mothers of adolescents and adults with autism. *Dev Psychol* 2011, 47:551–561, doi: 10.1037/a0021268

18. Bennett T, Boyle M, Georgiades K, Georgiades S, Thompson A, Duku E et al. Influence of reporting effects on the association between maternal depression and child autism spectrum disorder behaviors. *J Child Psychol Psychiatry* 2012, 53: 89–96, doi: 10.1111/j.1469-7610.2011.02451.x

19. Ingersoll B, Hambrick DZ. The relationship between the broader autism phenotype, child severity, and stress and depression in parents of children with autism spectrum disorders. *Res Autism Spectr Disord* 2011, 5:337–344, doi: 10.1016/j.rasd.2010.04.017

20. Weitlauf AS, Vehorn AC, Taylor JL, Warren ZE. Relationship satisfaction, parenting stress, and depression in mothers of children with autism. *Autism* 2014, 18:194–198, doi: 10.1177/1362361312458039

21. Zablotsky B, Bradshaw CP, Stuart EA. The association between mental health, stress, and coping supports in mothers of children with autism spectrum disorders. *J Autism Dev Disord* 2013, 43:1380–1393, doi: 10.1007/s10803-012-1693-7

22. Montes G, Halterman JS. Psychological functioning and coping among mothers of children with autism: A population-based study. *Pediatrics* 2007, 119: 1040–1046, doi: 10.1542/peds.2006-2819

23. Karaivazoglou K, Papadaki E, Iconomou G, Touliatos G, Kotsopoulos S, Assimakopoulos K. Psychological distress and health-related quality of life in parents of children referred to an outpatient service for children with developmental disorders. *Australas Psychiatry* 2019, 27: 152–156, doi:10.1177/1039856218815754

24. Ntre V, Papanikolaou K, Triantafyllou K, Giannakopoulos G, Kokkosi M, Kolaitis G. Psychosocial and financial needs, burdens and support, and major concerns among Greek families with children with autism spectrum disorder (ASD). *Intern J Caring Sci* 2018, 11 985-995.

25. Pattini E, Carnevali L, Troisi A, Matrella G, Rollo D, Fornari M, Sgoifo A. Psychological characteristics and physiological reactivity to acute stress in mothers of children with autism spectrum disorder. *Stress Health* 2019, 35:421–431, doi: 10.1002/smi.2870

26. Lai WW, Oei TPS. Coping in parents and caregivers of children with autism spectrum disorders (ASD): A review. *Rev J of Autism Dev Disord* 2014, 1: 207–224, doi: 10.1007/s40489-014-0021-x

27. Miranda A, Mira A, Berenguer C, Rosello B Baixauli I. Parenting stress in mothers of children with autism without intellectual disability. Mediation of behavioral problems and coping strategies. *Front Psychol* 2019, 10:464, doi: 10.3389/fpsyg.2019.00464

28. Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. *Appl Psychol Meas* 1997, 1:385–401, doi:10.1177/014662167700100306

29. Fountoulakis K, Iacovides A, Kleanthous S, Samolis S, Kaprinis SG, Sitzoglou K et al. Reliability, validity and psychometric properties of the Greek translation of the Center for Epidemiological Studies-Depression (CES-D) Scale. *BMC Psychiatry* 2001, 1: 1-8, doi: 10.1186/1471-244X-1-6

30. McCubbin HI, Olson D, Larsen A. Family crisis oriented personal evaluation scale. In McCubbin HI, Thompson AI, McCubbin MA (eds) *Family assessment: Resiliency, coping and adaptation – Inventories for research and practice*. Madison: University of Wisconsin System; 1996

31. Gouva M, Dragioti E, Konstanti Z, Kotrotsiou E, Koulouras V. Translation and Validation of a Greek version of the Family Crisis Oriented Personal Evaluation Scales (F- COPES). *Interscientific Health Care* 2016, 8:64–72

32. Abidin RR. Parenting Stress Index: Professional Manual. 3rd ed. Psychol Assess Resources, Odessa, FL, 1995

33. Haskett ME, Ahern LS, Ward CS, Allaire JC. Factor structure and validity of the parenting stress index-short form. *J Clin child Adolesc Psychol* 2006, 35:302–312, doi:10.1207/s15374424jccp3502_14

34. Hastings RP, Kovshoff H, Brown T, Ward NJ. Espinosa FD, Remington B. Coping strategies in mothers and fathers of preschool and school-age children with autism. *Autism* 2005, 9: 377–391, doi: 10.1177/1362361305056078

35. Hadjicharalambous D, Demetriou L. Investigating the influences of parental stress on parents parenting practices. *Int J Sci Acad Res* 2021, 2:1140–1148

36. Dabrowska A, Pisula E. Parenting stress and coping styles in mothers and fathers of pre-school children with autism and Down syndrome. *J Intellect Disabil Res* 2010, 54:266–280, doi: 10.1111/j.1365-2788.2010.01258.x

37. Reed P. Child behavior problems moderate effectiveness of coping strategies except for reframing for mothers of children with ASD. *Res Autism Spectr Disord* 2020, 76: 101589, doi: 10.1016/j.rasd.2020.101589

38. Loomes R, Hull L, Polmear W, Mandy WPL. What is the male-to-female ratio in autism spectrum disorder? A systematic review and meta-analysis. *J Am Acad Child Adolesc Psychiatry* 2017, 56:466–474, doi: 10.1016/j.jaac.2017.03.013

39. Papadopoulos Ch, Lodder A, Constnantinou G, Randhawa G. Systematic review of the relationship between autism stigma and informal caregiver mental health. *J Autism and Dev Disord* 2019, 49: 1665–1685, doi: 10.1007/s10803-018-3835-z

40. Dunn ME, Burbine T, Bowers CA, Tantleff-Dunn S. Moderators of stress in parents of children with autism. *Community Ment Health J* 2001, 37: 39–52, doi: 10.1023/a: 1026592305436

41. Loomes R, HullL, Polmear W, Mandy L. What is the male-to-female ratio in autism spectrum disorder? A systemic review and meta-analysis. *J Am Acad Child Adolesc Psychiatr* 2017, 56:466–474, doi: 10.1016/j.jaac.2017.03.013

Ερευνητική εργασία

Στρατηγικές αντιμετώπισης των μητέρων με παιδιά με διαταραχές του φάσματος του αυτισμού: Η σχέση με το μητρικό στρες και την κατάθλιψη

Βασιλική Ντρε,[1] Κατερίνα Παπανικολάου,[2] Ειρήνη Αμανάκη,[3] Καλλιόπη Τριανταφύλλου,[4] Χαρά Τζαβάρα,[4] Γεράσιμος Κολαΐτης[2]

[1]*Καρδιολογική και Καρδιοχειρουργική Κλινική, Νοσοκομείο Παίδων «Η Αγία Σοφία», Ιατρική Σχολή, Εθνικό & Καποδιστριακό Πανεπιστήμιο Αθηνών,*

[2]*Παιδοψυχιατρική Κλινική, Νοσοκομείο Παίδων «Η Αγία Σοφία», Ιατρική Σχολή, Εθνικό & Καποδιστριακό Πανεπιστήμιο Αθηνών, Αθήνα,*

[3]*Μεταπτυχιακό Πρόγραμμα Σπουδών, Σχολή Ανθρωπιστικών Επιστημών, Ελληνικό Ανοικτό Πανεπιστήμιο, Πάτρα,*

[4]*Ιατρική Σχολή, Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών, Αθήνα*

ΙΣΤΟΡΙΚΟ ΑΡΘΡΟΥ: Παραλήφθηκε 11 Ιουνίου 2021/Αναθεωρήθηκε 11 Οκτωβρίου 2021/Δημοσιεύθηκε Διαδικτυακά 21 Φεβρουαρίου 2022

ΠΕΡΙΛΗΨΗ

Η ύπαρξη παιδιού με αυτισμό έχει ισχυρό αντίκτυπο σε ολόκληρη την οικογένεια και ειδικά στις μητέρες, οι οποίες είναι συνήθως οι κύριοι φροντιστές των παιδιών αυτών. Οι γονείς παιδιών με αυτισμό αναφέρουν περισσότερα προβλήματα ψυχικής υγείας, σε σύγκριση με τους γονείς παιδιών με άλλες αναπτυξιακές αναπηρίες ή γονείς παιδιών φυσιολογικής ανάπτυξης. Οι γονικές στρατηγικές αντιμετώπισης άγχους μπορεί να διαδραματίσουν σημαντικό ρόλο όταν οι γονείς έρχονται αντιμέτωποι με στρεσογόνες καταστάσεις κατά τη διάρκεια της ανάπτυξης του παιδιού. Σκοπός της παρούσας έρευνας ήταν να διερευνήσει τις στρατηγικές αντιμετώπισης (διαχείριση δύσκολων καταστάσεων και αλληλεπίδραση με το περιβάλλον) σε μητέρες με παιδιά με αυτισμό και τη σχέση αυτών των στρατηγικών με το μητρικό στρες και την κατάθλιψη. Στην παρούσα μελέτη συμμετείχαν 143 μητέρες (μέση ηλικία 42,7 ετών) παιδιών με αυτισμό (6–17 ετών) που είχαν απευθυνθεί στο Ειδικό Ιατρείο Διαταραχών Φάσματος Αυτισμού της Πανεπιστημιακής Παιδοψυχιατρικής Κλινικής στο Γενικό Νοσοκομείο Παίδων. Οι συμμετέχουσες στην έρευνα συμπλήρωσαν τα ακόλουθα ερωτηματολόγια: Ερωτηματολόγιο δημογραφικών στοιχείων, την Κλίμακα κατάθλιψης (Center for Epidemiologic Studies Depression Scale, CES-D), την Κλίμακα στρατηγικών αντιμετώπισης (Family Crisis Oriented Personal Scales, F-COPES) και το ερωτηματολόγιο γονεϊκού στρες (Parenting Stress Index Short-Form, PSI-SF). Οι μητέρες με υψηλότερο μορφωτικό επίπεδο σημείωσαν σημαντικά χαμηλότερη βαθμολογία στην υποκλίμακα «αναπλαισίωση» του F-COPES και στη συνολική βαθμολογία του F-COPES. Οι αυξημένες καθημερινές ώρες που αφορούσαν στη φροντίδα του παιδιού και η φαρμακευτική αγωγή του παιδιού ήταν επιπρόσθετοι παράγοντες που συσχετίζονταν σημαντικά με χαμηλότερες βαθμολογίες στην υποκλίμακα «αναπλαισίωση». Η υποκλίμακα αυτή συσχετίστηκε επίσης αρνητικά με τα επίπεδα γονικής δυσφορίας, ενώ η υποκλίμακα «παθητική αξιολόγηση» του F-COPES συσχετίστηκε θετικά με τα καταθλιπτικά συμπτώματα των μητέρων. Οι χαμηλότερες βαθμολογίες σχετικά με την κινητοποίηση της οικογένειας για απόκτηση και αποδοχή βοήθειας συσχετίστηκαν με σοβαρή επιβάρυνση στην οικογενειακή ζωή. Οι στρατηγικές αντιμετώπισης των μητέρων παιδιών με αυτισμό σχετίζονται με διάφορους παράγοντες όπως τα προσωπικά χαρακτηριστικά των φροντιστών, τη θεραπεία των παιδιών και τα οικογενειακά χαρακτηριστικά. Οι επαγγελματίες ψυχικής υγείας είναι σημαντικό να εξετάζουν προσεκτικά παράγοντες που μπορεί να ενισχύσουν τις στρατηγικές αντιμετώπισης, οι οποίες βοηθούν τις μητέρες να διαχειριστούν τις προκλήσεις που συναντούν, όταν μεγαλώνουν παιδί με αυτισμό.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: Διαταραχές φάσματος αυτισμού, στρατηγικές αντιμετώπισης, κατάθλιψη, γονεϊκό στρες

Συγγραφέας επικοινωνίας: Βασιλική Ντρε, Νοσοκομείο Παίδων «Η Αγία Σοφία» Θηβών & Παπαδιαμαντοπούλου, 115 27 Αθήνα, Διεύθυνση e-mail: vassilikintre@yahoo.gr

https://doi.org/10.22365/jpsych.2022.074 / Psychiatriki 2022, 33:219–227

Research article

Mental health of unaccompanied refugee minors in Greece living "in limbo"

Ioanna Giannopoulou, Lida Mourloukou, Vasiliki Efstathiou, Athanassios Douzenis, Panagiotis Ferentinos

Second Department of Psychiatry, National and Kapodistrian University of Athens, Attikon University Hospital, Athens, Greece

ARTICLE HISTORY: Received 8 September 2021/Revised 9 December 2021/Published Online 27 April 2022

ABSTRACT

The closure of the Balkan migration route in 2016, had implications for unaccompanied refugee minors (URMs), given that the vast majority, who perceived Greece as "stopover" for their desired final destination, were forced to remain in the country for an indeterminate period of time. This created for URMs a challenging situation of living "in limbo" uncertain about their future awaiting for a long time the outcome of their asylum application. This cross-sectional study aimed to explore the mental health of URMs, who arrived in Greece in 2016. The sample comprised of 90 URMs (76 boys), aged 13–17 years, consisting of 46 Syrians and 44 originating from other countries. Participants completed socio-demographic information and a range of clinical measures, including Children's Revised Impact of Events Scale (CRIES), Depression Self-Rating Scale (DSRS), Children's Post-Traumatic Cognitions Inventory (cPTCI), a measure of trauma exposure and perceived social support. Syrian URMs were significantly more likely than URMs originating from other countries to score within the probable clinical depression range (71.7% versus 47.7% respectively, p=0.020), to display probable posttraumatic stress disorder (PTSD), i.e., score within clinically significant range of posttraumatic stress symptoms and negative post-trauma cognitions (87% versus 65.9%, p=0.018), and meet the comorbidity PTSD/depression criterion (65.2% versus 40.9%, p=0.021). Multiple linear stepwise regression analyses showed that legal status (seeking asylum in Europe through family reunification procedure) significantly predicted higher levels of depressive symptoms (β=0.29, p=0.004), posttraumatic stress symptoms (β=0.21, p=0.034) and negative cognitions (β=0.33, p=0.001). The total number of stressful/traumatic experiences and male gender were found to be significantly related only with posttraumatic symptoms severity score (β=0.29, p=0.003), whereas lower levels of perceived social support were associated with increased levels of depressive symptoms (β=0.24, p=0.018) and negative cognitions and appraisals of the world and the self (β=0.26, p=0.008). These findings highlight the burden of living "in limbo" situation and add weight to the argument for amending restrictive EU asylum policies and accelerating the family reunification procedure under Dublin-III Regulation, as well as the pressing need for improved URMs access to mental health services and psychosocial support.

KEYWORDS: Unaccompanied refugee minors, PTSD, post-trauma negative cognitions, depression, traumatic experiences.

Introduction

Unaccompanied refugee minors (URMs) are a particularly vulnerable group for developing mental health problems, as they face unique challenges. Several studies in the context of 2015–2017 European migrant crisis have documented across national and settlement contexts high rates of mental health problems, such as post-traumatic stress symptoms (PTSS), post-traumatic stress disorder (PTSD), depression, anxiety, internalizing and externalizing behaviors and somatic complaints among URMs,[1] in keeping with previous research on refugee children resettled in high-income countries.[2] Most studies were conducted in heterogeneous sam-

Corresponding author: Ioanna Giannopoulou, Second Department of Psychiatry, National and Kapodistrian University of Athens, Attikon University Hospital, 1 Rimini street, GR-124 62 Athens, Greece • e-mail: igianno@med.uoa.gr

ples, including groups of accompanied and unaccompanied minors comparing outcomes between the two but not with respect to country of origin. A cross-sectional study of children in Syria exposed to war-associated daily stresses found that 60.5% met the criteria for at least one psychological disorder.[3] Prospective cohort studies indicated that severe exposure to trauma, female gender, older age, being denied asylum and high resettlement and social integration stressors were associated with persistent psychopathology.[1]

Greece is one of the major gateway countries for asylum to the EU.[4] The closure of the Balkan migration route to central and northern Europe, in March 2016 and the development of inhospitable climate in most European countries had implications for URMs. Even though most had neither planned nor wished to settle in Greece they were forced to remain in the country for an indefinite period of time.[4] This created for them a challenging situation of living in a state of prolonged uncertainty and limbo, compounded by enduring stress concerning their future and fear of deportation, in the context of the delays in the asylum procedure including family reunification (Dublin III Regulation) and frequent changes affecting the degree of continuity and life stability.

The present study aimed: (a) to explore for the first time in a standardized way the experience of trauma and levels of psychological distress among URM that have arrived in Greece in the wake of the so-called European migrant crisis, shortly before or after the closure of Balkan migration route, (b) to examine whether URMs originating from Syria compared with those originating from other countries differ with respect to mental health outcomes; we hypothesized that URMs fleeing war, i.e. Syrians, will display higher rates of PTSD and depression, and (c) to identify sociodemographic characteristics and stressors that predict higher levels of PTSS and depression symptoms, as well as negative cognitions.

Material and Method

Participants

The total sample comprised of 90 URMs (76 boys), between 13 and 17 years of age, consisting of 46 Syrians and 44 originating from other countries, housed in nine long-stay residential facilities, so called shelters for UMRs in Athens, run by a Non-Governmental Organization (NGO).

Procedure

The study was approved by the Ethics Committee of Attikon University Hospital. All shelters were contacted and given detailed information about the study and agreed to support it. Written permission to carry out the study was obtained from the Prosecutor for Minors, acting as a legal guardian. Participants were recruited between January 2018 and June 2018. Participation in the study was voluntary. The second author set up appointments for those who agreed to take part in the study; the completion of the questionnaires by the participant was carried out in a quiet room within his/her facility, with the presence of the second author and an interpreter. All measures were available in English, Arabic, Dari, and Farsi but the interpreter's help was sought only in case a participant didn't have adequate competency to read the questions or asked for clarifications. Participants were asked to sign a consent form after being informed about the aims of the study, the option to opt out at any point, the anonymity, and the obligation to confidentiality of all involved. In case the young person got distressed by the questions, the researcher was available for immediate psychological support and for giving contact details and appointment at the 2nd Department of Psychiatry of Attikon University Hospital. No case of emergency was documented throughout the study.

Measures

Socio-demographic characteristics

Participants completed a brief questionnaire regarding their age, gender, religion, spoken language, length of schooling, legal status, length of journey and stay in Greece, length of stay in Reception Identification Centre (RIC), contact with family, contact with mental health services, participation in organized leisure and learning language activities.

Exposure to trauma

An event checklist, based on the War Trauma Questionnaire (WTQ)[5] was adapted for use in the present study. It included 12 events the young person may have witnessed or personally experienced during pre-flight period (7 no/yes questions) and during the flight-journey (5 no/yes questions). The total score (range 0–12) derived from summing the endorsed items gives an indication of the youth's level of trauma exposure.

Depression Self-Rating Scale (DSRS)[6]

This is an 18-item scale designed to measure symptoms of depression. Each item is scored on the direction of the disturbance on a 3-point Likert-type scale ranging from 0 (never) to 2 (most of the time). The item scores are summed to give the severity depression score, which ranges from 0 to 36, with higher scores denoting higher levels of depression; a cutoff score of 15 points and

above is used to indicate probable depression. The DSRS has been used as a screening instrument in different cultural settings, including Palestinian children who were exposed to war,[7] Iranian adolescents,[8] as well as Nepali[9] and Burundi[10] children. The internal consistency of the scale in the present study was found to be adequate (Cronbach's alpha=0.83; for Arabic version 0.78, for Farsi/Dari 0.89 and for Urdu 0.90).

Children's Revised Impact of Events Scale[11]

This is a 13-item scale adapted from the Impact of Event Scale (IES)[12] that assesses intrusive thoughts and images, avoidance of thoughts or reminders of the event, and the degree of arousal. Participants are asked to rate how frequently each statement was true for them during the past seven days on a 4-point Likert scale scored as 0 (not at all), 1 (rarely), 3 (sometimes), 5 (often). Reliability and validity of the scale has been supported in studies of children and adolescents 8–18 years old exposed to war and conflict,[11,13,14] as well as natural disasters.[15] However, not all translations have been validated. In the present study we used the eight-item version (CRIES-8), comprising intrusion and avoidance items, and applied a cutoff score≥17 indicating a high probability of suffering PTSD.[14,16] The item scores are summed to give the post-traumatic stress symptoms (PTSS) severity score, which ranges from 0 to 40, with higher scores denoting higher levels of PTSS. The internal consistency of the CRIES-8 scale in the present study was found to be adequate (Cronbach's alpha = 0.83; for Arabic version 0.78, for Farsi/Dari 0.89 and for Urdu 0.90).

Children's Post-Traumatic Cognitions Inventory (cPTCI)[17]

This is a 25-item self-report questionnaire that measures maladaptive or overly negative posttraumatic thoughts and appraisals of the world and the self in young people following exposure to trauma. It comprises of statements describing the trauma-exposed child as a feeble person in a scary world (e.g., "Anybody could hurt me"; "I can't stop bad things from happening to me") and their post-trauma life as disturbing and permanently negatively changed (e.g., "My life has been destroyed by the frightening event"; "Not being able to get over all my fears means that I am a failure"). Children are asked to indicate on a 4-point Likert scale to what extent they agree or disagree with each statement (1=don't agree at all; 2=don't agree a bit; 3=agree a bit; 4=agree a lot). The item scores are summed to give a total cPTCI score, ranging from 25 to 100. A score in the range of 46 to 48 on the cPTCI is indicative of clinically significant negative post-trauma appraisals of the world and the self, typical of children and adolescents with PTSD. The measure has been used in a psychosocial group intervention study with war-affected children.[18] The internal consistency of the scale in the present study was found to be good (Cronbach's alpha = 0.86; for Arabic version 0.85, for Farsi/Dari 0.84 and for Urdu 0.90).

Social support index

Participants were asked to indicate whether or not (yes/no) they got support from various sources, i.e., recreational, spiritual, educational, close friends, staff, and mates in the accommodation facility. The total score (range 0–5) derived from summing the endorsed items gives an indication of the youth's perceived social support level.

Statistical analysis

All analyses were carried out with SPSS 26.0.[19] Prevalence rates were calculated on the basis of available cut off scores for each measure. For group comparisons we used independent samples t-test for continuous and chi-square for categorical variables. Multiple linear stepwise regression analyses were carried out to identify significant predictors of mental health outcome measures, i.e., CRIES, DSRS and cPTCI (dependent variables). Independent predictor variables included in the analysis were demographic data (gender; legal status, i.e., asylum seeking in Europe vs asylum seeking in Greece), trauma exposure (i.e., the total number of traumatic experiences during pre-flight and flight journey), the length of stay in Greece and perceived social support index. Age was not used due to restricted age range.

Results

Participant characteristics

Demographic information is reported in table 1. Regarding the country of origin, most were from Syria (n=46, 47.8%); followed by Afghanistan (n=13, 14.4%), Pakistan (n=9, 10%), Iran (n=7, 7.8%), Iraq (n=5, 5.6%), North African (n=7, 7.8%), and African countries (n=3, 3.3%). With regards to spoken language, 62.2% (n=56) used Arabic, 26.7% (n=24) Farsi/Dari, 10% (n=9) Urdu, and 1.1% (n=1) Lingala. Most entered Greece via the Aegean islands (n=75, 83.3%). Compared to URMs from other countries, Syrians URMs were more likely to have applied for asylum in central or northern European country through family reunification procedure (Dublin III Regulation), were less likely to attend leisure, Greek language and foreign language activities. The two groups of URMs did not differ with respect to further socio-demographic characteristics.

Table 1. Socio-demographic characteristics of the sample.

	URMs from Syria (N=46)	URMs from other countries (N=44)	Total Sample (N=90)	p*
Age in years, M(SD)	16.1 (1.2)	16.2 (1.2)	16.2 (1.2)	0.637[a]
Gender				0.098[c]
Male, n (%)	36 (78.3)	40 (90.9)	76 (84.4)	
Female, n (%)	10 (21.7)	4 (9.1)	14 (15.6)	
Religion				0.001[c]
Islamic faith, n (%)	46 (100)	33 (75)	79 (87.8)	
Other, n (%)	0	11 (25)	11 (12.2)	
Legal status				0.019[c]
Seeking asylum in Europe, n (%)	27 (58.7)	15 (34.1)	42 (46.7)	
Seeking asylum in Greece, n (%)	19 (41.3)	29 (65.9)	48 (53.3)	
Years of schooling, Median (Q1, Q3)	7 (4.8, 8)	7 (5, 8)	7 (5, 8)	0.678[b]
Months of journey to Greece, Median (Q1, Q3)	2 (1, 3)	2 (1, 3)	2 (1, 3)	0.535[b]
Months of stay in RIC, M(SD)	2.5 (0.7)	2.4 (0.8)	2.4 (0.8)	0.665[a]
Months of stay in Greece, Median(Q1, Q3)	15 (10, 19)	18 (12.5, 25)	15.5 (12, 22)	0.051[b]
Contact with the family, n (%)	44 (95.7)	39 (88.6)	83 (92.2)	0.396[c]
Mental Health services contact since arrival, n (%)	17 (37)	11 (25)	28 (31.1)	0.319[c]
Attending Greek lessons, n (%)	2 (4.3)	15 (34.1)	17 (18.9)	0.001[c]
Attending foreign lessons, n (%)	9 (19.6)	19 (43.2)	28 (31.1)	0.028[c]
Participating in organized activities by the shelter, n (%)	10 (21.7)	24 (54.4)	34 (37.8)	0.003[c]

Abbreviations: URMs: Unaccompanied Refugee Minors; RIC: Reception and Identification Center
Percentages calculated for columns
* comparison between URMs from Syria and URMs from other countries
a t-test; b Mann-Whitney U test; c chi-square test
bold, p<0.05

Trauma exposure

Table 2 displays the trauma-related experiences encountered by URMs. Comparison between URMs from Syria and URMs originating from other countries revealed significantly higher trauma exposure scores among Syrians, t(88)=3.25, p=0.002, (M=5.89, SD=2.22 vs. M=4.44, SD=2.03, respectively); significant difference between the groups in pre-flight trauma exposure, t(88)=3.49, p=.001, (M=3.89, SD=1.65 for Syrians vs. M=2.68, SD=1.64 for others); no significant group difference in trauma exposure during the journey (M=2.00, SD=1.19 for Syrians vs. M=1.70, SD=0.90 for others); t(88)=1.32, p=0.190.

Gender differences in mental health outcomes

Boys scored significantly higher than girls on CRIES-8 (M=27.26, SD=9.77 vs. M=18.71, SD=7.89, respectively), t(88)=3.09, p=0.003, but no significant gender differences were found in the average levels of negative post-trauma cognitions (M=62.56, SD=13.85 vs. M=64.36, SD=9.91, respectively), t(88)=-0.47, p=0.643, neither in the mean depression score (M=16.84, SD=6.34 for boys vs. M=19.14, SD=4.04 for girls), t(26.535)=–1.77, p=0.088.

Group differences in mental health outcomes

Table 3 provides an overview of mental health outcome measures for URMs participating in the study. Syrians URMs scored significantly higher than URMs from other countries on depression symptoms severity scores (p=0.016), but no differences were found in mean PTSS (p=0.344) and negative post-trauma cognitions (p=0.125) scores.

Applying clinical cutoffs on DSRS, Syrian URMs were more likely, than their counterparts from other countries of origin, to score within the likely clinical depression range, x^2 (1, N=90) =5.40, p=0.02, but not within the likely clinical PTSD range, x^2 (1, N=90) =0.49, p=0.48. However,

Table 2. Experience of trauma amongst URMs from Syria and other countries.

	URMs from Syria N (%)	URMs from other countries N (%)	Total Sample N (%)	p*
Pre-flight period				
Displacement/change of residence and/or school	38 (82.6)	23 (52.3)	61 (67.8)	0.002
Separated from parents	41 (89.1)	31 (70.5)	72 (80.0)	0.027
Witnessed violent acts	35 (76.5)	24 (54.5)	59 (65.6)	0.032
Being victim of violent acts	20 (43.5)	18 (40.9)	38 (42.2)	0.805
Death of a close family member (mother, father, sibling)	15 (32.6)	15 (34.1)	30 (33.3)	0.881
Death of significant loved one (e.g., friend, neighbor, teacher	21 (45.7)	6 (13.6)	27 (30.0)	0.001
Suffered serious physical injury	9 (19.6)	4 (9.1)	13 (14.4)	0.158
Flight period, i.e., journey to Greece				
Experienced kidnapping, robbery or being cheated	32 (69.6)	31 (70.5)	63 (70.0)	0.927
Witnessed drowning in the sea	10 (21.7)	11 (25.0)	21 (23.3)	0.715
Death of a loved one	16 (34.8)	2 (4.5)	18 (20.0)	<0.001
Experienced ambiguous loss (e.g. not knowing the fate of a loved one)	7 (15.2)	8 (18.2)	15 (16.7)	0.706
Other stressful events	27 (58.7)	22 (50.0)	49 (54.4)	0.408

Abbreviations: URMs: Unaccompanied Refugee Minors
Percentages calculated for columns; comparisons were performed with chi-square tests
* comparison between URMs from Syria and URMs from other countries
bold, p<0.05

when applying more stringent criteria for identifying probable PTSD cases (i.e., scoring above the clinical cut offs on both CRIES-8 and cPTCI), Syrian URMs (87%) were significantly more likely, than URMs from other countries of origin (65.9%), to score within the clinically significant range of PTSD and negative post-trauma cognitions, x^2 (1, N=90) =5.57, p=0.018.

Comorbid probable PTSD/depression diagnosis, determined by the participant scoring above threshold values on all mental health outcome measures, i.e., CRIES-8, cPTCI and DSRS, was found in 48 URMs (53.3%); of those, 20 (41.7%) had contact with mental health services. Syrian URMs (N=30, 65.2%) were more likely than URMs from other countries of origin (N=18, 40.9%) to meet the comorbidity of probable PTSD/depression criterion, x^2 (1, N=90)=5.34, p=0.021.

Predictors of self-report mental health outcomes

Table 4 provides the results of the linear stepwise regressions analyses. With regards to trauma-related mental health outcomes, the regression analysis demonstrated that the total number of traumatic experiences, male gender, and seeking asylum in Europe significantly predicted the CRIES severity score, accounting for 22% of variance in PTSS scores. The legal status (seeking asylum in Europe through family reunification procedure) was the strongest predictor of post-trauma negative cognitions followed by lower levels of social support accounting all together for 16% of variation in cPTCI scores.

In terms of depression, the regression analysis demonstrated that the legal status (seeking asylum in Europe) and lower levels of social support predicted the depression severity score, accounting together for 12% of variance in DSRS scores.

Discussion

The present study examined the rates of traumatic experiences and levels of psychological distress, including PTSS, depression and negative cognitions in a sample of 90 URMs who arrived in Greece shortly before or after the closure of the Balkan migration route in March 2016. As expected, the results indicate high levels of war/violence-related trauma among URMs, including death of a family member or significant others (66.3%) and/or ambiguous loss, i.e., not knowing the fate of significant others (16.7%). Substantial proportion (70%) experienced being kidnapped, robbed or cheated and having witnessed drowning of another person in the Aegean Sea (23.3%) during the flight pe-

Table 3. Mental health outcome measures by URMs groups

	URMs from Syria (N=46)	URMs from other countries (N=44)	Total (N=90)	p*
DSRS, M (SD)	18.70 (5.35)	15.64 (6.44)	17.20 (6.07)	0.016[a]
CRIES-8, M (SD)	24.96 (8.79)	26.95 (11.06)	25.93 (9.96)	0.344[a]
cPTCI, M (SD)	64.93 (12.96)	60.64 (13.40)	62.83 (13.28)	0.125[a]
DSRS ≥15, n (%)	33 (71.7)	21 (47.7)	54 (60)	0.020[b]
CRIES ≥ 17, n (%)	41 (89.1)	37 (84.1)	78 (81.8)	0.482[b]
cPTCI ≥ 48, n (%)	42 (91.3)	34 (77.3)	76 (84.4)	0.066[b]

Abbreviations: URMs: Unaccompanied Refugee Minors; DSRS: Depression Self-Rating Scale; CRIES: The Children's Revised Impact of Events Scale; cPTCI: The Children's Post-Traumatic Cognitions Inventory
* comparison between URMs from Syria and URMs from other countries
a t-test; bchi-square test
bold, p<0.05

Table 4. Linear stepwise regression analysis for variables predicting CRIES, cPTCI and DSRS outcome measures

	B (SE)	β	*p*
CRIES-8 (F=9.25, df=3, 86, p<0.001, adj. R^2=0.218)			
Trauma exposure	1.269 (0.425)	.286	0.004
Gender (Male=0, Female=1)	–7.827 (2.598)	–.286	0.003
Asylum seeking (in Europe=0, in Greece=1)	–4.127 (1.920)	–.208	0.034
cPTCI (F=9.26, df=2, 87, p<0.001, adj. R^2=0.157)			
Asylum seeking (in Europe=0, in Greece=1)	–8.809 (2.578)	–.333	0.001
Social support	–2.028 (0.748)	–.264	0.008
DSRS (F=7.02, df=2, 87, p<0.001, adj. R^2=0.119)			
Asylum seeking (in Europe=0, in Greece=1)	–3.544 (1.205)	–.293	0.004
Social support	–0.840 (0.350)	–.239	0.018

Abbreviations: URMs: Unaccompanied Refugee Minors; DSRS: Depression Self-Rating Scale; CRIES: The Children's Revised Impact of Events Scale; cPTCI: The Children's Post-Traumatic Cognitions Inventory

riod, confirming the high level of challenges and risks URMs face during their migration journey. As expected, Syrians fleeing from war experienced more traumatic events than youth from other countries, which were accounted for by higher levels of trauma exposure during the pre-flight period.

The rate of PTSS above the clinical threshold (86.7%) in our sample was higher than the reported in recent review by Kien et al[20] who found the point prevalence for PTSD between 19.0 and 52.7%. However, adapting a cut off indicative of clinically significant negative cognitions and appraisals of the world and the self that are typical of children and adolescents with PTSD and combining it with the clinical threshold of PTSS, led to a drop in the prevalence rate of probable PTSD diagnosis, which nevertheless still remained high (75.6%). As expected, Syrian URMs (84.8%) were more likely, than URMs from other countries of origin (65.9%), to score above the clinical cut-off for PTSS and post-traumatic negative cognitions. This may be explicable in terms of combination of the effects of mass uprooting conditions from the area from which they come and living "in limbo", which contributes to the accumulation of stressful and traumatic experiences. Similarly to the PTSD, depression rate in the present sample (67.4%) was in the upper range of most studies concerning URMs.[21] The rate of probable comorbid PTSD and depression (53.3%) found in the present study, comparable to the reported (57%) in URMs previously held in British detention centers,[22] most likely underscores the ongoing uncertainty regarding decision on their asylum status and the enduring fear of deportation. This high rate of comorbidity warrants attention, given that individuals who suffer from both

PTSD and depression usually display greater psychological burden, lower levels of global functioning and a more chronic course of impairment.[23] Furthermore, it is of concern that only 41.7% of URMs with comorbid PTSD/depression were in some contact with mental health services. The higher rates of probable PTSD and depression in our study, as compared to recent ones from central and northern European countries, might be due to different measures employed across studies, but also to different sample composition. It is important to stress that our sample comprised URMs whose living situation differs from those who have reached the final destination country. Living "in limbo" conceivably affects URMs emotionally, interfering with many aspects of their daily life (e.g., learning the language, participation in leisure activities, school activities, establishing social networks and new connections). Indeed, only about third of our sample participated in any organized leisure and learning foreign language activities, whereas only less than a fifth of the sample was learning Greek.

In terms of different factors possibly associated with the mental health of URMs, demographic data (gender, legal status), the total number of traumatic experiences, the length of stay in Greece, and social support were analyzed as predictors for the mental health outcome measures. Consistent with findings from other studies,[21] the total number of traumatic experiences was found to be a significant predictor for PTSS and depression symptoms severity score. The legal status (seeking asylum in Europe through family reunification procedure under the Dublin III Regulation) significantly predicted all self-reported mental health outcomes, a finding that draw attention to the detrimental effects of delaying or denying children's rights to family reunion. For these traumatized young people, it is much more important to reunite with their loved ones (safe haven), since any other context cannot adequately meet their basic psychological needs. Mental health impacts of stresses related to a decision regarding the residence permit or refugee status have been highlighted in previous studies.[24,25] Lower levels of perceived social support predicted increased levels of depression symptoms and negative cognitions and appraisals of the self and the world. Post-migration social-environmental factors, such as long wait for outcome of asylum application, poor social support, poor language proficiency of host country, experience of discrimination and experience of daily hassles, precarious living conditions have been shown to impact URMs mental health outcomes and capacity to focus on school and learning the language, making integration difficult.[1,26,27]

The findings of this study should be interpreted in light of a number of limitations in its design. First, the sample comprised of URMs living in long-stay accommodation facilities run by one NGO, which limits the generalizability of findings to URMs living in Greece. Further research on representative samples should be carried out, allowing for comparisons between different types of care facilities. Precarious living conditions in camps, for example, may further exacerbate mental health difficulties. Second, estimates of PTSD and depression are based on cut-off values on the self-report questionnaires, therefore are subject to recall bias. Studies based on clinical interviews have shown lower levels of PTSD and depression than those based on self-report questionnaires. However, none of the previous studies, using self-report measures, assessed negative trauma-related cognitions and appraisals of the self and the world, which are part of DSM-5 criteria for diagnosing PTSD. Combining clinical cut offs on both CRIES and cPTCI measures allowed for applying a more stringent criterion for calculating the prevalence rates of probable PTSD. Third, the cross-sectional nature of data does not allow for causal assertions. Longitudinal study design would allow for examining the course of symptoms among URMs over time and how mediating and moderating factors contribute through their effect to mental health outcomes for those who are granted a refugee status and attempt to rebuild their life in Greece or reunite with their families in another European country.

Although our results may be subject to sampling and recall bias, the unexpectedly high rates of PTSD and depression warrant an urgent call to action. The delays and high rate of rejected applications seem to have detrimental consequences of shrinking the right to family reunification, family life, children's rights and other individual rights.[28] Our findings provide evidence on the detrimental consequences for URMs' mental health and need for provision of mental health and psychosocial support services. Clinicians need to be aware of post-trauma negative cognitions and appraisals of the self and the world as a result of traumatic experiences that URMs encounter, as they often are linked to the development and maintenance of trauma-related disorders and display of behavior problems. EU politicians need to be aware that the uncertainty about the future of URMs living "in limbo" situation, might not only have a debilitating impact on their mental health and compromise the chance of future young people's psychosocial adjustment in host countries, but also violates substantial welfare principles, such as the family unity and the best interest of the child.

References

1. Bamford J, Fletcher M, Leavey G. Mental Health Outcomes of Unaccompanied Refugee Minors: a Rapid Review of Recent Research. *Curr Psychiatry Rep* 2021, 23:46, doi: 10.1007/s11920-021-01262-8
2. Fazel M, Reed RV, Panter-Brick C, Stein A. Mental health of displaced and refugee children resettled in high-income countries: risk and protective factors. *Lancet* 2012, 379:266–282, doi: 10.1016/s0140–6736 (11)60051-2
3. Perkins JD, Ajeeb M, Fadel L, Saleh G. Mental health in Syrian children with a focus on post-traumatic stress: a cross-sectional study from Syrian schools. *Soc Psychiatry Psychiatr Epidemiol* 2018, 53:1231–1239, doi: 10.1007/s00127-018-1573-3
4. Hodes M, Anagnostopoulos D, Skokauskas N. Challenges and opportunities in refugee mental health: clinical, service, and research considerations. *Eur Child Adolesc Psychiatry* 2018, 27:385–388, doi: 10.1007/s00787-018-1115-2
5. Macksoud MS. Assessing war trauma in children: A case study of Lebanese children. *J Refug Stud* 1992, 5:1–15, doi: 10.1093/jrs/5.1.1
6. Birleson P, Hudson I, Buchanan DG, Wolff S. Clinical evaluation of a self-rating scale for depressive disorder in childhood (Depression Self-Rating Scale). *J Child Psychol Psychiatry* 1987, 28:43–60, doi: 10.1111/j.1469-7610.1987.tb00651.x
7. Sanchez-Cao E, Kramer T, Hodes M. Psychological distress and mental health service contact of unaccompanied asylum-seeking children. *Child Care Health Dev* 2013, 39:651–659, doi: 10.1111/j.1365-2214.2012.01406.x
8. Taghavi MR. Factor structure of the Depression Self-Rating Scale in an Iranian adolescent sample. *Psychol Rep* 2006, 99:709–716, doi: 10.2466/pr0.99.3.709-716
9. Kohrt BA, Jordans MJ, Tol WA, Luitel NP, Maharjan SM, Upadhaya N. Validation of cross-cultural child mental health and psychosocial research instruments: adapting the Depression Self-Rating Scale and Child PTSD Symptom Scale in Nepal. *BMC Psychiatry* 2011, 11:127, doi: 10.1186/1471-244x-11-127
10. Ventevogel P, Komproe IH, Jordans MJ, Feo P, De Jong JT. Validation of the Kirundi versions of brief self-rating scales for common mental disorders among children in Burundi. *BMC Psychiatry* 2014, 14:36, doi: 10.1186/1471-244x-14-36
11. Smith P, Perrin S, Dyregrov A, Yule W. Principal components analysis of the impact of event scale with children in war. *Pers Individ Dif* 2003, 34:315–322, doi: 10.1016/S0191-8869(02)00047-8
12. Horowitz M, Wilner N, Alvarez W. Impact of Event Scale: a measure of subjective stress. *Psychosom Med* 1979, 41:209–218, doi: 10.1097/00006842-197905000-00004
13. Barron IG, Abdallah G, Smith P. Randomized control trial of a CBT trauma recovery program in Palestinian schools. *J Loss Trauma* 2013, 18:306–321, doi: 10.1080/15325024.2012.688712
14. Perrin S, Meiser-Stedman R, Smith P. The Children's Revised Impact of Event Scale (CRIES): Validity as a screening instrument for PTSD. *Behav Cogn Psychother* 2005, 33:487–498, doi: 10.1017/S1352465805002419
15. Giannopoulou I, Strouthos M, Smith P, Dikaiakou A, Galanopoulou V, Yule W. Post-traumatic stress reactions of children and adolescents exposed to the Athens 1999 earthquake. *Eur Psychiatry* 2006, 21:160–166, doi: 10.1016/j.eurpsy.2005.09.005
16. Stallard P, Velleman R, Baldwin S. Psychological screening of children for post-traumatic stress disorder. *J Child Psychol Psychiatry* 1999, 40:1075–1082, PMID: 10576537
17. Meiser-Stedman R, Smith P, Bryant R, Salmon K, Yule W, Dalgleish T, et al. Development and validation of the Child Post-Traumatic Cognitions Inventory (CPTCI). *J Child Psychol Psychiatry* 2009, 50:432–440, doi: 10.1111/j.1469-7610.2008.01995.x
18. Kangaslampi S, Punamaki RL, Qouta S, Diab M, Peltonen K. Psychosocial Group Intervention Among War-Affected Children: An Analysis of Changes in Posttraumatic Cognitions. *J Trauma Stress* 2016, 29:546–555, doi: 10.1002/jts.22149
19. IBM Corp. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp. 2019.
20. Kien C, Sommer I, Faustmann A, Gibson L, Schneider M, Krczal E, et al. Prevalence of mental disorders in young refugees and asylum seekers in European Countries: a systematic review. *Eur Child Adolesc Psychiatry* 2019, 28:1295–1310, doi: 10.1007/s00787-018-1215-z
21. El Baba R, Colucci E. Post-traumatic stress disorders, depression, and anxiety in unaccompanied refugee minors exposed to war-related trauma: a systematic review. *Int J Cult Ment Health* 2018, 11:194–207, doi: 10.1080/17542863.2017.1355929
22. Ehntholt KA, Trickey D, Harris Hendriks J, Chambers H, Scott M, Yule W. Mental health of unaccompanied asylum-seeking adolescents previously held in British detention centres. *Clin Child Psychol Psychiatry* 2018, 23:238–257, doi: 10.1177/1359104518758839
23. Angelakis S, Nixon RDV. The Comorbidity of PTSD and MDD: Implications for Clinical Practice and Future Research. *Behaviour Change* 2015, 32:1–25, doi: 10.1017/bec.2014.26
24. Smid GE, Lensvelt-Mulders GJ, Knipscheer JW, Gersons BP, Kleber RJ. Late-onset PTSD in unaccompanied refugee minors: exploring the predictive utility of depression and anxiety symptoms. *J Clin Child Adolesc Psychol* 2011, 40:742–755, doi: 10.1080/15374416.2011.597083
25. Müller LRF, Gossmann K, Hartmann F, Büter KP, Rosner R, Unterhitzenberger J. 1-year follow-up of the mental health and stress factors in asylum-seeking children and adolescents resettled in Germany. *BMC Public Health* 2019, 19:908, doi: 10.1186/s12889-019-7263-6
26. Höhne E, van der Meer AS, Kamp-Becker I, Christiansen H. A systematic review of risk and protective factors of mental health in unaccompanied minor refugees. *Eur Child Adolesc Psychiatry* 2020, Epub ahead of print, doi: 10.1007/s00787-020-01678-2
27. Jensen TK, Skar AS, Andersson ES, Birkeland MS. Long-term mental health in unaccompanied refugee minors: pre- and post-flight predictors. *Eur Child Adolesc Psychiatry* 2019, 28:1671–1682, doi: 10.1007/s00787-019-01340-6
28. Refugee Support Aegean (RSA)-PRO ASYL: The systematic rejections of family reunifications requests from Greece by Germany and their detrimental impact upon the right to family life and the best interest of the child. Available from https://rsaegean.org/en/refugee-families-torn-apart (2019)

Ερευνητική εργασία

Ψυχική υγεία των ασυνόδευτων ανηλίκων προσφύγων στην Ελλάδα που διαβιούν σε «κατάσταση αβεβαιότητας»

Ιωάννα Γιαννοπούλου, Λήδα Μουρλούκου, Βασιλική Ευσταθίου, Αθανάσιος Δουζένης, Παναγιώτης Φερεντίνος

Β΄ Ψυχιατρική Κλινική, Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών, Αττικόν Νοσοκομείο, Αθήνα

ΙΣΤΟΡΙΚΟ ΑΡΘΡΟΥ: Παραλήφθηκε 8 Σεπτεμβρίου 2021/Αναθεωρήθηκε 9 Δεκεμβρίου 2021/Δημοσιεύθηκε Διαδικτυακά 27 Απριλίου 2022

ΠΕΡΙΛΗΨΗ

Το κλείσιμο της μεταναστευτικής διαδρομής των Βαλκανίων το 2016, είχε ως αποτέλεσμα ένας σημαντικός αριθμός ασυνόδευτων ανήλικων (ΑΑ) προσφύγων, που θεωρούσε την Ελλάδα ως «πέρασμα» για τον τελικό επιθυμητό προορισμό τους, να «εγκλωβιστεί» για απροσδιόριστο χρονικό διάστημα στη χώρα. Κατά συνέπεια δημιουργήθηκε για τους ΑΑ μία δύσκολη συνθήκη διαβίωσης "in limbo", χαρακτηριζόμενη από αβεβαιότητα γύρω από το μέλλον τους, στο πλαίσιο της μακράς αναμονής για την έκβαση της αίτησής τους για χορήγηση ασύλου. Σκοπός της παρούσας συγχρονικής μελέτης ήταν να διερευνήσει την ψυχική υγεία των ΑΑ που έφθασαν στην Ελλάδα μετά το 2016 και τους προβλεπτικούς παράγοντες της βαρύτητας των καταθλιπτικών συμπτωμάτων, των συμπτωμάτων μετατραυματικού στρες και των αρνητικών γνωσιών τους. Το δείγμα αποτέλεσαν 90 ΑΑ (76 αγόρια), ηλικίας 13-17 χρονών, εκ των οποίων οι 46 ήταν Σύριοι και οι 44 διαφορετικής εθνοτικής καταγωγής. Οι συμμετέχοντες συμπλήρωσαν στη μητρική τους γλώσσα τις κλίμακες: Children's Revised Impact of Events Scale (CRIES-8), Depression Self-Rating Scale (DSRS), Children's Post-Traumatic Cognitions Inventory (cPTCI). Επιπλέον, συλλέχτηκαν πληροφορίες σχετικές με τα κοινωνικο-δημογραφικά χαρακτηριστικά, τις στρεσογόνες και τραυματικές εμπειρίες που βίωσαν και την κοινωνική στήριξη. Οι Σύριοι ΑΑ είχαν πολύ μεγαλύτερη πιθανότητα από τους ΑΑ άλλων εθνοτήτων να εμφανίσουν κλινική κατάθλιψη (71,7% έναντι 47,7%, αντίστοιχα, p=0,020), να παρουσιάσουν συμπτώματα διαταραχής μετατραυματικού στρες (ΔΜΣ), δηλαδή βαθμολογία εντός κλινικά σημαντικού εύρους συμπτωμάτων μετατραυματικού στρες και αρνητικών μετατραυματικών γνωσιών (87% έναντι 65,9% αντίστοιχα, p=0.018) και συννοσηρότητας ΔΜΣ/κατάθλιψης (65,2% έναντι 40,9% αντίστοιχα, p=0.021). Οι αναλύσεις πολλαπλής γραμμικής παλινδρόμησης με τη μέθοδο βηματικής απαλοιφής έδειξαν ότι το νομικό καθεστώς (αιτούντες άσυλο-οικογενειακή επανένωση στην Ευρώπη) αποτελεί προβλεπτικό παράγοντα αυξημένων επιπέδων καταθλιπτικής συμπτωματολογίας (β=0,29, p=0,004), συμπτωμάτων μετατραυματικού στρες (β=0,21, p=0,034) καθώς και αρνητικών γνωσιών (β=0,33, p=0,001). Ο συνολικός αριθμός στρεσογόνων/τραυματικών εμπειριών και το άρρεν φύλο (β=0,29, p=0,004) βρέθηκε να σχετίζονται σημαντικά μόνο με τη βαρύτητα των συμπτωμάτων μετατραυματικού στρες, ενώ χαμηλότερα επίπεδα αντιλαμβανόμενης κοινωνικής στήριξης συσχετίζονταν με αυξημένα επίπεδα συμπτωμάτων κατάθλιψης (β=0,24, p=0,018) και αρνητικών γνωσιών (β=0,26, p=0,008). Τα ευρήματα υπογραμμίζουν την ψυχική επιβάρυνση των ΑΑ που ζουν σε συνθήκη "in limbo" και ενισχύουν το επιχείρημα για την τροποποίηση των περιοριστικών πολιτικών ασύλου της Ευρωπαϊκής Ένωσης και την επιτάχυνση των διαδικασιών οικογενειακής επανένωσης σύμφωνα με τον Κανονισμό του Δουβλίνου. Επίσης, επισημαίνουν την άμεση ανάγκη για βελτίωση της πρόσβασης των ΑΑ σε υπηρεσίες ψυχικής υγείας και ψυχοκοινωνικής υποστήριξης.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: Ασυνόδευτοι ανήλικοι πρόσφυγες, διαταραχή μετατραυματικού στρες, μετατραυματικές αρνητικές γνωσίες, κατάθλιψη, τραυματικές εμπειρίες.

Συγγραφέας επικοινωνίας: Ιωάννα Γιαννοπούλου, Β΄ Ψυχιατρική Κλινική, Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών, Αττικόν Νοσοκομείο, Ρίμινι 1, 124 62 Αθήνα, Διεύθυνση e-mail: igianno@med.uoa.gr

https://doi.org/10.22365/jpsych.2022.073 / Psychiatriki 2022, 33:228–242

Review

Dietary interventions for autism spectrum disorder: An updated systematic review of human studies

Cecilia N. Amadi,[1] Chinna N. Orish,[2] Chiara Frazzoli,[3] Orish E. Orisakwe[1,4]

[1]*Department of Experimental Pharmacology & Toxicology, Faculty of Pharmacy, University of Port Harcourt, Choba,*
[2]*Department of Anatomy, Faculty of Basic Medical Sciences, College of Health Sciences, University of Port Harcourt, Choba, Nigeria*
[3]*Department for Cardiovascular, Dysmetabolic and Aging Diseases, Istituto Superiore di Sanità, Rome, Italy,*
[4]*African Centre of Excellence for Public Health and Toxicological Research (ACE-PUTOR), University of Port Harcourt, PMB, Choba, Nigeria*

ARTICLE HISTORY: Received 18 January 2022/Revised 10 February 2022/Published Online 24 April 2022

ABSTRACT

Autism is a complex spectrum of disorders (ASD) with genetic, epigenetic, autoimmune, oxidative stress, and environmental aetiologies. Treatment of ASD using dietary approaches is a promising strategy, especially owing to its safety and availability. Our study critically analysed the roles and efficacy of antioxidants, probiotics, prebiotics, camel milk and vitamin D. This systematic review provides an updated synopsis of human studies that investigated therapeutic benefits of these dietary interventions in autism. A total of 943 papers were identified out of which 21 articles were included in the systematic review. The selected studies investigated the impact of 5 different dietary supplementations in ASD symptoms and behaviours. These agents include; antioxidants/polyphenolic compounds, probiotics, prebiotics, camel milk and vitamin D. From the results of the present review, antioxidants/polyphenolic compounds decreased the levels of inflammatory cytokines and improved behavioural symptoms. Probiotics improved behavioural and GI symptoms as well as restored gut microbiota equilibrium. Prebiotics decreased levels of inflammatory cytokines, improved behavioural and GI symptoms and improved gut microbiota. Vitamin D improved behavioural symptoms and offered protective effects against neurotoxicity. Camel milk reduced inflammatory responses and oxidative stress. Given the chronic nature as well as early onset of ASD, dietary supplements become useful to complement nutritional deficiencies in children with ASD. Key benefits of these agents stem from their ability to target multiple physiological areas via the gut brain-axis while they are devoid of potential harmful or aggravating effects on ASD patients. The evidence collated in this review propose that dietary intervention may provide a new platform for the management of autism.

KEYWORDS: Autism spectrum disorder (ASD), dietary intervention, gut microbiota, public health.

Introduction

Autism spectrum disorder (ASD) is a complex developmental disorder characterized by a wide array of symptoms such as impaired verbal skills, social withdrawal, repetitive behavior, insistence to routines, and abnormal response to sensory stimuli.[1,2] ASD is associated with a spectrum of metabolic, mitochondrial, immune, inflammatory, and behavioral anomalies involving different parts of the body that appear in the first years of life and continue throughout the lifespan of the patient.[3] The disease condition generally manifests in the first 3 years of life. It is estimated that 1 out of every 88 children is diagnosed with an autism spectrum disorder.[4,5] Although ASD is regarded to be heritable with complex genetic heterogeneity,[6] growing evidence indicates that the to-

Corresponding author: Orish E. Orisakwe, African Centre of Excellence for Public Health and Toxicological Research (ACE-PUTOR), University of Port Harcourt, PMB, 5323 Port Harcourt, Choba, Nigeria • e-mail: orishebere@gmail.com, orish.orisaakwe@uniport.edu

tal fraction of ASD ascribable to genetic inheritance may only be 30–40%.[7] Out of the remaining 60–70%, about half have different kinds of polymorphisms and the other half have de novo mutations with little or no similarities. These findings suggest that factors of non-genetic origin may play important roles in the aetiology of ASD.[8]

A growing evidence shows that the gut-brain axis plays a key role in the pathogenesis of ASD.[9,10] The gut–brain axis is regarded as a bidirectional pathway of communication between the gut and the brain.[10] The gut microbiota modulates brain function via the neuroendocrine, neuro-immune and autonomic nervous systems and through microbiological toxin production.[11,12] Cases of altered gut microbiome have been found in children with autism, a condition known as dysbiosis.[13–15] Dysbiosis is characterized by an imbalance between beneficial microorganisms and pathogenic microorganisms resident in the gut.[15] Gut dysbiosis also results in systemic inflammation and neuro-inflammation which subsequently impair brain functions (Gut-Brain Axis).[10] In addition, children with ASD exhibit picky eating habits and food selectivity which can result in nutritional deficiencies.[16–18]

While some studies have highlighted some level of efficacy of elimination diets in autism, certain leading systematic reviews remain doubtful about their effectiveness.[19–21] Examples include the gluten-free and casein-free (GFCF) diets on children with autism. The use of GFCF diets is based on the framework of the "opioid excess theory", the disorder symptoms that are comparable to the behavioural effects of opiate which hypothesizes that certain food proteins such as gluten and casein can be metabolized into opioid peptides. These peptides might subsequently enter the blood stream and act upon the central nervous system. Therefore, a diet with minimal proteins (gluten-free and casein-free) was highlighted to ameliorate the behavioural symptoms of children with autism.[21] Another nutritional strategy-ketogenic diet (KD), which is a high fat diet that forces the body to use fat as a fuel source was also proposed for ASD.[16] However, KD has been associated with adverse events such as constipation, increased serum cholesterol, hemolytic anemia, decreased serum protein, as well as vomiting and dehydration which may worsen ASD symptoms.[22]

On the other hand, recent evidence indicates that supplementation with certain dietary agents is beneficial in reducing the severity of ASD symptoms, as well as in improving behavioural anomalies in children with autism.[2,4,23,24] Some of these agents such as antioxidants (flavonoids, polyphenols), probiotics, prebiotics, vitamin D, and camel milk, contribute to overall protection against oxidative stress, exert a neuroprotective effect, strengthen intestinal barrier, decrease GI symptoms and inflammation and also improve gut microbiota.[25–30] These agents come out as safer alternatives to elimination and ketogenic diets because of their ability to target multiple physiological areas via the gut brain-axis and are devoid of potential harmful or aggravating effects on ASD patients. Even though the therapeutic evidence of dietary interventions and their mechanisms of actions are very new, they provide a promising platform for designing future treatments for alleviating ASD symptoms. This systematic review provides an updated synopsis of dietary interventions in autism to evaluate their therapeutic efficacy and beneficial effects.

Material and Method

Information sources and search strategy

Relevant studies were identified from scientific databases such as PubMed, Google scholar, and Scopus. This systematic review was performed according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines.[31] Using the keywords: ("probiotics" OR "prebiotics" OR "polyphenols" OR "antioxidants" OR "camel milk" OR "vitamin D" OR "dietary interventions") in ("autism" OR "ASD"), ("gut-brain axis" AND "autism"). Titles and abstracts were screened to select articles of interest. For relevant abstracts, full articles were obtained and reviewed. A backward search was done from which the reference lists of retrieved results were screened.

Inclusion and Exclusion Criteria

The present systematic review identified studies that evaluated dietary interventions in autism. As recommended by the PRISMA guidelines and graphically illustrated in figure 1, the study selection was performed using the procedure composed of four main steps: identification, screening, eligibility and inclusion. Articles were included if they met the following criteria: (1) Studies involving dietary interventions in humans, (2) articles that provided sufficient data, including dietary agents, study/experimental design, sample size, study population, duration of study and clinical findings. Articles were excluded for the following reasons: (1) articles that were not published in English language, (2) articles had no focus on dietary interventions in autism, (3) articles were not original research, (4) articles reported *in vitro* data, (5) articles reported animal studies, (6) articles without full texts. No limits were applied to the year of study.

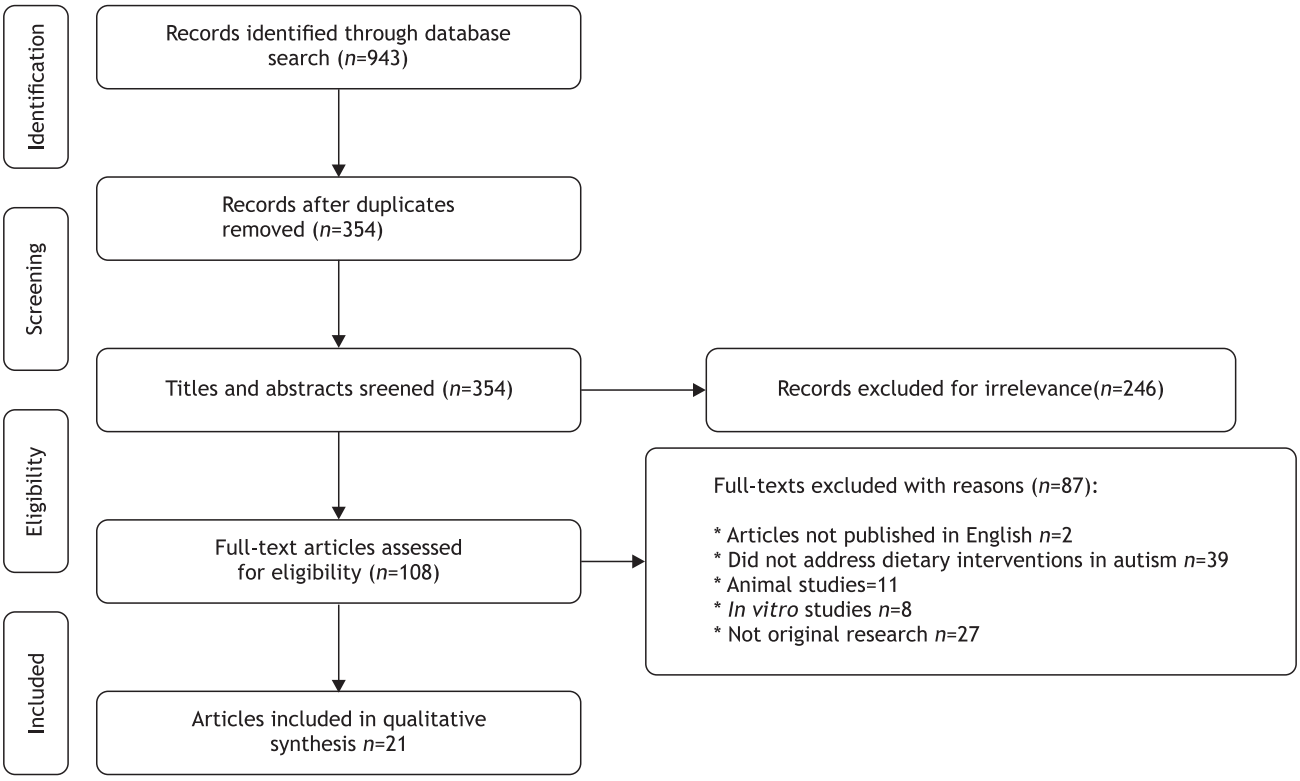

Figure 1. PRISMA flow diagram summarizing search study and selection process.

Study quality assessment

We used the Cochrane collaboration's tool for risk of bias assessment[32] to evaluate whether the authors took adequate steps to reduce the risk of bias across six domains: sequence generation, allocation concealment, blinding (of participants, and outcome assessors), incomplete outcome data, selective outcome reporting, and other sources of bias. The judgment was grouped into low, high or unclear risk of bias.[32]

Results and Discussions

As shown in figure 1, a total of 943 articles were identified from the initial search, and duplicates were removed (n=589). Following title and abstract screening, 246 articles were excluded, while the remaining 108 articles were reviewed in detail. Based on our review, 87 additional publications were excluded due to the following reasons: 27 articles did not contain original research; 39 articles had no focus on dietary interventions; 11 articles reported only animal studies; 8 articles reported *in vitro* studies; 2 articles were not published in English language. A total of 21 articles were included in the review (table 1). While 8 articles examined the use of probiotics,[33–40] 6 articles investigated antioxidants/polyphenolics,[41–46] 2 articles examined the use of prebiotics-only regimen[47,48] and 3 articles investigated camel milk.[49–51] Furthermore, 1 article examined vitamin D3[29] and 1 article examined a combined probiotic + prebiotic regimen.[52]

The data obtained from the assessment of the study quality of the included studies are shown in figures 2 and 3. While 9 studies[36,41,44,45,48–52] showed unclear risks of performance bias, 3 studies[36,44,52] showed unclear risks of selection bias and two studies[33,45] showed high risk of selection bias. The risk of other biases in the included studies are unclear.

Generally, there was 100% low risk of attrition and reporting bias in the selected studies

Dietary interventions in autism

Antioxidants/Polyphenolics

Antioxidant-containing foods may offer promising therapeutic benefits in autism.[53] Studies have suggested that supplementation with antioxidants (such as polyphenolics, flavonoids) ameliorates symptoms of autism,[54,55] but the evidence is not sufficient to recommend an antioxidant-based therapeutic practice for autism.

Recent findings have shown that dietary polyphenols are metabolized by gut microbiota resulting in metabo-

Table 1. Summary of human studies that investigated dietary interventions in autism.

Dietary agent	Study design	Sample size (n)	Study population	Study duration	Findings	References
Camel Milk	Randomized controlled trial	60	2-12-year-old children with ASD (Saudi Arabia)	2 weeks	Significantly ($p<0.5$) increased levels of glutathione, superoxide dismutase, and myeloperoxidase; improved autistic behaviour detected by Childhood Autism Rating Scale (CARS)	Al-Ayadhi and Elamin 201351
Camel milk	Randomized controlled trial	65	2-12-year-old children with ASD (Saudi Arabia)	2 weeks	Improvements were detected by CARS, Social Responsiveness Scale (SRS) and Autism Treatment Evaluation Checklist (ATEC) scales, following 2 weeks of camel milk consumption, but not in the placebo group	Al-Ayadhi et al. 201549
Camel milk	Randomized controlled trial	45	2-12-year-old children with ASD (Saudi Arabia)	2 weeks	Camel milk significantly improved clinical symptoms (CARS score) of autism and decreased serum level of thymus and activation-regulated chemokine (TARC) in autistic children	Bashir and Al-Ayadhi 201450
Antioxidants - (Luteolin + quercetin) containing dietary formulation	Open-label controlled trial	40	4–10-year-old children with ASD (Greece)	26 weeks	Decreased levels of inflammatory cytokines (IL-6 and TNF); improvements in overall behaviour in patients and reduction in ASD symptoms and	Tsilioni et al. 201542
Antioxidants (Flavonoid and Luteolin)	Open-label controlled trial	50	4–10-year-old children with ASD (Greece)	26 weeks	Improvement in overall behavior as indicated by a reduction in ABC (Aberrant Behaviour checklist) scores	Taliou et al. 201346
Antioxidants (Sulforaphane derived from broccoli sprouts)	Randomized controlled trial	44	13–27-year-old young men with moderate to severe ASD (US)	4-18 weeks	Significant decrease (improvement of behaviour) in ABC ($p<0.001$) and SRS scores ($p=0.017$) and improvement in social interaction	Singh et al. 201443
Avmacol®, a sulforaphane-producing dietary supplement	Open-label controlled trial	15	5–22-year-old children/young adults with ASD(USA)	12 weeks	Improvements (decreases) in mean scores of SRS and ABC over the study period; Identification of urinary metabolites associated with clinical improvements in participants	Bent et al. 201844
High antioxidant cacao	Pilot study	17	4–17-year-old children with ASD (USA)	4 weeks	Significant improvements on ABC-2 subscales of irritability ($p=0.03$); social withdrawal ($p=0.01$); stereotypic behaviour ($p=0.05$); hyperactivity/noncompliance ($p=0.04$); inappropriate speech ($p=0.05$). Significant improvements on the ASRS subscales of social/communication ($p=0.04$), abnormal behaviours ($p=0.003$), self-regulation ($p=0.02$).	Sadek et al. 201845
Antioxidants (Cysteine-Rich Whey Protein (CRWP)	Randomized controlled trial	46	3–5-year-old children with ASD (USA)	3 months	CRWP nutritional intervention significantly improved behaviours associated with ASD as well as glutathione levels	Castejon et al., 202141

Continues

Table 1. Continued.

Dietary agent	Study design	Sample size (n)	Study population	Study duration	Findings	References
Probiotics (*Lactobacillus acidophilus, Lactobacillus rhamnosus, Bifidobacteria longum*)	Open-label controlled trial	30	5–9-year-old children with ASD (Egypt)	3 months	Enhanced levels of *Bifidobacteria* in stool samples, Behavioral improvement, Improved GI symptoms following assessment with using a six-item GI Severity Index (6-GSI) questionnaire and Autism Treatment Evaluation Checklist (ATEC)	Shaaban et al 201834
Probiotics (3 strains of *Lactobacillus*, 2 strains of *Bifidobacteria*, 1 strain of *Streptococcus*)	Open-label controlled trial	29	2–9-year-old children with ASD (Slovakia)	4 months	Probiotic supplementation normalized bacterial balance in fecal microbiota in children with ASD	Tomova et al 201535
Probiotics (VISBIOME) (8 probiotic species of *Lactobacillus* and *Bifidobacterium*)	Randomized controlled trial	13	3-12-year-old children with ASD (USA)	8 weeks	A parent-selected target symptom showed significant improvement in GI complaints with probiotic supplementation compared with placebo (p=0.02)	Arnold et al 201936
Probiotics (*Lactobacillus plantarum* PS128)	Randomized controlled trial	80	7-15-year-old children with ASD (Taiwan)	28 days	PS128 ameliorated opposition/defiance behaviours; Improved behavioural symptoms compared to placebo	Liu et al 201937
Probiotics (*Lactobacillus plantarum* PS128)	Open-label controlled trial	131	45-127-month-old children with ASD (Italy)	6 months	Improved attention, improved communication skills, improved personal autonomies	Mensi et al 202133
Probiotics Vivomixx® oor Visbiome® (*Streptococcus thermophilus, Bifidobacterium breve, Bifidobacterium longum, Bifidobacterium infantis, Lactobacillus acidophilus, Lactobacillus plantarum, Lactobacillus para-casei, Lactobacillus delbrueckii subsp. Bulgaricus)*	Randomized controlled trial	85	18-72 months old children with ASD (Italy)	6 months	Improvements in GI symptoms, adaptive functioning, and sensory profiles compared with placebo	Santocchi et al 202038
Probiotics + prebiotics (*Bifidobacterium* infantis) + colostrum supplement (bovine colostrum product)	Randomized controlled trial	8	2-11-year-old children with ASD (USA)	12 weeks	– Reduced frequency of GI symptoms in both BCP and BCP only+ *B. infantis* group – Improved intestinal microflora profile and reduced behavioral abnormalities with combination therapy	Sanctuary et al 201952
Probiotics (*Lactobacillus plantarum* WCFS1)	Randomized controlled trial	22	4–16-year-old children with ASD (UK)	12 weeks	– Increased *lactobacilli* and *enterococci* counts and significantly reduced *Clostridium* cluster counts compared to placebo – Significant improvements in TBPS (Total Behaviour Problem Score)	Parracho et al 201040

Continues

Table 1. Continued.

Dietary agent	Study design	Sample size (n)	Study population	Study duration	Findings	References
Probiotics (*Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus delbrueckii, Bifidobacteria longum, Bifidobacteria bifidum*)	Open-label controlled trial	33	3–16-year-old children with ASD (USA)	21 days	Improved behavioural symptoms Improved GI symptoms (constipation and diarrhea)	West et al 201339
Prebiotics (*Bimuno® galactooligosaccharide* (B-GOS®))	Randomized controlled trial	30	4–11-year-old children with ASD (UK)	6 weeks	– Improved ant-social behaviour – Enhanced gut microbiota – Reduced gastrointestinal (GI) discomfort	Grimaldi et al 201847
Prebiotics (partially hydrolyzed guar gum)	Randomized controlled trial	13	4–9-year-old children with ASD (Japan)	2 months	– Decreased behavioural irritability – Improved gut microbiota – Relieved constipation and gut dysbiosis symptoms – Decreased concentrations of inflammatory cytokines (IL-1b, IL-6 and TNF-α)	Inoue et al 201948
Vitamin D3	Case-controlled cross-sectional study	122	3-9-year-old children with ASD (Egypt)	3 months	Improved behavioural outcome (Improved CARS and ABC scores)	Saad et al. 201629

lites that are more bioactive as well as possessing more antioxidant capacity than the native form.[27,56–58] The gut microflora break down polyphenols into metabolites that are readily absorbed from the intestine and transported via the blood to the brain where the metabolites exert biological activities.[59]

Polyphenolic compounds act as natural antioxidants specifically due to their radical-scavenging properties (figure 4) which are linked to the number of free hydroxyl groups in their skeleton capable of donating H. to the oxidizing compound.[60] Polyphenolic compounds with multiple hydroxyl groups possess more potent radical scavenging properties than those with only one hydroxyl group.[61]

An imbalance between generation of reactive oxygen species (ROS) and their elimination especially by the antioxidant defence system in the body results in oxidative stress (figure 4). While oxidative stress-induced mechanisms are associated with the aetiology of ASD,[62,63] disruptions in the antioxidant defence systems could lead to changes in neuronal structure and general brain function, inflammation and dysregulation of immune function.[62,64] Interestingly, polyphenolic compounds act as natural antioxidants attributable to their free radical scavenging properties linked to their chemical structure.[27,59]

Six articles that investigated antioxidants/polyphenolics were included in this review.[41–46]

In an open-label clinical trial by Tsilioni et al, 4-10-year-old children with ASD in Greece were treated with Luteolin+quercetin-containing dietary formulation for 26 weeks.[42] At the end of the treatment, a significant decrease in the mean serum IL-6 and TNF was observed ($p=0.036$ and $p=0.015$, respectively) compared with levels before treatment. Improvements in behavioural pattern of the participants were also noted after treatment.[42] A randomized trial was conducted in 13–27 years old young men with moderate to severe ASD in the United States.[43] This was carried out for a period of 4–18 weeks using daily oral doses of sulforaphane (50–150 μmol). At the end of the treatment period, participants receiving sulforaphane showed significant decrease (improvement in behaviour) in ABC ($p<0.001$) and SRS scores ($p=0.017$). A significantly ($p=0.015$–0.007) greater number of participants that received sulforaphane demonstrated improvement in social interaction, verbal communication and abnormal behaviour.[43] Similarly, Bent et al. conducted an open-label study with sulforaphane supplements (Avmacol®) in 5–22 years old children/young adults with ASD in the United States.[44] Approximately 2.5 μmol glucoraphanin (GR)/lb) (sulforaphane precursor) was administered for 12 weeks.

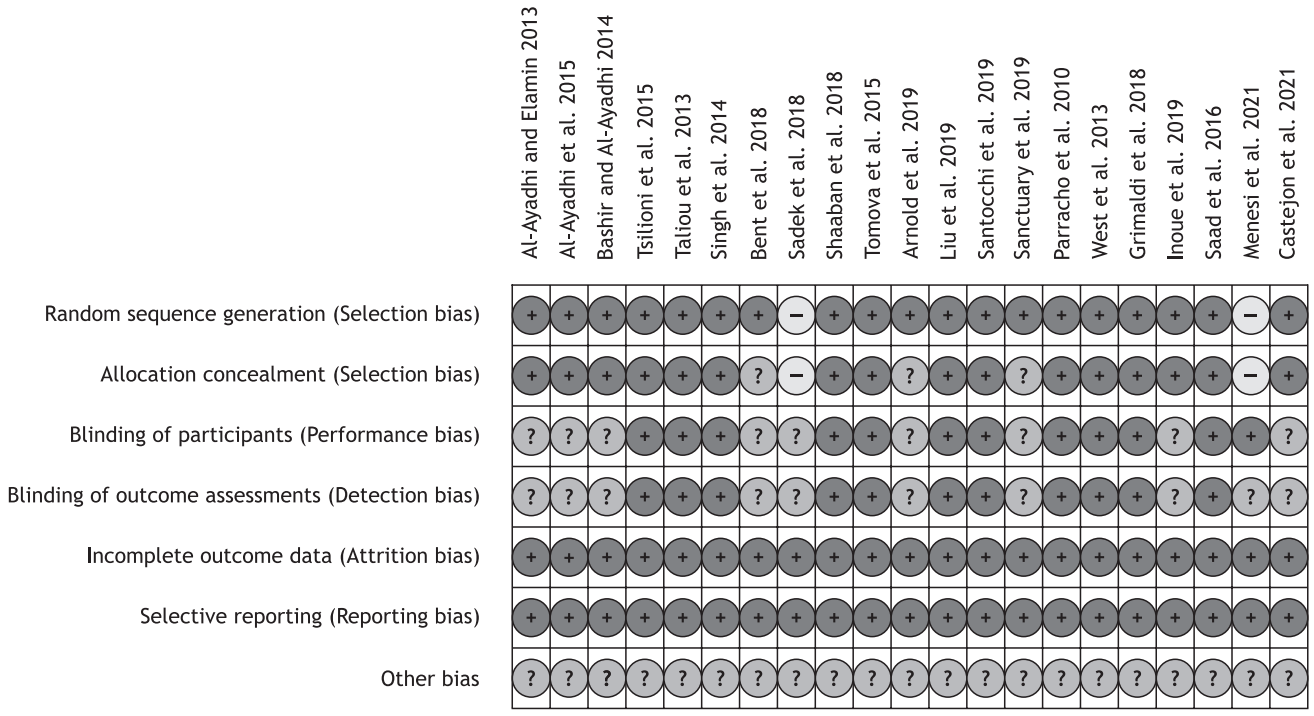

Figure 2. Summary of risk of bias of the included studies. Risk of bias for individual studies was determined using the Cochrane tool for assessment of risk of bias.

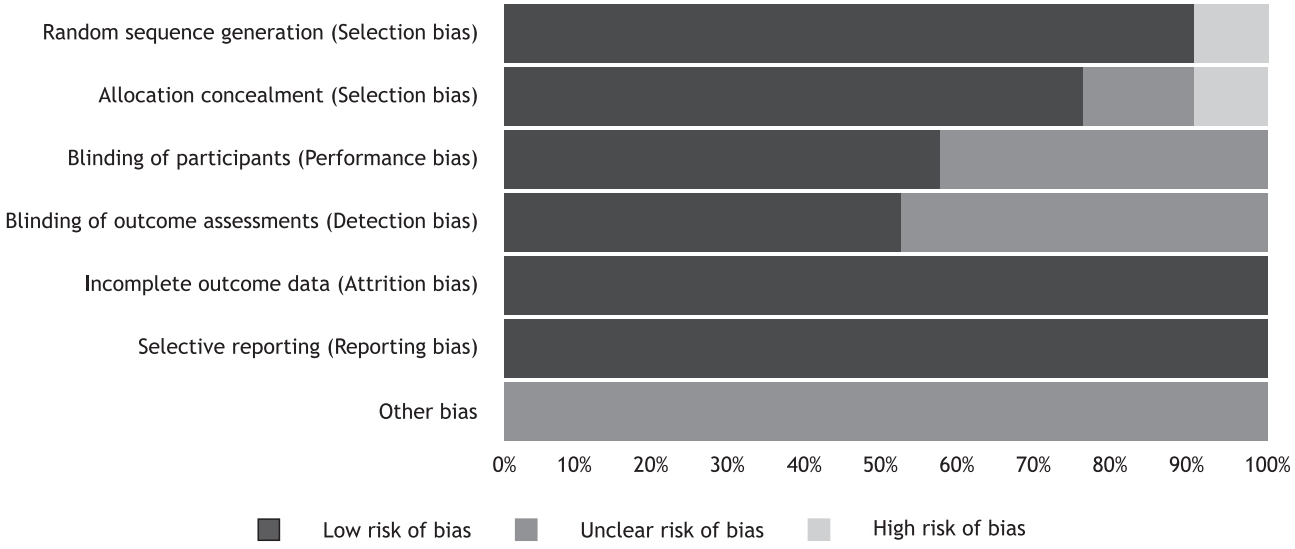

Figure 3. Risk of bias graph: summary of risk of bias is presented as percentage across all included studies

Fasting urinary metabolites as well as measures of behaviour (ABC and SRS) were evaluated at the start and at the end of the study. Mean scores of both ABC and SRS showed improvements (decreases) over the study period. Urinary metabolites associated with clinical improvements in participants were identified.[44]

A pilot study reported by Sadek et al revealed that administration of high antioxidant cacao for 4 weeks significantly improved behaviours of children with ASD.[45] Participants received 16 g per day of dark chocolate. ABC and ASRS (Autism Spectrum Rating Scale) were completed at baseline, end of 2nd and 4th week. Results obtained revealed significant improvements in the behavioural measures.[45] In Greece, Taliou and colleagues supplemented flavonoid and luteolin in 4-10-year-old children with autism for 26 weeks.[46] Results obtained from that study revealed improvement in general behaviour as shown by a reduction in ABC scores.[46]

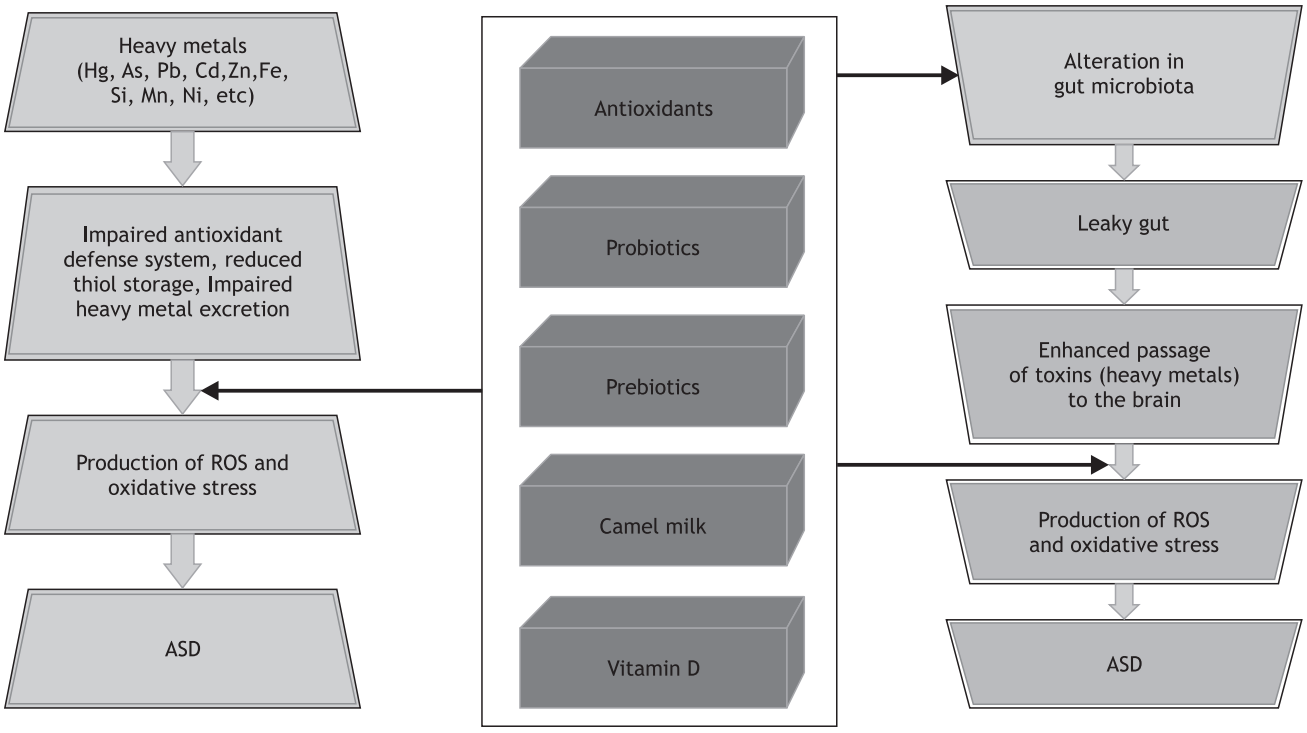

Figure 4. Interconnections between ASD and the possible mechanisms/beneficial effects of dietary agents.

Castejon et al, performed a 3 months' study to probe the effectiveness of Cysteine-Rich Whey Protein (CRWP) intervention in children with ASD and to ascertain whether improvements in intracellular glutathione (reduced and oxidized) correlated with behavioural changes.[41] Findings from that study demonstrated that intervention with CRWP significantly improved both glutathione levels and abnormal behaviours associated with ASD.[41]

Probiotics

Probiotics are live microorganisms which have the capacity to maintain or restore the microbiota balance in the intestinal tract when consumed in adequate amounts.[65] Probiotics consist of bacteria that are identical to those that naturally inhabit the human gut. These bacteria are basically of two groups -Lactobacillus and Bifidobacterium spp.[65]

Imbalance in gut microbiota or dysbiosis has been implicated in the pathogenesis of ASD.[59,66] Several pieces of evidence have indicated that the gut microbiota composition of patients with autism differed significantly in comparison to healthy controls.[67–71] Such disruptions in the gut microbiome may predispose an individual to altered gut motility and secretion, resulting in diarrhoea or constipation, which are common symptoms reported in patients with autism.[72] Dysbiosis occurs majorly due to an altered integrity of the intestinal barrier which enhances passage of toxins (produced by pathogenic bacteria) from the gut lumen to the brain ('leaky gut) (figure 5).[14] These toxic molecules influence neurotransmitter function in the brain, resulting in abnormalities in behavioural patterns such as impaired socialization, decreased pain response, communication abnormalities and self-abusive or repetitive behaviours, delirium, confusion, which are core symptoms of ASD.[73] Interestingly, probiotics enhance gut microbiota equilibrium and enhance the integrity of the gut mucosa.[28]

From our review, 8 articles examined the use of probiotics in children with autism.[33–40] Tomova et al. probed the GI microbiome composition and also examined the changes in the faecal microbiota, hormone and cytokine levels following probiotic administration in ASD children, their healthy siblings and control children.[35] Daily supplementation with three *Lactobacillus* strains, two *Bifidobacterium strains* and a *Streptococcus strain* for a period of 4 months decreased the level of *Desulfovibrio spp*., *Bifidobacteria* and also normalized the Bacteroidetes/Firmicutes ratio in the faeces of children with autism. The study showed that ASD severity has a positive correlation with the severity of GI dysfunctions in the subjects. The level of TNF-α was decreased following probiotic supplementation. Generally, probiotic supplementation altered gut microbiota composition in ASD children.[35]

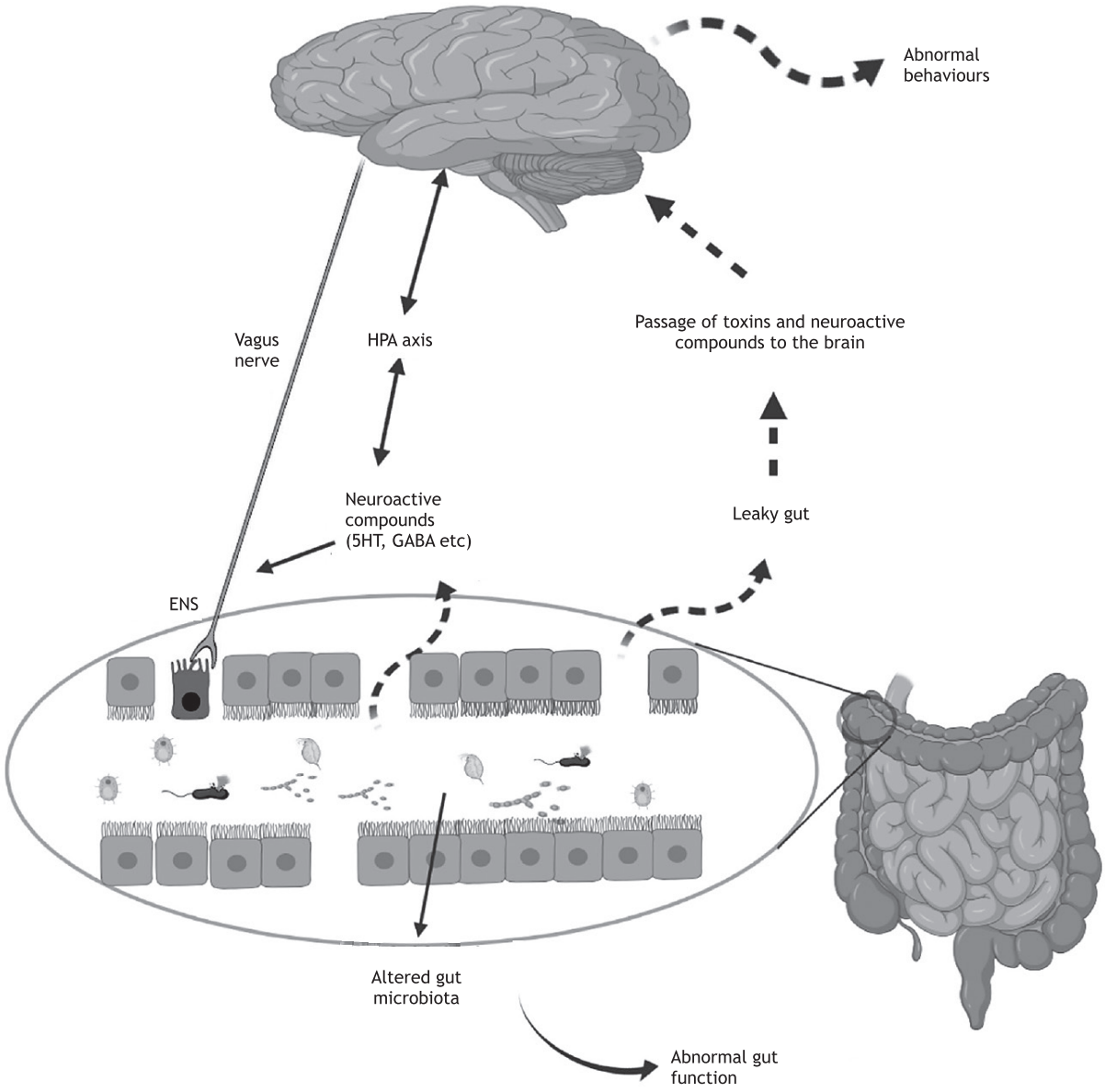

Figure 5. Relationships between the microbiota, gut brain axis and ASD: Toxins and neuroactive compounds (e. 5-HT and GABA) produced by certain microbiota can cross the "leaky gut" to affect brain function and induce abnormal behaviours. These neuroactive compounds can influence the HPA Axis directly and increase circulating levels of cortisol. Certain microbiota, metabolites produced and neuroactive compounds can activate enteric nervous system (ENS) and affect brain function via the vagus nerve.

In an open-label controlled trial, the supplementation of a mixture of 3 probiotic strains (*B. longum, L. rhamnosus, L. acidophilus* (100x10^6 CFU per gram; 5 g per day) for 3 months significantly altered the faecal microbiota (*Bifidobacteria* and *Lactobacilli*) of ASD children in Egypt.[34] The abdominal symptoms and the severity of the ASD, were quantified using a six-item GI Severity Index (6-GSI) questionnaire and Autism Treatment Evaluation Checklist (ATEC) respectively, before and after probiotics supplementation. These were found to be reduced in ASD children compared to baseline. The study demonstrated that probiotic supplementation improves the behavioural pattern, gut microbiota and the abdominal discomforts in ASD children.[34] Arnold et al. investigated GI symptoms, and anxiety following VISBIOME® supplementation (mixture of 8 probiotic species, mostly *Lactobacillus* and *Bifidobacterium*) in an 8-week crossover trial separated by a 3-week washout. The study was carried out in 13 children with ASD aged 3–12 years. A parent-selected target symptom revealed significant improvement in GI complaints with probiotic supplementation compared to placebo (p=0.02).[36] A

4-week, randomized controlled trial evaluated the effects of *Lactobacillus plantarum* PS128 (PS128) on boys with ASD, aged 7–15 in Taiwan. Following a 28-day period of PS128 supplementation, results obtained showed improved behavioural pattern as well as improved total score of SNAP-IV (Swanson, Nolan, and Pelham-IV-Taiwan version) compared with the placebo group.37 Recently, a similar study was carried out by Mensi et al. investigating the effectiveness of *Lactobacillus plantarum* PS128 (PS128) in children with ASD.[33] In that study, patients supplemented with *Lactobacillus plantarum* (PS128) showed greater improvements and minimal side effects compared to patients that ingested other probiotics. Their data was consistent with results of earlier studies validating the therapeutic effects of *Lactobacillus plantarum* PS128 in Autism.[33]

West and co-workers[39] probed the supplementation of probiotics in 3-16-year-old children with autism in the USA. Their data showed improved behavioural symptoms and improved GI symptoms (constipation and diarrhoea).[39] In the UK, Parracho et al[40] investigated the supplementation of probiotics in 4–16-year-old children with autism. Supplementation with *Lactobacillus plantarum* for 12 weeks produced a significantly reduced Clostridium cluster counts compared to placebo and enhanced Lactobacilli and enterococci counts compared to placebo. There was also a significant improvement in TBPS (Total Behaviour Problem Score).[40] Finally, Santocchi et al[38] evaluated the effects of probiotics in ASD in a randomized trial of 85 pre-schoolers in Italy. Data obtained demonstrated greater improvements in adaptive functioning, GI symptoms, and sensory profiles compared to placebo. This study suggests potentially beneficial effects of probiotics on core autism symptoms.[38]

Prebiotics

Colonization of the gut by toxin-producing bacteria in the gut is associated with bowel problems in autism.[74] Prebiotics can enhance the growth of healthy bacteria and reduce the overgrowth of pathogenic *Clostridium difficile*.[75] Prebiotics are non-digestible dietary agents that modulate gut microbiota and are selectively utilized by beneficial microorganisms for growth within the host, thereby conferring health benefits to the host.[76] While probiotics (live microorganisms) can balance, or normalize gut microbiota, prebiotics inhibit the growth of pathogenic micro-organisms by nourishing beneficial micro-organisms. In essence, both prebiotics and probiotics work together to maintain healthy gut microbiota.[74] Non-digestible carbohydrates such as fructo-oligosaccharides, galacto-oligosaccharides and trans-galacto-oligosaccharides are common examples of prebiotics which modify the composition and function of gut microbiota.[77,78] Beneficial gut micro-organisms ferment and degrade these non-digestible dietary substances and obtain energy for survival while influencing gut microbiota in the long run.[77,79]

Studies have also indicated that prebiotics exert antioxidant and direct radical scavenging effects, thereby counteracting oxidative stress and the development of ROS-related diseases (figure 4).[80,81] These effects are mediated by the action of short-chain fatty acids produced from their fermentation in the colon.[80] Prebiotics can also stimulate the activity of antioxidant enzymes Glutathione S- Transferases (GSTs) indicating possible antioxidant effects.[82]

From our review, 2 studies examined the use of prebiotics-only regimen;[47,48] while one RCT study investigated a combined probiotics+prebiotics regimen,[52] respectively. Gremaldi and colleagues investigated the effect of exclusion diets and a 6-week Bimuno® galacto-oligosaccharide (B-GOS®) prebiotic intervention in 30 children with autism.[47] From this study, children on exclusion diets showed significantly lower incidence of abdominal pain and abnormal bowel movement, as well as decreased levels of *Bifidobacterium spp* and *Veillonellaceae* family, but higher levels of *Faecalibacterium prausnitzii* and *Bacteroides spp*. In addition, B-GOS® intervention resulted in improved anti-social behaviour, significant changes in gut microbiota, as well as pronounced changes in faecal and urine metabolites.[47] In another study, supplementation with partially hydrolyzed guar gum for 2 months in 4–9-year-old children with autism normalized gut microbiota and significantly increased defecation frequency per week.[48] In addition, the intervention significantly decreased levels of serum interleukin-1β ($p<0.05$) and tumor necrosis factor-α ($p=0.07$), respectively. Behavioral irritability was also ameliorated as per ABC, Japanese Version.[48]

Sanctuary et al[52] used a combined regimen of probiotic and prebiotic [containing *Bifidobacterium* infantis + colostrum supplement (bovine colostrum product)] vs bovine colostrum product alone for 12 weeks in a randomized controlled trial. Results obtained revealed a reduction in the severity of GI symptoms and improved intestinal microflora profile as well as reduced behavioral abnormalities. These results were linked to a reduction in IL-13 and TNF-α production in some participants.[52]

Camel milk

While low plasma levels of GSH (glutathione) and cysteine have been associated with autism, camel milk has been shown to enhance levels of GSH-Px (glutathione

peroxidase) and superoxide dismutase with an improvement in ASD clinical symptoms.[4] The unique composition of camel milk makes it different from other ruminants' milk. Camel milk contains more minerals such as calcium, iron, magnesium, copper, zinc, potassium; and more vitamins (A, B2, E, C); less fat, less cholesterol, and less lactose, when compared to cow milk. While cow milk contains beta-lactoglobulin and beta-casein, these components are absent in camel milk.[51] Due to the unique composition of camel milk, its use has been indicated to provide improvements in the behaviour of children with autism by increasing the levels of superoxide dismutase (SOD), myeloperoxidase (MPO), and plasma GSH, thereby reducing oxidative stress-a major component of autism's aetiology (figure 4).[51,83] Camel milk also reduces oxidative stress via downregulation of mitogen-activated protein kinase (MAPK) signalling pathways.[30]

In the present review, 3 studies[49–51] sought to investigate the effects of camel milk on the clinical outcomes of autism and oxidative stress markers. Al-Ayadhi et al. investigated the effects of camel milk supplementation on oxidative stress parameters in children with autism.[51] Findings from that study revealed significantly ($p<0.5$) increased levels of glutathione, superoxide dismutase, and myeloperoxidase, as well as improved autistic behaviour validated by the Childhood Autism Rating Scale (CARS).[51] A later study by the same authors probed the impacts of raw and boiled camel milk on the Childhood Autism Rating Scale (CARS) and oxidative stress biomarkers such as GSH, SOD, and MPO.[49] Participants aged between 2 to 12 years were randomized into 3 different groups: boiled camel milk, raw camel milk, cow milk (control) which received 500 mL milk products daily for 2 weeks. Significant reductions in the CARS and oxidative stress markers were noted following 2 weeks' consumption of raw and boiled camel milk compared to cow milk (control).[49] Lastly, Bashir and Al-Ayadhi[50] used a randomized trial to probe the impact of camel milk on the CARS assessment and serum levels of thymus and activation-regulated chemokine (TARC). Results obtained revealed that raw camel milk correlated with significant improvements in the CARS score compared with baseline, whereas, both raw and boiled camel milk correlated with significant decreases in TARC serum levels. Cow milk (control) did not produce any significant changes in these measurements.[50]

Vitamin D

Reports have indicated that maternal vitamin D deficiency predisposes children to autism[84,85] suggesting that supplementation with vitamin D may prove beneficial in ameliorating autism symptoms.[86] This evidence is associated with neuro-protective effects of vitamin D, attributable to neuronal calcium regulation, anti-oxidative pathway, immunomodulation and detoxification.[87] Earlier studies have demonstrated that vitamin D upregulates the levels of glutathione in the brain.[88,89] Asides being a potent antioxidant, glutathione scavenges oxidative products,[90,91] protects nerve cells from toxins, and enhances conduction in the nerves critical to mental processing.[92] Hence, it can be deduced that vitamin D plays important roles in the detoxification of the brain. All these mechanisms in conjunction with other factors may account for the neuroprotective effects of vitamin D and its ameliorative effects in autism.[86]

In the present review, one cross-sectional study examined the impact of vitamin D in children with autism.[29] In that study, 57% of the patients had vitamin D deficiency, while 30% had vitamin D insufficiency. Results obtained from that study demonstrated significantly improved outcome (CARS and ABC) subscales that measured eye contact, behaviour, attention span and stereotype behaviour).[29]

Limitations of the study

Some limitations were observed across the studies included in this review. Two studies lacked control groups,[33,45] one study used a narrow age group and carried out work only in male children,[41] while five studies[36,44,45,48,52] used small sample sizes in their trials. These factors limit the generalizability of the results obtained from these studies; therefore, more robust randomized controlled trials (with sufficient group sizes) are required to validate and elaborate on findings. Secondly, we were not able to conduct quantitative analysis of current evidence due to significant heterogeneity in interventions and inconsistencies in outcome measures, hence we only performed qualitative review of the included studies. Lastly, Studies on dietary agents were typically short-term (<7 months) and provided limited evidence regarding the potential effects of these interventions.

Conclusion

The collated evidence in the present review indicate that dietary intervention may hold a promise in the management of autism. Dietary agents are generally available, accessible and considered safe because of their natural origin. The preliminary evidence is encouraging, however, given the limitations associated with these studies, the future direction will depend on larger, long-term and well-designed studies. Taken together, results from this study add to existing literature on the potential benefits and effectiveness of dietary interventions in improving symptoms associated with autism.

References

1. Masi A, DeMayo MM, Glozier N, Guastella AJ. An overview of autism spectrum disorder, heterogeneity and treatment options. *Neurosci Bull* 2017, 33:183–193, doi: 10.1007/s12264-017-0100-y
2. Yong L, Ou J-J, Li Y-M, Xiang D-X. Dietary supplement for core symptoms of autism spectrum disorder: Where are we now and where should we go? *Front Psychiatry* 2017, 8:155, doi: 10.3389/fpsyt.2017.00155
3. Klein N, Kemper KJ. Integrative approaches to caring for children with autism. *Curr Probl Pediatr Adolesc Health Care* 2016, 46:195–201, doi: 10.1016/j.cppeds.2015.12.004
4. Cekici H, Sanlier N. Current nutritional approaches in managing autism spectrum disorder: A review. *Nutr Neurosci* 2019, 22:145–155, doi:10.1080/1028415X.2017.1358481
5. Lundin AA, Dwyer JT. Autism-Can Dietary Interventions and Supplements Work? *Nutr Today* 2014, 49:196–206, doi: 10.1097/NT.0000000000000037
6. AlSagob M, Colak D and Kaya N. Genetics of autism spectrum disorder: an update on copy number variations leading to autism in the next generation sequencing era. *Discov Med* 2015, 19:367–379, PMID:26105700
7. Tărlungeanu DC, Deliu E, Dotter CP, Kara M, Janiesch PC, Scalise M et al. Impaired amino acid transport at the blood brain barrier is a cause of autism spectrum disorder. *Cell* 2016, 167:1481–1494, e18, doi: 10.1016/j.cell.2016.11.013
8. Kern JK, Geier DA, Sykes LK, Haley BE, Geier MR. The relationship between mercury and autism: A comprehensive review and discussion. *J Trace Elem Med Biol* 2016, 37:8–24, doi: 10.1016/j.jtemb.2016.06.002
9. Fattorusso A, Di Genova L, Dell'Isola GB, Mencaroni E, Esposito S. Autism spectrum disorders and the gut microbiota. *Nutrients* 2019, 11:521, doi: 10.3390/nu11030521
10. Li Q, Han Y, Dy ABC, Hagerman RJ. The gut microbiota and autism spectrum disorders. *Front Cell Neurosci* 2017, 11:120, doi: 10.3389/fncel.2017.00120
11. Grenham S, Clarke G, Cryan J, Dinan T. Brain-gut-microbe communication in health and disease. *Front Physiol* 2011, 2:94, doi: 10.3389/fphys.2011.00094
12. Mayer EA, Tillisch K, Gupta A. Gut/brain axis and the microbiota. *J Clin Investig* 2015, 125:926–938, doi: 10.1172/JCI76304
13. Fasano A. Intestinal permeability and its regulation by zonulin: diagnostic and therapeutic implications. *Clin Gastroenterol Hepatol* 2012, 10:1096–1100, doi: 10.1016/j.cgh.2012.08.012
14. Goldani AA, Downs SR, Widjaja F, Lawton B, Hendren RL. Biomarkers in autism. *Front Psychiatry* 2014, 5:100, doi: 10.3389/fpsyt.2014.00100
15. Sivamaruthi BS, Suganthy N, Kesika P, Chaiyasut C. The role of microbiome, dietary supplements, and probiotics in autism spectrum disorder. *Int J Environ Res Public Health* 2020, 17:2647, doi: 10.3390/ijerph17082647
16. Doenyas C. Dietary interventions for autism spectrum disorder: New perspectives from the gut-brain axis. *Physiol Behav* 2018, 194:577–582, doi: 10.1016/j.physbeh.2018.07.014
17. Sharp WG, Berry RC, McCracken C, Nuhu NN, Marvel E, Saulnier CA et al. Feeding problems and nutrient intake in children with autism spectrum disorders: a meta-analysis and comprehensive review of the literature. *J Autism Dev Disord* 2013, 43:2159–2173, doi:10.1007/s10803-013-1771-5
18. Ma NS, Thompson C, Weston S. Brief report: scurvy as a manifestation of food selectivity in children with autism. *J Autism Dev Disord* 2016, 46:1464–1470, doi: 10.1007/s10803-013-1771-5
19. Christison GW, Ivany K. Elimination diets in autism spectrum disorders: any wheat amidst the chaff? *J Dev Behav Pediatr* 2006, 27:S162–S171, doi: 10.1097/00004703-200604002-00015
20. Mari-Bauset S, Zazpe I, Mari-Sanchis A, Llopis-González A, Morales-Suarez-Varela M. Evidence of the gluten-free and casein-free diet in autism spectrum disorders: a systematic review. *J Child Neurol* 2014, 29:1718–1727, doi: 10.1177/0883073814531330
21. Reissmann A, Hauser J, Makulska-Gertruda E, Tomsa L, Lange KW. Gluten-free and casein-free diets in the treatment of autism. *Functional Foods in Health and Disease* 2014, 4:349–361, doi: 10.31989/ffhd.v4i8.146
22. El-Mallakh R, Paskitti M. The ketogenic diet may have mood-stabilizing properties. *Med Hypotheses* 2001, 57:724–726, doi: 10.1054/mehy.2001.1446
23. Grossi E, Melli S, Dunca D, Terruzzi V. Unexpected improvement in core autism spectrum disorder symptoms after long-term treatment with probiotics. *AGE Open Medical Case Rep* 2016, 4:2050313X16666231
24. Ruskin DN, Fortin JA, Bisnauth SN, Masino SA. Ketogenic diets improve behaviors associated with autism spectrum disorder in a sex-specific manner in the EL mouse. *Physiol Behav* 2017, 168:138–145, doi 10.1016/j.physbeh.2016.10.023
25. Dua TK, Dewanjee S, Khanra R, Bhattacharya N, Bhaskar B, Zia-Ul-Haq M et al. The effects of two common edible herbs, Ipomoea aquatica and Enhydra fluctuans, on cadmium-induced pathophysiology: a focus on oxidative defence and anti-apoptotic mechanism. *J Transl Med* 2015, 13:245, doi: 10.1186/s12967-015-0598-6
26. Li X, Jiang X, Sun J, Zhu C, Li X, Tian L et al. Cytoprotective effects of dietary flavonoids against cadmium-induced toxicity. *Ann N Y Acad Sci* 2017, 1398:5–19, doi: 10.1111/nyas.13344
27. Di Meo F, Margarucci S, Galderisi U, Crispi S, Peluso G. Curcumin, gut microbiota, and neuroprotection. *Nutrients* 2019, 11:2426, doi: 10.3390/nu11102426
28. Gaisawat MB, Iskandar MM, MacPherson CW, Tompkins TA, Kubow S. Probiotic supplementation is associated with increased antioxidant capacity and copper chelation in C. difficile-infected fecal water. *Nutrients* 2019, 11:2007, doi: 10.3390/nu11092007
29. Saad K, Abdel-rahman AA, Elserogy YM, Al-Atram AA, Cannell JJ, Bjørklund G et al. Vitamin D status in autism spectrum disorders and the efficacy of vitamin D supplementation in autistic children. *Nutr Neurosci* 2016, 19:346–351, doi: 10.1179/1476830515Y.0000000019
30. Zhu W-W, Kong G-Q, Ma M-M, Li Y, Huang X, Wang L-P et al. Camel milk ameliorates inflammatory responses and oxidative stress and downregulates mitogen-activated protein kinase signaling pathways in lipopolysaccharide-induced acute respiratory distress syndrome in rats. *J Dairy Sci* 2016, 99:53–56, doi:10.3168/jds.2015-10005.,
31. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021, 372, doi: 10.1016/j.ijsu.2021.105906
32. GS HJ. Cochrane handbook for systematic reviews of interventions version 5.1. 0. *Naunyn-Schmiedebergs Archiv für experimentelle Pathologie und Pharmakologie* 2011, 5:S38, Available from: www.cochrane-handbook.org
33. Mensi MM, Rogantini C, Marchesi M, Borgatti R, Chiappedi M. Lactobacillus plantarum PS128 and Other Probiotics in Children and Adolescents with Autism Spectrum Disorder: A Real-World Experience. *Nutrients* 2021, 13:2036, doi: 10.3390/nu13062036
34. Shaaban SY, El Gendy YG, Mehanna NS, El-Senousy WM, El-Feki HS, Saad K et al. The role of probiotics in children with autism spectrum disorder: A prospective, open-label study. *Nutr Neurosci* 2018, 21:676–681, doi:10.1080/1028415X.2017.1347746
35. Tomova A, Husarova V, Lakatosova S, Bakos J, Vlkova B, Babinska K et al. Gastrointestinal microbiota in children with autism in Slovakia. *Physiol Behav* 2015, 138:179–187, doi: 10.1016/j.physbeh.2014.10.033

36. Arnold LE, Luna RA, Williams K, Chan J, Parker RA, Wu Q et al. Probiotics for Gastrointestinal Symptoms and Quality of Life in Autism: A Placebo-Controlled Pilot Trial. *J Child Adolesc Psychopharmacol* 2019, 29:659–669, doi: 10.1089/cap.2018.0156
37. Liu YW, Liong MT, Chung YE, Huang HY, Peng WS, Cheng YF et al. Effects of Lactobacillus plantarum PS128 on Children with Autism Spectrum Disorder in Taiwan: A Randomized, Double-Blind, Placebo-Controlled Trial. *Nutrients* 2019, 11:820, doi: 10.3390/nu11040820
38. Santocchi E, Guiducci L, Prosperi M, Calderoni S, Gaggini M, Apicella F et al. Effects of Probiotic Supplementation on Gastrointestinal, Sensory and Core Symptoms in Autism Spectrum Disorders: A Randomized Controlled Trial. *Front Psychiatry* 2020, 11:550593, doi: 10.3389/fpsyt. 2020. 550593
39. West R, Roberts E, Sichel L, Sichel J. Improvements in gastrointestinal symptoms among children with autism spectrum disorder receiving the Delpro® probiotic and immunomodulator formulation. *J Probiotics Health* 2013, 1:1–6, doi: 10.4172/2329-8901.1000102
40. Parracho HM, Gibson GR, Knott F, Bosscher D, Kleerebezem M, McCartney AL. A double-blind, placebo-controlled, crossover-designed probiotic feeding study in children diagnosed with autistic spectrum disorders. *Int J Probiotics Prebiotics* 2010, 5:69
41. Castejon AM, Spaw JA, Rozenfeld I, Sheinberg N, Kabot S, Shaw A et al. Improving Antioxidant Capacity in Children With Autism: A Randomized, Double-Blind Controlled Study With Cysteine-Rich Whey Protein. *Front Psychiatry* 2021, 12:669089, doi: 10.3389/fpsyt.2021.669089
42. Tsilioni I, Taliou A, Francis K, Theoharides T. Children with autism spectrum disorders, who improved with a luteolin-containing dietary formulation, show reduced serum levels of TNF and IL-6. *Transl Psychiatry* 2015, 5: e647–e647, doi: 10.1038/tp.2015.142
43. Singh K, Connors SL, Macklin EA, Smith KD, Fahey JW, Talalay P et al. Sulforaphane treatment of autism spectrum disorder (ASD). *Proc Natl Acad Sci* 2014, 111:15550–15555, doi: 10.1073/pnas.1416940111
44. Bent S, Lawton B, Warren T, Widjaja F, Dang K, Fahey JW et al. Identification of urinary metabolites that correlate with clinical improvements in children with autism treated with sulforaphane from broccoli. *Mol Autism* 2018, 9:35, doi: 10.1186/s13229-018-0218-4
45. Sadek A, Berk LS, Mainess K, Daher NS. A Pilot Study: Parent Perceptions of Behavior Change in Their Child With Autism Spectrum Disorder Following High Antioxidant Cacao Consumption. *Integr Med* (Encinitas), 2018, 17:31–38, PMCID: PMC6469451
46. Taliou A, Zintzaras E, Lykouras L, Francis K. An open-label pilot study of a formulation containing the anti-inflammatory flavonoid luteolin and its effects on behavior in children with autism spectrum disorders. *Clin Ther* 2013, 35:592-602, doi: 10.1016/j.clinthera.2013.04.006
47. Grimaldi R, Cela D, Swann J, Vulevic J, Gibson G, Tzortzis G. Costabile, (2017). *In vitro* fermentation of B-GOS: impact on faecal bacterial populations and metabolic activity in autistic and non-autistic children. *Microb Ecol* 2017, 93, doi: 10.1186/s40168-018-0523-3
48. Inoue R, Sakaue Y, Kawada Y, Tamaki R, Yasukawa Z, Ozeki M et al. Dietary supplementation with partially hydrolyzed guar gum helps improve constipation and gut dysbiosis symptoms and behavioral irritability in children with autism spectrum disorder. *J Clin Biochem Nutr* 2019, 64:217–223, doi: 10.3164/jcbn.18-105
49. Al-Ayadhi LY, Halepoto DM, Al-Dress AM, Mitwali Y, Zainah R. Behavioral benefits of camel milk in subjects with autism spectrum disorder. *J Coll Physicians Surg Pak* 2015, 25:819-823, PMID: 26577969
50. Bashir S, Al-Ayadhi LY. Effect of camel milk on thymus and activation-regulated chemokine in autistic children: double-blind study. *Pediatr Res* 2014, 75:559–563, doi: 10.1038/pr.2013.248
51. Al-Ayadhi LY, Elamin NE. Camel Milk as a Potential Therapy as an Antioxidant in Autism Spectrum Disorder (ASD). *Evid Based Complement Alternat Med* 2013:602834, doi: 10.1155/2013/602834
52. Sanctuary MR, Kain JN, Chen SY, Kalanetra K, Lemay DG, Rose DR et al. Pilot study of probiotic/colostrum supplementation on gut function in children with autism and gastrointestinal symptoms. *PloS One* 2019, 14:e0210064, doi:10.1371/journal.pone.0210064
53. Lysiuk R, Oliynyk P, Antonyak H, Voronenko D. Development of Phyto-Antidotes Against Adverse Chemical Agents. *Poisonous Plants and Phytochemicals in Drug Discovery* 2020:249–268, doi: 10.1002/9781119650034.ch12
54. Dolske MC, Spollen J, McKay S, Lancashire E, Tolbert L. A preliminary trial of ascorbic acid as supplemental therapy for autism. *Prog Neuropsychopharmacol Biol Psychiatry* 1993, 17:765–774, doi: 10.1016/0278-5846(93)90058-z
55. Nye C, Brice A. *Combined vitamin B6-magnesium treatment in autism spectrum disorder.* Cochrane Database Syst Rev 2005, 4:CD003497, doi: 10.1002/14651858.CD003497.pub2
56. Rowland I, Gibson G, Heinken A, Scott K, Swann J, Thiele I et al. Gut microbiota functions: metabolism of nutrients and other food components. *Eur J Nutr* 2018, 57:1–24, doi: 10.1007/s00394-017-1445-8
57. Duda-Chodak A, Tarko T, Satora P, Sroka P. Interaction of dietary compounds, especially polyphenols, with the intestinal microbiota: a review. *Eur J Nutr* 2015, 54:325–41, doi: 10.1007/s00394-015-0852-y
58. Landete JM, Arqués J, Medina M, Gaya P, de Las Rivas B, Muñoz R. Bioactivation of Phytoestrogens: Intestinal Bacteria and Health. *Crit Rev Food Sci Nutr* 2016, 56:1826–1843, doi:10.1080/10408398.2013.789823
59. Filosa S, Di Meo F, Crispi S. Polyphenols-gut microbiota interplay and brain neuromodulation. *Neural Regen Res* 2018, 13:2055–2059, doi: 10.4103/1673-5374.241429
60. Treml J, Šmejkal K. Flavonoids as potent scavengers of hydroxyl radicals. *Comprehensive reviews in food science and food safety* 2016, 15:720–738, doi: 10.1111/1541-4337.12204
61. Bendary E, Francis R, Ali H, Sarwat M, El Hady S. Antioxidant and structure–activity relationships (SARs) of some phenolic and anilines compounds. *Ann Agric Sci* 2013, 58:173–181, doi: 10.1016/j.aoas.2013.07.002
62. Essa M, Braidy N, Waly M, Al-Farsi Y, Al-Sharbati M, Subash S et al. Impaired antioxidant status and reduced energy metabolism in autistic children. *Res Autism Spectr Disord* 2013, 7:557–565, doi: 10.1016/j.rasd.2012.12.006
63. Chauhan A, Chauhan V, Brown WT, Cohen I. Oxidative stress in autism: Increased lipid peroxidation and reduced serum levels of ceruloplasmin and transferrin-the antioxidant proteins. *Life Sci* 2004, 75:2539–2549, doi: 10.1016/j.pathophys.2006.05.007
64. Smaga I, Niedzielska E, Gawlik M, Moniczewski A, Krzek J, Przegaliński E et al. Oxidative stress as an etiological factor and a potential treatment target of psychiatric disorders. Part 2. Depression, anxiety, schizophrenia and autism. *Pharmacol Rep* 2015, 67:569–580, doi: 10.1016/j.pharep.2014.12.015
65. Sánchez B, Delgado S, Blanco-Míguez A, Lourenço A, Gueimonde M, Margolles A. Probiotics, gut microbiota, and their influence on host health and disease. *Mol Nutr Food Res* 2017, 61:1600240, doi: 10.1002/mnfr.201600240
66. Srikantha P, Mohajeri MH. The possible role of the microbiota-gut-brain-axis in autism spectrum disorder. *Int J Mol Sci* 2019, 20:2115, doi: 10.1016/j.nut.2011.08.002
67. Krajmalnik-Brown R, Lozupone C, Kang DW, Adams JB. Gut bacteria in children with autism spectrum disorders: challenges and promise of studying how a complex community influences a complex disease. *Microb Ecol Health Dis* 2015, 26:26914, doi: 10.3402/mehd.v26.26914
68. Finegold SM. Desulfovibrio species are potentially important in regressive autism. *Med Hypotheses* 2011, 77:270–274, doi: 10.1016/j.mehy.2011.04.032

69. Finegold SM, Downes J, Summanen PH. Microbiology of regressive autism. *Anaerobe* 2012, 18:260–262, doi: 10.1016/j.anaerobe.2011.12.018

70. Williams BL, Hornig M, Parekh T, Lipkin WI. Application of novel PCR-based methods for detection, quantitation, and phylogenetic characterization of Sutterella species in intestinal biopsy samples from children with autism and gastrointestinal disturbances. *mBio* 2012, 3, doi: 10.1128/mBio.00261-11

71. Adams JB, Johansen LJ, Powell LD, Quig D, Rubin RA. Gastrointestinal flora and gastrointestinal status in children with autism--comparisons to typical children and correlation with autism severity. *BMC Gastroenterol* 2011, 11:22, doi: 10.1186/1471-230X-11-22

72. Critchfield JW, Van Hemert S, Ash M, Mulder L, Ashwood P. The potential role of probiotics in the management of childhood autism spectrum disorders. *Gastroenterol Res Pract* 2011, 2011:161358, doi: 10.1155/2011/161358

73. Martin CR, Osadchiy V, Kalani A, Mayer EA. The brain-gut-microbiome axis. *Cell Mol Gastroenterol Hepatol* 2018, 6:133–148, doi: 10.1016/j.jcmgh.2018.04.003

74. Aabed K, Bhat RS, Moubayed N, Al-Mutiri M, Al-Marshoud M, Al-Qahtani A et al. Ameliorative effect of probiotics (Lactobacillus paracaseii and Protexin®) and prebiotics (propolis and bee pollen) on clindamycin and propionic acid-induced oxidative stress and altered gut microbiota in a rodent model of autism. *Cell Mol Biol* (Noisy-le-grand) 2019, 65:1–7, PMID: 30782287

75. Aabed K, Bhat RS, Al-Dbass A, Moubayed N, Algahtani N, Merghani NM et al. Bee pollen and propolis improve neuroinflammation and dysbiosis induced by propionic acid, a short chain fatty acid in a rodent model of autism. *Lipids Health Dis* 2019, 18:200, doi: 10.1186/s12944-019-1150-0

76. Gibson GR, Hutkins RW, Sanders ME, Prescott SL, Reimer RA, Salminen SJ et al. The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. *Nat Rev Gastroenterol Hepatol* 2017, 14:491–502, doi: 10.1038/nrgastro.2017.75

77. Davani-Davari D, Negahdaripour M, Karimzadeh I, Seifan M, Mohkam M, Masoumi SJ et al. Prebiotics: definition, types, sources, mechanisms, and clinical applications. *Foods* 2019, 8:92, doi: 10.3390/foods8030092

78. Walker AW, Ince J, Duncan SH, Webster LM, Holtrop G, Ze X et al. Dominant and diet-responsive groups of bacteria within the human colonic microbiota. *The ISME journal* 2011, 5:220–230, doi: 10.1038/ismej.2010.118

79. Flint HJ, Scott KP, Louis P and Duncan SH. The role of the gut microbiota in nutrition and health. *Nat Rev Gastroenterol Hepatol* 2012, 9:577, doi: 10.1038/nrgastro.2012.156

80. Guarino M, Altomare A, Cocca S, Emerenziani S, De Gara L. Effect of Prebiotics on Gastrointes-tinal System. *J Dig Dis Hepatol* 2017, JDDH-125

81. Van den Ende W, Peshev D, De Gara L. Disease prevention by natural antioxidants and prebiotics acting as ROS scavengers in the gastrointestinal tract. *Trends Food Sci Technol* 2011, 22:689–697, doi: 10.1016/j.tifs.2011.07.005

82. Van den Ende W, Valluru R. Sucrose, sucrosyl oligosaccharides, and oxidative stress: scavenging and salvaging? *J Exp Bot* 2009, 60:9–18, doi: 10.1093/jxb/ern297

83. Gizachew A, Teha J, Birhanu T, Nekemte E. Review on medicinal and nutritional values of camel milk. *Nature and Science* 2014, 12:35–41

84. Alfawaz HA, Bhat RS, Al-Ayadhi L, El-Ansary AK. Protective and restorative potency of Vitamin D on persistent biochemical autistic features induced in propionic acid-intoxicated rat pups. *BMC Complement Altern Med* 2014, 14:416, doi: 10.1186/1472-6882-14-416

85. Holick MF. The vitamin D epidemic and its health consequences. *J Nutr* 2005, 135:2739S–2748S, doi: 10.1093/jn/135.11.2739S

86. Bölte S, Girdler S, Marschik PB. The contribution of environmental exposure to the etiology of autism spectrum disorder. *Cell Mol Life Sci* 2019, 76:1275–1297, doi: 10.1007/s00018-018-2988-4

87. Uberti F, Morsanuto V, Bardelli C, Molinari C. Protective effects of 1α, 25-Dihydroxyvitamin D3 on cultured neural cells exposed to catalytic iron. *Physiol Rep* 2016, 4: e12769, doi: 10.14814/phy2.12769

88. Garcion E, Wion-Barbot N, Montero-Menei CN, Berger F, Wion D. New clues about vitamin D functions in the nervous system. Trends *Endocrinol Metab* 2002, 13:100–105, doi: 10.1016/s1043-2760(01)00547-1

89. Baas D, Prüfer K, Ittel ME, Kuchler-Bopp S, Labourdette G, Sarlième LL et al. Rat oligodendrocytes express the vitamin D3 receptor and respond to 1, 25-dihydroxyvitamin D3. *Glia* 2000, 31:59–68, doi: 10.1002/(sici)1098-1136(200007)31:1<59::aid-glia60>3.0.co;2-y

90. Kern JK, Jones AM. Evidence of toxicity, oxidative stress, and neuronal insult in autism. *J Toxicol Environ Health - B: Crit Rev* 2006, 9:485–499, doi: 10.1080/10937400600882079

91. Jia F, Wang B, Shan L, Xu Z, Staal WG, Du L. Core symptoms of autism improved after vitamin D supplementation. *Pediatrics* 2015, 135: e196–e198, doi: 10.1542/peds.2014-2121

92. Cannell JJ. Autism, will vitamin D treat core symptoms? *Med Hypotheses* 2013, 81:195–198, doi: 10.4161/derm.24356

Ανασκόπηση

Διατροφικές παρεμβάσεις για τη διαταραχή αυτιστικού φάσματος: Μία επικαιροποιημένη συστηματική ανασκόπηση των μελετών σε ανθρώπους

Cecilia N. Amadi,[1] Chinna N. Orish,[2] Chiara Frazzoli,[3] Orish E. Orisakwe[1,4]

[1]*Department of Experimental Pharmacology & Toxicology, Faculty of Pharmacy, University of Port Harcourt, Choba,*

[2]*Department of Anatomy, Faculty of Basic Medical Sciences, College of Health Sciences, University of Port Harcourt, Choba, Nigeria,*

[3]*Department for Cardiovascular, Dysmetabolic and Aging Diseases, Istituto Superiore di Sanità, Rome, Italy,*

[4]*African Centre of Excellence for Public Health and Toxicological Research (ACE-PUTOR), University of Port Harcourt, PMB, Choba, Nigeria*

ΙΣΤΟΡΙΚΟ ΑΡΘΡΟΥ: Παραλήφθηκε 18 Ιανουαρίου 2022/Αναθεωρήθηκε 10 Φεβρουαρίου 2022/Δημοσιεύθηκε Διαδικτυακά 24 Απριλίου 2022

ΠΕΡΙΛΗΨΗ

Ο αυτισμός είναι ένα σύνθετο φάσμα διαταραχών (ΔΑΦ) με αιτιολογία σχετιζόμενη με παράγοντες γενετικούς, επιγενετικούς, αυτοάνοσους, οξειδωτικού στρες και περιβαλλοντικούς. Η θεραπεία της ΔΑΦ με τη χρήση διατροφικών προσεγγίσεων είναι μια πολλά υποσχόμενη στρατηγική, ειδικά λόγω της ασφάλειας και της διαθεσιμότητάς της. Η μελέτη μας ανέλυσε κριτικά τους ρόλους και την αποτελεσματικότητα των αντιοξειδωτικών, των προβιοτικών, των πρεβιοτικών, του γάλακτος καμήλας και της βιταμίνης D. Αυτή η συστηματική ανασκόπηση παρέχει μια επικαιροποιημένη σύνοψη των μελετών σε ανθρώπους που διερεύνησαν τα θεραπευτικά οφέλη αυτών των διατροφικών παρεμβάσεων στον αυτισμό. Εντοπίστηκαν συνολικά 943 εργασίες από τις οποίες 21 άρθρα συμπεριλήφθηκαν στη συστηματική ανασκόπηση. Οι επιλεγμένες μελέτες διερεύνησαν την επίδραση 5 διαφορετικών συμπληρωμάτων διατροφής στα συμπτώματα και στις συμπεριφορές της ΔΑΦ. Αυτοί οι παράγοντες περιλαμβάνουν: αντιοξειδωτικά/πολυφαινολικές ενώσεις, προβιοτικά, πρεβιοτικά, γάλα καμήλας και βιταμίνη D. Από τα αποτελέσματα της παρούσας ανασκόπησης, οι αντιοξειδωτικές/πολυφαινολικές ενώσεις μείωσαν τα επίπεδα των φλεγμονωδών κυτοκινών και βελτίωσαν τα συμπτώματα συμπεριφοράς. Τα προβιοτικά βελτίωσαν τη συμπεριφορά και τα γαστρεντερικά συμπτώματα καθώς και αποκατέστησαν την ισορροπία μικροβιακής χλωρίδας του εντέρου. Τα πρεβιοτικά μείωσαν τα επίπεδα των φλεγμονωδών κυτοκινών, βελτίωσαν τη συμπεριφορά και τα γαστρεντερικά συμπτώματα καθώς και τη μικροβιακή χλωρίδα του εντέρου. Η βιταμίνη D βελτίωσε τα συμπτώματα συμπεριφοράς και προσέφερε προστατευτικά αποτελέσματα έναντι της νευροτοξικότητας. Το γάλα καμήλας μείωσε τις φλεγμονώδεις αντιδράσεις και το οξειδωτικό στρες. Δεδομένης της χρόνιας φύσης καθώς και της πρώιμης έναρξης των ΔΑΦ, τα συμπληρώματα διατροφής είναι χρήσιμα για τη συμπλήρωση των διατροφικών ελλείψεων σε παιδιά με ΔΑΦ. Τα βασικά οφέλη αυτών των παραγόντων προέρχονται από την ικανότητά τους να στοχεύουν πολλαπλές φυσιολογικές περιοχές μέσω του άξονα του εγκεφάλου του εντέρου, ενώ και στερούνται πιθανών επιβλαβών ή επιβαρυντικών επιδράσεων σε ασθενείς με ΔΑΦ. Τα στοιχεία που συγκεντρώθηκαν από αυτήν την ανασκόπηση υποδεικνύουν ότι η διατροφική παρέμβαση μπορεί παρέχει ένα νέο σύστημα για τη διαχείριση του αυτισμού.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: Διαταραχή αυτιστικού φάσματος (ΔΑΦ), διατροφική παρέμβαση, μικροβιακή χλωρίδα εντέρου, δημόσια υγεία.

Συγγραφέας επικοινωνίας: Orish E. Orisakwe, African Centre of Excellence for Public Health and Toxicological Research (ACE-PUTOR), University of Port Harcourt, PMB, 5323 Port Harcourt, Choba, Nigeria, Διεύθυνση e-mail: vik.gkot@hua.gr orishebere@gmail.com; orish.orisaakwe@uniport.edu

https://doi.org/10.22365/jpsych.2022.075 / Psychiatriki 2022, 33:243–246

Brief communication

Cognitive changes in health locus of control attributions after behavioral analysis in patients with panic disorder and/or agoraphobia

Yiannis Kasvikis, Titika Mitsopoulou, Evangelia Alexiou

Behavior Treatment Unit, Hellenic Center of Mental Health and Research, Athens, Greece

ARTICLE HISTORY: Received 3 September 2021/Revised 5 December 2021/Published Online 27 April 2022

ABSTRACT

Patients with panic disorder and/or agoraphobia (PD +/– Ag) attribute their mental health more to external factors and less to internal, while after behavior treatment (BT) their external attributions decrease and internal attributions increase. We examined whether these cognitive changes observed at the end of BT, begin earlier. Forty patients with PD +/– Ag were assessed on the Multidimensional Health Locus of Control Scale, before and after the diagnostic and psychoeducational sessions that precede the clinical implementation of BT. Decreased health attributions to significant others ($t=4.22$, $p<0.01$) and an increase trend to self ($t=-0.78$, $p=0.43$) were observed, which are compatible with the active role patients need to adopt in the clinical application of BT.

KEYWORDS: Health locus of control, panic disorder, agoraphobia, behavioral assessment, behavior therapy.

Introduction

It has been observed that certain characteristics of patients with panic disorder and/or agoraphobia (PD+/–Ag), such as the attribution of their health locus of control, are associated with a predisposition to the development and maintenance of the disorder.[1] In particular, patients with PD+/–Ag tend to attribute their mental health locus of control less to themselves and more to external factors, namely significant other people and chance, compared to healthy controls.[2] This particular cognitive profile enhances avoidant behavior, while at the same time it seems to share many symptoms with learned helplessness.[3] The devaluation of one's abilities leads to a catastrophizing interpretation of bodily sensations and to the avoidance of situations and behaviors that may cause them.[4]

The attribution of health locus of control was initially considered a stable personality trait, but is now indicated to be modifiable through life experiences, education and treatment.[5] In a retrospective clinical study conducted in our country, 250 patients with anxiety disorder, obsessive compulsive disorder and post-traumatic stress disorder who completed their BT, showed a decrease in the attribution of their mental health locus of control to external factors, while at the same time showed a significant increase in attributing their health-related behaviors to internal factors like their own efforts.[6] In a subsequent study Greek patients with PD+/–Ag who completed BT reported decreased health attributions to significant others and increased health attributions to self, a change that was maintained in the one-year follow-up, in contrast to those who refused or discontinued.[2]

The question of whether these cognitive changes are solely due to the successful completion of the BT or can be achieved at earlier points by improving the patient's cooperation is crucial, due to the active participation that the BT requires. In the present study, the mental health locus of control attributions of patients with PD+/–Ag were assessed before the clinical initiation of the BT and after the first preparatory sessions, so that any changes observed are not related to experiential/therapeutic experiences.

Corresponding author: Evangelia Alexiou, Behavior Treatment Unit, Hellenic Center of Mental Health and Research, Metsovou 33, GR-106 83 Athens, Greece • e-mail: evalexioy@gmail.com

Material and Method

Participants and process

The study involved 40 patients with PD+/–Ag who requested treatment at the Behavior Treatment Unit (BTU) of the Hellenic Center of Mental Health and Research in Athens. Their age ranged from 19 to 73 years with a mean age of 36.43 years (SD=12.1). All patients signed an inform consent before entry and were assigned to treatment, with the sole criterion of the availability of each therapist. The sessions were conducted by five different therapists with many years of clinical experience, while diagnosis was confirmed by the clinical team and the supervising psychiatrist.

The design of this preliminary study was one group pre-post- test design. The Multidimensional Health Locus of Control (MHLC) Scale[7] was administered at two different time points, the same for all participants, before the first assessment session and immediately after the completion of the assessment (before the fourth session). In these preparatory sessions, were performed: (a) completion of psychiatric history, (b) behavioral analysis, including patient's feedback on the factors of maintenance of the disorder, c) psychoeducation for pathological anxiety and (d) explanation of the BT rationale, which clarified the active participation of the patient as a necessary condition for the achievement of his/her therapeutic goals.

Multidimensional Health Locus of Control (MHLC) Scale

The questionnaire consists of three subscales which include 18 items: six to evaluate the attribution of mental health locus of control to self, that is one's own behavior (internal health locus of control, IHLC), six to evaluate the attribution of mental health to significant others, such as healthcare professionals, family, friends (powerful others health locus of control, POHLC) and six to evaluate the attribution of mental health to chance, e.g. fate, luck (chance health locus of control, CHLC). The degree of agreement or disagreement with each item is evaluated on a six-point Likert scale (from 1=strongly disagree to 6= totally agree). The three subscales are calculated independently and the proposed scoring range is: 25+/–5 in the IHLC, 20+/–5 in the POHLC and 15+/–5 in the CHLC subscale.[7] The validity and reliability of the Greek version of the Multidimensional Health Locus of Control Scale has been tested[6,8] and in our sample, the internal consistency was a=0.72 for the self-dimension, a=0.80 for significant others and a=0.83 for chance.

Statistical analysis

The data collected were analyzed with the SPSS statistical package, version 25. The distribution of the data was normal (Shapiro-Wilk test) and parametric tests were used.

Results

Table 1 presents the demographic and clinical characteristics of the sample in detail.

In the dependent samples paired t-test analyses, a decrease in mental health locus of control attributions to significant others was observed (t=4.22, p<0.01). The dimension of internal control (attribution to self) showed an increase trend between the two time points, which was not yet significant (t=–0.78, p=0.43), while in the chance dimension (t=1,63, p=0.11) no change was observed (table 2).

Discussion

Immediately after their first three preparatory sessions our patients with PD+/–Ag showed a decrease in the external mental health locus of control attribution to significant others and an increase trend in the self-dimension, cognitive changes that are consistent with BT rationale. Psychoeducation and explanation of the BT have been shown to foster the development of a different psychological way of thinking with emphasis on self-management and the adoption of responsibility of oneself. This may be a first form of cognitive exposure to the avoidant and depressive established thoughts and habits of patients with PD+/–Ag.

Table 1. Demographic and clinical characteristics of the 40 participants at the time of their admission to the study.

Sex	n (%)
Men	13 (32.5%)
Women	27 (67.5%)
Marital status	
Single	17 (42.5%)
Married/In a relationship	23 (57.5%)
Education Level	
Primary	5 (12.5%)
Secondary	23 (57.5%)
Higher	12 (30%)
Profession	
Employed	24 (60%)
Unemployed	16 (40%)
Diagnosis	
Panic Disorder	16 (40%)
Panic Disorder and Agoraphobia	19 (47.5 %)
Agoraphobia	5 (12.5%)
Treatments they have tried in the past	
Other psychotherapeutic interventions	10 (25%)
Pharmacotherapy	14 (35%)
Psychotherapeutic interventions and pharmacotherapy	7 (17.5%)
Initiation of BT with medication	22 (55%)

Table 2. Comparison of mental health locus of control attributions before and after the assessment.

	Before	After		
Dimensions	M (SD)	M (SD)	t	p
Internal control attribution (self)	27.94 (4.72)	28.54 (4.38)	–0.78	0.43
External control attribution (significant others)	26.00 (6.21)	23.,57 (5.43)	4.22	0.00**
External control attribution (luck)	16.97 (7.09)	15.31 (7.85)	1.63	0.11

M=Mean, SD=standard deviation, ** p<0.01

A qualitative study that examined the experiences of patients with PD+/–Ag, suggested that understanding the individual factors that maintain the disorder during the first BT sessions, is a key component for patients' subsequent therapeutic involvement.[9] The successful manualized exposure-based BT of patients with PD+/–Ag in a single session, accompanied by personalized self-help manual,[10] has confirmed the usefulness of active participation in the treatment outcome. Moreover, their emotional and functional gains and reduced relapses in long-term evaluations, may be due to this experiential training and empirical feedback, which seems to significantly modify the attribution of mental health locus of control.[10,11]

Studies in other psychiatric disorders have similar results. In postpartum depression and bipolar disorder, the content of psychoeducation seems to modify pre-existing mental health locus of control attributions, changes that are predictive and positively correlated with increased patients' cooperation in treatment and reduced prevalence of psychiatric morbidity.[12,13]

The lack of change in mental health locus of control attribution to luck in this study may be due to the fact that the vast majority of participants had previously tried other psychotherapeutic or pharmaceutical interventions (77.5%), or were already on medication (55%) when they requested treatment at the BTU, so they knew in part that their mental health or illness could not be attributed to random factors. Further study with people without any prior familiarity with psychiatric care services, e.g., patients visiting a mental health specialist for the first time, may clarify how pre-existing control attributions are formed after the first informational contact.

The results of this study, although innovative, are preliminary. The size of the sample limits their generalization and the design of the study cannot explore cause-and-effect relationships. Verification is required on the basis of methodologically improved experimental research.

In conclusion, the findings are compatible with the active role that the patient with PD +/– Ag is called to adopt from the beginning of the clinical application of BT, reducing his/her dependence on external factors and focusing on his/her self-management. The emphasis on self-management may contribute to the empowerment of patients,[14] a continuous process that involves the concept of health control attributions, which is necessary not only in anxiety disorders but also in other chronic illnesses, such as diabetes and hypertension, where self-regulation is required.[15]

References

1. Gallagher MW, Bentley KH, Barlow DH. Perceived Control and Vulnerability to Anxiety Disorders: A Meta-analytic Review. *Cognit Ther Res* 2014, 38:571–584, doi: 10.1007/s10608-014-9624-x
2. Kasvikis Y, Skaloubaka D, Mitskidou P. Effects of exposure treatment on locus of control attributions in agoraphobics. *Psychiatriki* 2003, 14:191–199 (In Greek)
3. Maier SF, Seligman MEP. Learned helplessness at fifty: Insights from neuroscience. *Psychol Rev* 2016, 123:349–367, doi: 0.1037/rev0000033
4. White KS, Brown TA, Somers TJ, Barlow DH. Avoidance behavior in panic disorder: The moderating influence of perceived control. *Behav Res Ther* 2006, 44:147–157, doi: 10.1016/j.brat.2005.07.009
5. De las Cuevas C, Peñate W, Betancort M, Cabrera C. What Do Psychiatric Patients Believe Regarding Where Control Over Their Illness Lies? *J Nerv Ment Dis* 2015, 203:81–86, doi: 10.1097/nmd.0000000000000244
6. Kasvikis Y. Routine monitoring of outcome of the Behavior Treatment Unit – Center of Mental Health: 15 years of functioning. 1st WPA Regional and Intersectional Congress, 12–15 March 2005, Athens
7. Wallston KA, Wallston BS. Development of the Multidimentional Health Locus of Control Scales. *Health Educ Monogr* 1978, 6:160-170, doi: 10.1177/109019817800600107
8. Roussi P. Health Locus of Control Scale (HLC). In: Stalikas A, Triliva S, Roussi P (eds) *Greek psychometric tools* (6th ed). Pedio, Athens, 2009:276–277 (In Greek)
9. Tzavela EC, Mytskidou P, Mertika A, Stalikas A, Kasvikis Y. Treatment engagement in the early phase of cognitive-behavior therapy for panic disorder: A grounded theory analysis of patient experience. *Psychother Res* 2018, 28:842–860, doi: 10.1080/10503307.2016.1246769
10. Mitsopoulou T, Kasvikis Y, Koumantanou L, Giaglis G, Skapinakis P, Mavreas V. Manualized single-session behavior treatment with self-help manual for panic disorder with or without agoraphobia. *Psychother Res* 2020, 30:776-787, doi:10.1080/10503307.2019.1663956
11. Bandelow B, Sagebiel A, Belz M, Görlich Y, Michaelis S, Wedekind D. Enduring effects of psychological treatments for anxiety disorders: meta-analysis of follow-up studies. *Br J Psychiatry* 2018, 212:333–338, doi: 10.1192/bjp.2018.49
12. Even C, Thuile J, Kalck-Stern M, Criquillion-Doublet S, Gorwood P, Rouillon F. Psychoeducation for patients with bipolar disorder receiving lithium: short and long term impact on locus of control and knowledge about lithium. *J Affect Disord* 2010, 123:299–302, doi: 10.1016/j.jad.2009.09.008
13. Mollard E. Women's health locus of control during pregnancy may predict risk for postpartum depression. *Evid Based Nurs* 2013, 18:73 doi: 10.1136/ebnurs-2014-101985
14. Aymé S, Kole A, Groft S. Empowerment of Patients: Lessons from the Rare Diseases Community. *Lancet* 2008, 371:2048–2051, doi: 10.1016/S0140-6736(08)60875-2
15. Chen J, Mullins CD, Novak P, Thomas SB. Personalized Strategies to Activate and Empower Patients in Health Care and Reduce Health Disparities. *Health Educ Behav* 2015, 43:25–34, doi: 10.1177/1090198115579415

Σύντομο άρθρο

Γνωσιακές αλλαγές της απόδοσης ελέγχου υγείας μετά την ανάλυση συμπεριφοράς σε ασθενείς με διαταραχή πανικού ή/και αγοραφοβία

Γιάννης Κασβίκης, Τιτίκα Μητσοπούλου, Ευαγγελία Αλεξίου

Μονάδα Θεραπείας Συμπεριφοράς, Ελληνικό Κέντρο Ψυχικής Υγιεινής και Ερευνών, Αθήνα, Ελλάδα

ΙΣΤΟΡΙΚΟ ΑΡΘΡΟΥ: Παραλήφθηκε 3 Σεπτεμβρίου 2021/Αναθεωρήθηκε 5 Δεκεμβρίου 2022/Δημοσιεύθηκε Διαδικτυακά 27 Απριλίου 2022

ΠΕΡΙΛΗΨΗ

Οι ασθενείς με διαταραχή πανικού και/ή αγοραφοβία (ΔΠ+/–Αγ.) αποδίδουν τον έλεγχο της ψυχικής τους υγείας περισσότερο σε εξωτερικούς παράγοντες και λιγότερο σε εσωτερικούς, ενώ μετά από θεραπεία συμπεριφοράς (ΘΣ) παρατηρείται αύξηση της απόδοσης ελέγχου στον εαυτό και μείωση σε εξωτερικούς παράγοντες. Ερευνήσαμε εάν οι γνωσιακές αυτές μεταβολές που παρατηρούνται στη λήξη της ΘΣ ξεκινούν σε πρωθύστερα χρονικά σημεία, προς όφελος της συνεργασιμότητας στη θεραπεία. Σαράντα ασθενείς με ΔΠ+/–Αγ. που προσήλθαν στη Μονάδα Θεραπείας Συμπεριφοράς του Ελληνικού Κέντρου Ψυχικής Υγιεινής και Ερευνών αξιολογήθηκαν στο Πολυδιάστατο Ερωτηματολόγιο Απόδοσης Ελέγχου Υγείας, μετά τις διαγνωστικές και ψυχοεκπαιδευτικές συνεδρίες που προηγούνται της κλινικής έναρξης της ΘΣ. Η αξιολόγηση και η ενημερωμένη συμμετοχή στη ΘΣ, πριν την κλινική εφαρμογή οποιασδήποτε παρέμβασης, τροποποίησε τις αποδόσεις ελέγχου των ασθενών μας, με μείωση στην απόδοση ελέγχου ψυχικής υγείας στους σημαντικούς άλλους ανθρώπους ($t=4,22$, $p<0,01$) και μία τάση αύξησης στην απόδοση ελέγχου στον εαυτό ($t=-0,78$, $p=0,43$). Τα ευρήματα είναι συμβατά με τον ενεργητικό ρόλο που καλείται να υιοθετήσει ο ασθενής στην κλινική εφαρμογή της ΘΣ.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: Απόδοση ελέγχου ψυχικής υγείας, διαταραχή πανικού, αγοραφοβία, ανάλυση συμπεριφοράς, θεραπεία συμπεριφοράς.

Συγγραφέας επικοινωνίας: Ευαγγελία Αλεξίου, Μονάδα Θεραπείας Συμπεριφοράς, Ελληνικό Κέντρο Ψυχικής Υγιεινής και Ερευνών, Μετσόβου 33, 106 83 Αθήνα, Διεύθυνση e-mail: evalexioy@gmail.com

https://doi.org/10.22365/jpsych.2022.076 / Psychiatriki 2022, 33:247–248

Letter to the Editor

Regarding "Stress management and *In Vitro* Fertilization (IVF): A pilot randomized controlled trial"

ARTICLE HISTORY: Received 18 January 2022/Published Online 27 April 2022

To the Editors,

Koumparou et al[1] recently published a randomized controlled trial (RCT) on the effectiveness of psychological interventions (stress management training, SMT) for women planning *in vitro* fertilization (IVF). They concluded that while the effect of SMT was limited in terms of IVF outcome, it resulted in a significant reduction of stress levels in infertile patients. Since most women undergoing infertility treatment are exposed to high psychological stress,[2] this study may be of great value in demonstrating the need for proactive SMT to maintain infertile women's mental health and motivation to continue treatment. However, we are concerned that the reliability of this RCT has been compromised in several ways.

First, the registration of the RCT was not clearly stated. According to The CONsolidated Standards of Reporting Trials (CONSORT) 2010 guidelines, a prospective registration of the RCT is required, which prevents unnecessary concerns about the bias of results selection.[3,4]

Second, the lack of specific figures on the background of the participants in the case and control groups risks distorting the RCT results. The article states that there was no significant difference between the two groups. However, since aging and prolonged infertility treatment increase the psychological burden on infertile patients,[5] detailed background information is necessary to interpret the results of an RCT accurately. Selection bias could not be determined, which weakened the validity of this RCT.

Furthermore, the absence of any mention of case dropout makes the conclusions of this RCT uncertain; a discussion of cases demonstrating difficulty in completing an 8-week psychological program would clarify whether temporary SMT would show efficacy for patients.

Finally, it is essential to note that the details of IVF have not been clarified. Since the timing of the SMT and IVF-ET cycles or details of the IVF-ET protocol were not shown, this RCT could not be used as a reference for IVF facilities to actually operate SMT. There is no doubt that psychological interventions are necessary for infertile patients exposed to high psychological stress, but this RCT has many details that have not been clarified and the conclusions are attenuated. As details become clearer, this RCT will provide a foundation for the active use of SMT in infertility treatment settings.

Acknowledgments. We would like to thank Editage (http://www.editage.jp) for English language editing.

Shinnosuke Komiya
Department of Obstetrics and Gynecology, Kansai Medical University Graduate School of Medicine, Osaka, JAPAN, HORAC Grand Front Osaka Clinic, Kita-ku, Osaka, JAPAN, e-mail: komiya0703@gmail.com

Masahiro Banno
Department of Psychiatry, Seichiryo Hospital, Nagoya, JAPAN, Department of Psychiatry, Nagoya University Graduate School of Medicine, Nagoya, JAPAN, Scientific Research WorkS Peer Support Group (SRWS-PSG), Osaka, JAPAN

Yuki Itagaki
Department of Surgery, Japanese Red Cross Asahikawa Hospital, Hokkaido, JAPAN, Scientific Research WorkS Peer Support Group (SRWS-PSG), Osaka, JAPAN

References

1. Koumparou M, Bakas P, Pantos K, Economou M, Chrousos G. Stress management and *In Vitro* Fertilization (IVF): A pilot randomized controlled trial. *Psychiatriki* 2021, 32:290–299, doi: 10.22365/jpsych.2021.029
2. Volgsten H, Svanberg AS, Olsson P. Unresolved grief in women and men in Sweden three years after undergoing unsuccessful *in vitro* fertilization treatment. *Acta Obstet Gynecol Scand* 2010, 89:1290–1297, doi: 10.3109/00016349.2010.512063
3. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010, 23, 340:c869, doi: 10.1136/bmj.c869
4. Page M, Boutron I. *RoB 2 Domain 5: bias in selection of the reported result*. Available from: https://training.cochrane.org/resource/rob-2-domain-5-bias-selection-reported-result. Accessed 12 Jan 2022
5. Gonda KJ, Domar AD, Gleicher N, Marrs RP. Insights from clinical experience in treating IVF poor responders. *Reprod Biomed Online* 2018,36:12-19, doi: 10.1016/j.rbmo.2017.09.016

https://doi.org/10.22365/jpsych.2022.077 / Psychiatriki 2022, 33:249–250

Letter to the Editor

Authors Reply: Regarding "Stress management and *in Vitro* Fertilization (IVF): A pilot randomized controlled trial"

ARTICLE HISTORY: Received 16 February 2022/Published Online 27April 2022

To the Editors,

Komiya et al recently sent a letter to the editor[1] raising issues of reliability and validity of our study "Stress management and *in Vitro* Fertilization (IVF): A pilot randomized controlled trial".[2] Their comments focused on the default of the registration, the absence of any mention of case dropout, the ambiguity in the details of IVF treatment and the lack of specific figures on the background of the participants.

However, the principles of CONSORT 2010 cannot be applied to Pilot Randomized and Feasibility Trials, only to Randomized Trials (RTs) or Randomized Controlled Trials (RCTs). Similarly, the CONSORT Extension 2016 suggested some principles for Pilot and Feasibility Trials, but again it does not directly apply to internal pilot studies, non-randomized pilot and feasibility studies, or phase II studies.[3,4] Many international journals do not require registration for Pilot and Feasibility Trials, but only for RTs or RCTs,[5] granted that clinical trial registration is not an indicator of low risk of bias.[6]

Thanks to the useful comments by Komiya et al, our article[2] now includes online "Supplementary Materials" in which we clarify all their points one by one. Specifically, the Material and Method section of Supplementary Materials includes details for the Registration, the Flow Chart and the IVF Treatment, and the Results section includes details for the Background of the Participants. Thus, we believe that the level of reliability and validity of the study can be now examined and ensured.

Maria Koumparou
Second Department of Obstetrics and Gynecology, National and Kapodistrian University of Athens, Aretaieio Hospital, Athens, Greece
Email: mkoympar@med.uoa.gr

Panagiotis Bakas
Second Department of Obstetrics and Gynecology, National and Kapodistrian University of Athens, Aretaieio Hospital, Athens, Greece

Konstantinos Pantos
IVF Unit at Genesis Athens Clinic, Athens, Greece

Marina Economou
First Department of Psychiatry, National and Kapodistrian University of Athens, Eginition Hospital, Athens, Greece

George Chrousos
University Research Institute of Maternal and Child Health and Precision Medicine, National and Kapodistrian University of Athens, Medical School

References

1. Komiya S, Banno M, Itagaki Y. Regarding "Stress management and *In Vitro* Fertilization (IVF): A pilot randomized controlled trial". Psychiatriki 2022, 33:247–248, 10.22365/jpsych.2022.076
2. Koumparou M, Bakas P, Pantos K, Economou M, Chrousos G. Stress management and *In Vitro* Fertilization (IVF): A pilot randomized controlled trial. *Psychiatriki* 2021, 32:290–299, doi: 10.22365/jpsych.2021.029
3. Eldridge SM, Chan CL, Campbell MJ, Bond CV, Hopewell S, Thabane L, Lancaster GA; PAFS consensus group. CONSORT 2010 statement: extension to randomized pilot and feasibility trials. *BMJ* 2016, 355: i5239, doi.org/10.1136/bmj.i5239.
4. Thabane L, Hopewell S, Lancaster GA, Bond CM, Coleman CL, Campbell MJ, Eldridge SM. Methods and processes for development of a CONSORT extension for reporting pilot randomized controlled trials. *Pilot Feasibility Stud* 2016, 20:25, doi.org/10.1186/s40814-016-0065-z
5. Trinquart L, Dunn AG, Bourgeois FT. Registration of published randomized trials: a systematic review and meta-analysis. *BMC Med* 2018, 16:173, doi.org/10.1186/s12916-018-1168-6
6. Farquhar CM, Showell MG, Showell EAE, Beetham P, Baak N, Mourad S, Jordan VMB. Clinical trial registration was not an indicator for low risk of bias. *J Clin Epidemiol* 2017, 84:47–53, doi: 10.1016/j.jclinepi.2016.11.011