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Eating disorders in the era of the COVID-19 pandemic

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COVID-19 pandemic and its socioeconomic consequences have been influencing considerably the Greek population and especially those people that are vulnerable or are actually suffering from a mental disorder. Considering eating disorders (ED) there are reports of a number of factors that increase the stress experienced by patients. The most important of them are:¹

- A. Quarantine and house confinement. Many ED patients report poor relationships with other family members or in some cases falling victim to some type of abusive behavior by other family members. Prolonged compulsory house confinement could have a negative impact on the course of ED. It should be noted that a similar negative impact of the pandemic has been observed in family members that have unsuccessfully tried to balance the need of the patients with the need of the rest of the family.
- B. Changes in exercising. Quarantine has severely influenced patients that have been doing vigorous and compulsive exercise.
- C. Food fear. During the first quarantine in March 2020, there were rumors of forthcoming extreme shortages of necessary products and food.
- D. Restrictions on access to mental health facilities and therapists. In many countries, a substantial number of mental health programs were temporarily shut down during the first wave of the pandemic.
- E. Isolation of people residing alone in cities far away from the family home.
- F. Financial adversities due to slow down of economic activities caused by quarantine.
- G. Increase in obsessive fear concerning body health and food purity due to orthorexia nervosa onset or relapse.²

Research conducted during the pandemic showed that women suffering from ED reported more often than men increase in ED symptomatology, in the number of hours spent exercising, and in the intensity of preoccupation with their body image and social appearance.² A meta-analysis of ED studies during the pandemic showed that 65% of the patients reported a deterioration of ED symptomatology.³ Contrary to the above, the longitudinal studies that were included in the meta-analysis did not report any substantial difference in BMI and ED symptomatology before and after the first quarantine.³ Anorexia nervosa patients seemed to be more influenced than patients suffering from bulimia nervosa and ED non-otherwise specified.³ Other longitudinal studies reported that bulimia nervosa patients were greatly influenced during the quarantine showing signs of slower remission or even relapse of the bulimic symptoms.⁴ Family conflict and intense fear for the life of loved ones could predict a relapse of the ED symptomatology.⁴

Young people were often caught in the following dilemma. On the one hand, the consumption of palatable food could be used as a coping mechanism for regulating emotions such as anxiety, sorrow, and loneliness caused by prolonged house isolation. On the other hand, the increasing presence in the virtual reality environment of social networks has intensified the need for a perfectly slim and fit body that could attract more followers and ensure social approval and success.^{5,6} A special interest group that was affected by the pandemic, was university students. ED symptomatology increased, especially among female students. Stress and depression related to social isolation and disruption of educational activities have been correlated with ED manifestation, especially bulimia nervosa.⁷

Fortunately, young patients seem to adjust adequately to internet-based treatments. There are indications that therapy through teleconference could prove quite effective for the treatment of ED.⁸ There are reports that this type of treatment is not attractive for anorexia nervosa patients, while all other ED patients are well adjusted to it.¹

The consequences of the pandemic considerably affected mental health experts that have been treating ED patients as the number of new and relapsed clients raised dramatically. The situation was worsened by the fact that a large number of those patients had to be treated distantly. It has been reported that often conduct with other colleagues, the feeling of higher purpose or duty, recognition of their effort and supervision are some of the factors that can protect therapists from professional burn-out.¹

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Οι διαταραχές πρόσληψης τροφής στην περίοδο της πανδημίας COVID-19

ΙΣΤΟΡΙΚΟ ΑΡΘΡΟΥ: Παραλήφθηκε 30 Οκτωβρίου 2022/Δημοσιεύθηκε Διαδικτυακά 17 Νοεμβρίου 2022

Η πανδημία του COVID-19 και οι κοινωνικο-οικονομικές συνέπειές της επηρέασαν και εξακολουθούν να επηρεάζουν τον πληθυσμό της χώρας μας και ιδιαίτερα άτομα που πάσχουν ή έχουν την προδιάθεση να νοσήσουν από μια ψυχική διαταραχή. Ειδικότερα για τις διαταραχές πρόσληψης τροφής (ΔΠΤ) έχει αναφερθεί μια σειρά από παράγοντες που φαίνεται να επιτείνουν το στρες των πασχόντων. Οι σημαντικότεροι από αυτούς είναι:¹

- A. Η καραντίνα και ο περιορισμός των ατόμων εντός της οικείας. Πολλοί από τους πάσχοντες από ΔΠΤ έχουν κακή σχέση με την οικογένειά τους ή υφίστανται κάποια μορφή κακοποίησης από μέλη της οικογενείας τους. Η παρατεταμένη υποχρεωτική παραμονή εντός της οικείας επέδρασε αρνητικά στην πορεία της ΔΠΤ. Να σημειωθεί ότι παρόμοια αρνητική επίπτωση παρατηρήθηκε και στην οικογένεια που προσπαθούσε να ισορροπήσει ανάμεσα στη φροντίδα του πάσχοντος μέλους και τη φροντίδα των υπολοίπων μελών της.
- B. Αλλαγές στις δυνατότητες για άσκηση. Από τον εγκλεισμό επηρεάστηκαν ιδιαίτερα οι πάσχοντες που έκαναν παρατεταμένη και καταναγκαστική άσκηση.
- Γ. Ο φόβος για την έλλειψη τροφίμων. Ιδιαίτερα στην πρώτη φάση της καραντίνας, τον Μάρτιο 2020, υπήρχε έντονη φημολογία ότι θα υπάρχουν σημαντικές ελλείψεις σε είδη πρώτης ανάγκης και τρόφιμα.
- Δ. Η δυσκολία πρόσβασης σε θεραπευτικά προγράμματα και ειδικούς της ψυχικής υγείας. Σε πολλές χώρες οι μονάδες ψυχικής υγείας περιόρισαν τη λειτουργία τους για πολλούς μήνες ιδιαίτερα στην πρώτη φάση της πανδημίας.
- E. Η απομόνωση ατόμων που διέμεναν μόνα τους και σε πόλεις μακριά από τους οικείους τους.
- ΣΤ. Οικονομικά προβλήματα που προέκυψαν από τον περιορισμό της εμπορικής δραστηριότητας λόγω της καραντίνας.
- Z. Η αύξηση των καταναγκαστικών φόβων για την υγεία και την καθαρότητα των τροφών στα πλαίσια εμφάνισης ή επιδείνωσης προηγούμενων ορθορεκτικών συμπεριφορών.²

Οι μελέτες που έχουν γίνει έδειξαν ότι οι γυναίκες που έπασχαν από ΔΠΤ ανέφεραν επιδείνωση της πρόσληψης τροφής, αύξηση των ωρών της άσκησης και περισσότερο έντονη ενασχόληση με την εμφάνιση και το σώμα τους.² Μετα-ανάλυση των μελετών που αφορούσαν στις ΔΠΤ στην περίοδο της πανδημίας, έδειξε ότι 65% των πασχόντων ανέφερε επιδείνωση των συμπτωμάτων της ΔΠΤ.³ Οι διαχρονικές μελέτες όμως που συμπεριλήφθηκαν στη μετα-ανάλυση δεν έδειξαν σημαντικές διαφορές στον δείκτη μάζας σώματος και τη συμπτωματολογία των ΔΠΤ πριν και μετά την πρώτη καραντίνα.³ Από τους τύπους των διαταραχών φαίνεται ότι η μεγαλύτερη επίδραση υπήρχε στα άτομα που έπασχαν από ψυχογενή ανορεξία.³ Αντίθετα άλλες διαχρονικές μελέτες έδειξαν ότι επηρεάζονται κυρίως οι πάσχοντες από ψυχογενή βουλιμία που κατά τη διάρκεια της πανδημίας και ενώ βρίσκονταν σε ψυχοθεραπεία μέσω τηλεδιάσκεψης, παρουσίαζαν επιβράδυνση της ίασης ή ακόμα και επιδείνωση της διαταραχής.⁴ Στους ασθενείς αυτούς οι ενδοοικογενειακές συγκρούσεις και ο φόβος για την υγεία αγαπημένων ατόμων φαίνεται να προέβλεπαν την επιδείνωση της συμπτωματολογίας.⁴

Το δίλημμα που θέτει η πανδημία, κυρίως στους νέους ανθρώπους, είναι ότι από τη μία πλευρά το φαγητό είναι ένας τρόπος να διαχειριστεί κανείς το άγχος, τη θλίψη και τη μοναξιά που έφερε η πανδημία στην καθημερινότητά τους, και από την άλλη πλευρά η παραμονή στο σπίτι αύξησε κατακόρυφα την παραμονή τους στον εικονικό διαδικτυακό χώρο των κοινωνικών δικτύων, εκεί δηλαδή που η εικόνα του ατόμου είναι τρομακτικά σημαντική καθώς είναι ο κεντρικός δίαυλος επικοινωνίας και προσέλευσης «ακροατών».^{5,6} Μία ιδιαίτερη κατηγορία νεαρών ενηλίκων που επηρεάστηκε σημαντικά από την πανδημία, είναι οι φοιτητές των πανεπιστημίων. Η συμπτωματολογία των ΔΠΤ φαίνεται να αυξήθηκε σημαντικά ιδιαίτερα στις γυναίκες. Το στρες και η κατάθλιψη που σχετιζόταν με την απομόνωση της καραντίνας και τη διακοπή των εκπαιδευτικών δραστηριοτήτων, φαίνεται να οδήγησε σε αύξηση των ΔΠΤ και ιδιαίτερα της βουλιμίας.⁷

Είναι βέβαια παρήγορο ότι τα νεαρά άτομα φαίνεται να προσαρμόζονται εύκολα στη θεραπεία μέσω διαδικτύου. Στην περίπτωση των ΔΠΤ υπάρχουν σημαντικές ενδείξεις ότι η θεραπεία με τηλεδιάσκεψη μπορεί να έχει καλή αποτελεσματικότητα.⁸ Φαίνεται ότι αυτή η μορφή θεραπείας δυσκολεύει περισσότερο τα άτομα που πάσχουν από ψυχογενή ανορεξία, ενώ γίνεται καλά αποδεκτή από τους πάσχοντες των υπολοίπων ΔΠΤ.¹

Τις επιπτώσεις της πανδημίας βίωσαν και οι ειδικοί της ψυχικής υγείας που ασχολούνται με τις ΔΠΤ, καθώς κλήθηκαν να συνδράμουν έναν αυξημένο αριθμό πασχόντων που ορισμένοι από αυτούς βρίσκονταν σε υποτροπή. Στο παραπάνω πρέπει να προστεθούν και οι δυσκολίες που προέκυψαν λόγω των μέτρων της πανδημίας, κάτι που σε αρκετές περιπτώσεις επέβαλε την τηλεδιάσκεψη ως το μόνο μέσο επαφής με τον πάσχοντα. Έχει βρεθεί ότι η συχνή επαφή με τους συναδέλφους, το αίσθημα επιτέλεσης του καθήκοντος, η αναγνώριση της προσπάθειας από τους άλλους και η εποπτεία είναι μερικοί σημαντικοί παράγοντες προστασίας των θεραπειών από την επαγγελματική εξουθένωση.¹

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Research article

The effect of COVID-19 pandemic on mental health and quality of life in the Athens area – Greece

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ABSTRACT

This study examines the associations of the COVID-19 pandemic stressors with the mental health and quality of life (QoL) of the general population in different demographic areas of Athens. The random sample of the study consisted of 602 participants, 389 (64,6%) women and 213 (35,4%) men residing in Attica (Greece). It was conducted with telephone interviews during the first wave of the pandemic. The instruments used were: the World Health Organization Quality of Life Instrument (WHOQOL-BREF), Depression Anxiety Stress Scale (DASS-21), Body Vigilance Scale (BVS), Dimensional Obsessive-Compulsive Scale (Category 1: contamination obsessions -decontamination compulsions) (DOCS) and a set of socio-demographic data and questions on stressors related to the COVID-19 outbreak. A range of statistical analyses was used, including descriptive statistics, examination of the questionnaires' internal consistency, calculating Cronbach's alpha coefficient, as well as multiple linear regression analyses with dependent variables the WHOQOL-BREF, DASS-21, DOCS, and BVS scales. According to the results of our study: (a) The greater the extent of negative emotions due to the pandemic and the imposed restrictive measures, such as worry and fear, the higher the score of depression, anxiety, stress, obsessive-compulsive symptomatology, body vigilance and the lower the scores of the WHOQOL domains (Physical Health, Psychological Health, Social Relationships, Environment), (b) the fear of being contaminated by the virus seems to have intensified depression-anxiety-stress (DASS-21), obsessive-compulsive (DOCS) and hypochondriacal (BVS) symptomatology. (c) The independent variables of depression, stress and anxiety, and obsessive-compulsive and hypochondriacal symptomatology were negatively associated with QoL d) The most vulnerable groups in terms of QoL and the mental health indicators in our study were those with psychiatric or/and physical illness, the elderly, the unemployed during the lockdown period, those with low educational/socioeconomic status and those living alone. In conclusion, the negative emotions associated with the COVID-19 outbreak and the imposed restrictive measures had a serious impact on the mental health and QoL of the population. This and other similar findings should be taken into account by authorities and decision-makers to prevent and deal with the effects of the pandemic. Unfortunately, the COVID-19 pandemic is still continuing and the imposition of new restrictive measures is being considered. This increases the relevance of research like the one presented here.

KEYWORDS: Covid-19 stressors, quality of life, depression, stress, contamination obsessions -decontamination compulsions, body vigilance.

Introduction

The sudden coronavirus pandemic has spread at an alarming rate worldwide provoking millions of deaths. Especially in Greece, a total of 4336 cases had been confirmed as of July 30th 2020 and the number of deaths was 203 whereas on November 29th, 2020 the number

of confirmed cases was 104.227 and the number of accumulated deaths was 2.321. Up to now (July 2022), over 30.000 people passed away due to COVID-19.

Beyond the physical impacts, the COVID-19 pandemic had various serious mental health effects. Indeed, relevant studies and meta-analyses have shown high levels

of psychological distress in the general population, with higher levels of anxiety and depression in people with underlying diseases, and in those actually infected by the virus,¹ as well as post-traumatic stress symptoms.² The rapid spread of the disease, its high mortality rate, and concerns about the future are probably the main sources of anxiety.³ In addition, according to the findings of several studies, the fear and distress linked to the virus spread have contributed to high levels of depression, anxiety,^{4–6} obsessive-compulsive disorder (OCD) symptomatology as well as health anxiety.⁷ Moreover, the concern about COVID-19 was positively correlated with both obsessive-compulsive symptomatology (OCS) and health anxiety symptoms.⁸

Pandemics overall have a significant impact on individuals' quality of life (QoL) in different dimensions such as psychological and physical health, social and family relationships, issues related to work-unemployment, etc.^{9–11} Indeed, research referring to the impact of coronavirus disease and related restrictions on mental health and QoL of the general population in Austria, showed an increase of depression and decrease of QoL in times of COVID-19 as compared to the pre- COVID-19 period.¹²

Also, as mentioned in a recent review,¹³ of those who have been quarantined, have reported a significantly high prevalence of psychological distress, emotional disturbance, depression, stress, low mood, irritability, insomnia, post-traumatic stress, anger, and emotional exhaustion. It seems that the lockdown, the loss of normal routine, and reduced social and physical contact with others are stressors that probably contribute to boredom, irritability, and isolation from the rest of the world.

The present study was conducted by the Society of Preventive Psychiatry. We investigated the impact of the COVID-19 outbreak and of the related imposed restrictive measures on mental health and QoL of the general population in Attica, Greece. The objectives of the study were:

- To assess QoL, stress-anxiety-depression, contamination obsessions/ decontamination compulsions, and the degree of body vigilance.
- To investigate the associations of QoL with stress-anxiety-depression, contamination obsessions/ decontamination compulsions, and the degree of body vigilance.
- To detect the effect of sociodemographic characteristics and of stressors related to the COVID-19 outbreak on QoL and on the rest of the variables of the study.

Material and Method

Participants and procedures

The sample consisted of 602 persons, 389 (64.6%) women and 213 (35.4%) men with mean age 47.8 (SD= 17.0) years. Table 1 provides descriptive summaries of the demographic characteristics of the sample. Our research was carried out during the first period of restrictions imposed in Greece to minimize the spread of the pandemic. It was carried out using telephone interviews, with the application of systematic sampling. Specifically, a random sample was taken from several districts in Athens, by selecting 5 citizens' telephone numbers every 10 pages of the Attica region telephone directory, maintaining the anonymity of personal data. The interviews were conducted during a three-month time span (from April to June 2020). The number of 602 participants refers to the individuals who answered our phone calls and accepted to participate in our research during the above time span.

Measures

The instruments used were:

*World Health Organization QOL Instrument (WHOQOL-BREF):*¹⁴ The Greek version of WHOQOL-BREF includes 30 questions assessing an overall quality of life/general health facet, and 4 domains: physical health, psychological health, social relationships, and environment. This instrument has been adapted to the Greek population¹⁵ with satisfactory internal consistency (Cronbach's alpha coefficient: 0,67–0,81) and satisfactory construct, convergent, and discriminant validity. In our study, the calculation of Cronbach's alpha coefficient per domain was performed, which resulted in satisfactory alpha values ranging from 0.70–0.76.

*Depression Anxiety Stress Scale (DASS-21):*¹⁶ It includes 21 questions. The depression, scale measures: dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest/involvement, anhedonia, and inertia. The anxiety scale estimates autonomic arousal, skeletal musculature effects, situational anxiety, and subjective experience of anxious affect. The stress scale measures: difficulty relaxing, persistent arousal, agitation, irritability/over reactivity, and impatience. The DASS was shown to possess satisfactory psychometric properties, and the factor structure was substantiated both by exploratory and confirmatory factor analysis.¹⁶ This instrument has been adapted to the Greek population¹⁷ with satisfactory internal consistency for the total scale (Cronbach's alpha coefficient: 0,93) and satisfactory psychometric properties concerning validity. In our study, the calculation of Cronbach's alpha coefficient per each subscale

Table 1. Socio-demographic characteristics.

Variables		N	%
Gender	Women	389	64.6
	Men	213	35.4
Age, mean (SD)		47.8 (17.0)	
Number of children	0	316	52.5
	1	108	17.9
	≥2	178	29.5
Number of habitants at home, mean (SD) median (IQR)		1.8 (1.2)	2 (1–3)
Years of Education, mean (SD)		15 (3.9)	
Family status	Married	242	40.2
	Living together	50	8.3
	Unmarried	225	37.4
	Widowed	35	5.8
	Divorced	43	7.1
	Separated	7	1.2
Living circumstances	With own family	281	46.7
	With parental family	110	18.3
	Alone	147	24.4
	With partner (unmarried)	64	10.6
Professional status	Full-time employed	315	52.3
	Part-time employed	33	5.5
	Student (graduate/postgraduate)	23	3.8
	Retired	119	19.8
	Household	30	5.0
	Unemployed	41	6.8
	Other	41	6.8
Individuals under suspension of work	No	254	73.0
	Yes	94	27.0
Job condition	At work	150	55.4
	Remotely	121	44.6
Socioeconomic status	Upper class	32	5,3
	Upper middle class	123	20.4
	Middle class	333	55,3
	Middle-lower class	92	15,3
	Lower class	22	3,7

was performed, which resulted in satisfactory alpha values ranging from 0.83–0.93.

Body Vigilance Scal–BVS:¹⁸ a four-item questionnaire measuring conscious attention focused on internal bodily sensations. There are three items that assess the degree of Attentional focus on bodily sensations, the Perceived sensitivity to changes in bodily sensations,

and the Average amount of time spent attending to bodily sensations. The fourth item involves separate ratings for Attention to 15 sensations (e.g., heart palpitations). An overall score is also calculated.

The Body Vigilance Scale has been validated in clinical and nonclinical samples with satisfactory psychometric properties (reliability-validity).¹⁸ BVS scale underwent

a rigorous translation in Greek, back translation, and cross-examination by bilingual subjects. In our study, the calculation of Cronbach's alpha coefficient for the BVS total score was performed, which resulted in a satisfactory alpha value (0.75).

Dimensional Obsessive-Compulsive Scale (DOCS):¹⁹ assessing contamination obsessions and decontamination compulsions (Category 1: Concerns about Germs and Contamination), which includes 5 questions and an overall score, acquiring satisfactory psychometric properties (reliability and validity).¹⁹ DOCS (Category 1) underwent a rigorous translation in Greek, back translation, and cross-examination by bilingual subjects. In our study, the calculation of Cronbach's alpha coefficient for DOCS and especially for the subscale "Concerns about Germs and Contamination" was performed, which resulted in a satisfactory alpha value (0.80).

Set of socio-demographic data and questions-stressors related to the COVID-19 outbreak, which refer to sex, age, residence, educational status, years of education, professional status, income, family status, number of children, living circumstances, socioeconomic status, job status during quarantine, job condition, category of respondents regarding COVID-19 infection.

The questions-stressors related to the COVID-19 outbreak evaluate the following: frequency and reasons of movements outside the home, accuracy, and frequency of getting mass media information about the virus, negative feelings due to the pandemic and restrictive measures, fear of contamination, negative feelings due to social isolation, insecurity due to job and economic matters.

Statistical analysis

Statistical analyses were conducted using SPSS statistical software (version 22.0). A range of statistical analyses was used, including descriptive statistics and examination of the questionnaires' internal consistency, calculating Cronbach's alpha coefficient. Also, multiple linear regression analyses in a stepwise method (p for entry 0.05, p for removal 0.10) were used with dependent variables the WHOQOL-BREF, DASS-21, DOCS, and BVS scales. The regression equation included also terms for demographic characteristics and stressors regarding the pandemic. The adjusted regression coefficients (β) with standard errors (SE) were computed from the results of the linear regression analyses. When DOCS or BVS scales were the dependent variables, multiple linear regression was conducted after having logarithmically transformed the dependent variable. All reported p values are two-tailed. Statistical significance was set at $p < 0.05$.

Results

Sample characteristics

Regarding the stressful conditions that have been developed due to COVID-19 and the related restrictive measures: the majority of the participants ($n=497$, 82.6%) reported that they were satisfied with the accuracy of mass media information about COVID-19 and many of them ($n=238$, 39.5%) were getting information 2–3 times per day. Many participants used to get out of the house during the quarantine period several times per week ($n=202$, 33.6%), getting out mostly for shopping ($n=480$, 79.9%).

The most prevalent negative feelings reported by the majority of the participants were worry ($n=491$, 81.6%), stress ($n=386$, 64.1%), and fear ($n=288$, 47.8%). A significant percentage of the participants ($n=171$, 28.7%) reported high levels of negative feelings due to social isolation and moderate levels of negative feelings ($n=207$, 34.4%) due to the pandemic and the restrictive measures in general. Also, a significant proportion of the population ($n=222$, 36.9%) exhibited moderate levels of fear of being contaminated and high levels of fear of loved ones getting the virus ($n=232$, 38.5%). Finally, a significant number of participants ($n=260$, 43.2%) reported high/very high levels of insecurity due to financial matters and a restricted proportion of the sample showed high/very high levels of job insecurity ($n=191$, 31.8%).

Associations of WHOQOL- BREF

According to multiple linear regression analysis, men, older people, those with lower socioeconomic status, unemployed participants during the quarantine, and those with mental or/and physical illness showed lower scores in the majority of WHOQOL-BREF domains. Also, married people exhibited higher QoL scores.

Concerning the stressors related to the COVID-19 outbreak: the greater the extent of negative emotions due to the pandemic and the restrictive measures, the lower the scores of all QoL domains. Higher scores of the fear of significant others contracting the virus and of occupational insecurity were associated with lower scores in certain QoL domains.

Depression and stress scores were significantly negatively associated with WHOQOL-BREF domain scores. A higher score of the average amount of time spent attending to bodily sensations was associated with lower scores in WHOQOL-BREF domains (table 2)

Associations of DASS-21

According to multiple linear regression analysis, participants with the lower score of educational and soci-

Table 2. Multiple linear regression analysis with WHOQOL– BREF domains as dependent variables.

		β	SE	b	P
<i>Dependent: WHOQOL–BREF Overall QoL/ and general health</i>					
Gender	Women (reference)				
	Men	–2.73	1.17	–0.08	0.020
Age		–0.14	0.05	–0.13	0.006
Socioeconomic status		–2.04	0.79	–0.10	0.010
Group	Healthy (reference)				
	Patients with psychiatric illness	–8.70	2.22	–0.14	<0.001
	Patients with physical illness	–8.23	1.49	–0.19	<0.001
	Patients with psychiatric and physical illness	–8.43	2.64	–0.11	0.002
Negative feelings due to pandemic/restrictive measures		–2.73	0.61	–0.17	<0.001
Depression		–1.10	0.23	–0.25	<0.001
Average amount of time spent attending to bodily sensations		–1.01	0.31	–0.15	0.001
<i>Dependent: WHOQOL–BREF Physical health</i>					
Socioeconomic status		–1.66	0.61	–0.09	0.006
Group	Healthy (reference)				
	Patients with psychiatric illness	–6.59	1.15	–0.18	<0.001
	Patients with physical illness	–10.89	2.04	–0.17	<0.001
	Patients with psychiatric and physical illness				
Fear of beloved ones being contaminated		–1.38	0.56	0.09	0.014
Negative feelings due to pandemic/restrictive measures		–1.37	0.47	–0.10	0.004
Depression		–1.51	0.18	–0.39	<0.001
Stress		–0.37	0.16	–0.11	0.025
Average amount of time spent attending to bodily sensations		–1.03	0.24	–0.17	<0.001
<i>Dependent: WHOQOL–BREF Psychological health</i>					
Married/ Living together	No (reference)				
	Yes	2.90	1.13	0.10	0.011
Socio–economic status		–1.26	0.63	–0.07	0.045
Negative feelings due to pandemic/restrictive measures		–1.26	0.49	–0.09	0.010
Depression		–1.79	0.18	–0.48	<0.001
Stress		–0.36	0.17	–0.11	0.037
<i>Dependent: WHOQOL–BREF Social relationships</i>					
Age		–0.10	0.05	–0.11	0.046
Married/ Living together	No (reference)				
	Yes	5.38	1.42	0.17	<0.001
Negative feelings due to pandemic/restrictive measures		–1.49	0.61	–0.10	0.015
Depression		–1.41	0.23	–0.35	<0.001
<i>Dependent: WHOQOL–BREF Environment</i>					
Socioeconomic status		–2.74	0.61	–0.20	<0.001
Working during quarantine	No (reference)				
	Yes	–2.93	1.21	–0.12	0.016
Negative feelings due to pandemic/restrictive measures		–1.86	0.47	–0.17	<0.001
Insecurity due to job matters		–1.19	0.43	–0.13	0.006
Depression		–0.70	0.18	–0.23	<0.001

+regression coefficient ++Standard Error ‡Standard Regression Coefficient

Note: only significant variables are presented

oeconomic status and those with mental or/and physical illness exhibited higher scores in DASS-21 domains. Also, people who shared accommodation showed a lower score in significant DASS-21 dimensions.

The greater the extent of negative emotions due to the pandemic and the restrictive measures and the greater the fear of being infected by the virus, the higher the scores of DASS-21 dimensions. Participants who reported that they had accurate information about COVID-19 from the media showed lower scores in DASS-21 dimensions (table 3).

Associations of DOCS

According to multiple linear regression analysis, people with lower educational levels, those with higher monthly income, and patients with mental or/and physical illness, in comparison to healthy individuals, exhibited high scores soon on the DOCS scale. The more frequent updates provided to the participants about COVID-19, the greater the fear of getting the virus, and the greater the extent of negative emotions, the higher the score on the DOCS scale (table 4).

Associations of BVS

According to multiple linear regression analysis, older participants, those with higher educational and socioeconomic status, and patients with physical or/and mental illness showed higher scores in significant BVS dimensions, in comparison to healthy individuals.

Negative emotions, insecurity about financial matters, and the fear of being contaminated by the virus, are positively correlated with BVS scores (table 5).

Discussion

The present study evaluated the impact of the COVID-19 outbreak and the imposed measures on QoL and mental health of the general population in the Region of Attica, Greece. In particular, it examined its effect with reference to QoL, stress-anxiety and, depression symptomatology as well as contamination obsessions/ decontamination compulsions, and degree of body vigilance.

Men, older people, singles, those with lower socioeconomic status, and participants with physical or/ and mental illness exhibited lower levels in certain QoL domains. These findings are in line with the results of research in China demonstrating that health-related quality of life in the general population deteriorated significantly with aging, chronic disease, and lower income.²⁰ This can be explained by the fact that the elderly are affected disproportionately by the pandemic because

they constitute a high-risk group for developing severe illnesses.²¹ Also it seems that elderly people have a poor QoL associated with restrictive measures.²² With reference to the differential effect of the pandemic on men and women, contrary to our findings, Italian research showed that women had an overall worse psychological, physical, and environmental QoL during the pandemic compared to men.²³ Our findings are also consistent with the results of other studies in Saudi Arabia and Morocco, according to which people with chronic medical conditions reported significantly lower QoL scores during the COVID-19 pandemic.^{24,25} Accordingly, another study concerning US young adults during the initial months of the COVID-19 pandemic, showed a deteriorated health-related QoL among those with either a suspected or reported mental health diagnosis.²⁶

As expected, the wider the extent of negative emotions arising from the pandemic and the restrictive measures, the more likely the occurrence of a low level of QoL. Also, the higher the levels of depression, stress, and of body vigilance, the more likely it was that the QoL would decline. In accordance with the results of our study, in a cross-sectional survey in Saudi Arabia, it was demonstrated that participants who had experienced anxiety, depression, and stress were at an increased risk of exhibiting lower levels of QoL.²⁴

With reference to the association of depression-anxiety-stress with sociodemographic characteristics, those who resided alone and those with a lower educational and socioeconomic status seemed to exhibit higher levels of stress. Moreover, it was observed that the lower the educational level of the participants, the higher the possibility to have depressive symptomatology. Our findings are in line with the results of some other studies in Greece^{27,28} and in Mexico,²⁹ according to which, persons with lower educational levels were more likely to develop depressive and anxiety symptomatology during the pandemic period. Also, participants who suffered from physical or/and psychiatric disorders were more likely to exhibit higher levels of anxiety and stress. These findings are in accordance with the results of an Italian study³⁰ which indicate that persons with a medical history were more likely to have higher scores of anxiety and depression.

According to our findings, the higher the negative feelings due to COVID-19 and the higher the fear of contamination, the higher the possibility of developing depression, anxiety, and stress. This finding is in line with other Greek studies which indicated that young people who worried more about being contaminated by COVID-19, were more likely to develop psychological distress.³¹ Similarly, according to other studies,

Table 3. Multiple linear regression analysis with DASS-21 dimensions dependent variables and sociodemographic characteristics and stressors related to COVID-19 as predictors.

		β ±	SE±±	b±	P
<i>Dependent: DASS-21 Depression</i>					
Educational status		-0.20	0.09	-0.10	0.033
Group	Healthy (reference)				
	Patients with psychiatric illness	2.13	0.54	0.15	<0.001
	Patients with physical illness	0.76	0.37	0.08	0.041
	Patients with psychiatric and physical illness	3.55	0.64	0.21	<0.001
Fear of being contaminated		0.38	0.17	0.10	0.030
Negative feelings due to pandemic/restrictive measures		1.10	0.14	0.30	<0.001
<i>Dependent: DASS-21 Anxiety</i>					
Educational status		-0.30	0.09	-0.15	0.001
Living circumstances	Alone (reference)				
	With others	-0.76	0.35	-0.09	0.032
Group	Healthy (reference)				
	Patients with psychiatric illness	2.34	0.50	0.18	<0.001
	Patients with physical illness	0.59	0.34	0.07	0.083
	Patients with psychiatric and physical illness	3.33	0.59	0.21	<0.001
Fear of being contaminated		0.63	0.16	0.18	<0.001
Fear of beloved ones being contaminated		0.35	0.17	0.10	0.035
Negative feelings due to pandemic/restrictive measures		0.70	0.13	0.20	<0.001
<i>Dependent: DASS-21 Stress</i>					
Educational status		-0.31	0.11	-0.13	0.004
Socioeconomic status		-0.46	0.22	-0.09	0.040
Group	Healthy (reference)				
	Patients with psychiatric illness	2.16	0.61	0.13	<0.001
	Patients with physical illness	0.68	0.42	0.06	0.106
	Patients with psychiatric and physical illness	3.18	0.72	0.16	<0.001
Accurate information about COVID-19	No (reference)				
	Yes	-1.17	0.42	-0.10	0.006
Fear of being contaminated		0.49	0.20	0.12	0.012
Fear of beloved ones being contaminated		0.52	0.20	0.12	0.011
Negative feelings due to pandemic/restrictive measures		1.31	0.16	0.31	<0.001
<i>Dependent: Total DASS-21</i>					
Educational status		-0.82	0.25	-0.14	0.001
Living circumstances	Alone (reference)				
	With others	-2.00	1.01	-0.08	0.049
Socio-economic status		-1.09	0.52	-0.08	0.036
Group	Healthy (reference)				
	Patients with psychiatric illness	6.67	1.43	0.17	<0.001
	Patients with physical illness	2.02	0.98	0.08	0.039
	Patients with psychiatric and physical illness	10.04	1.69	0.21	<0.001

Continues

Table 3. Continued.

		β +	SE++	b‡	P
Accurate information about COVID-19	No (reference)				
	Yes	-2.07	0.98	-0.07	0.035
Fear of being contaminated		1.51	0.46	0.15	0.001
Fear of beloved ones being contaminated		1.19	0.48	0.11	0.013
Negative feelings due to pandemic/restrictive measures		3.10	0.37	0.31	<0.001

+regression coefficient ++Standard Error ‡standardized regression coefficient
Note: only significant variables are presented

Table 4. Regression analysis with the total DOCS score as dependent variable and sociodemographic characteristics and stressors related to COVID-19 as predictors.

		β +	SE++	b‡	P
Educational status		-0.24	0.08	-0.11	0.002
Monthly income		0.22	0.11	0.07	0.042
Group	Healthy (reference)				
	Patients with psychiatric illness	2.37	0.49	0.17	<0.001
	Patients with physical illness	0.84	0.34	0.09	0.014
	Patients with psychiatric and physical illness	2.13	0.59	0.12	<0.001
Frequency of getting information		0.66	0.17	0.14	<0.001
Fear of being contaminated		1.40	0.13	0.37	<0.001
Negative feelings due to pandemic/restrictive measures		0.65	0.13	0.17	<0.001

+regression coefficient ++Standard Error ‡standardized regression coefficient
Note: only significant variables are presented

the perceived high risk of contracting the virus as well as the fear and anxiety about COVID-19 are associated with high levels of depression and stress.^{32,5,6} Our participants who had precise information from the media about COVID-19 had a lower score of depression and stress. This finding is in line with other studies, according to which higher satisfaction with the health information concerning COVID-19 was associated with a lower psychological impact of the outbreak.^{33,29}

In reference to contamination obsession and decontamination compulsions, our findings indicate that unhealthy participants and those with higher incomes were more likely to develop OCS. In the same direction, according to other studies persons with mental disorders³⁴ and higher income groups were more likely to exhibit higher levels of OCS during the pandemic situation.³⁵ It appears that rich people are probably more "careful" and value their lives more than the less financially privileged.

Also, the more negative emotions (such as fear) the participants developed due to the pandemic, the more

likely they were to develop OCS. This is consistent with previous reports maintaining that obsessions and compulsions (such as washing rituals) were often motivated by fear of contracting a disease.^{36,37}

Regarding body vigilance, our findings indicated that older participants, those with higher educational status, and those suffering from mental or/and physical illness were more likely to develop hypochondriacal symptomatology. In accordance with these findings, other study results indicated that persons with past or present psychiatric illnesses had greater sensitivity to and awareness of their body sensations.³⁸

The great extent of negative emotions developed, the fear of contamination by the virus, and the high degree of financial insecurity seems to have intensified hypochondriacal symptomatology. These findings are consistent with the results of other studies^{39,7} that revealed a positive relationship between excessive concern about COVID-19 and health anxiety.

In conclusion, the more negative feelings that the participants developed due to the COVID-19 pandemic,

Table 5. Multiple regression analysis with BVS as dependent variable and sociodemographic characteristics and stressors related to COVID-19 as predictors.

		β +	SE++	b‡	P
<i>Dependent: BVS Attentional focus on bodily sensations</i>					
Age		-0.02	0.01	-0.16	<0.001
Group	Healthy (reference)				
	Patients with psychiatric illness	0.96	0.35	0.11	0.006
	Patients with physical illness	0.84	0.26	0.14	0.001
	Patients with psychiatric and physical illness	1.76	0.44	0.16	<0.001
Fear of being contaminated		0.65	0.09	0.28	<0.001
Insecurity due to economic matters		0.16	0.08	0.07	0.048
<i>Dependent: BVS Perceived sensitivity to changes in bodily sensations</i>					
Age		-0.03	0.01	-0.18	<0.001
Socioeconomic status		-0.35	0.12	-0.11	0.003
Group	Healthy (reference)				
	Patients with psychiatric illness	0.91	0.35	0.10	0.009
	Patients with physical illness	0.81	0.26	0.13	0.002
	Patients with psychiatric and physical illness	2.20	0.44	0.20	<0.001
Fear of being contaminated		0.77	0.09	0.32	<0.001
<i>Dependent: BVS Average amount of time spent attending to bodily sensations</i>					
Age		-0.01	0.01	-0.08	0.050
Group	Healthy (reference)				
	Patients with psychiatric illness	0.76	0.33	0.09	0.025
	Patients with physical illness	0.97	0.25	0.16	<0.001
	Patients with psychiatric and physical illness	1.71	0.43	0.16	<0.001
Fear of being contaminated		0.80	0.09	0.34	<0.001
<i>Dependent: BVS Attention to 15 sensations</i>					
Educational status		0.10	0.04	0.09	0.028
Group	Healthy (reference)				
	Patients with psychiatric illness	1.20	0.28	0.17	<0.001
	Patients with physical illness	0.57	0.20	0.11	0.004
	Patients with psychiatric and physical illness	0.07	0.35	0.12	0.002
Fear of being contaminated		0.30	0.09	0.16	0.001
Fear of beloved ones being contaminated		0.25	0.10	0.12	0.009
Negative feelings due to pandemic/restrictive measures		0.40	0.08	0.21	<0.001
<i>Dependent: BVS Total score</i>					
Age		-0.08	0.02	-0.17	<0.001
Group	Healthy (reference)				
	Patients with psychiatric illness	3.91	1.06	0.14	<0.001
	Patients with physical illness	3.27	0.80	0.16	<0.001
	Patients with psychiatric and physical illness	7.00	1.36	0.20	<0.001
Fear of being contaminated		2.83	0.29	0.37	<0.001

+regression coefficient ++Standard Error ‡standardized regression coefficient

Note: only significant variables are presented

the higher the possibility of developing depression, anxiety, stress, obsessive-compulsive and hypochondriacal symptomatology. These conditions in turn seem to contribute to the deterioration of QoL.

The main limitation of this study is that the cross-sectional design used limits drawing conclusions regarding causality, therefore further longitudinal studies could capture the ongoing psychological impact of the COVID-19 pandemic and the related effect on QoL over a longer duration of time. Such a longitudinal study is scheduled to be published soon. Also, another limitation is that the random population, specifically targeted the Attica region excluding the rest of Greece, does not constitute a national representation.

A positive aspect of our work is that it included the study of the impact of the pandemic not only with reference to depression, anxiety, and stress (which has been the subject of most studies), but also with reference to obsessive-compulsive and hypochondriacal symptomatology, as well as to QoL. Quality of life is a broad multi-dimensional indicator and “can be used in daily clinical practice for the assessment of therapeutic interventions and for the health need assessment of populations”,^{40,41} especially in response to disasters and crises such as the COVID-19 pandemic. The findings of our study have demonstrated that the greater the extent of negative emotions due to the pandemic the lower the QoL scores. Also, our study shows the significant effect of negative emotions due to the pandemic and fear of contamination on hypochondriacal and obsessive-compulsive symptomatology, a very important finding since only a few researchers^{7,8} have addressed this issue.

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Moreover, the sample of our study included not only healthy subjects but also patients with physical and/or mental diseases, thus rendering possible the comparison between these groups. Finally, another positive feature of our study was that it was carried out with telephone interviews, (rather than internet questionnaires), each interview lasting almost one hour and thus allowing clarification of concepts and issues related to the questionnaires.

The findings of this and other related studies should be taken into consideration by the authorities so that appropriate interventions to improve quality of life can be designed and actions to prevent and treat psychopathological conditions associated with the COVID-19 pandemic can be implemented.

The recent Athens Mental Health Summit Declaration of the WHO European Region (July 2021) “on actions required to address the impact of the COVID-19 pandemic on mental health” is a good response to this need. However, this is just a starting point. It should be followed by substantial attention to the needs and adequate and consistent funding. Finally, vulnerable population groups suffering from mental or/and physical diseases will certainly require specific and targeted support to cope with the negative impact of disasters such as the COVID-19 pandemic on their mental health and quality of life.

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Ερευνητική εργασία

Η επίδραση της πανδημίας COVID-19 στην ψυχική υγεία και την ποιότητα ζωής του γενικού πληθυσμού στην Αττική

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Εταιρεία Προληπτικής Ψυχιατρικής

ΙΣΤΟΡΙΚΟ ΑΡΘΡΟΥ: Παραλήφθηκε 16 Αυγούστου 2022/Αναθεωρήθηκε 10 Νοεμβρίου 2022/Δημοσιεύθηκε Διαδικτυακά 17 Νοεμβρίου 2022

ΠΕΡΙΛΗΨΗ

Με την παρούσα μελέτη επιδιώκεται η εκτίμηση της επίδρασης στρεσογόνων παραγόντων που σχετίζονται με την πανδημία COVID-19 στην ψυχική υγεία και την ποιότητα ζωής (ΠΖ) του γενικού πληθυσμού σε περιοχές της Αττικής. Το δείγμα της μελέτης, που επελέγη με τυχαία δειγματοληψία, αποτέλεσαν 602 άτομα του γενικού πληθυσμού, κάτοικοι διαφορετικών περιοχών της Αττικής, εκ των οποίων 389 (64,6%) ήταν γυναίκες και 213 (35,4%) άνδρες. Η έρευνα πραγματοποιήθηκε με τηλεφωνικές συνεντεύξεις κατά το πρώτο κύμα της πανδημίας. Τα ερωτηματολόγια που χρησιμοποιήθηκαν ήταν: το Ερωτηματολόγιο Ποιότητας Ζωής του Παγκόσμιου Οργανισμού Υγείας (WHOQOL-BREF), το Ελληνικό Ερωτηματολόγιο Μέτρησης της Κατάθλιψης, του Άγχους και του Στρες (DASS-21), η Κλίμακα εστίασης της προσοχής σε σωματικές αισθήσεις-συμπτώματα (BVS), η Πολυδιάστατη Κλίμακα Ιδεοψυχαναγκαστικής συμπτωματολογίας (Κατηγορία 1: ιδεοληψίες μόλυνσης και καταναγκασμοί απολύμανσης) (DOCS) και ένα δελτίο κοινωνικοδημογραφικών χαρακτηριστικών και ερωτήσεων που αφορούν σε στρεσογόνους παράγοντες σχετιζόμενους με την πανδημία της COVID-19. Σύμφωνα με τα αποτελέσματα της μελέτης: (α) Όσο μεγαλύτερη είναι η έκταση των αρνητικών συναισθημάτων εξαιτίας της πανδημίας και των περιοριστικών μέτρων που επεβλήθησαν για τη μείωση της εξάπλωσης της πανδημίας, τόσο υψηλότερα είναι τα επίπεδα της κατάθλιψης, του άγχους, του στρες, της ιδεοψυχαναγκαστικής συμπτωματολογίας, της εστίασης στα σωματικά συμπτώματα και τόσο χαμηλότερο είναι το επίπεδο της ΠΖ, (β) Ο φόβος μόλυνσης από τον ιό φαίνεται να επιδεινώνει την κατάθλιψη, το άγχος και το στρες (DASS-21), την ιδεοψυχαναγκαστική (DOCS) και την υποχονδριακή (BVS) συμπτωματολογία, (γ) Οι ανεξάρτητες μεταβλητές της κατάθλιψης, του στρες, του άγχους, της ιδεοψυχαναγκαστικής και της υποχονδριακής συμπτωματολογίας φαίνεται να συσχετίστηκαν αρνητικά και να επέδρασαν στην ποιότητα ζωής του πληθυσμού, (δ) Οι πιο ευάλωτες ομάδες όσον αφορά στην ΠΖ και την ψυχική υγεία ήταν τα άτομα που έπασχαν από ψυχική ή/και σωματική νόσο, οι ηλικιωμένοι, οι άνεργοι κατά την περίοδο του lockdown, τα άτομα χαμηλού εκπαιδευτικού επιπέδου και χαμηλής κοινωνικοοικονομικής κατάστασης και όσοι ζούσαν μόνοι τους. Εν κατακλείδι, τα αρνητικά συναισθήματα που σχετίζονται με την πανδημία της COVID-19 και τα περιοριστικά μέτρα είχαν πιθανώς σοβαρό αρνητικό αντίκτυπο στην ψυχική υγεία και στην ΠΖ του πληθυσμού. Το εύρημα αυτό καθώς και άλλα παρόμοια ερευνητικά πορίσματα θα πρέπει να αξιοποιηθούν από τις αρχές και τους υπεύθυνους λήψης αποφάσεων, για την πρόληψη και την αντιμετώπιση των επιπτώσεων της πανδημίας. Μιας πανδημίας που δυστυχώς συνεχίζεται και δημιουργεί ήδη προβληματισμό ως προς την ανάγκη εκ νέου εφαρμογής αυστηρών περιοριστικών μέτρων. Κάτω από αυτό το πρίσμα, εργασίες όπως η παρούσα μπορεί να αποδειχθούν χρήσιμες.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: Στρεσογόνοι παράγοντες COVID-19, ποιότητα ζωής, κατάθλιψη, στρες, ιδεοληψίες μόλυνσης και καταναγκασμοί απολύμανσης, εστίαση στα σωματικά συμπτώματα.

Research article

The impact of COVID-19 on people under opioid substitution treatment

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ABSTRACT

Given the aggravation on the general population's quality of life due to COVID-19 and the vulnerability of People Who Use Drugs (PWUD) to acute stress, the current study aimed to better comprehend the impact of COVID-19 on quality of life and mental health of PWUD as well as their drug use patterns. Another study had been conducted before the COVID-19 outbreak, which assessed the quality of life, indicative PTSD symptoms, and drug use patterns of people who were attending an Opioid Substitution Treatment (OST), in Athens, Greece. As a continuation of the aforementioned study, the same variables were assessed in May and June 2020, after the first lockdown measures. 104 patients agreed to participate. The World Health Organization Quality of Life Questionnaire (WHOQOL) and the Post-Traumatic Stress Scale (PCL-C) were used as well as toxicology tests. The only statistically significant outcome was a reduction regarding the dimension referring to the relationship between the individual and their environment. People with low quality of life were found to experience more severe Post-Traumatic Stress Disorder (PTSD) symptoms after the lockdown comparing to those with high quality of life. There was also a statistically non-significant increase in PTSD scores before and after lockdown measures. Regarding drug use patterns, the present research reveals an overall decline in drug use during quarantine. There was a statistically significant decrease in opioid (22.3%) and in benzodiazepine (35%) use after the lockdown. Also, a statistically significant increase in mean scores of indicative PTSD symptoms of people who decreased opioid use during and after lockdown measures was found. In regards to amphetamine use, research findings underline a non-significant increase in use (8.7%). The pandemic's impact on the life of people on opioid substitution treatment should be taken into consideration and further studies need to be conducted to protect this population's quality of life and maximize the potential benefits such as reduced access to illicit substances.

KEYWORDS: COVID-19, post-traumatic stress disorder, quality of life, opioid substitution treatment.

Introduction

Within the first few months of the declaration by the WHO about the COVID-19 pandemic, this disease has escalated with intimidating speed and has turned into an unprecedented global crisis.^{1,2} COVID-19 has led to over 6.320.600 deaths globally³ and constitutes a big chal-

lenge for healthcare systems and public health policies around the world.⁴

Literature suggests that large-scale disruptive events, like natural disasters, are associated with depression, anxiety, and mainly with the manifestation of PTSD symptoms.⁵ Studies found that tobacco, alcohol, and

cannabis users increased their substance consumption in the aftermath of terrorist attacks.^{6–8} Moreover, people with a history of trauma and anxiety disorders were more likely to experience aggravated symptoms of irritability and nervousness after exposure to such events⁶, and participants with increased substance consumption, mainly alcohol and tobacco, had higher scores on post-traumatic stress scales.⁹

Regarding the psychological impact of disease outbreaks worldwide, there is a lack of studies in this field. Nevertheless, the occurrence of new diseases in the 21st century has rekindled interest in this underdeveloped area.¹⁰ Jalloh et al¹¹ researched the impact of the Ebola virus and found that depression and PTSD symptoms usually manifested one year after the disease outbreak and mainly in people who were somehow exposed to the consequences of the virus. Considering that epidemic situation in the past enhanced PTSD symptoms and the fact that humanity is experiencing the most severe pandemic since the Spanish Influenza, we may safely hypothesize that COVID-19 may significantly impact the manifestation of PTSD symptoms.^{12–14}

Research has shown that the psychological impact of “quarantine” may have long-lasting effects and that social distancing is associated with increased psychological distress and PTSD symptoms.¹⁵ Several studies have investigated the prevalence of PTSD in the general population, in students, health care practitioners, and psychiatric patients, following the first wave of the COVID-19 outbreak.^{16–18} A cross-sectional study in China revealed that 4.6% of the population experienced severe PTSD symptoms,² whereas one-third of psychiatric patients presented PTSD symptoms and scored higher than the general population for depression, anxiety, and suicidal ideation scales.¹⁷

Furthermore, the pandemic’s impact on quality of life has been explored. This term describes ‘an individual’s perception of their position in life considering their culture, goals, expectations and their concerns.’¹⁹ During the first months of the pandemic Liu et al²⁰ studied, the quality of life in young adults with a psychiatric disorder and found that it was worse than those without a diagnosis.

Within this context, the impact on PWUD has not been adequately investigated, even though premorbid physical health conditions, which are overrepresented within this group, are also high-risk factors for severe morbidity from COVID-19.⁴ A cross-sectional study in the USA found a correlation between loneliness, binge drinking and severe drug use during the COVID-19 pandemic.²¹ When it comes to people on OST, measures taken to manage the pandemic could compromise access to

treatment services and their quality. These measures could lead to increased rates of treatment discontinuation and hence relapses to opiate use, accidental overdoses, and augmentation of PTSD symptomatology.^{2,22}

According to research findings regarding the lockdown’s effect on the mental health of individuals with SUD in Barcelona, symptoms of clinical anxiety were found in 58.7% of the sample, 48.2% of participants scored above the clinical threshold for depression and 50.3% of the individuals reported a deterioration in depression and anxiety symptoms during lockdown.²³ Fuchs-Leitner et al.²⁴ found that more than a quarter of patients in Opioid Substitution Treatment services in Austria developed an increased risk for PTSD and that 30–50% of the patients displayed elevated levels of depression and stress symptoms. Moreover, given that the quality of life of PWUD is generally lower than the quality of life of the general population of people with physical health problems²⁵ and considering the impact of previous crises (e.g., economic) on people attending drug treatment programs,⁴ it is worth investigating the impact of the pandemic on their quality of life.

Furthermore, it can be hypothesized that any traumatic event may affect drug use patterns. The impact of the COVID-19 pandemic on these patterns must be studied.²⁴ In the first three months of the pandemic there was a reduction in drug use, possibly due to lockdown measures which might affect the availability of certain substances.²⁶ However, there has been an increased use of prescribed drugs, such as benzodiazepines. A Global Drug Survey, conducted in New Zealand came to the same conclusions.²⁷ On the contrary, a study in Spain found that the frequency of use for the majority of individuals with SUD remained stable during lockdown compared to the pre-lockdown era, while there was a reduction in tobacco, alcohol, cannabis, and cocaine use.²³

The current study was an effort to better comprehend the impact of COVID-19 on PWUD who attend OST services. It further adds to the data of a cross-sectional study that took place from November 2019 to March 2020,²⁸ just before the implementation of the lockdown measures in Athens, Greece, on 13th March 2020, with further data collection from the same sample during and immediately after the relaxation of the lockdown measures in spring 2020.

Materials and Method

Participants

Participants were attending an OST service in Athens, operated by the Organization Against Drugs (OKANA, the national public agency providing opioid substitution treatment), and were recruited for another study.

Ethics approval was extended, and participants were approached again after the lockdown period. Participants were prescribed methadone or buprenorphine.

Research process

The research tools were first administered from November 2019 to March 2020 before the implementation of the lockdown measures. To maintain continuity, the same research tools (see below) were administered once more after the lockdown measures, from May to June 2020. Participants were given an adapted information sheet and signed a new consent form. The questionnaires were anonymous and a unique patient code for each participant was used. Participants had to complete these measures outside the premises of the treatment Unit of the Organization against Drugs – OKANA (General University Hospital “ATTIKON”), due to the COVID-19 restrictions.

Research tools

The research tools that were used both in the study before COVID-19 and this study are the World Health Organization Quality of Life Questionnaire (WHOQOL-BREF)²⁸ and the Post-Traumatic Stress Scale (PTSD Check List).²⁹

The WHOQOL-BREF includes 26 questions that assess the quality of life in four dimensions: physical health, mental health, social relationships, and the relationship between the individual and their environment. This questionnaire presents internal consistency reliability, with Cronbach's alpha ranging from $\alpha=.67$ to $.81$.³⁰

The Post Traumatic Stress Scale (PCL-C) contains 17 elements that correspond to the main symptoms of PTSD according to DSM-IV. Regarding its internal consistency, it ranges from $\alpha=.94$ to $.97$.³¹ This questionnaire has been adapted into Greek.³²

Drug use was assessed with toxicology tests (urine) at three-time points (before the enforcement of lockdown measures, and during and after the lifting of these measures).

Statistical analysis

Paired Sample t-tests were performed to explore whether indicative symptoms of PTSD, quality of life, and drug use profiles have changed. Independent sample t-tests, one-way ANOVA, and multivariate analysis (linear and multiple regression analyses) were also conducted. Analyses were performed using the statistical package SPSS 25.0.

Results

Demographic and clinical characteristics

As shown in table 1, 86 males (82.7%) and 18 females (17.3%) took part in the study. The age range was 23 to 71 years, with an average age of 46.2 years old ($SD=9.17$) (results summarized in table 2). The mean age of participants' most severe early traumatic experience was 16.5 years old ($SD=11.72$), while substance abuse was initiated at 17.74 years old ($SD=4.77$). The onset of psychotic symptoms was 27.57 years old ($SD=12.58$).

Quality of Life and PTSD

A paired sample t-test was performed to compare the mean scores of WHOQOL-BREF results. As shown

Table 1. Socio-demographic characteristics

	(%)	N
Gender		
Males	82.7%	86
Females	17.3%	18
Age		
23-44	49%	51
45-54	31.7%	33
55-71	19.2%	20
Nationality		
Greeks	96.2%	100
Foreigners	3.8%	4
Marital Status		
Unmarried	55.8%	58
Married	21.2%	22
Divorced	19.2%	20
Widowed	3.8%	4
Children		
Exist	43.3%	45
Non-existent	56.7%	59
Education level		
Secondary education	91.3%	95
Higher education	7.7%	8
Advanced education	1%	1
Employment status		
Employed	28.8%	30
Unemployed	71.2%	74
Residential area		
Urban	91.3%	95
Rural	8.7%	9

Note: N=104

Table 2. Clinical characteristics (N=104).

		N	%
Substitute	Methadone	32	30.8
	Buprenorphine	72	69.2
Substance of preference	Alcohol	1	1.0
	Benzodiazepine	2	1.9
	Heroin	67	64.4
	Cannabis	14	13.5
	Tobacco	2	1.9
	Cocaine	13	12.5
	Pharmaceutical pills	1	1.0
	Speedball	1	1.0
	Hallucinogenic	1	1.0
	Opiates	2	1.9
Discontinuation of the Program (voluntarily or involuntarily)	Yes	46	44.2
Psychotic Symptoms	Yes	45	43.3

Note: N=104

in table 3 there is no statistically important change in participants' physical, and mental health, and social relations, $p > 0.05$. The only statistically significant change was found in the scores of the dimension which refers to the relationship between the individual and their environment, before lockdown $M = 12.31$ ($SD = 2.57$), after lockdown $M = 12.06$ ($SD = 2.76$); $t(103) = -.626$, $p = 0.05$.

A multiple regression analysis was performed to explore the impact of quality of life on PTSD scores after lockdown, yet there were no statistically important results found $p > 0.05$. However, when the sample was divided into those with high and those with low quality of life, it was found that those with low quality of life had higher PTSD scores after lockdown, $M = 49.98$ ($SD = 15.64$), than those with high quality of life, $M = 37.31$ ($SD = 17.81$); $t(102) = 3.649$, $p < 0.001$.

The independent sample t-test analysis showed no statistically significant differences between men and women in any dimensions of quality of life ($p > 0.05$) nor in PTSD scores.

The sample was divided into three age groups (23–44, 45–54, 55–71). The one-way ANOVA analysis showed no statistically significant differences between these groups ($p > 0.05$) in PTSD scores. Regarding the quality of life, only the dimension which refers to the relationship between the individual and their environment was statistically significant $F(103) = 5.418$, $p = .006$. More specifically, the first age group ($M = 12.92$, $SD = 2.18$) scored higher than the second group ($M = 11.40$, $SD = 3.09$), $p = 0.012$ and the third group ($M = 10.95$, $SD = 2.98$), $p = 0.006$ on this dimension.

Drug use patterns

As shown in table 4, it was found that before the lockdown 32% of the sample tested positive for opioid use, during lockdown it increased to 35% and after lockdown, it reduced to 22.3%. A repeated measures ANOVA determined a statistically significant decrease in opioid use between time points, $F(1.936, 385.263) = 7.719$, $p = 0.001$. Post hoc analysis with a Bonferonni adjustment revealed that opioid use was higher before, $M = 0.29$ ($SD = 0.45$), than after lockdown, $M = 0.21$ ($SD = 0.41$). It was also higher during, $M = 0.32$ ($SD = 0.47$) than after the lockdown. Regarding benzodiazepine use, there was a reduction during, $M = 0.33$ ($SD = 0.47$), and after lockdown, $M = 0.30$ ($SD = 0.46$), $F(1.816, 361.412) = 25.742$, $p < 0.001$. The percentage of participants who tested positive for cannabis and cocaine use remained stable both during and after the lockdown ($p > 0.05$). Regarding amphetamine use, no differences were found between time points ($p > 0.05$).

Regarding opioid use, it was found that the average age of participants that stopped using opioids ($N = 13$) was 48.7 years old ($SD = 9.8$). The majority were on (or prescribed) buprenorphine (76.9%). This group showed a significant increase in mean scores of indicative PTSD

Table 3. Differences in mean scores of WHOQOL-BREF domains and PCL-C (N=104).

	Before lockdown		After lockdown		t (df=103)	p
	M	SD	M	SD		
PTSD	44.77	17.98	46.07	17.27	0.552	0.453
Physical health	12.06	3.05	12.13	3.35	0.145	0.691
Mental health	11.80	3.16	11.20	3.32	-1.33	0.941
Social relations	11.60	3.99	11.46	4.44	-0.230	0.323
Environment	12.31	2.57	12.06	2.76	-0.626	0.037*

Note: * $p < 0.05$

Table 4. Frequencies of substances used before, during and after quarantine (N=103).

Substances	Before	During	After
Opioid	32%	35%	22.3%
Benzodiazepines	75.7%	35%	35%
Cocaine	10.7%	9.7%	7.8%
Cannabis	32%	32%	30.1%
Amphetamines	3.9%	8.7%	5.7%

symptoms before ($M=42.61$, $SD=17.92$) and after lockdown ($M=54.76$, $SD=21.06$); $t(12)=-2.326$, $p<0.05$. There is also, a statistically significant decrease in the dimension 'environment' of quality of life before ($M=12.42$, $SD=2.99$) and after lockdown ($M=10.26$, $SD=3.13$); $t(12)=-1.417$, $p<0.05$. The decrease in mean scores of physical health before and after the lockdown was just below significance levels ($p=0.08$). Moreover, the average age of participants that stopped using benzodiazepines during and after lockdown ($N=42$) was 46.8 years old ($SD=8.9$) and the majority was on buprenorphine (69%). There were no statistically significant changes in the mean scores of indicative PTSD symptoms before and after lockdown, $p>0.05$; or in the mean scores of the four dimensions of quality of life.

The average age of participants that started using amphetamines ($N=5$) was 48 years old ($SD=15.8$) and the majority were on buprenorphine (60%). There were no significant differences between the mean scores of indicative PTSD symptoms or the dimensions of quality of life before and after the lockdown.

Discussion

It is evident from the results of this study that the prevalence of indicative PTSD symptoms remained stable during and after the lockdown period suggesting no impact of the COVID-19 pandemic. This finding was against researchers' predictions and not consistent with existing literature. PTSD constitutes the most common psychological impact on people who are exposed to the threat of a new, frightening disease and it is generally considered the most likely consequence of a major disaster.^{2,12,17} Martinotti et al³² argued that there is a high prevalence of depression, anxiety, and PTSD in their sample, which consisted of PWUD.

Regarding adverse mental health effects of the pandemic, findings from OST services in Spain have shown that a high percentage of patients displayed clinical levels of anxiety and/or depression and that 50.5% of the patients reported worsening of these symptoms due to lockdown.²³

The absence of a statistically significant increase following the experience of the pandemic and the lockdown measures could be attributed to several factors, which also reflect possible limitations of the present study: (i) the small sample size, and (ii) the timing of the second screening which was immediately after the lifting of the lockdown measures and too close to the experience of what was hypothesized as the traumatic experience. Literature suggests that it sometimes takes up to six months for the diagnosis of PTSD to be made or for the first symptoms of the disorder to appear.³³ This time-lapse hypothesis is indicatively well considered by Jalloh et al,¹¹ who assessed PTSD one year after the outbreak of the Ebola virus. Perhaps further follow-up studies are needed to assess the short and long-term effects of the COVID-19 pandemic on individual and collective mental health.

As far as participants' quality of life, scores on the dimensions of physical, and mental health, and social relations remained stable before and after the lockdown measures. PWUD continued to evaluate their quality of life as mediocre, without any deterioration against predictions. This was also inconsistent with Zhang and Ma³⁴ findings that suggested a major impact of COVID-19 on the Chinese population's quality of life, with 50% feeling terrified and unsafe because of the pandemic. Our findings revealed a significant relationship between PCL-C and WHO-QOL scores, with those with a low quality of life scoring higher on PCL-C than those with a higher quality of life. This finding is consistent with previous research results which underlined the negative correlation between general PTSD symptom levels and subjective quality of life.^{35,36}

It could be argued that the experience of the pandemic was not severe or long enough to compromise further the pre-existing mediocre quality of life of PWUD, as opposed to the good quality of life of the general population; or that PWUD is somehow better equipped to cope with such threatening experiences and traumas. However, there was a decrease in the scores of dimension, referring to the participant's relationship with their environment. After the lockdown participants felt insecure in their daily life to a greater extent than they did before and they were not satisfied with their living conditions and their financial status.²³ Martinotti et al³² came to the same conclusion by associating low quality of life with an increased craving for drug use during the lockdown period.

Regarding the drug use pattern, the use of opioids was reduced and possibly was substituted by an increase in the use of crack cocaine or amphetamines.³⁷ However, these changes might reflect a change in substance

availability due to the impact of COVID-19 restrictions on drug production and trafficking. Similar findings have been reported from other European countries.²⁶ It is of great interest that this reduction seems to be associated with an increase in indicative PTSD symptoms. Furthermore, studies indicate that opioid reduction leads to increased benzodiazepine use, which aims to help people deal with stress and withdrawal symptoms caused by other substances.^{26,27} This is not confirmed in the current study, where benzodiazepine use during and after the quarantine was reduced. Cocaine and cannabis use remained stable during lockdown measures. However, amphetamine use rates doubled during the lockdown, but changes during time points were not statistically significant. This outcome is not consistent with studies conducted in northern Europe.²⁵ This could be a result of the small sample size used.

The less severe than anticipated immediate impact of COVID-19 on patients with high levels of drug depend-

ency reported here has also been reported by another survey conducted in Austrian OST services.³⁸ This outcome is evident in many European countries, without overlooking the national variations, which depend on the sub-population and the availability of a substance.²⁶ Drug use patterns seem to be affected by the new social reality under COVID-19, but it is still uncertain whether the identified changes will remain or not. The pandemic's impact on PWUD should also be taken into consideration during the readjustment and the repair of possible ruptures in the therapeutic interventions in Substitution Units for PWUD. Scientific reviews have already highlighted the importance of service adaptability to respond to COVID-19's effects on drug market disruption, heightened risk of psychological distress, and drug-related harms.^{39,40} Therefore, this area needs to be further studied, to raise awareness of the long-term effects of the pandemic on drug users' mental health needs, service delivery, and treatment efficacy.

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Ερευνητική εργασία

Η επίδραση της πανδημίας σε άτομα με διαταραχή χρήσης ουσιών υπό θεραπεία υποκατάστασης

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ΠΕΡΙΛΗΨΗ

Δεδομένης της επιδείνωσης της ποιότητας ζωής του γενικού πληθυσμού λόγω της COVID-19 και της ευαισθησίας των ανθρώπων που κάνουν χρήση ουσιών στο έντονο στρες, ο στόχος της παρούσας έρευνας είναι η καλύτερη κατανόηση της επίδρασης που έχει η πανδημία της COVID-19 στην ποιότητα της ζωής, στην ψυχική υγεία των χρηστών ουσιών και στο μοτίβο χρήσης ουσιών. Πριν την έξαρση του ιού είχε διεξαχθεί μία έρευνα η οποία αξιολογούσε την ποιότητα ζωής, τα ενδεικτικά συμπτώματα Διαταραχής Μετα-τραυματικού Στρες (PTSD) και το μοτίβο χρήσης ουσιών των ατόμων που λάμβαναν υπηρεσίες από μία Μονάδα Ολοκληρωμένης Θεραπείας της Εξάρτησης, θεραπεία με υποκατάστατο, στην Αθήνα. Σε συνέχεια της μελέτης αυτής, αξιολογήθηκαν οι ίδιες μεταβλητές τον Μάιο και τον Ιούνιο του 2020, έπειτα από την άρση των περιοριστικών μέτρων. 104 ασθενείς δέχθηκαν να συμμετάσχουν και συμπλήρωσαν το ερωτηματολόγιο Ποιότητας Ζωής του Παγκόσμιου Οργανισμού Υγείας (WHOQOL-BREF) και την Post-Traumatic Stress Scale (PCL-C). Για την αξιολόγηση του μοτίβου χρήσης ουσιών λήφθηκαν υπόψη οι τοξικολογικοί έλεγχοι. Μία στατιστικά σημαντική διαφορά που αναδείχθηκε ήταν η μείωση στον παράγοντα της ποιότητας ζωής που αφορά τη σχέση του ατόμου με το περιβάλλον του. Βρέθηκε ότι τα άτομα με χαμηλή ποιότητα ζωής βίωσαν πιο σοβαρά συμπτώματα PTSD μετά την άρση των περιοριστικών μέτρων σε σχέση με τα άτομα με υψηλή ποιότητα ζωής. Γενικότερα βρέθηκε μία στατιστικά μη σημαντική αύξηση στα σκορ του PTSD πριν και μετά τα περιοριστικά μέτρα. Όσον αφορά στο μοτίβο χρήσης ουσιών, η παρούσα έρευνα αναδεικνύει μία συνολική μείωση στη χρήση ουσιών κατά τη διάρκεια των περιοριστικών μέτρων. Υπήρξε, επίσης, μία στατιστικά σημαντική μείωση στη χρήση οπιοειδών (22.3%) και βενζοδιαζεπινών (35%) μετά την άρση των περιοριστικών μέτρων. Τα άτομα που μείωσαν τη χρήση οπιοειδών κατά τη διάρκεια και μετά τα περιοριστικά μέτρα παρουσίασαν αυξημένο σκορ στα ενδεικτικά συμπτώματα PTSD. Όσον αφορά στη χρήση αμφεταμινών, βρέθηκε μία στατιστικά μη σημαντική αύξηση (8.7%). Η επίδραση της πανδημίας στη ζωή των ωφελούμενων μίας θεραπευτικής μονάδας υποκατάστασης οπιοειδών χρειάζεται να ληφθεί υπόψη και να διερευνηθεί περισσότερο ώστε να προστατευθεί η ποιότητα ζωής του πληθυσμού αυτού και να μεγιστοποιηθούν πιθανά οφέλη, όπως η περιορισμένη πρόσβαση σε παράνομες ουσίες.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: COVID-19, διαταραχή μετα-τραυματικού στρες, ποιότητα ζωής, θεραπευτική μονάδα υποκατάστασης οπιοειδών.

Review

The effect of physical activity interventions on cognitive function of older adults: A systematic review of clinical trials

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ABSTRACT

Prevalence of dementia or of milder form of cognitive impairment is increasing and a pharmaceutical treatment remains pending. These facts underline the need of identifying modifiable factors and targeted interventions that could reduce the incidence of the disease or control its progression. Physical activity (PA) has been shown to have a beneficial effect on cognitive function, however findings to date remain controversial. The aim of this systematic review is to summarize the most recent data from clinical studies investigating the relationship between cognitive impairment and PA in adults older than 60 years of age. For this purpose, PubMed, Scopus and Google Scholar searches were conducted, and a total of thirty-five studies were selected and reviewed. Eleven studies investigated the effect of PA on individuals without cognitive impairment and seven of them presented some significant improvement, mostly on specific cognitive domains and only one in global cognition. Fourteen studies included populations with mild cognitive impairment (MCI) and twelve of them reported significant improvements in cognitive function. The majority of them presented a beneficial effect on global cognition and executive function. Finally, nine studies investigated interventions on populations with a diagnosis of dementia and only four of them showed any cognitive benefit following their interventions. There was no consistently observed association of a specific type of exercise and greater improvement or improvement in certain domains of cognition nor was there a minimum duration of intervention required for the improvements to take effect. In conclusion, the majority of the latest published literature suggests a protective role of PA on cognitive function. People with MCI seem to benefit the most from PA interventions, benefits in people with normal cognition are more subtle and harder to detect, while findings from studies in people with dementia remain contradictory. As findings are not currently in total agreement, further long-term prospective intervention studies are required in order to elucidate the reasons of this heterogeneity.

KEYWORDS: Cognitive function, cognitive decline, aging, healthy aging, physical activity, clinical studies, review.

Introduction

The number of people living with dementia was estimated at 50 million in 2019 by World Health Organization (WHO) and has been forecasted to affect 135 million by 2050.¹ Mild cognitive impairment (MCI) is a condition between dementia and the expected cognitive decline of normal aging. Many population studies have been

conducted in the recent years aiming to document the frequency of MCI, and estimates ranged between 15–20% in the population over 60 years of age.² It has been hypothesized that compared to the general population people suffering from MCI are at increased risk to develop dementia in the following years, with a great number of these people progressing annually from one stage to the next.³ Cognitive frailty is another term used

to describe MCI accompanied with mild physical frailty in geriatric populations.⁴ MCI and dementia can be considered as a continuum with the risk of progressing with aging. Given that currently there is no pharmacological cure for dementia, there is an imperative need for the identification of modifiable risk factors and targeted interventions that could reduce the burden of the disease by delaying or even reversing the progression of MCI to dementia and preventing further cognitive deterioration in people already diagnosed.

Physical activity (PA) is considered a promising intervention for the prevention of cognitive impairment in older adults. The meta-analyses of prospective, observational studies by Santos-Lozano et al,⁵ and Guure et al,⁶ reported an association of physical activity with lower probability of development of Alzheimer's Disease (AD) and a protective effect in the rate of cognitive decline in patients with AD and other forms of dementia, respectively. In addition, a meta-analysis of randomized controlled trials (RCTs) of Northey et al,⁷ reported that PA interventions improved cognitive function of older adults regardless of their cognitive status, while the meta-analysis of Falck et al, presented a beneficial impact of PA on cognitive function of healthy older adults.⁸ Similar results have been reported regarding PA interventions on patients with AD or other forms of dementia.^{9,10} On the other hand, in a meta-analysis of twelve clinical trials, Young et al reported no evidence that physical activity interventions have any cognitive benefit for healthy older adults.¹¹ Conclusively, the published literature is not in total agreement over the effects of PA on cognitive function, as some findings remain conflicting for reasons that are still elusive. Additionally, to our knowledge, there is no published work assessing the effect of PA comparatively among populations of different cognitive status (normal cognition, MCI and dementia) and little is known about the characteristics of PA interventions that seem to be associated with the most beneficial effects for cognition.

The aim of this systematic review was to report recent results from clinical trials assessing the effect of PA interventions (including type, duration, etc.) on cognition of non-institutionalized older people, compare the effects among populations of different cognitive status and discuss the potential mechanisms that link PA and cognition.

Material and Method

Search strategy

For the purpose of this review, a literature search on PubMed, Scopus and Google Scholar, was conducted. The search query included the following terms: "aging",

"older", "physical activity", "exercise", "cognition", cognitive performance", "cognitive function", "cognitive functioning", "cognitive impairment". Reference list from the studies obtained were used for additional content.

Inclusion criteria

Methodological filters used in the present review included: (i) studies in humans only, (ii) randomized clinical trial design (defined by WHO as a type of research that studies new tests and treatments and evaluates their effects in human health outcomes), (iii) older people (>60 years of age) of both sexes; (iv) non-institutionalized, (v) who had not known major health conditions (aside from cognitive impairment or dementia). Tai-Chi and yoga-type interventions were excluded, since they cannot be entirely considered as PA. The search in the literature was restricted to studies that have been published over the past 10 years (from May 2010 to May 2020) and were written in English language.

Study selection

The retrieved papers were firstly screened by Title and then by Abstract by 2 authors (VG and EM). The papers that passed this process underwent full text screening by the same 2 authors; in the case of opposing opinions, the third author (DP) had the role of a judge. Main results, and potential mediating factors reported by studies included were extracted, in order to summarize findings and compare studies. No data analysis was performed, since this is a narrative review.

Results

Search query provided 1535 results. Fifty-five remained after Title and Abstract screening, upon completing full text screening a total of 35 studies met the inclusion criteria and were included in the review. The quality of the selected studies was assessed using the RoB 2 Cochrane tool for the estimation of risk of bias (table 1). All included studies fulfilled the basic principles of randomized clinical (intervention) trials.

Effect of PA on participants without Cognitive Impairment

A summary of characteristics of the studies included in this section is presented in table 2. Eleven studies investigated the effect of various forms of PA on older adults without any form of cognitive impairment or dementia. Table 2 summarizes the characteristics of these studies.

Table 1. Estimated risk of bias.

Authors	Year	Estimated Risk
Song D et al	2019	Low Risk
De Oliveira Silva F et al	2019	Some Concerns
Marston KJ et al	2019	Low Risk
Lamb et al	2018	Some Concerns
Langoni CS et al	2018	Some Concerns
Bademli K et al	2018	High Risk
Shimada H	2018	Some Concerns
Amjad I.et al	2018	Some Concerns
Choi W et al	2018	Low Risk
Yoon DH et al	2018	High Risk
Zhu Y et al	2018	Low Risk
Iuliano E et al	2017	Low Risk
Hong SG et al	2017	Low Risk
Liu Ambrose et al	2016	Low Risk
Mavros Y et al	2016	Some Concerns
Ohman H et al	2016	Some Concerns
Hoffman K et al	2016	Low Risk
Tarazona-Santabalbina FJ.	2016	Low Risk
Alghadir AH et al	2016	Low Risk
Sink MK et al	2015	Low Risk
Yang SY et al	2015	Low Risk
Holthoff VA et al	2015	Low Risk
Iuliano E et al	2015	High Risk
Lu J et al	2015	Low Risk
Fiatarone Singh MA et al	2014	Low Risk
Linde K et al	2014	Some Concerns
Ruiz JR et al	2014	Low Risk
Nouchi R et al	2013	Low Risk
Vreugdenhill A et al	2012	Some Concerns
Venturelli M et al	2011	Some Concerns
Maki Y et al	2011	Some Concerns
Yaguez LK et al	2010	Some Concerns
Muscari A et al	2009	Low Risk

Effect on Global Cognition

Regarding global cognition, the study by Muscari et al¹² presented stabilization of MMSE scores of the trained group, while the control group showed a significant decrease of 1.21 points after twelve months of intervention (endurance exercise), indicating a small to moderate effect size (Cohen's $\alpha=0.48$). However, the studies by Shimada et al and Ruiz et al,^{13,14} studies that set the MMSE as their primary cognitive outcome, did not show any significant difference compared to their controls after the intervention period.

Effect on Specific Domains of Cognition

The study by Marston et al¹⁵ revealed that their trained groups presented a statistically significant improvement in delayed verbal memory following their twelve-week intervention of resistance training. In the study of Linde et al,¹⁶ the trained group, with a sixteen-week combined aerobic and strengthening intervention, presented significant improvements in cognitive speed. Furthermore, the study by Maki et al¹⁷ presented significant improvement in word fluency, following a twelve-week intervention of walking. The study by Nouchi et al¹⁸ investigating the effect of combined aerobic, strength and stretching exercise showed significant improvements in executive functions, episodic memory and processing speed of their trained group, but not in working memory, reading ability and attention which were also tested. Alghadir et al in their study¹⁹ used a set of tests evaluating orientation, visual perception, spatial perception, motor praxis, vasomotor organization, thinking operations and attention-concentration to assess the effect of a 24-week aerobic intervention. This study showed significant improvements for their trained group in each subcategory of the test. Finally, in the clinical study by Iuliano et al, (2015)²⁰ that compared different types of exercise interventions (aerobic, resistance, postural) and a control group, it was shown that the aerobic group presented improvements in the Attentive Matrices Test, as well as Raven's Progressive Matrices Test that evaluate attention and abstract reasoning, respectively, the resistance group improved in Drawing Copy Test, which assesses praxis abilities, whereas postural and control group did not show any improvements. However, the studies by Iuliano et al (2017) and Hong et al^{21,22} that investigated the effect of different physical activity interventions on various domains of cognition and specifically memory performance did not present any benefits in their trained groups.

MCI and Cognitive Frailty

Fourteen studies investigated the effects of physical activity interventions on the cognitive function of people with MCI or at cognitive frailty. A summary of characteristics of the studies included in this section is presented in table 3.

Effect on Global Cognition

Ten studies²³⁻³² assessed the effect of their interventions on global cognition setting having as primary outcomes MMSE, Clinical Dementia Rating (CDR), Alzheimer's Disease Assessment Score ADAS-cog, or Montreal Cognitive Assessment (MoCA) scores. In their

Table 2. Study's characteristics in people with no cognitive impairment.

Authors	Year	Sample	Intervention	Duration	Cognitive Outcome	Results
Marston KJ et al	2019	N=45 Age 41–69	High Load Resistance vs Moderate Load vs Controls	Twice a week/ 12 weeks	CogState computerized battery	Improved in Some Domains Cognition Delayed verbal memory
Shimada H.	2018	N=100 Age over 65	Golf training vs Controls	Once a week/ 24 weeks	MMSE	No Difference in Cognition
Iuliano E et al	2017	N=80 Mean Age=67	Resistance training vs Cardio Training vs Postural Training vs Control	12 weeks	Various cognitive tests	No Difference in Cognition
Hong SG et al	2017	N=47 Age over 65	Resistance training vs Controls	12 weeks	Various cognitive tests	No Difference in Cognition
Alghadir AH et al	2016	N=100 Ager 65–95	Moderate Aerobic Training vs Control	24 weeks	LOTCA battery	Improved Cognition
Iuliano E et al	2015	N=80 Age over 55	Aerobic vs Resistance vs Postural vs Controls	12 weeks	Various cognitive tests	Improved Different domains of Cognition based on intervention
Linde K et al	2014	N=70 Age 60–75 years	Physical training vs Cognitive training vs Combined vs controls	16 weeks	Various cognitive tests	Improved Cognition for all interventions vs controls Cognitive Speed
Ruiz JR et al	2014	N=20 Age over 90	Aerobic and Resistance vs Control	8 weeks	MMSE, GDS	No difference in Cognition
Nouchi R	2013	N=64 Age over 60	Combined Exercise vs Controls	4 weeks	Various Cognitive tests	Improved Cognition
Maki Y et al	2011	N=150 Age Over 65	Walking vs Controls	12 weeks	5–Cog Test	Improvement in Word Fluency
Muscari A et al	2009	N=120 Age 65–74	Endurance Exercise Training vs Controls	12 months	MMSE	Stabilized Cognition

ADAS cog: Alzheimer's Disease Assessment Scale-cognition, ADL: Activities of Daily Living, GDS: Geriatric Depression Scale, LOTCA: Lowenstein Occupational Therapy Cognitive Assessment, MMSE: Mini Mental State Examination, MoCA: Montreal Cognitive Assessment

studies Song et al,²⁴ Bademli et al²⁵ and Amjad et al²⁶ included aerobic exercise interventions; Lu et al,²⁷ Mavros et al²⁸ and Fiatarone Singh et al²⁹ included resistance training; Tarazona-Santabalbina et al,³⁰ de Oliveira Silva et al,³¹ Langoni et al³² and Choi et al³³ included multimodal programs that combined different types of exercise (aerobic, strength, flexibility, endurance etc.). All of the studies mentioned above presented significant improvements in global cognition of their trained groups compared to controls, except for the study of de Oliveira Silva et al.³¹

Effect on Specific Domains of Cognition

Seven studies used tests that assessed the effect of their interventions on different domains of cognitive function and five of them presented improvements for their trained groups. Specifically, the study by de Oliveira Silva et al³¹ showed significant improvement in Clock Drawing Test (associated with executive function) and Verbal Fluency (associated with semantic memo-

ry) following a 12-week multimodal training program. Four more studies presented significant improvements in Trail Making Tests (which are associated with processing speed and executive function) following a six-week aerobic,²⁶ a twelve-week resistance (dumbbell),²⁷ a sixteen-week resistance³⁴ and a twelve-week aerobic (dancing)³⁵ training intervention. The dancing intervention was also associated with improvements in Logical Memory, as depicted by the Wechsler Memory Scale.

Dementia

Nine studies investigated the effect of various forms of physical activity on the cognitive function of people with Alzheimer's disease (AD) or other forms of dementia. A summary of characteristics of the studies included in this section is presented in table 4.

Effect on AD patients

Seven of the reviewed studies included populations with a confirmed diagnosis of Alzheimer's Disease.^{31,36–41}

Table 3. Study's characteristics in people with mild cognitive impairment (MCI).

Authors	Year	Sample	Intervention	Duration	Cognitive Outcome	Results
Song D et al	2019	N=120 Age over 60	Moderate Intensity Aerobic	16 weeks	MoCA	Improved Cognition
De Oliveira Silva F et al	2019	N=56 Age over 65	Multimodal Training vs Controls	12 weeks	CDR, MMSE, CDT, VF	Improved Cognition
Langoni CS et al	2018	N=52 Age over 60	Multicomponent exercise vs Controls	24 weeks	MMSE	Improved Cognition
Bademli K et al	2018	N=60 Age over 65	Physical Activity Program vs Controls	20 weeks	MMSE	Improved Cognition
Amjad I. et al	2018	N=40 Mean Age=59	Aerobic vs Controls	6 weeks	MMSE, MoCA, TMT A and B	Improved Cognition
Choi W et al	2018	n=60 Mean age=74 years	GKP vs Controls	6 weeks	MoCA score	Improved Cognition for both, more for trained
Yoon DH et al	2018	N=45 Age over 65	Resistance Training vs Controls	16 weeks	Various Cognitive Tests	Improved Cognition
Zhu Y et al	2018	N=60 Age 50-85	ADR vs Controls	12 weeks	Various cogni- tive tests	Improved Cognition
Hong SG et al	2017	N=47 Age over 65	Resistance training vs Controls	12 weeks	Various cogni- tive tests	No Difference in Cognition
Mavros Y et al	2016	N=100 Age over 55	Progressive Resistance Training vs Controls	6 months	ADAS-cog,	Improvements in Cognition
Tarazona- Santabalbina FJ	2016	N=100 Age over 70	Multimodal Exercise vs Controls	24 weeks	MMSE	Improved Cognition
Sink MK et al	2015	N=1635 Age over 70	Multimodal Exercise vs Controls	24 months	DSC, HVLT-R	No difference in cognition
Lu J et al	2015	N=45 Age over 65	Dumbbell training vs Controls	12 weeks	ADAS-cog, TMT B, DST,	Improved Cognition
Fiatarone Singh MA et al	2014	N=100 Mean Age=70	PRT vs Cognitive Training vs Combined vs Controls	6 months	ADAS-cog	Improved Cognition for PRT only

ADAS cog: Alzheimer's Disease Assessment Scale-cognition, ADL: Activities of Daily Living, CANTAB: Cambridge Neuropsychological Test Automated Battery, CDR: Clinical Dementia Rating, CDT: Clock Drawing Test, DSC: Digit Symbol Coding, DST: Digit Span Test, HIFE: High Intensity Functional Exercise

HVLT-R: Hopkins Verbal Learning Test revised, GDS: Geriatric Depression Scale, GKP: Ground Kayak Paddling

LOTCA: Lowenstein Occupational Therapy Cognitive Assessment, MCI: Mild Cognitive Impairment, MMSE: Mini Mental State Examination, MoCA: Montreal Cognitive Assessment, SDMT: Symbol Digit Modalities Test, SIB-s: Severe Impairment Battery- short form, TMT: Trail Making Test, VF: Verbal Fluency, WMS-R LM: Wechsler Memory Scale-Revised Logical Memory

All these studies used a validated tool to assess global cognition. Six of these used MMSE and/or ADAS-cog, while the remaining one³⁶ used The Cambridge Neuropsychological Test Automated Battery (CANTAB), which is a computerized neuropsychological test that can detect early stages of dementia and distinguish them from depression. Three of the studies mentioned above, those conducted by Yaguez et al,³⁶ Vreugdenhil et al³⁷ and Yang et al,³⁸ presented significant improvements following six weeks of movement training (a multimodal program that consists of fifteen exercises), sixteen weeks of walking and twelve weeks of aerobic

interventions, respectively. The studies by Vreugdenhil et al and Yang et al presented improvements in global cognition (Cohen's $d=0.32$ and 6.1 , respectively), while the study by Yaguez et al presented improvements in the domains of attention, visual memory and working memory. On the contrary, the remaining four studies conducted by de Oliveira et al,³¹ Ohman et al,³⁹ Hoffman et al⁴⁰ and Holthoff et al⁴¹ did not report any improvement in global cognition for individuals with Alzheimer's disease following aerobic or multimodal exercise interventions. Regarding specific domains of cognition, like executive function, assessed with Clock

Table 4. Study's characteristics in people with dementia.

Authors	Year	Sample	Intervention	Duration	Cognitive Outcome	Results
De Oliveira Silva F et al	2019	N=56 Age over 65	Multimodal Training vs Controls	12 weeks	CDR, MMSE, CDT, VF	Improved Cognition for MCI not AD
Lamb SE et al	2018	N=494 Age 78	Aerobic and Strength Exercise vs Controls	16 weeks	ADAS-cog	No difference in Cognition
Liu Ambrose T et al	2016	N=70 Mean Age=74	Aerobic Training vs Controls	6 months	ADAS-cog	Improvements in Cognition
Ohman H et al	2016	N=210 Age over 65	Home Exercise vs Group Exercise vs Control	12 months	MMSE, VF, CDT, CDR	No Difference in Cognition
Hoffman K et al	2016	N=200 Age 50–90	Moderate to High Intensity Aerobic vs Controls	16 weeks	SDMT, MMSE, ADAS-cog	No Difference in Cognition
Yang SY et al	2015	N=50 Age 50–80	Aerobic Exercise	12 weeks	MMSE, ADAS-cog	Improved Cognition
Holthoff VA et al	2015	N=30 Age 50–90	Multimodal Exercise vs Controls	12 weeks	MMSE	No Difference in Cognition
Vreugdenhill A et al	2012	n=40 Mean Age=74	Home Based Exercise and walking vs Controls	16 weeks	MMSE, ADAS-cog	Improved Cognition
Yaguez L K et al	2010	N=27 Mean Age=72.5 Years	Movement Training vs Controls	6 weeks	CANTAB	Improved Cognition

AD: Alzheimer's Disease, ADAS cog: Alzheimer's Disease Assessment Scale– cognition, ADL: Activities of Daily Living, CANTAB: Cambridge Neuropsychological Test Automated Battery, CDR: Clinical Dementia Rating, CDT: Clock Drawing Test, DSC: Digit Symbol Coding, DST: Digit Span Test, GDS: Geriatric Depression Scale, HIFE: High Intensity Functional Exercise, HVLT–R: Hopkins Verbal Learning Test revised LOTCA: Lowenstein Occupational Therapy Cognitive Assessment, MCI: Mild Cognitive Impairment, MMSE: Mini Mental State Examination, MoCA: Montreal Cognitive Assessment, SDMT: Symbol Digit Modalities Test SIB–s: Severe Impairment Battery– short form, TMT: Trail Making Test, VF: Verbal Fluency

Drawing Test, and Semantic Memory, evaluated with Verbal Fluency test that were examined in the studies of Ohman et al and de Oliveira Silva et al^{39,31} the trained groups did not show any benefit compared to the controls.

Other Forms of Dementia

The study by Lamb et al⁴² investigated the effect of a twenty-four-week combined aerobic and strength program on the cognitive function of people with clinically diagnosed dementia, without further specifying its form. This study reported that there was no improvement or stabilization of the cognitive function of their trained group compared to the control group. Finally, Liu-Ambrose et al⁴³ in their study investigated the effect of a six-month aerobic training intervention on the cognitive function of individuals with ischemic vascular cognitive impairment. This study showed a significant improvement in global cognition of the trained group relatively to the controls as depicted by the ADAS-cog test score that was, however, diminished in the 6-month follow-up assessment.

Discussion

This review of clinical studies confirmed that there is evidence linking physical activity interventions to improvements of cognitive function, with the majority of the studies reporting significant benefits for their trained groups in global cognition or at least in some cognitive domains, regardless of their cognitive status. Regarding specific aspects of cognitive function, executive function was the one that was most consistently reported to improve after the physical activity interventions, which is in accordance with previous published literature.^{7,8}

Regarding the effects of PA on specific populations, seven out of the eleven studies on healthy older adults reported some cognitive benefits for their intervention groups. Additionally, people without cognitive impairment seemed to benefit more in specific cognitive domains and not in global cognition. However, due to the multitude of cognitive tests that were used, no consistent link could be identified between interventions and a specific cognitive domain. This heterogeneity is also reflected in the latest meta-analyses and systematic reviews, as some report mild to moderate benefits in

specific cognitive domains,^{44–46} while others do not.^{11–47} This can be partly attributed to the fact that cognitive deterioration in healthy older adults is slow and subtle, making differences between intervention and control groups hard to detect, especially with crude tests that are designed to diagnose dementia, such as MMSE.

On the other hand, people with MCI were consistently presented to benefit in global cognition in the present review. In a meta-analysis by Sanders et al,⁴⁸ there was a similar trend with healthy older adults to benefit more in specific domains of cognition, while those with MCI benefit more in global cognition after PA interventions. Recently published literature seems to be in agreement with the findings of the present review, as PA interventions are consistently reported to have a beneficial effect on the cognitive function of people with MCI.^{49,50} This might be attributed to the fact that cognitive impairment is progressing faster in people with MCI compared to healthy older adults, but it could also indicate that it can be reversed, making people with MCI potentially the ones that might benefit the most out of targeted PA interventions.

Finally, regarding studies in populations with dementia, five out of nine studies (n=244) presented significant benefits for their trained groups, while the remaining four (n=934) did not present any. Recently published literature is also contradictory as PA interventions are reported to either provide some cognitive benefits⁵¹ or not.⁵² This can be attributed to many reasons that may have to do with the quality of the studies (small samples, insensitive cognitive tests, etc.). However, it may also reflect the fact that as cognitive deterioration progresses passed a certain point it may be more challenging to be reversed or slowed down.

Concerning the duration of the intervention, its intensity and the types of exercise, a minimal duration threshold was not found nor a consistent link between cognitive benefits and a specific type of physical activity or intensity level. Only one study²⁰ presented association of different types of exercise with specific domains of cognition, however, given its small sample and the number of the comparisons that were conducted its findings should be interpreted with great caution.

The observed heterogeneity regarding studies in populations with dementia can be attributed to several reasons. Dementia is a clinical diagnosis based on the deterioration of cognitive function experienced by the patients, that may result from various causes. Distinguishing between different causes of dementia can be challenging, even for specialists, as characteristic findings of different pathological entities frequently co-exist. In addition, the exact pathophysiological mechanisms for specific types

of dementia are not yet fully clarified, even for Alzheimer's Disease, which is the most common etiology of dementia contributing to the 60–70% of total cases according to WHO. Taking all these into account, it is clear that individuals with a clinical diagnosis of Dementia may vary greatly even when stratified for gender, age and cognitive performance and thus respond differently to interventions, causing studies to produce these conflicting results.

The effects of PA on cognitive function can be categorized as direct and indirect. Cerebral blood flow progressively declines with aging.⁵³ This deterioration of cerebral perfusion has been linked with poorer cognitive performance.⁵⁴ Physical exercise has been shown to directly impact cerebral circuitry, by increasing its flow⁵⁵ and promoting vascular growth factors.⁵⁶ Aside from benefiting brain blood circulation, PA may also have a direct effect on brain neuronal function by the stimulation of Brain Derived Neurotrophic Factor (BDNF),⁵⁷ which is considered to play a key role in neurogenesis and neuronal function.⁵⁸ Finally, oxidative stress is currently believed to play some role in the pathophysiology of neurodegenerative diseases and Alzheimer's Disease in particular,^{59–61} contributing to the cascade of events that lead to accumulation of amyloid- β , neuronal apoptosis and eventually dementia. Current knowledge suggests that physical activity can reduce oxidative stress and thus have a protective role in the development of these conditions. The indirect links of PA with cognitive function could be explained by the interplay with sleep quality and depressive mood.²⁴

Physical exercise might seem a promising intervention for the prevention of cognitive impairment, however, there are some limitations that cannot be depicted by the studies mentioned above. Firstly, aging is often associated with health problems that limit mobility and may make individuals less willing and able to engage in physical activity. Another important issue is that the interventions of randomized trials are usually supervised by exercise experts, which is not possible in everyday life. Unless they are easily structured in a way that they can be incorporated in the every-day life of the individuals it is unlikely that they will adhere to them and benefit in the long term.

Conclusion

The comparative analysis of the effects of PA on cognitive function of populations with different cognitive status suggested that PA may have a protective role against cognitive impairment at the stages preceding dementia, while its effect on demented people is controversial. However, its value should be highlighted as an essential part of a healthy lifestyle.

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Ανασκόπηση

Η επίδραση της φυσικής άσκησης στη νοητική λειτουργία του πληθυσμού μεγαλύτερης ηλικίας: Μια συστηματική ανασκόπηση κλινικών δοκιμών

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ΠΕΡΙΛΗΨΗ

Ο επιπολασμός άνοιας ή ηπιότερων μορφών νοητικής έκπτωσης αυξάνεται και προς το παρόν δεν είναι διαθέσιμη κάποια αποτελεσματική φαρμακευτική θεραπεία. Αυτά τα γεγονότα υπογραμμίζουν την ανάγκη εντοπισμού τροποποιήσιμων παραγόντων και στοχευμένων παρεμβάσεων που θα μπορούσαν να μειώσουν τη συχνότητα εμφάνισης ή να ελέγξουν την εξέλιξη της νόσου. Η σωματική άσκηση (ΣΑ) έχει φανεί να έχει ευεργετική επίδραση στη νοητική λειτουργία, ωστόσο τα ευρήματα μέχρι σήμερα παραμένουν αμφιλεγόμενα. Ο σκοπός αυτής της συστηματικής ανασκόπησης είναι να συνοψίσει τα πιο πρόσφατα δεδομένα από κλινικές μελέτες που διερευνούν τη σχέση μεταξύ νοητικής έκπτωσης και ΣΑ σε ενήλικους άνω των 60 ετών. Για τον σκοπό αυτόν, πραγματοποιήθηκε αναζήτηση στο PubMed, το Scopus και το Google Scholar και επιλέχθηκαν συνολικά τριάντα πέντε μελέτες για ανασκόπηση. Έντεκα μελέτες διερεύνησαν την επίδραση της ΣΑ σε άτομα χωρίς νοητική έκπτωση και επτά από αυτά παρουσίασαν κάποια σημαντική βελτίωση, κυρίως σε συγκεκριμένους γνωστικούς τομείς και μόνο μία στη συνολική νοητική λειτουργία. Δεκατέσσερις μελέτες περιλάμβαναν πληθυσμούς με ήπια νοητική έκπτωση και δώδεκα από αυτές ανέφεραν σημαντικές βελτιώσεις στη νοητική λειτουργία. Η πλειοψηφία τους παρουσίασε ευεργετική επίδραση στη συνολική νοητική λειτουργία και εκτελεστική λειτουργία. Τέλος, εννέα μελέτες διερεύνησαν παρεμβάσεις σε πληθυσμούς με διάγνωση άνοιας και μόνο τέσσερις από αυτές έδειξαν οποιοδήποτε νοητικό όφελος μετά τις παρεμβάσεις τους. Δεν παρατηρήθηκε συνεπής συσχέτιση συγκεκριμένου τύπου άσκησης και μεγαλύτερη βελτίωση ή βελτίωση σε ορισμένους τομείς της νόησης ούτε υπήρχε ελάχιστη διάρκεια παρέμβασης για να τεθούν σε ισχύ οι βελτιώσεις. Συμπερασματικά, η πλειοψηφία της πιο πρόσφατης δημοσιευμένης βιβλιογραφίας προτείνει έναν προστατευτικό ρόλο του ΣΑ στη νοητική λειτουργία. Τα άτομα με ήπια νοητική έκπτωση φαίνεται να επωφελούνται περισσότερο από τις παρεμβάσεις ΣΑ, τα οφέλη σε άτομα με φυσιολογική νόηση είναι πιο περιορισμένα και πιο δύσκολο να εντοπιστούν, ενώ τα ευρήματα από μελέτες σε άτομα με άνοια παραμένουν αντιφατικά. Καθώς τα ευρήματα δεν είναι σε απόλυτη συμφωνία προς το παρόν, απαιτούνται περαιτέρω μακροπρόθεσμες μελέτες μελλοντικής παρέμβασης προκειμένου να διευκρινιστούν οι λόγοι αυτής της ετερογένειας.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: Νοητική λειτουργία, νοητική έκπτωση, γήρανση, υγιής γήρανση, σωματική άσκηση, κλινικές μελέτες, ανασκόπηση.

Special article

The role of the Mobile Mental Health Units in mental healthcare delivery in rural areas in Greece: current challenges and prospects

A position statement of the Coordinating Committee of the Mobile Mental Health Units

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ABSTRACT

The present paper aims to highlight the importance of Mobile Mental Health Units (MMHUs) in the delivery of mental health services in remote areas in rural Greece. Since the foundation of the first MMHUs in the eighties till nowadays, those services have expanded in many rural areas and there is some evidence that they are effective in the management of patients with severe mental disorders. The care of those patients seems to contribute to a significant reduction in voluntary and involuntary acute admissions and length of hospital stay. Cost/effectiveness analysis studies have also shown favorable results. Besides their regular clinical work, MMHUs conduct research, such as epidemiologic surveys. Other research explores the care of elderly patients in rural areas and the care of immigrants that permanently reside in Greece. Other research involves the study of psychotic disorders in the rural context, such as the long-term outcome, the patient's functioning, and the long-term treatment with benzodiazepines. Current challenges for MMHUs involve staffing, particularly for those run by public hospitals, and the retention of highly trained personnel. Other important challenges are related to the aging of the rural population and the refugee/migrant influx. The MMHUs of the islands that initially accept the refugee flow have already faced an increased number of new referrals. Given the disparities in mental healthcare between rural and urban areas, further enhancement of the MMHUs' operation is required, as well as continuing training of their workforce. Research at the national level is needed and could be the basis for the design and staffing of new services. The establishment of valid and broadly accepted clinical indices to measure treatment outcomes would facilitate research and ensure the recording and evaluation of the MMHUs' work and their effectiveness as well, and would highlight their utility within the contemporary health system.

KEYWORDS: Community mental health services, mobile mental health units, rural and remote areas, psychotic disorders, schizophrenia.

Introduction

The contemporary trend in the treatment of mental disorders involves the delivery of easily accessible community-based services, in a non-restrictive environment. Community mental health services offer a broad range of services for all mental disorders, with the emphasis being placed on long-term, severe mental illnesses (SMI), such as psychoses. The effectiveness of their interventions for SMI is supported by several studies, which demonstrate that the care provided contributes to the improvement of symptomatology; the reduction of the length of hospital stay; and the management of substance abuse comorbidity. In addition, community interventions improve patients' functioning and treatment adherence.¹ Nevertheless, mental health service delivery in remote rural areas is challenging for the healthcare system. For example, in Eastern European countries, the population of these areas does not receive adequate care, due to socioeconomic and geographical reasons and the lack of local services.² Moreover, there is evidence that the use of community mental health services is significantly affected by the distance that the patients have to travel.³ Similar results have been found in Greece,⁴ where a large part of the population resides in mountainous-rural areas, as well as islands, conditions that adversely affect the accessibility of psychiatric patients to mental health services. The introduction of Mobile Mental Health Units (MMHUs) in rural regions, seems to contribute to the solution to this problem.⁵

The present paper aims to present the activities of the MMHUs and highlights their prospects for the provision of quality services in remote rural areas. It also refers to the challenges that MMHUs face and puts forward specific proposals for the enhancement of their operation.

The MMHUs in Greece

Historical background

The first two MMHUs in Greece were founded in 1981, in Fokida, Central Greece, and Evros, Northeast Greece. The MMHU of Fokida was established by the Society of Social Psychiatry and Mental Health, headed by its President, Panagiotis Sakellaropoulos, who later became a Professor of Psychiatry at the Democritus University of Thrace. The MMHU in Evros was founded by the University Psychiatric Department of the General Hospital of Alexandroupolis, headed by its Director, Charalambos Ierodiakonou, who was at the time Professor of Psychiatry at the Alexandroupolis branch of the Aristotle University of Thessaloniki. In 1985, Panagiotis Sakellaropoulos who had become by then Professor of Psychiatry at the Democritus University of Thrace took over the management of the MMHU of the

Hospital of Alexandroupolis. Under his scientific responsibility, for almost a decade, these two first MMHUs operated on a converging course, with common aims and similar operating principles.⁶⁻⁸ Later, other MMHUs were established in the areas of Evia and Thessaloniki.

The first two MMHUs, in accordance with the principles of Social and Community Psychiatry, aimed at:⁶⁻⁸ (a) overcoming the problems created by traditional psychiatric methods for people with mental health problems, (b) the improvement of the accessibility of psychiatric services, for patients and their families, through the decentralization of these services, considering that at the time, remote rural areas lacked any kind of mental health services, (c) the systematic and consistent patients' follow-up near their place of residence or at their home, to prevent relapses and reduce hospitalizations, (d) the management of crises-relapses through home treatment, especially at the MMHU of Fokida, which lacked a psychiatric ward at the local hospital, (e) cultivating relationships with the community, to provide information and raise awareness regarding mental health issues (Community Sensitization). The aim of the cooperation with the community was, on one hand, to reduce the effects of stigma toward mental illness and on the other hand, to employ community resources for the support of people with severe psychiatric disorders.^{8,9}

Over the following decades, many more MMHUs were established and became an integral part of mental health services, within the framework of the psychiatric reform. By 2016, 25 MMHUs had been registered in Greece, whose operation was mainly under the responsibility of non-governmental organizations, as well as the psychiatric sectors of general hospitals.¹⁰ In 2019, their number had been reduced to 20.¹¹

Basic operational principles of the MMHUs

In our country, MMHUs are interdisciplinary teams that deliver services according to the principles of Social and Community Psychiatry. Their operation is based on both the Community Mental Health Teams model, which is very common in the UK, and the Assertive Community Treatment, which is the benchmark for community-based treatment of SMI in developed Western countries.¹² MMHUs are a modified version of the above models, adapted to the Greek reality and rural settings. Similar adaptations of the traditional community-based treatment models for mental health disorders in remote areas have been reported internationally.¹³⁻¹⁵

MMHUs deliver services in the non-restrictive context of the community and Primary Health Care (PHC). Referrals are made by the PHC, the psychiatric wards of general hospitals, and local services, such as the Home

Help service, whereas a significant percentage of patients are self-referrals or have been referred by their families. MMHUs undertake the care of all referred cases that require treatment, with emphasis on patients with long-term and severe mental disorders. They offer a wide range of evidence-based therapeutic interventions, such as medication and psychological therapies, along with support and training of the family and other caregivers. The MMHUs use the infrastructures of the local services, of PHC (Health Centers and Regional Medical Offices), whereas they may conduct home visits in selected cases of patients.^{16–19}

The operation of the MMHUs has been the subject of discussion and reflection. Professor Mavreas²⁰ previous remarks are still relevant:

1. Often, the networking of the MMHUs with the rest of the mental health services system does not exist. It is a problem that is directly related to the incomplete implementation of sectorization in Greece.¹⁰
2. The complete implementation of their work, as it has been determined by the relative legislation is difficult.
3. Scientific documentation and evaluation of their work are required.
4. Their operation in changing conditions, such as the current pandemic, must be protected.

Indications-Evidence for the effectiveness of the MMHUs

The small number of studies that have been conducted so far on MMHUs have shown some interesting results. They seem to ensure a significant degree of continuity of care for patients with psychoses, a prerequisite for the treatment of psychotic disorders in the community.²¹ Some studies showed that the operation of the MMHUs contributes to the reduction of hospitalizations, including involuntary hospitalizations, as well as in the reduction of the length of hospital stay of patients with schizophrenia-spectrum disorders and bipolar disorder.^{22,23} A recent study in an island population which was designed to investigate the effectiveness of community interventions, found that the care provided to patients with common psychiatric disorders by the Northeast and Western Cyclades MMHUs, led to a significant reduction in Disability Adjusted Life Years.²⁴ Other research suggests that the cost/effectiveness ratio of the MMHUs interventions at the islands is favorable. According to the authors, the improvement of the patient's mental health, forms the basis for reducing public costs of treatments, and may also be the basis for the improvement of patient's financial status by reducing productivity losses.²⁵ (table 1).

It is not clear whether the above findings are generalized nationwide. The design of large, multicenter studies with the participation of all MMHUs is necessary to produce robust evidence, to form conclusions regarding the effectiveness of their interventions.

Other research work of the MMHUs

Individual MMHUs' practices, such as home visits, appear to be useful for the care of elderly patients,^{26,27} who comprise a large proportion of the rural population and have increased needs. In a previous epidemiologic study by the MMHU of Northeastern Cyclades, the prevalence of common mental disorders in islands was assessed.²⁸ Other research projects of the MMHUs include the study of long-term outcomes in psychotic disorders in rural areas,²⁹ the study of functioning in patients with psychosis in this areas³⁰ and the study of the use of telepsychiatry for the treatment of patients in remote areas.³¹ In addition, more specific issues have been studied concerning patients with psychotic disorders, such as chronic treatment with benzodiazepines³² and gambling problems.³³ Very recently, the nutritional habits and obesity among patients with schizophrenia-spectrum disorders in parts of Epirus have been studied.³⁴ Other recent studies report on the correlation between depressive symptoms and family functioning among immigrants from Albania, who live permanently in Northwest Aegean islands³⁵ and the use of community mental health services by this population.³⁶ The most recent research by the MMHUs concerns the COVID-19 vaccination rates of patients with SMI, which were found to be similar to those of the general population.³⁷

Differences among MMHUs

As mentioned above, the operation of the MMHUs in Greece is determined by Social and Community Psychiatry principles and aspirations. Nevertheless, there may be significant differences between MMHUs.³⁸ Very recently, a systematic recording of the differences between the MMHU of the University General Hospital of Alexandroupolis (MMHU UGHA), and the MMHU of Ioannina and Thesprotia Prefectures (MMHU I-T) was attempted. The comparison revealed significant differences with regard to the units' staffing and the service users' demographic and clinical characteristics.³⁹ Moreover, the MMHUs on the islands deal with all kinds of referrals, in the absence of other mental health services. As a result, the proportion of patients with SMI receiving treatment by these units is relatively small, compared to the total number of cases treated.⁴⁰ Differences between MMHUs could be attributed to local factors, such as the availability of other services and access to other specialized ser-

Table 1. Studies that are suggestive of the effectiveness of the MMHUs

Study	MMHU	N	Research questions	Method	Results
Peritogiannis et al, 2013	Ioannina & Thesprotia	74 patients with psychotic disorders	Treatment engagement rates	Retrospective study, 5-year follow-up	The treatment engagement rate was 67.2%. treatment engagement was not correlated to clinical or demographic variables
Lykomitrou et al, 2020	Northeastern & Western Cyclades	724 (604 clinical cases and 120 certificates etc)	Evaluation of the operation of the MMHU	Economic analysis of cost/effectiveness	The operation of the MMHU reduced the treatment costs by almost 50%
Peritogiannis et al, 2020	Ioannina & Thesprotia	76 patients with psychotic disorders	The impact of the interventions of the MMHU on hospital admissions and length of hospital stay in patients with psychoses	Retrospective study, pre/post intervention mirror design (mean follow-up duration 5.3 years)	Reduction of hospitalizations by 80%, 2.6-fold reduction of length of hospital stay, 6-fold reduction in involuntary admissions
Lykomitrou et al, 2021	Northeastern & Western Cyclades	724 (604 clinical cases and 120 certificates etc)	Assessment of the effectiveness of the MMHU	Measurement of the outcome of the interventions with the use of the DALYs Index	6.4-fold reduction in DALYs, through the interventions of the MMHU. Over a year, 98 DALYs were averted, due to the prevention of premature mortality and the reduction of the mental health burden
Garbi et al, 2021	Kefalonia, Zakynthos & Ithaca	108 patients with psychotic or bipolar disorders	The impact of the interventions of the MMHU on hospitalizations and length of hospital stay	Retrospective study, pre/post intervention mirror design (mean follow-up duration 6.7 years)	Reduction of hospitalizations by 45.9% and reduction of involuntary admissions by 51%. Reduction of hospital stay by 54.4%

MMHU: Mobile Mental Health Unit, DALYs: Disability-Adjusted Life Years

vices, or to whether the MMHU is run by a hospital or a non-governmental organization (NGO).

Other differences between MMHUs in our country have not been adequately recorded. For instance, some of them provide children and adolescent care services, whereas others do not. Moreover, some of the MMHUs were selected to implement new programs for children and adolescents as well as the assertive community treatment program, funded by the National Strategic Reference Framework (NSRF).⁴¹ It is still unknown how many of the MMHUs that were selected to implement the above programs managed to adequately staff and operate the new services.

Challenges in the current situation

Refugees and immigrants

Refugees and immigrants, whose population is gradually increasing in our country, are at increased risk of developing psychiatric symptoms. These people are subject to intense mental strain due to their expatriation and various losses. In addition to the physical and emotional trauma, they have experienced, refugees and migrants face poverty, hostility, and racism in the host country. Other factors that contribute to the development of psychiatric symptoms are poor living conditions, lack of support, and detention, as well.⁴²

On islands with large reception centers and camps, local MMHUs have already been involved in the mental healthcare of refugees, especially over the last five years. Referrals of these individuals come from multiple sources, such as hospitals, accommodation structures, identification centers, the police, and non-governmental organizations operating in the camps. According to a recent study at the Reception and Identification Center in Chios, high rates of self-destructive behavior were observed among refugees and migrants, as well as high dropout rates, both in adults and children/adolescents. The most common diagnoses in adults were anxiety and stress-related disorders, as well as emotional disorders. In minors, the most common diagnoses were anxiety as well as stress-related disorders and developmental disorders.⁴³

Aging of the rural population

The population of our country is constantly aging and the phenomenon is more evident in the Greek countryside. This already affects the patient population profile treated by certain MMHUs, which deal with age-related mental disorders, such as dementia and other organic brain syndromes. In the absence of specialized psychogeriatric services, especially in the province, the best

prospects for the diagnosis and treatment of mental disorders in the elderly are the MMHUs, in close cooperation with the PHC.⁴⁴

Suggestions

Staffing

Working in rural areas presents significant challenges and is generally not considered attractive for health professionals.⁴⁵ Additionally, a shortage of qualified mental health professionals has been identified in Greek rural areas.⁴⁶ With regard to the MMHUs' understaffing, it may be even more obvious for units run by general hospitals. The bureaucratic procedures of hiring and replacing staff place obstacles in the staffing process. At the same time, the employment conditions of psychiatrists in the public sector MMHUs may not be attractive. Liaison with universities and access to research activities, financial incentives, and other work-professional incentives could be ways to strengthen the scientific staffing of the MMHUs.

Active participation in decision-making

The MMHUs' experience and expertise in providing mental health services in remote areas are remarkable and can be utilized by scientific organizations and state institutions. The extent to which this happens is not clear, but there are some negative examples, such as the recent drafting of guidelines for the community treatment of schizophrenia,⁴⁷ in which the MMHU representatives' participation was low. More active participation in the decision-making concerning the MMHUs is proposed, through their representation in bodies such as the Hellenic Psychiatric Association (community psychiatry branch) and the Sectoral Scientific Committees of Adult and Child-Adolescent Mental Health (ΤΕΠΕΨΥΕ-ΤΕΠΕΨΥΠΕ).

Research

The research conducted by the MMHUs can contribute to the collection of epidemiological data, which is lacking in Greek literature, especially for the provincial regions. In addition, conducting research is the most appropriate way to highlight the work of the MMHUs and document their effectiveness.

It is encouraging that, according to a relatively recent ministerial decision,⁴⁸ new funding is expected to be allocated to Community Mental Health Services for "conducting organized research initiatives". This would be a strong incentive for the personnel of the MMHUs to participate in research activities. A question that arises, however, is the extent to which this opportunity has

been utilized until today, and whether research proposals have been submitted to the Ministry of Health, as well as how many of them have already been approved and funded.

MMHUs Evaluation

In recent years, there has been an international trend towards the reduction of available mental health resources.⁴⁹ In an era of changing economic conditions in our country, due to the financial crisis and the current COVID-19 pandemic, linking funding to service effectiveness, as proposed by some experts,¹⁰ seems likely. Consequently, the need for a valid evaluation of MMHUs is emerging. Currently, there is only a rough link between funding and the number of monthly therapeutic sessions carried out by MMHUs run by NGOs, based on a controversial costing method. This method may distort the evaluation of the quality of the services provided and runs the risk of creating an artificial demand for services, such as the extension of treatment in cases where it is no longer necessary.

Some issues that are involved in research and evaluation, and need to be resolved, are highlighted below:

- A. The necessity for an extended (nationwide) population needs assessment survey, which should form the basis for sectorization, the design of new mental health services, including MMHUs, as well as their staffing.
- B. The need for the systematic use of widely accepted clinical indices regarding treatment, for the measurement and evaluation of the work of the MMHUs, as well as all the mental health units. Such indices could include the percentage of patients receiving treatment compared to the total referrals and requests; the hospitalizations (voluntary and involuntary) of patients with SMI receiving care; patients' symptomatology and functioning; patients' satisfaction with the services provided etc.
- C. The need for targeted research to evaluate the effectiveness of the MMHUs, as well as relevant external evaluation (with cost/effectiveness indices, SWOT analysis, etc.).
- D. The need to fill the gap of systematic and valid recording of the work of the MMHUs, as well as the entire system of mental health units in the country, that limits research and evaluation of all the issues listed above.

Staff training

The ongoing training of the MMHUs' staff is a key prerequisite for strengthening their skills and the prevention of burnout, to provide effective services.⁵⁰ Recognizing

the need for specialized training for the staff working in the community mental health services, Aris Liakos, Professor of Psychiatry at the University of Ioannina, in collaboration with Professor Panagiotis Sakellaropoulos and the Society of Social Psychiatry and Mental Health, founded the Postgraduate Program in Social Psychiatry-Child Psychiatry, in the Department of Medicine of the University of Ioannina, which operated for several years. This program contributed significantly to the training of young professionals and the promotion of the psychiatric reform. Since 2008, a Postgraduate Program with similar educational goals operates at the Department of Medicine of the Democritus University of Thrace, founded by Miltos Livaditis, Professor of Social Psychiatry.

The challenges regarding the treatment of the growing number of elderly patients by the MMHUs require further training in psychogeriatrics. At the same time, due to the high rate of physical comorbidities in patients with psychosis, the long-term training of MMHUs' staff in general medicine is considered essential.⁵¹ In addition, training in cross-cultural psychiatric issues is necessary for the MMHUs of those islands that shelter an increased number of refugees and immigrants.

Inequalities regarding the access to mental health services in remote rural areas have been highlighted in detail in the international and the Greek literature.^{4,52} Undoubtedly, MMHUs as secondary care services that have the potential to deliver interdisciplinary interventions can meet most of the needs of the population in rural areas. On the other hand, expectations regarding the operation of the MMHUs should always be adjusted to their existing capabilities and available resources. For instance, if the demanding care of migrants/refugees is allocated to the MMHUs, they should be further supported and appropriately funded.

Conclusion

As Professor Sakellaropoulos has aptly stated regarding community mental health services, "We do not change the diagnosis; we change the person's fate". This statement summarizes the history and operation of the MMHUs. Initially, the MMHUs was an important initiative in the context of the country's psychiatric reform, but in recent decades they have faced various challenges, such as the financial crisis and the refugee-migrant flow. Recently, their operation has expanded, with increasing expectations. MMHUs need to be further strengthened to continue to meet their demanding role, while at the same time it is necessary to evaluate their effectiveness, through organized research initiatives.

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Ειδικό άρθρο

Ο ρόλος των Κινητών Μονάδων Ψυχικής Υγείας στην παροχή φροντίδας ψυχικής υγείας σε περιοχές της επαρχίας: τρέχουσες προκλήσεις και προοπτικές

Διακήρυξη της Συντονιστικής Επιτροπής των Κινητών Μονάδων Ψυχικής Υγείας

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ΠΕΡΙΛΗΨΗ

Το παρόν κείμενο έχει σκοπό να αναδείξει τη σημασία των Κινητών Μονάδων Ψυχικής Υγείας (ΚΜΨΥ) στην παροχή υπηρεσιών ψυχικής υγείας σε απομακρυσμένες περιοχές της ελληνικής επαρχίας. Από την ίδρυση των πρώτων ΚΜΨΥ στη δεκαετία του '80 ως τις μέρες μας, οι υπηρεσίες αυτές εξαπλώθηκαν σε πολλές περιοχές και υπάρχουν ισχυρές ενδείξεις πως είναι αποτελεσματικές στη φροντίδα ασθενών με σοβαρές ψυχικές διαταραχές. Η φροντίδα ασθενών με τέτοιες διαταραχές φαίνεται να επιφέρει σημαντική μείωση των νοσηλείων, ακούσιων και εκούσιων και των ημερών νοσηλείας. Η σχέση κόστους/αποτελεσματικότητας επίσης δείχνει να είναι ευνοϊκή. Παράλληλα με το κλινικό έργο, κάποιες ΚΜΨΥ έχουν αναπτύξει ερευνητική δραστηριότητα, όπως διεξαγωγή επιδημιολογικών μελετών. Αντικείμενο μελέτης αποτελούν ακόμη η φροντίδα των ηλικιωμένων ασθενών και των μεταναστών που κατοικούν μόνιμα στη χώρα. Το ερευνητικό έργο των ΚΜΨΥ περιλαμβάνει και τη μελέτη των ψυχωτικών διαταραχών στο πλαίσιο της επαρχίας, όπως τη μακροχρόνια έκβαση, τη λειτουργικότητα των ασθενών και τη χρόνια θεραπεία με βενζοδιαζεπίνες. Οι τρέχουσες προκλήσεις για τις ΚΜΨΥ αφορούν στη στελέχωσή τους, ειδικά εκείνων που υπάγονται σε δημόσια νοσοκομεία και στη διατήρηση επιστημονικού προσωπικού υψηλής κατάρτισης. Άλλες σημαντικές προκλήσεις τίθενται λόγω της γήρανσης του πληθυσμού της επαρχίας και του προσφυγικού/μεταναστευτικού προβλήματος. Οι ΚΜΨΥ των νησιών υποδοχής προσφύγων δέχονται ήδη αυξημένο αριθμό αιτημάτων για περίθαλψη αυτού του πληθυσμού. Δεδομένων των ανισοτήτων στη φροντίδα ψυχικής υγείας μεταξύ της επαρχίας και των αστικών κέντρων, επιβάλλεται η περαιτέρω ενίσχυση της λειτουργίας των ΚΜΨΥ και η συνεχής εκπαίδευση του προσωπικού. Η έρευνα των αναγκών του πληθυσμού σε όλη τη χώρα θα μπορούσε να αποτελέσει τη βάση για έναν περισσότερο ορθολογικό σχεδιασμό και στελέχωση νέων υπηρεσιών. Η με συστηματικό τρόπο χρησιμοποίηση κλινικών δεικτών θεραπευτικού αποτελέσματος κοινής αποδοχής θα διευκόλυne την έρευνα και θα επέτρεπε την καταγραφή και αξιολόγηση του έργου των ΚΜΨΥ και της αποτελεσματικότητάς τους, ώστε να αναδειχθεί η χρησιμότητά τους στο σύγχρονο σύστημα υγείας.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: Απομακρυσμένες περιοχές, επαρχία, κινητές μονάδες ψυχικής υγείας, κοινοτικές υπηρεσίες ψυχικής υγείας, σχιζοφρένεια, ψυχωτικές διαταραχές.

Special article

Theophrastus's "Anaisthetos" ("The Obtuse Man"): the oldest "phenomenological" description of neurodevelopmental disorders in an adult

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ABSTRACT

Theophrastus (381–278 B.C.), was the first to adopt the term character for the description of distinct inner psychological and moral features of an individual. In his classic book 'Characters' in a simple style wording he analyses some of his contemporary individuals. The character "Αναίσθητος" (Anaisthetos) has been translated in English as "The Obtuse Man" and in Modern Greek both as "Αναίσθητος", meaning lack of appreciation and "Βραδύνους", meaning slowness of mind. Theophrastus' description of this particular character is compatible with the co-occurrence in an adult of two neurodevelopmental disorders: attention-deficit hyperactivity disorder (ADHD) and social pragmatic communication disorder (SPCD), according to the 5th Diagnostic and Statistical Manual of Mental Disorders. Ten out of the twelve statements support the possible occurrence of ADHD while five of them the occurrence of SPCD. The description does not justify a diagnosis of an intellectual disability; therefore, we consider that in the Modern Greek vocabulary the original term «Αναίσθητος» ("Anaisthetos"), meaning lack of appreciation, more accurately corresponds to this particular Theophrastus's character than "Βραδύνους" ("Obtuse"), which indicates the presence of low intellectual capacities. Also, the lack of repetitive and restrictive interests and behaviors excludes autism spectrum disorder as a possible diagnosis. Minor psychiatric disorders and traits according to the Peripatetic School were attributed to the lack of rational control over appetites and behavior. Accordingly, «Αναίσθητος» is a phenomenological description of a stigmatizing inappropriate social behavior and the only help that might give is in increasing self-awareness. In our contemporary clinical practice, though, the early recognition and appropriate treatment of neurodevelopmental disorders in affected individuals leads to better clinical care and may diminish stigmatization. The co-existence of these two disorders in a character in such a different historical context reinforces their validity as diagnostic constructs and provides an example of the co-occurrence of neurodevelopmental disorders.

KEYWORDS: Neurodevelopmental disorders, attention deficit hyperactivity disorder adult, social (pragmatic) communication disorder, Theophrastus, Obtuse man, Anaisthetos.

Introduction

Neurodevelopmental Disorders

According to DSM-5¹ and ICD-11² neurodevelopmental disorders (ND) 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 range of developmental deficits varies from very specific limitations of learning or control of executive functions to global impairments of social skills or intelligence. The most prevalent are intellectual disability (ID), autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder

(ADHD), and communication disorders (CD). ID includes both intellectual and adaptive functioning deficits in conceptual, social, and practical domains. ASD is characterized by persistent deficits in social communication and social interaction across multiple contexts together with a restricted repetitive pattern of behavior, interests, or activities. Symptoms of ADHD include a persistent pattern of inattention and/or hyperactivity/impulsivity while CD is related to deficits in language, speech, and communication. Social pragmatic communication disorder (SPCD) is classified in DSM-5 as a discrete diagnostic category among CD. It is manifested by deficits in using communication for social purposes, impairment of the ability to change communication to match context or the needs of the listener, difficulties following rules for conversation and story-telling, and difficulties in understanding what is not explicitly stated.

Frequently NDs co-occur. Most of the symptoms are present throughout life and their appearance depends on a person's developmental stage. There is a significant unmet clinical and research need though, to understand the persistence into adulthood.³⁻¹¹ Nevertheless, in the last decade, awareness of NDs, especially for ADHD and ASD, has significantly increased.³ This is attributed to clinical, financial, educational, and political influences, stigma reduction, and the increasing knowledge of treatment efficacy.¹²

Historical perspectives

Historical references help us understand the evolution and validity of nosological concepts.

In the medical literature, the roots of the concept of intellectual development are attributed to Etienne Jean Georget (1795–1826) who wrote that “Idiocy” is a lack of development of intellectual faculties. Within the larger group of idiots, he included a subtype of “imbeciles” with higher cognitive abilities. Esquirol stated that idiocy was not an illness, but a condition in which intellectual faculties could not achieve sufficient development. He also distinguished imbecility from the severe intellectual impairment of idiocy. Although Autism was first described in the medical literature by Kanner and Asperger in the middle of the 20th century, medical descriptions that separate ASD from ID was reported much earlier. In a series of lectures, Down JL described 10 cases of “savant idiots” with exceptional abilities in a narrow field that could now be considered as exhibiting restrictive and repetitive patterns of behavior or activities.¹³

SCPD is a newly recognized diagnosis. Although it has been supported that it is a dimensional symptom profile that may be evident across a range of ND,¹⁴ it is now included as a distinct disorder in both DSM-5 and ICD-11.

Descriptions of ADHD as a disorder are presented in the medical literature of the last two centuries. Weikard first published 1775 descriptions of attention deficit as a medical condition.^{15,16}

Attempts to find examples of behavioral problems in historical accounts akin to those currently identified as ADHD have been attempted by many clinicians and historians.¹⁷ Recently, (Victor et al, 2018),¹⁸ compared Theophrastus' descriptions of “The Obtuse Man” («Αναίσθητος») to the DSM-5 ADHD symptoms and considered them as the oldest description compatible with the current conception of ADHD in adults. In the present work, we suggest that this character also possesses symptoms that may be attributed to another neurodevelopmental disorder, namely SCPD.

Theophrastus

Theophrastus was born in the island of Lesbos (371 B.C.). The main source for his life comes from Diogenes Laertius' work “Lives of Philosophers” written during the third century C.E., i.e., 600 years after Theophrastus' birth date. His name was Tyrtamus and he moved to Athens to pursue an education at Plato's Academy. He was fourteen years younger than Aristotle and in the Academy, the two men built a strong intellectual partnership. After Plato died in 347 B.C., Theophrastus witnessed Aristotle's scientific methodology and his approach to data collection and classification in various scientific studies in Assos, a town opposite to the island of Lesbos. In 335 B.C. Aristotle established in Athens a philosophical school known as “Peripatos” (“Walk”) named after Aristotle's habit to walk up and down while discussing philosophy. Theophrastus was a member of the Peripatetic school and Aristotle changed his name from Tyrtamus to Theophrastus which means “he who expresses himself like a god” because of his eloquence. When Aristotle left the city of Athens and withdrew to Chalcis on the island of Euboea in 323 B.C., he indicated Theophrastus to succeed him as head of Peripatus. Under Theophrastus' leadership, the school grew as a preeminent teaching institute. His stewardship of the philosophical school lasted thirty-six years, a period almost three times longer than that of Aristotle's leadership. He produced over two hundred works of varying lengths over a diverse range of subjects. Unfortunately only the titles of the majority of Theophrastus' works remain. He has a reputation as the founding father of botanical science because his works are considered excellent in scientific and research classification. The surviving scientific works of Theophrastus are indicative of the objectives of the Peripatos, which were to classify and study a wide range of natural phenomena.¹⁹⁻²²

Theophrastus' Characters

In his work "Characters" Theophrastus describes internal psychological features related to moral types. "Charactir- χαρακτήρ" meaning "engraving" comes from an instrument that engraves in wood, marble, or copper letters or signs. The objects over which letters or signs have been engraved differ from other objects that have not been engraved and do not possess these letters or signs. Character is synonymous with the notion of distinct features, and traits. Theophrastus is the first to use the metaphorical meaning for internal traits, psychic or moral, among different people.¹⁹

In "Characters" he follows a specific methodology that contains traces of the Peripatetic methodology applied across different disciplines. The emphasis is on classification and differentiation which means grouping certain shared attributes. Each character portrait is representative of a type that can be differentiated by their distinctive appearance, attributes, manner of speech, and modes of behavior. His interest is in the comic distortion of the behavior of the characters that are out of social norms. He uses the notions of excess and deficiency relative to a particular virtue. Aristotle developed the analysis of individual virtues and vices but he indicates, in abstract and general terms, the circumstances or behavior which are associated with each virtue and vice. Instead of an abstract circumstance, Theophrastus gives us a real occasion, and instead of an anonymous agent, a real individual. He locates his characters in a specific time and place. The time is the late fourth century. The place is Athens. And it is in Athens whose daily life he recreates for us in dozens of dramatic pictures and incidents. Such scenes and such people, cannot be found elsewhere.²⁰

Diogenes Laertius cites Characters twice, as "ethikoi caractires" and as "characters ethikoi". It is supposed that this is because of different copies of the work in circulation. In general, the title and the text betray evidence of interference from others. Thirty Characters are described. The first edition (1527) included 15 characters and it was only in 1786 that all 30 characters were discovered.^{20,21}

«Αναίσθητος» ("Anaisthetos", "The Obtuse Man")

The character «Αναίσθητος» (Anaisthetos) is the 14th of the thirty characters and has been translated into English as "the Obtuse Man". The definition though "Obtuseness may be defined as slowness of mind in speech and action" is considered spurious and interference from others is evident. One might claim that the «Αναίσθητος» ("The Obtuse Man"), by his speech and behavior, shows that he is the kind of man who is slow to

take things in. But the definition is unsatisfactory since slowness to take things in does not define his behavior or speech. On the other hand, «Αναίσθητος» comes from the verb αισθάνομαι which means I sense (from the senses) or I feel (from emotions). The prefix α denotes reverse meaning and «Αναίσθητος» could be translated as a lack of appreciation.²⁰ In Modern Greek this particular character has been named both «Αναίσθητος» (Anaisthetos)¹⁹ when translated from the original ancient Greek text and Βραδύνου (Obtuse) when translated from the Latin text.²² In our opinion, when we take into consideration Theophrastus's description, the term «Αναίσθητος», meaning lack of appreciation, is more appropriate than Βραδύνου, meaning slowness of mind. We believe that the description of this character is consistent with traits indicative of impulsivity, hyperactivity, and attentional and social-pragmatic deficits (table 1). Below we present the twelve statements describing traits corresponding to DSM-5 symptoms of ADHD and SPCD.

After a calculation with his counters and after computing the total asks the person sitting next to him 'What does it come to?' (i), When he has a lawsuit to defend and should be going to court, he forgets about it and goes into the country (ii). Those two statements may be considered inattentive symptoms.

At the theatre, he is found asleep in his seat when the audience has left (iii). It is easy to fall asleep in the modern theatre when attention flags. But this man falls asleep on a stone bench and is not woken even by the noise and jostle of the departing audience. This symptom may be associated with somnolence.

After a large supper, he is bitten by his neighbor's dog when he gets up and goes to the lavatory during the night (iv). When getting up from bed to go to the lavatory (somewhere outside his house), the dog bites him because he is clumsy enough to wake it up, probably by blundering about in the street outside.²⁰ This statement indicates sleep and attention problems.

He searches for some item that he has acquired and he is unable to find it, even though he stored it away himself (v). This is typical of inattention.

When a message arrives notifying him of the death of a friend and inviting him to the funeral, his face darkens and he bursts into tears and says "And the best of luck to him!" (vi). The phrase best luck to him is accidentally used because it is a phrase that expresses a wish for a good outcome of an action or a journey. It indicates verbally impulsive and inappropriate behavior, inconsistent with what would be socially correct. This statement indicates difficulties in social (pragmatic) communication.

Table 1. Theophrastus's description of Character "Αναίσθητος" (Anaisthetos)

«Αναίσθητος»	The Obtuse Man	
Ἔστι δε ἡ ἀναισθησία, ὡς ὄρω εἰπεῖν, βραδυτῆς ψυχῆς ἐν λόγοις καὶ πράξεσιν, ὁ δὲ ἀναισθητος τοιοῦτός τις,	Obtuseness may be defined as slowness of mind in speech and action	DEFINITION
i οἷος λογισάμενος ταῖς ψήφοις καὶ κεφάλαιον ποιήσας ἐρωτᾷ τὸν παρακαθήμενον· Τί γίνεται;	after a calculation with his counters and after computing the total asks the person sitting next to him "What does it come to?" <i>Ancient Greeks and Romans calculated using small stones in an abacus.</i>	ATTENTION
ii καὶ δίκην φεύγων καὶ ταύτην εἰσιέναι μέλλων ἐπιλαθόμενος εἰς ἀγρὸν πορεύεσθαι.	When he has a lawsuit to defend and should be going to court he forgets about it and goes into the country	ATTENTION
iii καὶ θεωρῶν ἐν τῷ θεάτρῳ μόνος καταλείπεσθαι καθεύδων.	At the theatre he is found asleep in his seat when the audience has left	SLEEP
iv καὶ πολλὰ φαγῶν καὶ τῆς νυκτὸς ἐπὶ θάκου ἀνιστάμενος <ἀποπλανώμενος> ὑπὸ κυνὸς τῆς τοῦ γείτονος δηχθῆναι.	After a large supper he is bitten by his neighbor's dog when he gets up and goes to the lavatory during the night <i>In ancient Athens there were no laboratories. People, especially the poor, were going outside for their needs. It is possible that he went to his neighbor's garden and was attacked by his dog</i>	ATTENTION SLEEP
v καὶ λαβῶν <τι> καὶ ἀποθεῖς αὐτός, τοῦτο ζητεῖν καὶ μὴ δύνασθαι εὑρεῖν.	He searches for some item that he has acquired and he is unable to find it, even though he stored it away himself	ATTENTION
vi καὶ ἀπαγγέλλοντος αὐτῷ, ὅτι τετελευτήκε τις αὐτοῦ τῶν φίλων, ἵνα παραγένηται, σκυθρωπάσας καὶ δακρύσας εἰπεῖν· Ἀγαθὴ τύχη.	When a message arrives notifying him of the death of a friend and inviting him to the funeral, his face darkens and he bursts into tears and says "And the best of luck to him!" <i>The phrase best luck to him is accidentally used because it is a phrase that expresses a wish for a good outcome of an action or a journey</i>	SPC
vii δεινὸς δὲ καὶ ἀπολαμβάνων ἀργύριον ὀφειλόμενον μάρτυρας παραλαβεῖν.	He is also apt to get witnesses to support him when he is taking repayment of money that is owed him	ATTENTION
viii καὶ χειμῶνος ὄντος μάχεσθαι τῷ παιδί, ὅτι σικύους οὐκ ἠγόρασεν.	He is annoyed with his slave for not buying cucumbers during the winter	ATTENTION SPC
ix καὶ τὰ παιδιά ἑαυτοῖς παλαίειν ἀναγκάζων καὶ τροχάζειν [καὶ] εἰς κόπους ἐμβάλλειν.	He tires out his children by forcing them to wrestle and run races with him	HYPERACTIVITY SPC
x καὶ ἐν ἀγρῷ αὐτὸς φακῆν ἔψων δις ἄλας εἰς τὴν χύτραν ἐμβαλὼν ἄβρωτον ποιῆσαι.	In the country when he is boiling lentil soup he puts salt into the pan twice and makes it inedible	ATTENTION
xi καὶ ὕοντος τοῦ Διὸς εἰπεῖν· † ἡδύ γε τῶν ἀστρῶν νομίζει, ὅτι δὴ καὶ οἱ ἄλλοι λέγουσι πίσης †	If it is raining he says "How sweetly the stars smell," when everyone else says "the earth" <i>This phrase is considered the most difficult according to Adamantios Korais and "locum desperatum" according to Casaubon because there is no effective translation</i>	SPC
xii καὶ λέγοντός τινος· Πόσους οἶε κατὰ τὰς Ἡριαίας [Meursius: Ἴερὰς] πύλας ἐξενηρέχθαι νεκρούς; πρὸς τοῦτον εἰπεῖν· Ὅσοι ἐμοὶ καὶ σοὶ γένοιτο.	When someone remarks "You can't imagine how many bodies have been taken out to the cemetery through the Erian Gates," he answers "I wish you and I could have such a windfall" <i>Erian gates were in the eastern direction of Athens close to Keramikos cemetery</i>	SPC

He is also apt to get witnesses to support him when he is taking repayment of money which is owed him (vii). The payer needs proof that he has paid. But for the recipient to call witnesses needs no proof that he has been paid. He is annoyed with his slave for not buying cucumbers during the winter (viii). Both statements indicate problems with attention and poor social communication skills.

He tires out his children by forcing them to wrestle and run races with him (ix). According to Diggle²⁰ "it is a lack of appreciation to make them wrestle and run against himself: he takes no account of his greater strength". This statement may be attributed to hyperactivity and problems in social (pragmatic) communication.

In the country when he is boiling lentil soup he puts salt into the pan twice and makes it inedible (x). It is a statement for inattentive symptoms.

If it is raining, he says 'How sweetly the stars smell', when everyone else says 'the earth' (xi). When someone remarks 'You can't imagine how many bodies have been taken out to the cemetery through the Erian Gates', he answers 'I wish you and I could have such a windfall.' (xii) These two statements indicate that «Αναίσθητος» after processing an input of a message responds impulsively and erroneously indicating impulsivity and social (pragmatic) communication deficits.

Discussion

The public behavior presented by Theophrastus in the portrait of "The Obtuse Man" may be considered as the first historical description of an adult person presenting co-occurrence of ADHD and SPCD. Both disorders are included in the DSM-5 Neurodevelopmental Disorders group condition. Traits for inattention are present in statements i, ii, iv, v, vii, viii, and x, for hyperactivity in ix and impulsivity in vi, ix, and xii. Social communication problems are evident in statements vi, viii, ix, xi, and xii.

Our view is in line with Victor et al (2018)¹⁸ consideration that some of the communication problems are related to impulsivity or inattention, but we question his idea that they are caused by cognitive limitations. We propose instead, that they are attributable to SPCD, which is characterized by deficits in using language for social purposes, appropriately matching communication to the social context, and following rules of the communication context. According to DSM-5 the symptoms of SPCD are not better explained by ASD or ID and global developmental delay. The «Αναίσθητος» was an equal member of the Athenian Democracy with family and slaves, was able to calculate correctly and according to Theophrastus' description does not present intellectual and adaptive functioning deficits in all domains;

thus intellectual disability does not justify his pragmatic communication problems. Also, in Theophrastus' text, there is no description of rigid, repetitive, and restrictive interests and behaviors that would be indicative of ASD while there are five statements that support the possible occurrence of an SPCD.

Since ID is not justified by the description, in the Modern Greek language the original name of the character «Αναίσθητος» which includes the meaning of lack of appreciation is preferred to the translation "Βραδύνου" (Obtuse) indicating the presence of low intellectual capacities.

Theophrastus is following the Peripatetic school methodology to lead to certain shared attributes in a realistic setting that is the urban Athens from 330 to 319 B.C. The primary objective was the collection and interpretation of information to raise and attempt the resolution of theoretical difficulties. To achieve this objective, the Peripatetic method involved establishing a line of inquiry, amassing all the relevant evidence, examining the views of others in line with that evidence, and agreeing or disagreeing openly by showing weaknesses in logic and reasoning. Recently,²¹ it has been argued that the Characters can no longer be dismissed as a curiously lopsided offshoot of Aristotle's ethical philosophy or as the comic jottings of an inferior philosophical mind. It is an innovative vibrant and highly influential work that merits its unique contribution to the fields of ethics, comedy, and rhetoric. Centuries after his initial writing, Theophrastus' observations about human behavior still resonate with the audience and still give rise to humor. The "errors" of the character type are the inappropriate form of speech and conduct that unconsciously engage in. By giving a clear illustration of poor conduct, inappropriate speech, behavioral follies, bad timing, and misjudgments, Theophrastus underscores the importance of appropriate and well-timed social behavior.²¹

The peripatetic school adopted the Socratic school of philosophers²³ attributing minor psychiatric disorders or traits to the lack of rational control over appetites and behavior. It may be supported that Theophrastus' text has been adopted all these years because it leads to the recognition of inappropriate social behavior. Increasing self-awareness was then the only help offered to persons presenting with the portraits that the characters describe. In modern psychiatry, though, Neurodevelopmental Disorders such as ADHD can be appropriately and effectively treated.³ The treatment of these disorders in affected individuals not only leads to better clinical care but also may diminish stigmatization.^{24,25}

A limitation of the study is that ancient texts are by their nature difficult in their interpretation of psycho-

logical traits. It is noteworthy though, that centuries after his initial writing, Theophrastus' observations about human behavior still resonate with the audience, and each character is representative of a type that can be differentiated by their distinctive appearance, attributes, manner of speech, and modes of behavior. Another limitation is that the text does not provide us with information on the continuous persistence of the symptoms from childhood as one should have to give a neurodevelopmental diagnosis in adulthood.

In conclusion, we support the notion that the «Αναίσθητος» (Obtuse Man) as described by Theophrastus is the earliest description of neurodevelopmental symptoms corresponding to the co-occurrence of ADHD and SPCD and that in Modern Greek vocabulary the original term «Αναίσθητος» (Anaisthetos) instead of “Βραδύνουζ” (Obtuse) is more accurate for this particular character. The co-existence of these two disorders in a character in such a different historical context reinforces their validity as diagnostic constructs and provides an example of the co-occurrence of two NDs.

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Ειδικό άρθρο

Ο χαρακτήρας “Αναίσθητος”/“Βραδύνους” του Θεόφραστου: η πρώτη «φαινομενολογική» προσέγγιση νευροαναπτυξιακών διαταραχών σε ενήλικο

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ΠΕΡΙΛΗΨΗ

Ο Θεόφραστος (381–278 π.Χ.), χρησιμοποίησε πρώτος τον όρο χαρακτήρας για την περιγραφή εσωτερικών, ψυχικών ή ηθικών διακριτών γνωρισμάτων των ατόμων. Στο έργο του «Χαρακτήρες» με οξυδέρκεια, ακριβή διατύπωση και απλό, απέριττο ύφος πραγματοποιεί λεπτή ψυχολογική ανάλυση ατόμων της εποχής του. Ο χαρακτήρας «Αναίσθητος» έχει μεταφραστεί στην αγγλική γλώσσα ως «Βραδύνους» (“The Obtuse Man”) και στη σύγχρονη ελληνική γλώσσα είτε ως «Αναίσθητος» δηλώνοντας έλλειμμα στην κατανόηση είτε ως «Βραδύνους» δηλώνοντας χαμηλή νοητική λειτουργία. Η περιγραφή του Θεόφραστου στον συγκεκριμένο χαρακτήρα είναι συμβατή με τη συνύπαρξη σε ενήλικο άτομο δύο νευροαναπτυξιακών διαταραχών: της διαταραχής ελλειμματικής προσοχής υπερκινητικότητας (ΔΕΠΥ) και της διαταραχής κοινωνικής πραγματολογίας (ΔΚΠ) σύμφωνα με την 5η Έκδοση του Διαγνωστικού Ταξινομικού Συστήματος για τις Ψυχικές Διαταραχές (DSM-5). Δέκα από τις δώδεκα περιγραφές αντιστοιχούν σε συμπτώματα για τη ΔΕΠΥ ενώ σε πέντε περιγραφές αντικατοπτρίζονται συμπτώματα της ΔΚΠ. Θεωρούμε ότι η συνολική περιγραφή του χαρακτήρα δεν δικαιολογεί τη διάγνωση της νοητικής υστέρησης. Η απόδοση επομένως στην σύγχρονη ελληνική γλώσσα του χαρακτήρα ως «Αναίσθητος» που δηλώνει έλλειμμα στην κατανόηση αντιστοιχεί ακριβέστερα στην έννοια που περιγράφεται συγκριτικά με τον όρο «Βραδύνους» ο οποίος παραπέμπει σε χαμηλή νοητική λειτουργία. Επίσης, διάγνωση της διαταραχής του φάσματος του αυτισμού αποκλείεται διότι δεν περιγράφονται στερεότυπα και επαναληπτικά ενδιαφέροντα και συμπεριφορές. Σύμφωνα με τις αρχές της Περιπατητικής Σχολής οι ήσσονες ψυχικές διαταραχές και τα χαρακτηριστικά οφείλονται σε αδυναμία ελέγχου του λογικού ελέγχου στις επιθυμίες και τη συμπεριφορά. Στο πλαίσιο αυτό η φαινομενολογική περιγραφή του «Αναίσθητου» στιγματίζει την ακατάλληλη κοινωνική συμπεριφορά και η μόνη βοήθεια που δίνει είναι να αυξάνει την αυτεπίγνωση. Στη σύγχρονη κλινική πρακτική όμως, η πρώιμη αναγνώριση και αντιμετώπιση των νευροαναπτυξιακών διαταραχών στα πάσχοντα άτομα έχει ως αποτέλεσμα την καλύτερη κλινική φροντίδα και μπορεί να μειώσει τον στιγματισμό. Η ταυτόχρονη περιγραφή των δυο αυτών διαταραχών σε ένα τόσο διαφορετικό ιστορικό πλαίσιο ενισχύει την εγκυρότητά τους ως διαγνωστικών κατασκευών και αποτελεί χαρακτηριστικό παράδειγμα συνύπαρξης δύο νευροαναπτυξιακών διαταραχών.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: Νευροαναπτυξιακές διαταραχές, διαταραχή ελλειμματικής προσοχής υπερκινητικότητας ενηλίκων, διαταραχή κοινωνικής πραγματολογίας, Θεόφραστος, «Βραδύνους», «Αναίσθητος».

Brief communication

Tobacco and Alcohol and Cannabis Experience Questionnaires. Greek translation and test-retest reliability

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ABSTRACT

The Tobacco and Alcohol Questionnaire (TAQ) and the Cannabis Experience Questionnaire (CEQ) are two instruments employed in the evaluation of substance use. The First Episode Psychosis (FEP) study in Athens employed two versions of those questionnaires, as part of a battery of psychometric tools, detecting environmental and genetic factors associated with FEP and addressed specifically the distinctive characteristics of patients with FEP. The goal of the present study is to present those two versions, regarding their content, their use in international research, their translation in Greek, and their test-retest reliability. The two questionnaires were translated by two independent translators and administered to 32 subjects with FEP twice, in order to be tested for test-retest reliability. Cohen's kappa was used to measure agreement between qualitative variables and ICC between quantitative variables. Significant agreement was found between the two measurements in all items of the TAQ version and almost all items of the CEQ version. Our study is an indication that both translations are reliable, although a more thorough test of their psychometric properties is needed. Both might be used in the Greek research field as part of a broad package of psychometric tools, specifically addressed to patients with FEP.

KEYWORDS: Psychosis, tobacco, alcohol, cannabis, translation, reliability.

Introduction

First-episode psychosis (FEP) emergence and its clinical outcome might be attributed to various parameters and gene-environment interaction plays a pivotal role in it. The necessity of a battery of psychometric tools, to detect environmental and genetic factors associated with FEP and addressed specifically the distinctive characteristics of patients with FEP, is of importance to the relevant research field. The Athens FEP Study, a longitudinal prospective research project, has organized such an assessment schedule, oriented to FEP patients, which relies in a considerable amount on the working pack-

age of the EUGEL-versions of psychometric tools. EUGEL, (European Network of National Schizophrenia Networks Studying Gene-Environment interactions), is an international multi-center study aiming to explore gene-environment interaction in relation to the emergence and clinical course of schizophrenia.

Among the most important environmental risk factors for FEP is high potency cannabis (Adj OR from 4.5 to 8),¹ while other recreational substances, such as stimulants, tobacco, and alcohol, may have a role in the incidence variation of psychotic disorders.² Thus, two instruments employed in the evaluation of substance

use, the EUGEI versions of the Tobacco and Alcohol Questionnaire (TAQ) and the Cannabis Experience Questionnaire (CEQ), are included in the “Athens FEP Study” research battery.^{3,4}

The TAQ_{EUGEI} has been used in already published Multicenter EUGEI case-control studies, to address the potential confounding role of tobacco and alcohol, based on their possible association with cannabis use and variation in the incidence of psychotic disorders, as well as cannabis use and FEP symptom dimensions.^{5–7}

The CEQ_{EUGEI}⁵ is the second modified version of the original instrument.^{8,9}

The information from the CEQ_{EUGEI} was analyzed to investigate issues, such as differences in the patterns of cannabis use across Europe, the main effect of different cannabis exposure on the risk of psychosis, and the proportion of new cases of psychosis attributable to cannabis use across the different study sites.¹

The CEQ_{EUGEI} has been employed in several case-control studies across sites of the Multicenter EUGEI research project. Among the findings of those studies are the following:

1. Participants who used high-potency cannabis daily had nearly five times increased odds of psychosis, compared to never users, and the incidence of psychosis variation was associated with differences in frequency of cannabis daily use and in high-potency cannabis use.⁵
2. Regular cannabis use was among the environmental exposures that contributed, along with childhood trauma, to the positive additive interaction with genetic liability for schizophrenia spectrum disorders.¹⁰
3. FEP patients and controls who had ever used cannabis, exhibited a higher IQ by three points compared to never users. Furthermore, FEP patients who used cannabis occasionally or daily had better social premorbid adjustment than never-users. However, both patients and control daily-users had lower premorbid academic adjustment compared to occasional and never users.¹¹
4. FEP patients with lifetime daily use of high-potency cannabis exhibited more positive and fewer negative symptoms compared to non-users or low-potency users. Schizophrenia-polygenic-score and cannabis use, independently from each other, are related to more severe positive symptomatology.^{2,6,12}

The goal of the current study, which is part of the Athens-FEP Study, is to present the Greek translation of TAQ_{EUGEI} and CEQ_{EUGEI} and to examine the test-retest

reliability of the Greek translations of the two questionnaires.

Material and Method

Both the English version of TAQ_{EUGEI} as well as CEQ_{EUGEI} were provided to the primary investigator of the Athens-FEP project and through him to our team by the EUGEI and its official web-based training area. The researchers were considered qualified in the administration of the English versions of the questionnaires after being trained with a word package and after assessing acceptable scores for the Inter-Rater reliability measurement videos, both provided by that web-training area.

Both questionnaires were translated into Greek by two independent qualified translators, who reached an agreement, after their initial translations, in repeated meetings. The principal investigator checked the final version of the questionnaires. Subsequently, the FEP-project researchers administered the translated questionnaires to three patients, in group sessions and then checked if there was agreement in their answers and if the translated tools were comprehensible and handy.

The reliability of the Greek version of the two psychometric tools was tested by the test-retest method.

The two translated questionnaires were administered to 32 patients by three qualified researchers twice, with an intermediate period of three weeks between the first and second administration. All were diagnosed with FEP. Their sociodemographic characteristics and final diagnoses, after one year of follow-up, are presented in table 1. The patients were recruited from the Early Psychosis Intervention Outpatient Service¹³ of Eginition University Hospital and from the Psychiatric Clinic of Sismanoglion General Hospital. Twenty-four of our recruited subjects were followed up in Eginition and eight of them in Sismanoglion and all of them participated in the Athens-FEP research project. Informed consent was obtained from all patients, following a detailed description of the research objectives. The ethics committee and the Institutional Review Board at Eginition University Hospital approved the study protocol.

TAQ_{EUGEI} was used as follows:

Lifetime tobacco use was divided into 3 categories: (a) smoked <10 cigarettes per day, (b) smoked ≥10 cigarettes or more per day, (c) never used. Alcohol consumption was measured through the mean number of alcoholic drinks consumed daily on an average week.⁵

Current use of tobacco cigarettes: smoking 10 cigarettes or more per day =1

Table 1. Participants' sociodemographic characteristics, diagnoses.

	N=32 (%)
Gender	
Males:	19 (59.4)
Females:	13 (40.6)
Age (years), mean (SD)	26.2 (7.7)
Age of Onset	23.7 (7.7)
Years of education, mean (SD)	13.6 (2.4)
Ever Employed	
Yes	22 (68.7)
No	10 (31.3)
Migration	
Yes	3 (9.4)
No	29 (90.6)
Final ICD-10 diagnoses	
Schizophrenia (F20)	16 (50%)
Acute and transient psychotic disorders (F23)	4 (12.5%)
Delusional Disorders (F22)	1 (3.1%)
Schizoaffective Disorder (F25)	1 (3.1%)
Other non-organic psychotic disorders (F28)	1 (3.1%)
Unspecified non organic psychosis F29	1 (3.1%)
Severe depressive episode with psychotic symptoms (F32.3)	2 (6.3%)
Bipolar Disorder (F31)	3 (9.4%)
Mental and behavioral disorders due to use of cannabinoids (F12.5)	2 (6.3%)

Current use of alcohol: drinking 10 alcohol units or more per week=1.

Low or no use scored as 0 and use scored as 1 in categorical variables.⁶

Other investigators proposed a different way to evaluate tobacco use, by separating subjects into cigarette and non-cigarette users, with emphasis on the last thirty days of use.⁷

CEQ_{EUGEI} consists of 17 sections and its administration provides a thorough evaluation of the use of cannabis and other recreational drugs history. It includes the following dimensions: (1) age at first use, (2) frequency of current and lifetime use, (3) assessment of the type of use, through which cannabis potency is estimated, (4) methods of consuming cannabis, (5) money spent weekly on cannabis during the period of most frequent use, (6) subjective experiences reported by individuals as immediate effects of cannabis use, which are recorded in a list of nine predetermined paranoid-dysphoric and euphoric symptoms,⁹ and (7) history of other drugs

used as inhalants, crack, cocaine, amphetamines/stimulants, sedatives, and opioids.

The lifetime cannabis use history section aims to identify the pattern of most frequent use during three age periods: 0–11 years old, 12–16 years old, and 17 and older. It comprises questions on the type of cannabis use, the quantity, the methods, the setting (socially and/or alone), and the frequency of use for each of the above three age periods.

Frequency of use is estimated by a seven-point scale fluctuating from “every day” to “I have only used cannabis once or twice”.

The potency of cannabis is estimated through the type of cannabis use most commonly met across Europe. Two potency cannabis categories are described: The low (Δ^9 -tetrahydrocannabinol - THC<10%) and the high (THC >10%).¹⁰ “Hash (cannabis resin/solid)” and “Imported Herbal cannabis” are included in the low-potency, whereas “Home-grown skunk/Sensimilla” and “Super skunk” are in the high-potency category.¹⁴

The CEQ_{EUGEI} “lifetime cannabis use” section comprises questions investigating symptoms of cannabis dependency, both lifetime and in the last twelve months.

The final section of the instrument explores other drugs, patterns of use, and symptoms of dependency.

The statistical significance was set at 0.05 and analyses were conducted using SPSS statistical software (version 22.0). Cohen's kappa was used to measure the agreement between qualitative variables and ICC the agreement between quantitative variables.

Results

The translations of TAO_{EUGEI} and CEQ_{EUGEI} in Greek are presented as supplementary material.

A significant agreement was found between the two measurements in all items of TAO_{EUGEI} (table 2) and almost all items of CEQ_{EUGEI}, except seven (table S1). For five of those seven items, a tendency for the significant agreement was found between the two measurements ($P<0.1$). The two items that differed in the answers between the two measurements were one sub-item about the reasons that led the patient to use cannabis, described as “other”, allowing the respondent to choose among a multitude of different answers and an item regarding the current use of cannabis, which is a situation that might have changed from first to the second measurement. That is why the overall test-retest reliability of CEQ_{EUGEI} is not affected by the lack of agreement between those items. Significant agreement coefficients

Table 2. Tobacco and Alcohol Questionnaire (test-retest results)

		Test		Retest		Cohen's kappa or ICC	P
		N	(%)	N	(%)		
Section Tobacco: 1.a	NO	21	65.6	22	68.8	0.93+	<0.001
	YES	11	34.4	10	31.3		
Section Tobacco: 1.b	NO	30	96.8	32	100.0	0.65+	<0.001
	YES	1	3.2	0	0.0		
Section Tobacco: 1.c	NO	30	100.0	32	100.0	1.00+	<0.001
	YES	0	0.0	0	0.0		
Section Tobacco: 1.d	NO	30	100.0	32	100.0	1.00+	<0.001
	YES	0	0.0	0	0.0		
Section Tobacco: 2.a, mean (SD) median (interquartile range -IR)		21.9 (8)	22.5 (15–30)	23 (10)	23 (15–30)	0.96++	<0.001
Section Tobacco: 2.b, mean (SD) median (IR)		0 (0)	0 (0–0)			–	–
Section Tobacco: 2.c, mean (SD) median (IR)		0 (0)	0 (0–0)			–	–
Section Tobacco: 2.d, mean (SD) median (IR)		0 (0)	0 (0–0)			–	–
Section alcohol: 1.a	NO	23	71.9	24	75	0.92+	<0.001
	YES	9	28.1	8	25		
Section alcohol: 1.b, mean (SD) median (IR)		2.5 (2.3)	1.5 (1–3)	3 (2)	2 (1–3)	1.00++	<0.001
Section alcohol: 2.a	NO	31	96.9	31	96.9	1.00+	<0.001
	YES	1	3.1	1	3.1		
Section alcohol: 2.b, mean (SD) median (IR)		2 (–)	2 (2–2)	0 (0)	0 (0–0)	–	–
Section alcohol: 2.c, mean (SD) median (IR)		10 (–)	10 (10–10)	0 (2)	0 (0–0)	–	–
Section alcohol: 3.a	NO	30	96.8	31	96.9	1.00+	<0.001
	YES	1	3.2	1	3.1		
Section alcohol: 3.b, mean (SD) median (IR)		20 (–)	20 (20–20)	20 (–)	20 (20–20)	–	–
Section alcohol: 3.c, mean (SD) median (IR)		8 (–)	8 (8–8)	8 (–)	8 (8–8)	–	–

+Cohen's kappa (for qualitative variables), ++ICC (for quantitative variables)

ranged from 0.48 to 1.00, and insignificant agreement coefficients ranged from 0.07 to 1.00.

Discussion

The translated TAQ_{EUGEI} in Greek presents an excellent test-retest reliability for all items and the translated CEQ_{EUGEI} for almost all items. Both of them are important psychometric tools that might be used among psychotic patients for epidemiologic research or research in the field of drug-abuse as well. No reference was found for

TAQ_{EUGEI} or CEQ_{EUGEI} being employed in non-psychotic samples.

Our study is an indication that the two translations are reliable. Among its limitations, is the lack of a more thorough test of their psychometric properties and especially of their validity.

Compared to the Alcohol Use Disorders Identification Test (AUDIT), another tool translated and weighed in Greek for the assessment of alcohol intake, TAQ_{EUGEI} does not explore the levels of risk for alcohol use disorders as

AUDIT does,¹⁵ but it has been developed as an easily administered questionnaire to briefly record quantitatively both tobacco and alcohol consumption, to explore their association with the development of psychotic symptoms. CEQ_{EUGEI} on the other hand, with its list of paranoid-dysphoric and euphoric symptoms, is more suitable than any other psychometric tool for the evaluation

of the use of a wide range of recreational substances in patients with FEP.

More importantly, both questionnaires are part of a broad, well-established research package of psychometric tools, specifically addressed to patients with FEP, which might be used in the Greek research field.

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Σύντομο άρθρο

Ερωτηματολόγιο Καπνού και Αλκοόλ και Ερωτηματολόγιο για Εμπειρία από χρήση Κάνναβης. Ελληνική μετάφραση και αξιοπιστία ελέγχου-επανελέγχου

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ΠΕΡΙΛΗΨΗ

Το Ερωτηματολόγιο Καπνού και Αλκοόλ και το Ερωτηματολόγιο Εμπειρίας Χρήσης Κάνναβης είναι δύο ψυχομετρικά εργαλεία που χρησιμοποιούνται στην εκτίμηση της χρήσης ουσιών. Η μελέτη FEP της Αθήνας χρησιμοποίησε δύο εκδοχές των δύο ερωτηματολογίων, ως μέρος ενός πακέτου ψυχομετρικών εργαλείων, που διερευνούν την αλληλεπίδραση γονιδιακών και περιβαλλοντικών παραγόντων στην εκδήλωση FEP, ειδικά σχεδιασμένων για ασθενείς με τα ειδικά χαρακτηριστικά των ατόμων με FEP. Στόχος της παρούσας εργασίας είναι η παρουσίαση των δύο εκδοχών αναφορικά με το περιεχόμενό τους, τη χρήση τους στη διεθνή έρευνα, την ελληνική τους μετάφραση και την test-retest αξιοπιστία τους. Τα δύο ερωτηματολόγια μεταφράστηκαν από δύο ανεξάρτητους μεταφραστές και χορηγήθηκαν σε 32 άτομα με FEP δύο φορές. Για τη στατιστική ανάλυση χρησιμοποιήθηκε το στατιστικό πακέτο SPSS (version 22). Οι συντελεστές Cohen's kappa χρησιμοποιήθηκαν για τον έλεγχο συμφωνίας μεταξύ ποιοτικών μεταβλητών και τα ICC μεταξύ ποσοτικών μεταβλητών. Στατιστικά σημαντική συμφωνία διαπιστώθηκε σε όλα τα λήμματα της εκδοχής του TAQ ερωτηματολογίου και σχεδόν σε όλα της αντίστοιχης του CEQ. Η μελέτη μας αποτελεί μια ένδειξη ότι οι δύο μεταφράσεις είναι αξιόπιστες, παρότι ένας πιο ολοκληρωμένος έλεγχος των ψυχομετρικών ιδιοτήτων τους είναι απαραίτητος. Επιπλέον, θα μπορούσαν να χρησιμοποιηθούν στην Ελλάδα, ως μέρος ενός εκτεταμένου πακέτου ψυχομετρικών εργαλείων για άτομα με FEP.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: Ψύχωση, καπνός, αλκοόλ, κάνναβη, μετάφραση, αξιοπιστία.

Brief communication

Physicians' attitudes towards euthanasia and correlation with their spirituality

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ABSTRACT

"Suffering" patients' wishes concerning hastening their own death by means of euthanasia, raised by personal, psychological, social and other motives, are becoming increasingly common. This raises controversies and marks challenges within both the scientific community and the public. The aim of this study was to investigate physicians' attitudes towards euthanasia and its correlation with their spirituality. The final sample consisted of 93 physicians (64.5% men), whose attitudes on euthanasia were evaluated using Euthanasia Attitude Scale (EAS) and (DSES). Physicians' attitudes correlate with their specialty ($p=0.037$), years of service ($p=0.037$), as well as the number of end stage patients they cared for and died within the last 12 months ($p=0.016$). Oncologists and other physicians with similar specialty, those with longer clinical experience and those who treat more end-stage patients do strongly oppose to the above practices. Spirituality, estimated with Daily Spiritual Experience Scale –DSES, is correlated with a negative attitude toward euthanasia ($p<0.001$). Finally, a considerable gap in physicians' training regarding the management of end-stage patients has been highlighted. Physicians are opposed to euthanasia and they require the acquisition of competencies in end-of-life care, in order to fulfill their profession's current and future demands in the domain of palliative care.

KEYWORDS: Euthanasia, physicians, attitudes, spirituality.

Introduction

The Merriam-Webster Online Dictionary defined "euthanasia" as "The act or practice of killing or permitting the death of hopelessly sick or injured individuals (such as persons or domestic animals) in a relatively painless way for reasons of mercy..."¹

In ancient times, the term euthanasia was used not only to express the cessation of a painful life full of despair, but also to express the meaning of glorious and heroic death, the sacrifice for high ideals, the avoidance of an honorable death. On the contrary, the medical community of the time condemned euthanasia and

medically assisted suicide, as evidenced by the phrase in Hippocrates' oath: nor should I ever give such advice"²

The first attempt to legalize euthanasia took place in 1906 in Ohio, USA. The bill to the relevant state legislature sought to allow the administration of a lethal anesthetic to patients who are suffering from a fatal trauma, irreversible disease or incurable pain. The final decision was rejected and the issue gradually began to decline. In 1935 it was revived with the founding in England of the "Voluntary Euthanasia Legalization Society" which, renamed to the "Dignity in Dying" that continues its activities to this day with more than 25,000 members.³ In April

2002, the Netherlands became the first European country to legalize the termination of patients' lives by physicians.⁴

The aim of this study was to investigate Greek physicians' attitudes and beliefs towards euthanasia and physician-assisted suicide.

Material and Method

Participants

A cross-sectional study was conducted among 120 physicians, members of the Medical Association of Athens. Avalanche sampling was used to select the study sample. Physicians whose specialty is not related to a clinical subject, which limits their direct contact with end-stage patients (e.g., microbiologists) were excluded.

Measures

The questionnaire included information about demographics data on the relationship of physicians with end-stage patients.

The *Daily Spiritual Experience Scale (DSES)* consists of 16 items.⁵ The first 15 are scored on Likert six-point scale. All items are given in positive terms. The total score is accounted for by the sum of all 16 items and ranges from 16–94. Permission to translate the original English version of DSES into Greek was obtained from Lynn Underwood. The translation was done using the same process conducted with *Euthanasia Attitude Scale (EAS)*. Lynn Underwood reassured that psychometric properties for translated versions of the DSES are strong, with Cronbach's alphas ranging from 0.86–0.98.

EAS was developed by Holloway, Hayslip and Murdock, in 1995 and consists of a questionnaire with 30 items related to consent in passive or active euthanasia, the rights of end-stage patients, the place of modern technologies in life preservation, brain death, the role of the physician in the final phase of the patient and other ethical and legal issues.⁶

The answers are given on a 4-point Likert scale for each participant, the numbers chosen for the 30 sentences are added together creating a score, which can range from 30 to 120. Permission to translate the original version of EAS into Greek was obtained from Bert Hayslip. The translation was done using the guidelines for the process of cross-cultural adaptation of self-report measures.⁷ Cronbach's alpha, was calculated and found to be 0.944.

Statistical analysis

All data were analyzed using SPSS statistical program, version 22. Absolute (N) values, mean (M), and standard

deviation (\pm SD) were used for description of the sample and the EAS and DSES items. The normal distribution of the results was checked by the Kolmogorov-Smirnov test. Student's t-test was used to compare mean values in the two independent groups, and one-way ANOVA was used for more than two groups. The level of statistical significance was set at 5%.

Results

The study sample were 93 physicians (77.5%) while 64.5% were men with a mean age of 53.7 years (SD=7.4) and an average year of service of 25.4 (SD=8.0) years, while the vast majority of the sample (95.7%) were Orthodox.

Mean value of EAS total was found to be 74.62 (SD 14.33) and mean value of DSES was 52.25 (SD 16.17). Mean value (SD) of 5 factors of EAS questionnaire were found as follows: general orientation towards euthanasia: 24.1 (SD 7.4), patients' rights issues 19.5 (SD 3.5), role of life sustaining technology 13.2 (SD 2.5), professional's role 10.9 (SD 1.1), ethics and values 11.5 (SD 3.2).

The inter-correlation matrix for the EAS dimensions and DSES is presented in table 1. A very strong positive correlation was found between EAS-factors and EAS-total. Strong negative correlation was found between general orientation towards euthanasia, patients' rights issues, role of life sustaining technology, EAS total with DSES scale, while moderate negative correlation was found between ethics and values and DSES.

In table 2 it is shown that physicians with >21 years of service overall disapprove of euthanasia practices (mean<75) which is even more pronounced when clinical experience exceeds 30 years (mean EAS scale=69.9). In contrast, physicians who have been practicing the profession for less than 20 years seem to adopt positive views (mean=79.9). Also, physicians who cared for more than 10 patients who died in the last year scored significantly lower on the EAS scale than physicians with none or 1–10 patients and they clearly disapprove of euthanasia ($p=0.016$). And those physicians who have not treated such a category of patients seem to be in favor of euthanasia. Oncologists and physicians of related specialties were not in favor of euthanasia as compared to physicians of other specialties who not only are not opposed but seem to approve it ($p=0.037$). Physicians' visit in worship places seems to be related to their attitudes towards euthanasia ($p<0.001$). In particular, those who go to Church at least once a month have a negative attitude, while the rest express a more or less positive attitude. In fact, people who say they never attend Church show the highest average on the EAS scale.

Table 1. Intercorrelations between the EAS Factors, EAS total and DSES.

	Patients' rights issues	Role of life sustaining technology	Professional's role	Ethics and values	EAS Total	DSES
General orientation towards Euthanasia	0.841*	0.723*	0.311**	0.926*	0.973*	-.622*
Patients' rights issues		0.770**	0.262**	0.783**	0.897**	-.641**
Role of life sustaining technology			0.293**	0.695*	0.8288**	-.608*
Professional's role				0.346**	0.400*	-.162**
Ethics and values					0.933*	-.587*
EAS Total						-.654*

*p<0.01, **p<0.05

Table 2. Associations of the Euthanasia Attitude Scale (EAS) with demographics.

Category	n	Mean	SD	p-value
Years of service				
<=20	28	79.93	13.37	0.037
21-30	43	73.60	14.37	
>30	22	69.86	13.89	
Treating end-stage patients				
2-3 times a year	48	77.17	15.01	0.025
Once every 2-3 months	24	75.96	13.57	
More than once a month	21	67.29	11.31	
Number of end stage patients who were lost (died) in the last year				
0	31	77.74	16.71	0.016
1-10	49	75.35	12.32	
11+	13	64.46	11.37	
Need for training on psychological support in end stage patients				
no	37	73.70	12.55	0.060
yes	56	75.23	15.46	
Physicians' specialty				
Oncologists and related specialties	34	70.6	14.22	0.037
Physicians of other specialties	59	77.0	13.97	
Frequency of visits a place of worship.				
Every week	4	67.8	12.8	<0.001
Once/Month	21	64.3	8.4	
Only at special days	54	78.5	14.5	
Almost never	10	80.5	11.3	

Discussion

The study attempted to compare the demographics of physicians with their views on euthanasia. It was initially found that those attitudes were not related to their gender and age. Although this finding partially confirms a previous study concerning Greek physicians,⁸ literature review has shown that other researchers who sought to correlate the aforementioned factors with the views of physicians ended up with contradictory results.⁹ Our study results showed that physicians' views on euthanasia are influenced by years of professional experience.

This finding can be interpreted from the above-mentioned results as the view on euthanasia by younger physicians, because in general younger physicians are those with less clinical experience.

The number of end stage patients treated in the last year also seemed to correlate with physicians' attitudes towards euthanasia. Dany et al, also observed that the higher the number of end-stage patients cared for by physicians, the more negative they are about euthanasia.¹⁰ The specialty is also one of the factors that influence physicians' views on euthanasia. According to

Parker et al, oncologists and geriatricians are less likely to accept discussions about speeding up patients' lives.¹¹ We found that oncologists are negative about euthanasia, with their position differing significantly from that of physicians of other specialties who express a marginally positive view. Physicians who are more exposed to suffering patients (e.g., chronic, end-stage) ultimately form disparaging views on euthanasia.¹²

Subsequently, the finding that came out from our study is that Greek physicians' views on euthanasia were negatively correlated to the depth of their religious devotion and spiritual pursuits. This finding was to some extent expected, as the majority of the participants embraced the Christian religion and, as is well known, the deliberate haste of the end of an individual's life is inconceivable not only in the context of Orthodoxy but also of most religions. Many researchers have come to the same conclusion, which they also interpret with the same reasoning.^{13,14}

An important element that emerges from the present work is the lack but also the need for physicians for training in issues related to the management of end-stage patients. In fact, previous studies have found that physicians who report having been trained in palliative care feel more competent in caring for terminal patients and are therefore less likely to euthanize or assist in suicide.¹⁵

The majority of the Greek medical community opposes euthanasia and medically assisted suicide, mainly because of its spirituality. Other factors, such as specialty,

clinical experience, and frequent care of end-stage patients, also appear to be related to physicians' perceptions. However, the approaches are multifaceted and extensive studies of other factors, which may influence the attitudes and views of physicians on the subject, can work informatively and constructively in the broader dialogue.

Many physicians recognize the patient's right to an end-of-life choice that may differ from their personal views and therefore favor the prospect of decriminalizing euthanasia and medically assisted suicide. Greek physicians have not received any training in the management of end-stage patients. Health policy makers should select appropriate interventions and programs that will provide physicians with the support they need to understand the deeper meaning of end-stage patient's demands for speeding up their end, in order to provide them with objectivity and ethics, the best care possible.

One limitation of our study that places constraints on the ability to generalize from the results is the small study sample. Euthanasia is a complex issue with conflicting views and there is still the possibility of errors in the study due to an unconscious desire of participants to provide socially acceptable answers. In addition, the sample of physicians studied was dominated by Christian Orthodox, a fact that may limit the generalization of conclusions to other populations of physicians who may embrace other religions or follow other spiritual traditions, although in Greece they are a minority.

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Σύντομο άρθρο

Στάση των ιατρών απέναντι στην ευθανασία και η συσχέτιση της με την πνευματικότητά τους

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ΠΕΡΙΛΗΨΗ

Οι επιθυμίες των ασθενών που «υποφέρουν» σχετικά με την επιτάχυνση του θανάτου τους μέσω ευθανασίας ή αυτοκτονίας με τη βοήθεια του ιατρού, που προκλήθηκαν από προσωπικά, ψυχολογικά, κοινωνικά και άλλα κίνητρα, γίνονται όλο και πιο συχνές. Αυτό εγείρει αντιπαραθέσεις και σηματοδοτεί προκλήσεις τόσο στην επιστημονική κοινότητα όσο και στο κοινό. Σκοπός αυτής της μελέτης ήταν να διερευνήσει τις στάσεις ιατρών απέναντι στην ευθανασία και τη συσχέτισή τους με την πνευματικότητα. Το τελικό δείγμα περιελάμβανε 93 ειδικούς ιατρούς (64,5% άνδρες), των οποίων οι στάσεις αξιολογήθηκαν χρησιμοποιώντας την κλίμακα στάσης ευθανασίας (EAS) και την κλίμακα καθημερινής πνευματικής εμπειρίας (DSES). Οι στάσεις των ιατρών συσχετιζόνταν με την ειδικότητά τους ($p=0,037$), τα χρόνια επαγγελματικής εμπειρίας ($p=0,037$), καθώς και τον αριθμό των τελικού σταδίου ασθενών που φρόντισαν και που έχασαν τους τελευταίους 12 μήνες ($p=0,016$). Οι Ογκολόγοι και άλλοι ιατροί με παρόμοια ειδικότητα, με μεγαλύτερη κλινική εμπειρία, που φροντίζουν περισσότερους ασθενείς τελικού σταδίου είναι αντίθετοι στις παραπάνω πρακτικές. Η πνευματικότητα, που εκτιμάται με την κλίμακα Daily Spiritual Experience Scale-DSES, σχετίζεται με αρνητική στάση απέναντι στην ευθανασία ($p<0,001$). Τέλος, επισημαίνεται ένα σημαντικό κενό στην εκπαίδευση των ιατρών σχετικά με τη διαχείριση ασθενών σε τελικό στάδιο. Οι ιατροί αντιτίθενται στην ευθανασία, ενώ απαιτείται η απόκτηση ικανοτήτων στη φροντίδα ασθενών στο τέλος της ζωής τους, προκειμένου να εκπληρώσουν τις τρέχουσες και μελλοντικές απαιτήσεις του επαγγέλματός τους στον τομέα της παρηγορητικής φροντίδας.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: Ευθανασία, στάσεις, ιατροί, πνευματικότητα.

Case report

Delusions with content related to COVID-19 pandemic in non-infected psychiatric hospitalized patients: a six-case series

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ABSTRACT

We briefly present a case series of six patients hospitalized in the Department of Psychiatry, University General Hospital of Ioannina, between the first (starting March 23, 2020) and the second (starting November 7, 2020) lockdown in Greece who presented with COVID-19 - related delusional ideas. All patients had negative PCR before admission and no history of COVID-19 infection. The first three of our cases were admitted during the first lockdown, between March 23 and May 4, one involuntary and the other two voluntaries. The first one was diagnosed with acute and transient psychosis (F23 - First Episode Psychosis) and the other two with psychotic depression (F32.3). Three additional patients were admitted voluntarily after the end of the first lockdown. One was diagnosed with acute and transient psychosis (F23-First Episode Psychosis) and the other two were relapses of a known psychiatric disorder (Bipolar disorder F31.5 and Psychotic depression F32.3). At follow-up six months after discharge all patients were in remission following antipsychotic medication, among other medicines. These cases reveal that COVID-19 pandemic may have an impact on the delusional content of new or preexisting psychotic disorders during the COVID-19 pandemic.

KEYWORDS: COVID-19 pandemic, psychosis, psychotic reactions, delusional content.

Introduction

Mental Health consequences of the COVID-19 pandemic are of increasing concern worldwide.¹ Even though vaccines and treatments have been developed, we are currently facing threats of mutations. At present, more than 280 million cases and over 5,4 million deaths have been reported.² The impact of this unprecedented public health crisis on mental health and especially at the outset of a new onset psychosis is a growing concern.³ The delusional content relevant to the pandemic in people presenting with psychotic disorders is introduced in a limited number of reports.^{4–6} Similar findings have been reported in stressful life events.⁷ We report a six-case series of delusional content relevant to the COVID-19 pandemic in non-infected psychiatric hospitalized patients.

Case presentation

The department of psychiatry of the University of Ioannina covers a catchment area of approximately 200.000 people in Northwestern Greece. Its 32-bed psychiatric clinic is divided into two sectors, a 22-bed “open ward” and a 10-bed “emergency ward”. There is also an Early Intervention Unit⁸ providing care for patients presenting with a First Psychotic Episode and a Consultation-Liaison Psychiatric Unit.⁹

During the period of mandatory quarantine measures starting on March 23, 2020, all patients admitted underwent PCR testing before admission. During the present study's period (March 23, 2020, to November 7, 2020) six patients out of 464 total admissions presented with delusions with content relevant to the COVID-19 outbreak. Two of them presented with the First Episode of Psychosis

(FEP) (out of 15 FEP admissions). All patients had no history of SARS-CoV-2 infection. Clinical diagnosis was made by experienced psychiatrists according to the tenth revision of the International Classification of Diseases (ICD-10).¹⁰ Additionally, the Brief Psychiatric Rating Scale (BPRS) had been employed at admission and discharge as well as during the 6-month follow-up. This project is ongoing, but up to now (6 January 2022) no other cases with delusional content related to the pandemic have appeared.

The sociodemographic and clinical characteristics of those six patients are presented in table 1.

Case 1

Mr. X, a 35-year-old man, a married, car mechanic, living in Ioannina, was admitted involuntarily to the Psychiatric Emergency Department of our hospital, two days after the first national lockdown in Greece (March 23, 2020). His family noted he was afraid of getting infected with SARS-CoV-2 and to eliminate this possibility he closed his car repair shop and forbade his mother and his 4-month-pregnant wife to leave the house while telling them “we are all going to die”. He felt a sensation of tickling in his nose, leading him to the conviction that he has been infected and as a result, he stopped any contact with his family. His condition was worsening and three days before the admission he presented extreme insomnia, agitation, and refusal to drink and eat anything. The psychiatric evaluation revealed that he also suffered from auditory hallucinations, telling him “He should warm up people’s hearts to banish all diseases” and visual-olfactory hallucinations (he complained of having a sensation of a very disturbing smell of liquid gas all around his residence) as well as delusions of persecution, poisoning, and religious content. Mr. X reported a history of delusional ideas of reference and olfactory hallucinations of a gas that seemingly would be toxic 6 months ago. He had a rapid response to treatment (aloperidol 5mg and later aripiprazole 20mg) and was discharged after 17 days of hospitalization and referred to the First Episode of Psychosis Unit for follow-up.

Case 2

Mrs. A, an 88-year-old, retired, married woman living in a village near Ioannina, was admitted voluntarily after attempting suicide by cutting the veins of her right wrist, during the first month of national lockdown in Greece. Her relatives noticed severe anxiety, insomnia, and feelings of hopelessness associated with the delusional belief that a local shop owner infected her with SARS-CoV-2. According to her son, she was on a ten-day treatment (escitalopram and quetiapine) from a private psychia-

trist. The psychiatric evaluation revealed psychomotor agitation, dysphoric mood, anorexia, insomnia, and the delusional belief that she and her entire family were infected with SARS-CoV-2. She was convinced that the doctors were going to torture and kill her, and she begged for mercy. Three days before discharge she developed a fever, believing again that she was infected, but a urinary tract infection was detected. She was hospitalized for 20 days and the delusions of infection were eliminated, getting discharged in remission with a diagnosis of psychotic depression, F32.3.

Case 3

Mrs. K is a 64-year-old woman, retired teacher, and mother of two children, living with her husband in an urban area in Ioannina. Two weeks after the first national lockdown she began to suffer from severe anxiety, insomnia, and feelings of worthlessness. She was convinced that she was infected with SARS-CoV-2 and that the world was at the edge of destruction, a conviction followed by guilt, and by somatic, nihilistic content (that her internal organs were destroyed). She was admitted voluntarily and discharged in remission after 38 days of hospitalization, with a diagnosis of psychotic depression, F32.3.

Case 4

Mrs. P is a 36-year-old female, who occupied part-time in her husband’s business. She has a known history of bipolar disorder and positive psychiatric family history. She was admitted voluntarily eleven days after the end of the first national lockdown and three days after a suicide attempt with cleaning chemicals. The psychiatric evaluation revealed a delusional conviction of SARS-CoV-2 infection and a belief that the disease was spreading to her family. Psychomotor agitation, insomnia, disorganized speech, ideas of uselessness, and inability to take care of her children were detected. She was discharged in remission after 27 days of hospitalization with a diagnosis of bipolar disorder and present episode of severe depression, with psychotic features, F31.5.

Case 5

Mr. K is a 24-year-old male, living in Ioannina, Greece, with his parents and working at an NGO. He was admitted voluntarily due to emerging psychotic symptomatology and self-destructive ideations, a month after the end of the first lockdown in Greece. Mr. K described two months prior to admission of unusual stress and absent-mindedness. He presented with a delusion that he was the COVID-19 that came to earth to plague humankind and presented with psychomotor retardation, anhedonia, sleep difficulties, and suicidal thoughts. He

Table 1. Sociodemographic and clinical characteristics of the cases.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age	35	88	64	36	24	62
Gender (Male/Female)	M	F	F	F	M	F
ICD-10 Diagnosis	F23 (FEP)*	F32.3	F32.3	F31.5	F23 (FEP)*	F32.3
Admission	Involuntary	Voluntary	Voluntary	Voluntary	Voluntary	Voluntary
Personal history of mental illness	Negative	Negative	Negative	Positive	Negative	Positive
Family history of mental illness	Negative	Negative	Negative	Positive	Positive	Unknown
First day of hospitalization	March 25, 2020	April 14	April 21	May 17	June 8	August 8
Duration of hospitalization (days)	17	20	38	27	16	9
Type of delusions	Somatic Religious	Somatic Religious	Somatic Nihilistic	Somatic Nihilistic	Reference Persecutory (Beliefs that himself was the COVID-19)	Somatic Religious
Suicide attempt	No	Yes	No	Yes	No	No
Antipsychotic/antidepressant Treatment(s)	Haloperidol Olanzapine	Olanzapine Risperidone Escitalopram	Olanzapine Venlafaxine	Olanzapine Sertraline Chlorazepam Lithium	Risperidone	Olanzapine Escitalopram Alprazolam
BPRS Baseline	73	84	72	64	51	53
BPRS at discharge	29	42	29	41	26	34
BPRS during the second lockdown in Greece (starting November 7,2020)	30	33	25	23	28	24

was discharged in remission after 16 days of hospitalization with a diagnosis of acute and transient psychotic disorder, F23.

Case 6

Mrs. E is a 62-year-old married woman, mother of two children, living in Ioannina with her husband. She was referred voluntarily, after five days of hospitalization in the Internal Medicine Ward of our hospital, due to a severe suicide attempt with analgesics. She described two months prior to the attempt with symptoms of depressed mood, anhedonia, insomnia, and somatic symptoms (especially fatigue) which were attributed to the delusional belief that she had been infected with SARS-CoV-2. Mrs. E, had a previous episode of psychotic depression during the H1N1 pandemic in 2010, with delusional ideas of contamination and transmission of the virus. She was discharged in remission after 9 days of hospitalization with the diagnosis of psychotic depression, F32.3.

Discussion

Given the stress of the COVID-19 pandemic and the concerns about seclusion and mortality, several psychological stressors have emerged and may precipitate to the presentation of psychotic symptoms. The literature on COVID-19-related delusional themes in unaffected psychiatric patients remains limited. To the best of our knowledge, two other cases from Greece have been published that included patients in need of

hospitalization.^{11,12} One multicenter study from Spain¹³ with 57 non-infected cases reported that 33 had been diagnosed with a Brief Psychotic Episode triggered by the pandemic outbreak, confirming that 57,6% presented with delusional ideas relevant to the COVID-19 pandemic. Two of our cases were initially diagnosed with the First Episode of Psychosis and a transition to schizophrenia was later confirmed. The three cases of self-harm were similar, due to the self-conviction of COVID-19 infection⁶ that was present in them, even though it is known how isolation and loneliness alone may affect the suicide risk, especially in older patients.¹⁴ We are given to understand that although psychotic symptoms may have appeared during the first wave of the COVID-19 outbreak, a pandemic such as the current one has different phases, and depending on them a patient may react differently. Future long-term research is necessary to pinpoint the factors that may contribute to a probably different delusional content through different phases of the Pandemic in a new onset psychosis or a previous exacerbation.

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Παρουσίαση περίπτωσης

Παραληρητικές ιδέες με περιεχόμενο σχετικό με την πανδημία COVID-19 σε μη προσβεβλημένους νοσηλευθέντες ψυχιατρικούς ασθενείς: μια σειρά έξι περιπτώσεων

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ΠΕΡΙΛΗΨΗ

Παρουσιάζονται έξι περιπτώσεις ασθενών που νοσηλεύθηκαν στην Ψυχιατρική Κλινική του Πανεπιστημιακού Γενικού Νοσοκομείου Ιωαννίνων (ΠΓΝΙ) και εμφάνισαν παραληρητικές ιδέες με περιεχόμενο σχετιζόμενο με την πανδημία COVID-19, στο χρονικό διάστημα από τις 23 Μαρτίου 2020 (ημερομηνία της έναρξης των πρώτων καθολικών περιοριστικών μέτρων) έως τις 7 Νοεμβρίου 2020 (ημερομηνία έναρξης περιοριστικών μέτρων για δεύτερη φορά). Όλοι οι ασθενείς είχαν PCR αρνητικό για COVID-19 και κανείς δεν είχε ιστορικό νόσησης. Οι πρώτοι τρεις από τις περιπτώσεις ασθενών εισήχθησαν κατά τη διάρκεια του πρώτου lockdown, μεταξύ 23/3/2020 και 4/5/2020, ο ένας ακούσια και οι άλλοι δύο εκούσια. Ο πρώτος διαγνώστηκε με Οξεία Παροδική Ψύχωση (F23 - Πρώτο Επεισόδιο Ψύχωσης) και οι άλλοι δύο με Ψυχωτική Κατάθλιψη (F32.3). Τρεις ακόμη ασθενείς εισήχθησαν εκούσια μετά το τέλος του πρώτου lockdown. Ο ένας διαγνώστηκε με Οξεία Παροδική Ψύχωση (F23 - Πρώτο Επεισόδιο Ψύχωσης) και οι άλλοι δύο ήταν υποτροπές προϋπαρχόντων ψυχιατρικών διαταραχών (Διπολική διαταραχή F31.5 και Ψυχωτική κατάθλιψη F32.3). Η επανεκτίμηση έξι μήνες μετά την έξοδό τους από το Νοσοκομείο ανέδειξε σημαντική ύφεση σε όλους. Αυτές οι περιπτώσεις ασθενών αποκαλύπτουν ότι η πανδημία της COVID-19 ενδέχεται να λειτουργεί παθοπλαστικά σε ψυχωτικές διαταραχές με παραληρητικές ιδέες με περιεχόμενο σχετιζόμενο με την πανδημία COVID-19.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: Πανδημία COVID-19, ψύχωση, ψυχωτικές αντιδράσεις, παραληρητικές ιδέες.

Letter to the Editor

Elder financial abuse and the COVID-19 pandemic: A call to action through training programmes?

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To the Editors,

Within the last decade, there has been a growing debate regarding financial capacity and abuse as one of the most important challenges that older adults are facing in their everyday lives.¹ Currently older adults are highly impacted by pre-and post-COVID-19 measures and there is a massive increase in financial exploitation reports involving older adults worldwide,² an increase that can be attributed to a number of reasons, such as the higher rates of depression among socially isolated seniors (a diagnosis itself linked to abuse, as it can worsen elders' cognitive and physical condition by making them dependent and vulnerable), but also due to of mass redundancies, financial pressure and stress faced by younger family members (children and grandchildren).³ Although prior research emphasized mainly individual cognitive aspects (e.g., financial knowledge/self-beliefs/behaviors in the financial decision-making process), the interaction with emotional and socio-cultural factors are not thoroughly examined. Unfortunately, there are scarce organized large-scale research attempts at national and none at international level to focus on financial abuse of elders suffering from different types of neurocognitive disorders as well as healthy elders, not only before the COVID-19 era, but especially during and after COVID-19 health and social crisis.⁴ In addition to the lack of research neglecting the cross-cultural perspective, there is also a dire need to refocus previous research attempts that mainly examine perceptions of financial abuse with experimental manipulations, not in real world situations and only from the viewpoint of the patient/family, while disregarding the attitudes and education /educational needs of healthcare experts.⁵

Future research questions that deserve to be examined, but still remain unanswered, are: What are the cognitive-emotional characteristics of elders prone to abuse and of the persons in their social environment? How do medical-psychiatric conditions influence elders financial abuse? What and how do individuals and groups from different social and cultural settings define-perceive financial abuse and the characteristics of the 'offender' and 'victim'? Under what real-life conditions we-as-'guardians' detect and are willing to report elder financial abuse and how can we 'protect' elders? What do we expect from the state, legal systems and the important others to do? What do elders themselves think and feel about financial abuse and how do they react? What is the 'correct reaction/directives'? What are healthcare professionals' attitudes and knowledge on this topic? Could all the above-mentioned points be taught in programmes? All the above will not only give an alternative viewpoint on this hot, complex multifaceted ethical, legal and practical issue (that many of us are concerned with, but at the same time are unwilling to systematically explore), but may assist us in understanding, planning and acting 'appropriately'. For that to happen, different questions should be addressed and a combination of methods is needed (mixed quantitative and qualitative designs in cross-cultural settings). A final point that may help to elucidate this confusing problem is the introduction of new statistical approaches such as multilevel analyses, which allow simultaneous examination of group-level (society) and individual-level (elder) factors and thus reveal to us the broader context.

Financial education programmes for the prevention of financial exploitation use a wide and appropriate range of delivery methods and dissemination channels focusing on the deficits, strengths as well as needs of the target groups (older adults, family members/caregivers, healthcare professionals). Due to the complex social situation, it is imperative to educate older adults as well as their caregivers to make sound financial decisions with the resources available. Such programmes have already success, because they provide not only access to financial advisors available for advice and questions on financial issues, they provide resources which are user-friendly (based on the read-

ing level of the older individuals and caregivers), but include enough detail to be useful in planning.⁶ In the cases of individuals without computer access or without computer literacy, alternative options are offered, such as services accessible over the phone or in person, brochures, handouts, or other written materials, or individual sessions and classes.⁶ The aim of promotion of financial education on a regular basis, (both via interactive online and with the use of offline resources), includes information fostering knowledge of money management and scam prevention, not only on an individual, but at the community level.⁷

Revisiting existing research and asking for an update on emerging issues and unexplored realms is a researchers' obligation. So, are existing educational programmes adequate? A contemporary empirical re-assessment will tell us and old and new questions will make us ponder where to go next.

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