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PSIHIJATRIJA DANAS
Časopis Udruženja psihijatara Srbije*

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DOPAMIN, PROLAKTIN I TERAPIJA PSIHOZA

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Apstrakt: Prolaktin (*pro-lactis*, lat.) je hormon otkriven pre gotovo osam decenija, a funkcije koje ima u organizmu su brojne, od efekata na rast i razvoj, do uticaja na ponašanje, metabolizam, reprodukciju, itd. Antipsihotici, koji se koriste preko 60 godina, održavaju "laktotrofni" hormon u žiži psihijatrijske javnosti, jer praktično svi lekovi iz grupe D2-antagonista povezani su sa promenama nivoa prolaktina. Pojava hiperprolaktinemije tumačena je kako karakteristikama pacijenta (genetskim, funkcionalnim, itd), tako i osobinama samog molekula (prolaznost kroz krvno-moždanu barijeru; koeficijent disocijacije na D2 receptoru; kapacitet za antagonizaciju serotonergičkih receptora), ali pažljiv osvrt na podatke iz literature ukazuje da u ovoj oblasti postoji još uvek dosta nepoznanica. U aktuelnom radu biće diskutovani mehanizmi i dinamika promena nivoa prolaktina tokom lečenja dopaminergičkim antagonistima na molekularnom, kao i na kliničkom nivou i razmotren rizik od pojedinih akutnih vs. kasnih neželjenih efekata. Pored toga, biće sagledane različite tehnike koje se preporučuju u kliničkom radu psihijatra u cilju kontrole prolaktinemije, sa posebnim osvrtom na mogućnosti koje se otvaraju sintezom i sve širom dostupnošću antipsihotika treće generacije.

Ključne reči: *prolaktin, dopamin, antipsihotik, psihoza, neželjena dejstva*

Uvod

Molekularna osnova psihotičnih poremećaja najvećim delom leži u poremećenoj regulaciji dopamina, tj. u presinaptičkim nivoima neuronskog konektoma. Biohemijske specifičnosti psihotičnosti postoje na nivou sinteze transmitera, koncentracije raspoloživog monoamina i/ili na nivou oslobađanja transmitera u sinapsi. Prema opsežnoj analizi istraživačkih grupa iz Londona i Njujorka [1], postoje brojni dokazi da se radi o poremećaju dopaminergičke transmisije koji se generiše presinaptički (veličina efekta d=0.79), dok su promene u raspoloživosti dopaminskog transportera, odnosno porast koncentracije D2/3 receptora od manjeg značaja u sagledavanju monoaminske disfunkcije u psihozi.

Dopamin je, sa druge strane, značajan faktor regulacije hormona prednjeg režnja hipofize – prolaktina. U poređenju sa ostalim hormonima hipofize, prolaktin je jedini hormon koji je pod dominantno inhibitornom kontrolom iz hipotalamusa. Za inhibiciju prolaktina je zadužen dopamin, i to posredstvom D2 receptora na laktotrofnim ćelijama. Tako, u slučajevima oštećenja peteljke na kojoj "visi" hipofiza, jedna od najznačajnijih žlezda našeg organizma teška jedva 0.5gr, prečnika ne većeg od 1cm, koncentracije njenih hormona uglavnom opadaju (na primer luteinizirajućeg hormona, folikulostimulirajućeg hormona, tireostimulučućeg hormona, adrenokortikotropina, hormona rasta), uz izuzetak prolaktina čija koncentracija raste, jer oštećenje peteljke u slučaju laktotrofnih ćelija znači negaciju negacije (dvostruku negaciju), tj. pozitivan efekat na ishod.

Prolaktin (*pro-lactis*, lat.) je hormon otkriven pre gotovo osam decenija, a funkcije koje ima u organizmu su brojne, od efekata na rast i razvoj, do uticaja na ponašanje, metabolizam, reprodukciju, itd. Hormon ima važne, na izvestan način opozitne funkcije. S jedne strane deluje stimulativno (priprema dojki, stvaranje mleka i održavanje funkcije dojenja, kao i održavanje funkcije jajnika, uz podržavanje sekrecije progesterona), a sa druge strane ima i inhibitorni uticaj (inhibicija gonadotropnog oslobadjajućeg hormona - GnRH). Iako podaci ukazuju da prolaktin ima čak oko 300 funkcija u organizmima različitih živih vrsta [2], ostaje otvoreno pitanje šta je od svega toga zaista relevantno kod ljudi.

Antipsihotici, koji se koriste već preko 60 godina, doveli su početkom sedamdesetih godina prošlog veka tzv. "laktotrofni" hormon sve više i više u žižu psihijatrijske javnosti. Zašto? Razlog je jednostavan – praktično svi lekovi iz ove grupe povezani su sa promenama nivoa prolaktina [3], a koriste se sve više tj. u sve širem spektru indikacija [4], kako pojedinačno, tako i kroz politerapijske sheme [5]. Na koji način nastaje hiperprolaktinemija, koji antipsihotici nose veći rizik, kako se posledice hiperprolaktinemije manifestuju na kliničkom planu i koji su rizici povezani sa hiperprolaktinemijom kao pratećim efektom antipsihotične terapije pitanja su kojima će biti posvećeni naredni odeljci.

Dopamin i prolaktin

Projekcija dopaminergičkih neurona iz hipotalamičkog *nc. arcuatus*-a, tzv. tuberoinfundibularna projekcija, smatra se najvažnijim regulatornim putem u vezi sa lučenjem prolaktina. Pored nje, odredjenu ulogu ima i tuberohipofizni put, ali znatno manje u poredjenju sa prethodnim. Interesantno je pomenuti da se dopamin iz neurona oslobadja u perivaskularni prostor i regiju eminencije medijane, tj. u primarni kapilarni splet, koji se zatim oblikuje u duge portalne sudove i preko infundibuluma u adenohipofizi formira sekundarni kapilarni splet [6].

Na membranama laktotrofnih ćelija prednjeg hipotalamusa postoje receptori iz familije D2 receptora. Kada se dopamin, dospeo putem kapilarnih spletova, veže za njih, dolazi do inhibicije transkripcije gena za prolaktin, što je uzrok prestanka njegove sinteze i oslobadjanja, kao i prestanka proliferacije laktotorofa. Osim toga, u regulaciji prolaktinemije učestvuje i povratna sprega, koja omogućava da se povišenje prolaktina reguliše povišenjem aktivnosti neurona tuberoinfundibularne projekcije [7], i obratno. Po svemu sudeći, auto-regulacija prolaktina vrši se jednim delom i preko sinteze dopamina, i to posredtsvom tirozin-hidroksilaze, no ovi aspekti su od manjeg značaja za aktuelni pregled. Ono što je važno jeste da što je jača blokada dopamina, npr. antipsihoticima sa visokim afinitetom za D2 receptor [8], to je izraženija dezinhibicija lučenja prolaktina, tj. porast serumskog nivoa hormona, dok sa druge strane dopaminski agonist antagonist bromokriptin ima direktno suprotan efekat. Pored toga, zanimljivo je da se regulacija prolaktina menja i u stresu. Naime, većina trauma dovodi do sniženja aktivnosti tuberoinfundibularnog puta, tj. smanjenja inhibitornih efekata na lučenje prolaktina, zbog čega, na primer, i samo vadjenje krvi kod nekih osoba daje tzv. "lažno pozitivne" rezultate. U suštini, u stanju straha blokira se sistem unutrašnje nagrade, balans endogenih opijata, itd, ova blokada sistema nagrade korelira sa hipodopaminergijom, a nakon pada dopamina sledi skok prolaktina i kratkotrajne promene u laboratorijskim nalazima koje kliničari ne tako retko uočavaju u svojoj praksi.

Zanimljivo je i fokusirati se na efekte koje u sprezi dopamin-prolaktin ima manipulacija serotoninom.

Za razliku od dopamina, serotonin stimulativno deluje na lučenje prolaktina. Ovo dejstvo nije neposredno (kao u slučaju dopamina), već se ostvaruje na nivou paraventrikularnog jedra hipotalamusa (povezanog sa *nc. raphe*) indirektno tj. preko dva posrednika – oksitocina i vazoaktivnog intestinalnog peptida – VIP [2,9]. Pored puta koji uključuje posrednike (ositocin i VIP), pretpostavlja se da stimulativnom efektu serotonina na prolaktin doprinosi i inhibitorna uloga na nivou tuberoinfundibularnog puta (inhibicija inhibitornog dejstva dopamina), i to najverovatnije putem GABA-ergičkih (inter)neurona [10].

Uz dopamin i serotonin, dva monoamina preko kojih se ostvaruje najveći deo efekata antipsihotika na mozak i ponašanje, na lučenje prolaktina

utiče i složena interakcija peptida i steroidnih hormona (somatostatin, acetilholih, hormon rasta, tireostimulišući hormon, angiotenzin, estrogen itd). U tom smislu zanimljivo je bilo istraživanje nemačke grupe predvodjene dr Veselinovic [11], gde je pokazano da će kod žena, i to onih koje su dobijale preparate estrogena (u sklopu oralne kontraceptivne terapije), antipsihotici izazvati upadljiviju hiperporlaktinemiju. Kako se estrogen smatra protektivnim faktorom u etiopatogenezi psihoza [12], između ostalog i zato što snižava dopamin u hipotalamusu, vrlo je zanimljivo pitanje u kojoj meri i kojim mehanizmima višestruke veze ova dva hormona utiču na razvoj i održavanje psihopatologije. Retke studije koje iz etičkih razloga nije bilo moguće sprovesti duže i u više centara, podsetile su da estrogensku hipotezu u profilaksi i dodatnoj terapiji poremećaja iz grupe shizofrenija ne treba zanemarivati, posebno u sklopu personalizacije terapije žena u generativnim fazama [13].

Antipsihotici i rizik od hiperprolaktinemije

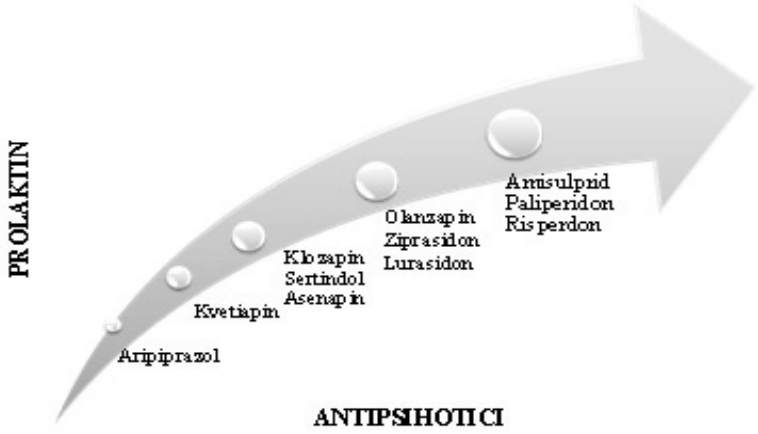
Hiperprolaktinemija se definiše kao povišen nivo prolaktina u serumu u odnosu na definisane normative laboratorija, sa napomenom da definisani normativi nisu apsolutno ujednačeni i da značajno zavise od pola (kod žena je fiziološki opseg viši u poredjenju sa muškarcima). Jedinice u kojima se izražava koncentracija ovog hormona su mlU/l (pretežno Evropa) ili ng/ml. Stanja kao što su trudnoća, dojenje, stres (disregulacija glikemije), stimulacija bradavica, san (posebno REM faza) i fizička aktivnost su primeri fiziološki uslovljenog povišenja prolaktina. Osim ovih stanja, postoje i umerene varijacije u dnevnom i sezonskom profilu lučenja prolaktina, ali amplituda oscilacija nije velika. U svakom slučaju, pravila koja važe za precizno merenje nivoa prolaktina u serumu su sledeća:

a) uzeti uzorak ujutru, *nadir*;
b) ponovljene analize obaviti u istoj laboratoriji;
c) pre daljeg ispitivanja inicijalnog nalaza povišenog nivoa hormona u krvi, obavezno ponoviti analizu tj. duplo proveriti "abnormalni" rezultat.

Ukoliko je kliničar uočio povišene nivoe prolaktina u serumu koji su *preko pet puta viši* od normativa, prvi dijagnostički zadatak je isključivanje mogućnosti da postoji prolaktinom (adenom hipofize). Nivoi niži od ovog takodje mogu ukazivati na prolaktinom (mikro- ili makro- adenom), ali u slučaju da pacijent koristi antipsihotike, verovatnoća da se radi o pratećem efektu terapije znatno nadmašuje verovatnoću da je u pitanju tumor. Zanimljivo je podsetiti se da je pituitarni tumor znatno češći nego što se klinički zapaža, jer se u literaturi pominje učestalost čak i do 10% u opštoj populaciji, ali ovaj podatak dobijen je tek na osnovu rezultata autopsije [2].

Do skora, u literaturi su antipsihotici najčešće bili deljeni u dve grupe [3]: lekovi koji "štede" prolaktin i oni koji podižu nivo prolaktina u krvi (*prolactine sparing potential*: olanzapin, kvetiapin, ziprasidon, klozapin i

prolactine raising potential: prva generacija antipsihotika i risperidon). Međutim, sa sve boljim zapažanjem razlika medju pojedinačnim molekulima, kao i nakon pojave treće generacije antipsihotika, dihotomna podela izgubila je preciznost, te je sve češće u upotrebi finiji, dimenzionalni konstrukt prikazan na slici 1.



Slika 1. Antipsihotici druge i treće generacije i rizik od povišenja prolaktina

Ako se traži jednostavan odgovor na pitanje koji antipsihotici nose najviši rizik od hiperprolaktinemije, odgovor je: amisulprid (prema autorima iz Grčke, čak 100% [14]), risperidon, paliperidon i antipsihotici prve generacije (supirid, flufenazin, haloperidol). Povišen nivo hormona može se registrovati u prvih nekoliko dana terapije, uglavnom ostaje povišen tokom tretmana i brzo se povlači nakon prekida terapije. Za amisulprid je karakteristično da hiperprolaktinemija nastaje nezavisno od doze i dužine lečenja, čak i sa dozama od 50mg dnevno [15]. U slučaju risperidona, oralna administracija nosi veći rizik nego što je slučaj sa dugodelujćom formom, a studije pokazuju i doznu zavisnost, što treba imati u vidu prilikom kontrole neželjenih dejstava. Ujedno, u dugoročnim studijama praćenja prolaktinemije tokom terapije risperidonom, kod grupe pacijenata praćene tokom pet godina [16] uočena je tendencija ublažavanja hiperprolaktinemije. Porast nivoa prolaktina tokom terapije risperidonom verovatno je bio posledica dejstva aktivnog metabolita, paliperidona, jer su nivoi paliperidona u krvi viši u poredjenju sa samim risperidonom, metabolit ima duži poluživot i slabije se vezuje za proteine plazme.

U našoj praksi (nepublikovani rezultati praćenja na Klinici za psihijatriju KCS – Odeljenje za naučno-istraživački rad i rane intervencije u psihijatriji, Beograd), uočili smo da se nivoi prolaktina tokom terapije olanzapinom

nalaze u opsegu od fiziološkog, do oko 1000mlI/l, na terapiji risperidonom raspon nivoa hormona u perifernoj krvi iznosi od 1500 do 3000 mlU/l, dok je u slučaju amisluprida opseg imao veću širinu, i dostizao povremeno i 6000 mlU/, i to već u samom početku lečenja i nezavisno od doze. U kliničkom smislu, kod pacijenatkinja dismenoreja je bila češća nego amenoreja kada je prolaktinemija ispod 2500 mlU/l, a galaktoreja je relativno retka ne samo u terapiji akutne faze, već i tokom terapijske faze održavanja. U slučajevima gde je došlo do pojave amenoreje, lek je obično bio zamenjen drugim antipsihotikom, a uspostavljanje ciklusa uočeno je uglavnom nakon 3-4 meseca, u redjim slučajevima do 6 meseci nakon prekida ekspozicije. Ginekomastija i galaktoreja su uočene nakon dužeg lečenja, čak i kada su pacijenti bili tretirani manjim dozama (npr. 2-3mg risperidona/dan), pa se mogu svrstati u kasne neželjene efekte. Poseban rizik od hiperprolaktinemije na terapiji manjim dozama antipsihotika uočili smo kod osoba sa izraženijim kognitivnim smetnjama, što je u skladu sa literaturom [17], i kod ovih pacijenata hiperprolaktinemija se uočava u samom početku terapije. U svakom slučaju, sve okolnosti u vezi sa promenama serumskog prolaktina tokom lečenja antipsihoticima jasno su bile predočene pacijentima u toku edukativnih terapijskih procedura i utisak je bio da su na ovaj način bile poboljšane i trenutna saradljivosti i trajnost terapijskog odnosa. Pacijenti su posebno dobro reagovali na priliku da prate jasno uočeni bio-marker i da na direktan način učestvuju u kontroli sopstvenog somatskog statusa, a bilo je i slučajeva kada je zbog efikasnosti leka umesto zamene antipsihotika strategija bila pažljivo titriranje doze istog leka i intenzivnije dispanzersko praćenje, što je takodje opisano i preporučeno i u literaturi [18]. U oba slučaja, komplijansa nije bila značajnije narušena. Naprotiv, utisak je bio da se saradnja čak i poboljšavala.

Koji je mehanizam nastanka hiperprolaktinemije tokom lečenja anitpsihoticima?

Prema većini studija iz savremene literature, pojava hiperprolaktinemije povezuje se sa razlikama koje, ako se tiču pacijenta obuhvataju polimorfizam gena za D2 receptor (DRD2 Taq1A polimorfizmi su povezani sa prolaktinemijom tokom lečenja antipsihoticima, dok DRD3 Ser9Gly polimorfizmi nisu [19]), a ako se odnose na lek, razlike potiču od nejednakosti izmedju antipsihotika u odnosu na:

1. Prolaznost kroz krvno-moždanu barijeru;
2. Koeficijent disocijacije na D2 receptoru;
3. Kapacitet za antagonizaciju serotonergičkih receptora.

Najviše dokaza ide u prilog prvoj tezi, tj. objašnjenju hiperprolaktinemije preko praćenja penetrantnosti molekula kroz BBB (*blood-brain-barrier*). Naime, hipofiza leži izvan BBB. Pošto je mehanizam pojave visokog prolaktina u serumu blokada D2 receptora na laktotrofnim ćelijama izvan BBB, očekuje se da lekovi koji slabije prolaze krvno-moždanu membranu dovode do izraženijih neželjenih efekata. Upravo tako i jeste: amisulprid i

risperidon su, u poredjenju sa olanzapinom i kvetiapinom, daleko slabiji u pogledu penetrantnosti, i samim tim duže se zadržavaju u "predvorju" centralnog moždanog konektoma, čime se povećava šansa da deluju na raspoložive D2 receptore u dostupnim laktotrofnim ćelijama [20]. Pored toga, ukoliko bi se D2 receptori blokirali molekulom koji specifično deluje izvan BBB, kakav je na primer domperidon (D2 blokator koji ne prelazi BBB) nastala bi takodje hiperprolaktinemija, što je i dokazano u više eksperimenata [21,22].

Ideja o značaju koeficijenta disocijacije na D-receptorima takodje zaslužuje pažnju, ali polako gubi dominaciju od kada je pokazano da se lekovi sa visokom verovatnoćom indukcije hiperprolaktinemije, npr. amisluprid ili čak i haloperidol, ustvari brzo "odvajaju" od receptora. U tom smislu, tzv. *fast dissociation* – hipoteza postala je nedovoljna da objasni fenomen hiperprolaktinemije tokom lečenja antidopaminergicima.

Medjutim, interesantno je proceniti da li i kako preko razlika u BBB penetrantnosti ili u koefinijentu D2 disocijacije može da se deluje i na kontrolu prolaktinemije. U tom smislu, korisni su podaci o mogućoj interakciji izmedju amisulprida i aripiprazola, gde se razmatraju efekti oba mehanizma. Naime, kao parcijalni agonist D2 receptora, aripiprazol deluje agonistički u okolnostima niske dopaminergije [23], i to na toničku komponentu dopaminergije, jer prema novijim razmatranjima, aktivnost dopamina je dvojaka: tonička i fazična, a aripiprazol je za sada jedini antipsihotik koji donekle pojačava toničku i snižava faličnu D-aktivnost, čime se izbegava ekstrapiramidni sindrom, ali i akutne manifestacije strijatalne hiperdopaminergije poput floridne psihotičnosti (za više informacija videti ref [24]). Zbog toga, dodatak malih doza aripiprazola u svrhu korekcije neželjene hiperprolaktinemije i kliničkih konsekvenci može imati odredjeni značaj za svakodnevnu praksu, ali treba imati u vidu da su opsežnije studije ove kombinacije lekova za sada još uvek retke, a podaci iz literature uglavnom bazirani na studijama slučaja.

Hiperprolaktinemija: kliničke manifestacije i rizici

Glavne kliničke manifestacije hiperprolaktinemije prikazane su u Tabeli 1. Najčeći poremećaji su poremećaji menstrualnog ciklusa, infertilitet i ginekomastija/eventulano galaktoreja, uz seksualnu disfunkciju, a redje se pojavljuju hirzutizam, gojaznost i promene gustine kostiju. Povezanost tumora hipofize sa lečenjem medikamentima koji uzrokuju hiperdopaminergiju je bila ispitivana u više navrata [25], ali nikada nije dokazana [2,26], no ipak treba imati u vidu da do danas ne raspolažemo potrebnim brojem kvalitetnih prospektivnih i/ili randomizovanih studija, što zaključuju i najnoviji pregledi literature. Slično tome, potencijalna povezanost hiperpolaktinemije i rizika od tumora dojke nije dokazana [27], medjutim ono na šta svakako treba obratiti pažnju jesu slučajevi gde postoji porodična predispozicija za onkološke

probleme dojke, jer se ne može isključiti mogućnost da visoki nivoi hormona mogu podsticati proliferaciju ćelija, redukujći apoptozu.

Tabela 1. Kliničke manifestacije hiperprolaktinemije*

Povišenje serumske koncentracije prolaktina	Gonade	Dojke	Menstrualni ciklus
Blago	Anovulacija Hipospermija		Skraćena lutealna faza
Umereno		Ginekomastija	Oligomenoreja
Jako	Hipogonadizam	Galaktoreja	Amenoreja

**hiperprolaktinemija ne mora biti praćena kliničkim simptomima*

Koliko su antipsihotici uzročnici promena u sferi seksualnog ponašanja, reprodukcije ili metabolizma kostiju [28], a koliko su ove promene posledica osnovnog poremećaja – psihoze, slabijeg kvaliteta života (ishrana, kretanje, navike), slabih kapaciteta za adaptaciju na stres i sl., teško je precizno reći. Pažljive analize u kojima se rezultati baziraju na detaljnom razmatranju velikog broja pratećih varijabli uglavnom se slažu u tome da su faktori nezavisni od medikacije [29-31], a blisko povezani sa fenomenologijom bolesti, načinom života i kumulativnim izlaganjem, ipak značajniji prediktori gore navedenih disfunkcija nego što je to hiperprolaktinemija *per se*.

Zaključak

Propisivanje antipsihotika dovodi svakog kliničara u situaciju da se suoči sa hiperprolaktinemijom. Jatrogena hiperprolaktinemija obavezuje terapeuta da potraži najbolje rešenje kako bi lečenje osnovnog poremećaja bilo i ostalo efikasno, kako bi se uspostavila i održala terapijska alijansa, ali i kako bi se kratkoročni i dugoročni rizici po opšte zdravlje sveli na minimum. U literaturi postoji jedna vrsta konsenzusa da, čak i kada su nivoi hormona laktacije desetostruku povišeni, ne postoje dokazi da kod osoba koje se leče antipsihoticima mogu nastati komplikacije koje su životno ugrožavajuće. Ovi dokazi baziraju se na solidnoj literaturi i na preko 50 godina pažljivog praćenja i iskustva, i na prvi pogled deluje da je ovaj period praćenja dug period, ali ne smemo zaboraviti da je to još uvek kraće nego prosečan ljudski vek, stoga imamo pravo da i dalje mislimo da je pitanje dugoročnih konsekvenci antipsihoticima uzrokovane hiperprolaktinemije otvoreno.

No, definitivno smo sigurni da su kratkoročne promene na D2 receptorima laktotrofnih ćelija koje nastaju dejstvom antagonista tog receptora reverzibilne, kao i da se kliničke manifestacije koje prate antagonizam na tuberoinfundibularnom putu povlače vrlo brzo nakon promene leka - antipsihoti-

ka. Pored promene leka, kliničari imaju mogućnost i da pažljivo kombinuju antipsihotike (na primer, sa aripiprazolom), ili eventualno pažljivo titriraju dozu ili promene farmaceutski oblik leka u cilju ravnomernijeg doziranja tj. oslobadjanja u krvi (na primer, umesto oralnog risperidona, u slučajevima hiperprolaktinemije odluče se za dugodelujući oblik ovog leka).

U sve većoj paleti antipsihotika leži daleko više mogućnosti nego organičenja. Na nama je da ih iskoristimo da bi lečili efikasno i sigurno i da bi se približili idealu tj. personalizovanoj terapiji duševnih poremećaja.

DOPAMINE, PROLACTIN AND TREATMENT OF PSYCHOSES

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Abstract: Prolactin (*pro-lactis*, lat.) is a hormone discovered around eight decades ago, with a numerous functions in human body including the effects on growth and development, influences on behavior, metabolism, reproduction, etc. More than 60 years after antipsychotic drugs were introduced, these medications have been keeping prolactin in the spotlight of the psychiatric research community as practically all D2-antagonists change prolactin levels. Hyperprolactinemia has been evaluated in several aspects, either related to patient's characteristics (genetic and functional individual features) or to some drug-related phenomena (penetrability across the blood-brain barrier; D2 receptor binding affinity; capacity to antagonize serotonin receptors), but a critical review of the current literature indicates many unknowns in the field. The present paper will discuss the mechanism and dynamics of changes in prolactin levels throughout treatment with dopamine antagonists on the molecular and clinical level, and the risk of certain acute *vs.* late adverse effects. Moreover, different techniques that could be applied in common psychiatric practice aiming to control prolactin levels will be considered, with a special emphasis on the possibilities following synthesis and increasing availability of a third generation antipsychotics.

Key words: *prolactin, dopamin, antipsychotic, psychoses, side effects*

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SUICIDE DURING YEARS OF STRESS – SERBIAN EXPERIENCE

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Abstract: Suicide is a global, ubiquitous phenomenon and one of the major causes of death at all ages and wide range of possible risk factors. Suicide and stress are intimately related, ranging from everyday life stressors, through global socioeconomic crises and economical disadvantages to major stressors such as natural or man made disasters. There is a strong association between suicidality and mental disorders, particularly depression and posttraumatic stress disorder (PTSD). Physicians should be alert to potential suicidal ideation when the history reveals risk factors for suicide, such as depression, PTSD, other psychiatric disorder, prior attempted suicide, recent divorce, separation, unemployment and bereavement. Dealing with consequences of stress, particularly suicidality, is a challenge to mental health professionals whose work during the years of stress has to be outside of their traditional roles. It is necessary to develop preventive strategies on high-risk population groups.

Key words: *suicide, stress, posttraumatic stress disorder, economic crisis*

Introduction

Suicide is a global, ubiquitous phenomenon throughout various historical epochs and societal groupings. This is, also, an anthropological-cultural phenomenon determined by biopsychosocial factors. Suicide is a huge public health problem, and one of the leading causes of premature mortality in the world. World Health Organization estimates that over 800,000 people die due to suicide every year. In addition, every 40 seconds a suicide takes place somewhere in the world [1]. The suicide rate is estimated as 11.6 per 100.000 inhabitants worldwide [2]. Although it is more common amongst older age groups, results from the recent studies reveal an increased suicide rate among younger people and as the second most common cause of death among young people worldwide. According to the United Nations Health Agency, more than 70% of suicides are among people from poor or middle-income countries [1].

The World Health Organization proposed an ecological model of suicide, whereby suicide results from a complex interplay of individual, interpersonal, social, cultural and environmental factors [3]. Societal factors such as economic and social crises, as well as, economic or social inequality, play an important role in suicidal risk.

A wide range of possible risks, protective and correlated factors for suicide were assessed. There is no single factor accepted as a universal cause of suicide. However, depression is a common condition among those who commit suicide, as well as some other mental disorders. Other risk factors are pain, stress, grief, trauma, catastrophic injury, financial loss, terrorism (especially related to religion suicide bombing and extreme nationalism) [4-6].

Trends of suicide in Serbia from 1950 to 2013

Serbia is located on the Balkan peninsula, which for centuries was crossroad between Central and Southern Europe, the East and the West [7]. The area of the Republic of Serbia covers 88.361 km^2, and its population according to the census in 2011 is 7.164,132. The country was exposed to prolonged stress since the beginning of the 1990s which caused a steady rise in mental and behavioural disorders.

According to Statistical Office of the Republic of Serbia, the total number of recorded suicide cases between 1950 and 2013 was 76.391.

Despite pledges to improve mental health care in the world as well as prevention efforts, during the last 50 years suicide rates have increased globally by 60%. A similar trend was found in Serbia as well. Overall suicide rates showed gradual, but irregular increase from 1950 to 2013 (11.2 vs. 16.7 per 100.000, respectively).

The number of suicides in the Serbian population almost doubled from 753 to 1.198 in the last 60 years, with a peak in 1992 (i.e. 1.638). Another peak occurred in 1999, during and after the NATO bombing (1.572).

During the reporting period, there were 52.305 (68.47%) male and 24.086 (31.53%) female suicides. From 1999 to 2002, the male suicide rates reached a peak of nearly 29 per 100.000 while the highest rates among females were in the years 1999-2000 (12.1 per 100.000) (Figure 1).

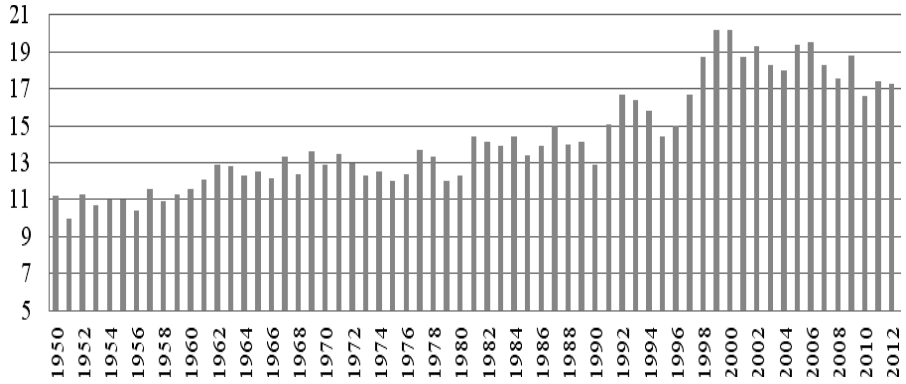

Figure 1. Suicide rate per year

Suicide during traumatic times

Major social changes and catastrophic events cause many factors that may have association with suicide. According to Knox [8], traumatic experiences can have deep impacts on mental health and may results in suicidal behaviour years and decades following the traumatic exposure. However, some authors have shown that huge catastrophic events, such as natural disaster or war, are associated with reduction in local suicide rates [9,10]. The grief and social disruption brought about by flood or earthquake is frequently accompanied by a sense of purpose, belonging and communal unity in the face of the 'common enemy' represented by the disaster. These human reactions appear to be also evident at times of war, when members of a community or society perceive themselves to be threatened and collectively charged with a shared purpose to face their common enemy [11-14].

However, some authors reported an increase in suicide rates at times of war [13]. Other studies have shown that, while suicide rates may rise, this is not necessarily a direct consequence of war per se, stating that relationship between war and suicide is a complex phenomenon mediated by other factors [15].

Serbian society was exposed to multiple and repeated stressful experiences during last three decades, man and nature caused. During early 90's a breakdown of former Yugoslavia began, with wars and exile, United Nations sanctions, which lasted 3.5 years, followed by 11 weeks of NATO bombing in 1999. The country has been facing a social transition, with economic difficulties, high unemployment rate, and political uncertainties.

Our data have shown that suicide rates in Serbia, during years of war at the area of former Yugoslavia, between 1991 and 2001, were lower, which is in accordance with other authors [11, 13, 14]. The lowest suicide rate was in 1995 and 1996, with the rate of 14.4 and 15.0 per 100.000, respectively. Furthermore, the lowest suicide rate was in August 1995 when Serbian population faced a humanitarian crisis with mass-exodus of refugees Croatia (around 250.000).

In contrast to that in the year 1999 in which there was bombardment of Serbia, the suicide increased significantly – 20.2 per 100.000, particularly in months after the bombing. During 2003 and 2004 suicide rates showed a pre-war level, with a small decrease in the following years, with the lowest level in 2008 (Figure 2).

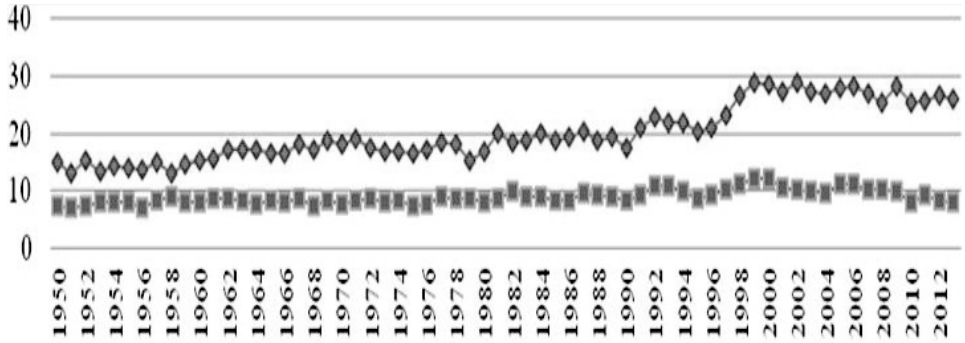

Figure 2. Suicide rate per year according to gender

Posttraumatic stress disorder and suicide

The aetiological pathway between traumatic experience and suicidality is still unclear. Most authors suggest that a psychological trauma contributes to development of mental disorders such as depression, posttraumatic stress disorder and substance abuse, which may in turn increase suicidality.

A significant association between PTSD and suicidal ideation, attempts and completions has been shown [16,17]. Some authors suggest that suicide risk is higher among those who experienced trauma due to the symptoms of PTSD [18,19], while others state that suicide risk is higher in these individuals because of related psychiatric conditions, more than because of PTSD symptomatology [20]. According to data of the National Comorbidity Survey, the PTSD without any of six anxiety diagnoses was significantly associated with suicidal ideation or attempts [21]. This study also revealed an association between suicidal behaviours, mood disorders and antisocial personality disorder and pointed to a robust relationship between PTSD and suicide after controlling for comorbid disorders. The Canadian Community Health Survey has also shown that persons with PTSD were at higher risk for

suicide attempts after controlling for physical disturbances and other mental disorders [22].

A multicentric, international epidemiological study "CONNECT" (supported by the EU within FP6) [23] carried out at the region of former Yugoslavia seven years after traumatic experiences including 640 subjects in Serbia, showed that the current PTSD prevalence rate among general adult Serbian population was 18.8% and lifetime PTSD prevalence 32.3% [24]. The suicidality in the Serbian sample was 13%, while comorbidity of PTSD and suicidality was 35%, which is accordance with others studies [17,25].

Local and global economic crisis

It is well known that social crises have significant impact on suicide rates. The highest inflation in the former Yugoslavia (i.e. Serbia & Montenegro) occurred during the 1992 and 1993 period. In the early '90 the unemployment increased with the peak of income decrease in 1993, which in addition to other aspects of economic and political crisis, were probably associated with an increased suicide rates. During that period the suicide rates were the highest since 1950, reaching nearly 16.4/100.000 and 15.8/100.000 during 1992 and 1993, respectively. Petrovic et al. (2001) reported that the peak of suicide rates in the southern-eastern part of Serbia occurred during the time of greatest economic depression (hyperinflation) in 1993, as well as during 1996 and 1999 [26].

During the post-war period at the area of former Yugoslavia, socio-economic factors were prevailing in generating high suicide rate - average rate for period of 2000-2013 was 18.29/100.000 [27].

In 2008 a global economic crisis affected Europe as well as the rest of the world. The Lopez-Ibor Foundation launched an initiative to study the possible impact of the economic crisis on European suicide rates [28]. The results of that study, carried out in 29 European countries, have shown that there is a relationship between suicide rates and the economic environment but have not confirmed a clear causal relationship between the current economic crisis and increase of suicide rates. The study has also shown that suicide rates are strongly correlated with gross domestic product (GDP) per capita and its changes, and to a lesser extent with the unemployment. Interestingly, Serbia and some other European countries (i.e. Greece, Spain, Portugal, Montenegro and Norway), showed a weak correlation of suicide rates with economic indices.

Conclusion

Suicide is a complex dynamical phenomenon, and one of the most important mental health indicators. Serbian suicide rate increased over the last decade of the XX century. According to the recent WHO data, Serbia is amongst the ten countries with the highest female suicide rates. During the past decades, our society was exposed to multiple and repeated stressfully

experiences, man and nature caused. The current global financial and economic crisis, superimposed on a difficult economic situation in the country may have negative effect on mental health of the population, including the suicide. Therefore, there is a need for national preventive programmes which should be in line with the new European WHO Mental Health Action Plan [29]. In the recent past, we carried out a one year pilot program for prevention of suicide in adolescents in collaboration with the Ministry of Health [30].

Declaration of interest

The authors report no conflicts of interest.

SUICID U GODINAMA STRESA – SRPSKO ISKUSTVO

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Apstrakt: Suicid je globalan, sveprisutan fenomen i jedan od glavnih uzroka smrti u svim uzrastima, sa širokim opsegom potencijalnih faktora rizika. Suicid i stres tesno su povezani, počevši od svakodnevnih životnih stresora, preko globalne socioekonomske krize i ekonomskih neprilika, do velikih stresora kao što su prirodne ili ljudskim faktorom izazvane katastrofe. Postoji snažna povezanost između suicidalnosti i mentalnih poremećaja, posebno depresije i posttraumatskog stresnog poremećaja (PTSP). Lekari bi trebalo da budu oprezni sa potencijalnom suicidalnom ideacijom kada istorija bolesti otkriva faktore rizika za suicid, kao što su depresija, PTSP, drugi psihijatrijski poremećaji, prethodni pokušaj suicida, nedavni razvod braka, razdvajanje, nezaposlenost i ožalošćenost. Nošenje sa posledicama stresa, posebno sa suicidalnošću, izazov je za psihijatre čiji je rad u godinama stresa izlazi iz okvira njihovih tradicionalnih uloga. Neophodno je razviti program prevencije suicida kao i preventivne strategije za visoko rizične populacione grupe.

Ključne reči: *suicid, stres, posttraumaski stresni poremećaj, ekonomska kriza*

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BODY DISSATISFACTION, TRAIT ANXIETY AND SELF-ESTEEM IN YOUNG MEN

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Abstract*: Background and purpose:* Body image dissatisfaction has recently been described as 'normative' for both men and women. Despite intense theoretical interest in a multidimensional concept of male body image, comprehensive models have rarely been assessed empirically. The aim of this study was therefore to examine the relationship between body image and self-esteem among men in a multivariate model. *Methods:* Participants of this cross-sectional questionnaire study were 239 male university students (mean age: 20.3 years, SD=2.78 years, range: 18–39 years). Measures: self-reported anthropometric data, weightlifting activity, importance of appearance, perceived weight status, satisfaction with body height, Body Shape Questionnaire – Short form, Muscle Appearance Satisfaction Scale, Rosenberg Self-Esteem Scale. *Results:* Structural equation modeling showed that after controlling for age, BMI, weightlifting activity, the importance of appearance, and trait anxiety, only muscle dissatisfaction predicted lower self-esteem (β=-0.11, p=0.033). Neither height dissatisfaction nor weight dissatisfaction showed significant association with self-esteem. Muscle dissatisfaction partially mediated the relationship between trait anxiety and self-esteem (β=-0.04, p=0.049, R^2=0.05). The model explained 50.4% of the variance in self-esteem. *Conclusions:* The results emphasize that trait anxiety might be a background variable in the relationship between males' body dissatisfaction and self-esteem, which should be considered in future studies and in the course of therapy.

Keywords: *male, body dissatisfaction, self-esteem, trait anxiety, structural equation modeling*

Introduction

Over the past few decades body image has become the focus of research. This can be partially explained by the observation that weight and shape concerns and body dissatisfaction have become a 'normative discontent' among women in Western cultures. As the gender difference in the emphasis on body appearance norms decreases, an increasing number of men experience appearance-related sociocultural pressure at levels similar to those affecting women [1]. Women are under social pressure to conform to a thin ideal, whereas the ideal for men is lean and muscular – sometimes referred to as a 'V-shaped figure'. Men may also experience dual pressure as the desire to be thinner and the desire to be more muscular are equally prevalent [2]. A recent study also described body image and muscle dissatisfaction as 'normative' for men [3].

For many years most research on male body image focused on body weight and muscularity, however, recent evidence suggests that male body image is complex and multidimensional, and discrepancies between the actual and the ideal can apply to various aspects of appearance [4]. One study found that men were dissatisfied with several aspects of their bodies: they wanted to be thinner, taller and more muscular; to have less body hair and more head hair; and to have a larger penis [5].

Men's increasing concern and dissatisfaction with body image are associated with the investment of a considerable amount of money and time in toiletries, cosmetic procedures and surgeries to improve appearance [5]. Nevertheless body image dissatisfaction often results in negative body image, which is often associated with maladaptive behaviors such as restrictive dieting, self-induced vomiting, excessive exercise, psychological distress, and social avoidance [6], which may also be factors contributing the extensive research interest in this area. It is important to note, however, that body image dissatisfaction does not always have negative consequences; for instance, some men who are dissatisfied with their bodies do not perceive that their bodies play an important role in their attractiveness. It is therefore essential to consider the importance of appearance when psychological correlates or consequences of body dissatisfaction are examined. A study of the predictors of appearance self-esteem found that dissatisfaction with body weight, muscularity and height, and the perception that body weight and penis size are important to physical attractiveness predicted lower appearance self-esteem [5].

The relationship between body image dissatisfaction and self-esteem in men has been also investigated in recent years; some authors have argued that body satisfaction is critical to self-esteem. The earlier studies of the association between self-esteem and body satisfaction examined the relationship between self-esteem and muscle dissatisfaction, and subsequent research investigated other aspects of body image such as satisfaction with body weight and height [3,7]. Bergeron and Tylka found a weak negative association between

dissatisfaction with body height, weight and muscularity and self-esteem [8]. In a multivariate model dissatisfaction with muscularity and body fat, but not dissatisfaction with body height, were independent predictors of self-esteem after adjusting for the drive for muscularity and body mass index (BMI). According to the authors' knowledge, multivariate models testing the negative psychological correlates of body dissatisfaction have rarely controlled for the potential psychological background variables. For instance, trait anxiety often contributes to lower self-esteem [9]. The aim of this study was therefore to examine the relationship between body image and self-esteem among men in a multivariate model adjusting for trait anxiety.

Method

Participants and Procedure

The participants were 239 male undergraduate students recruited from a large university located in Budapest. The students completed the paper-and-pencil questionnaire anonymously during or after a university class. Participation was voluntary, and the participants were not remunerated for participating. All participants provided informed consent. Ethical approval for this study was obtained from the relevant university's research ethics committee.

The mean age of the respondents was 20.3 years (*SD*=2.78 years, range: 18–39 years). The mean body weight was 75.6 kg (*SD*=14.71 kg, range: 50–185 kg). The mean body height of the sample was 181.6 cm (*SD*=7.49 cm, range: 160–201 cm). The mean BMI of the participants was 22.8 (*SD*=3.82, range: 15.9–55.2). Almost half of the participants (43.9%) lived in Budapest, 39.7% lived in another city and 16.3% lived in rural areas. Nearly all participants (90.2%) were unmarried; 9.8% were married or cohabited.

Measures

Sociodemographic and anthropometric data. All participants provided data on age, place of residence, marital status, height (cm) and weight (kg); BMI (weight [kg] / height2 [m]) was calculated based on self-reported height and weight.

Perceived weight status. The participants were asked to rate their weight status using the following response options: (1) very thin, (2) slightly thin, (3) about the right weight, (4) slightly overweight and (5) very overweight.

Dissatisfaction with body height. Height satisfaction was assessed with a single question, 'How satisfied are you with your body height?', with responses given on a nine-point Likert scale (-4=completely dissatisfied to 4=completely satisfied). This item was reverse coded to simplify interpretation; higher scores indicated greater dissatisfaction with body height.

Body Shape Questionnaire – Short form (BSQ–SF14) [10,11]. This fourteen-item scale measures psychopathological concern about body shape. Questions related to the respondent's state over the past two weeks are answered on a six-point Likert scale (1=never to 6=always). Higher scores indicate greater body weight concerns and body weight dissatisfaction.

Muscle Appearance Satisfaction Scale (MASS) [12,13]. This nineteen-item scale measures muscle dysmorphia symptoms using five subscales. In this study, we used only the three-item Muscle Satisfaction subscale. The items were rated on a five-point Likert scale (1=strongly disagree to 5=strongly agree). Higher scores indicate greater muscle dissatisfaction.

Rosenberg Self-Esteem Scale (RSES) [14,15]. This ten-item scale measures global self-esteem, which is defined as a person's overall evaluation of his or her worthiness as a human being. The items were rated on a four-point Likert scale (1=strongly disagree to 4=strongly agree). Higher scores indicate higher self-esteem.

State-Trait Anxiety Inventory (STAI) [16]. This forty-item self-report measure assesses both how a person feels at the time of responding (state anxiety) and how he or she generally feels (trait anxiety). We used only the twenty-item Trait Anxiety Scale. The items were rated on a four-point Likert scale (1=not at all to 4=very much so). Higher scores indicate greater trait anxiety.

Weightlifting activity. To assess current weightlifting activity one yes/no question was used: 'Do you currently engage in any weightlifting activity?'

Importance of body appearance. The importance of body appearance was assessed using a single question: 'How important do you consider your body appearance compared with other things in life?' Responses were given on a four-point Likert scale (1=not important at all, 2=not important, 3=slightly important, 4=very important).

The Cronbach's alpha coefficients for the scales were acceptable in the current study sample (Table 1).

Statistical analyses

Scale score reliability was assessed using Cronbach's alpha coefficient and its 95% confidence interval (95% CI). Associations involving categorical variables were examined using a chi-square test. The relationship between perceived weight status and self-esteem was investigated using ANOVA. Linear relationships were investigated with correlational analyses (Pearson's or Spearman's method). Effect sizes were interpreted according to Cohen's conventions: a correlation coefficient of 0.10 was assumed to represent a weak or small association, a correlation coefficient of 0.30 was considered a moderate correlation and a correlation coefficient of 0.50 or larger was assumed to represent a strong or large association [17].

The complex theoretical model was tested using structural equation modeling (SEM). Robust maximum likelihood estimation method (MLR

estimation) was applied. To evaluate the fit of the SEM model, we used recommended fit measures: the Comparative Fit Index (CFI), the Tucker-Lewis Fit Index (TLI), the root mean square error of approximation (RMSEA), and the standardized root mean square residual (SRMR). CFI and TLI values between 0.90 and 0.95 indicate an acceptable fit and values greater than 0.95 suggest a good fit. RMSEA assesses approximate fit, with values below 0.08 indicating an acceptable fit and values below 0.05 indicating a good fit. The SRMR can take a range of values between 0.0 and 1.0, with 0.0 indicating a perfect fit (i.e., the smaller the SRMR, the better the model fit). Chi-square values and their p-values are reported but are less suitable as indicators of model fit because they are extremely sensitive to sample size and model complexity [18]. Analyses were performed using the SPSS 21.0, and MPLUS 7.11 [19] statistical packages.

Results

Characteristics of the Sample

Forty-one participants (17.2%) reported current weightlifting activity. Based on the BMI 4.1% of the respondents were underweight (BMI<18.5), 76.2% were normal weight (BMI=18.5–24.9) and 19.7% were overweight or obese (BMI≥25.0). There was a significant difference between the frequency of perceived weight status and objective weight status (based on BMI): 29.9% of the respondents considered themselves underweight, 55.7% thought that they were about the right weight and 14.5% considered themselves overweight (McNemar $\chi^2(3)=59.831$, $p<0.001$).

Most participants considered body appearance important: body appearance was reported to be ‘very important’ (25.7%) or ‘slightly important’ (62.4%) compared with other things in life. Only 11.9% of the participants considered that body appearance was not important compared with other things in life. Descriptive statistics (means, standard deviations and Cronbach’s alphas) and correlations between variables are presented in Table 1.

Perceived Weight Status and Self-Esteem

Regarding to perceived weight status responses were divided into three categories (i.e., thin, about the right weight, overweight), combining the ‘very’ and ‘slightly’ options in the thin and overweight categories. The ANOVA revealed a significant association between perceived weight status and self-esteem ($F(2)=6.572$, $p=0.002$). Post-hoc tests (LSD) indicated that the participants who regarded themselves as thin or overweight had significantly lower self-esteem than participants who regarded themselves as being about the right weight. There was no difference in the self-esteem of those who perceived themselves as thin or overweight. The model explained 5.8% of the variance in self-esteem.

Psychological Correlates of Body Image Dissatisfaction

Correlation analyses revealed that there was no significant linear association between body height dissatisfaction and muscle dissatisfaction or weight dissatisfaction. There was a significant positive but weak association between body weight dissatisfaction and muscle dissatisfaction. All three aspects of body dissatisfaction showed a significant weak or moderate relationship with both self-esteem and trait anxiety (Table 1).

Table 1. Descriptive statistics for the measures and correlations between the variables.

Variables	Cronbach's α [95% CI] (number of items)	Mean *(SD)*	2. Weight dissatisfaction (BSQ–SF14)	3. Muscle dissatisfaction (MASS)	4. Self-esteem (RSES)	5. Trait anxiety (STAI)	6. Age	7. BMI
1. Height dissatisfaction	- (1)	-2.0 (2.27)	*0.11*	*0.02*	*-0.17**	*0.17***	*0.07*	*0.04*
2. Weight dissatisfaction (BSQ–SF14)	0.89 [0.87, 0.91] (14)	23.4 (8.86)	-	0.26***	-0.30***	0.32***	0.11^{+}	0.36***
3. Muscle dissatisfaction (MASS)	0.88 [0.85, 0.90] (3)	9.3 (2.98)		-	-0.36***	0.36***	0.08	-0.03
4. Self-esteem (RSES)	0.86 [0.83, 0.89] (10)	21.2 (5.07)			-	-0.72***	0.03	-0.02
5. Trait anxiety (STAI)	0.91 [0.90, 0.93] (20)	42.0 (10.47)				-	-0.05	-0.05
6. Age	- (1)	20.3 (2.78)					-	0.35***
7. BMI	- (1)	22.8 (3.82)						-

Note: $^{+}$ p<0.10, * p<0.05, ** p<0.01, *** p<0.001. Values in italics are Spearman's rank correlational coefficients.

Path Analyses

We hypothesized that all measured aspects of body dissatisfaction predict lower self-esteem. In the first model we adjusted for age, weightlifting activity, importance of appearance, and BMI. In the second model we adjusted for trait anxiety as well (Figure 1).

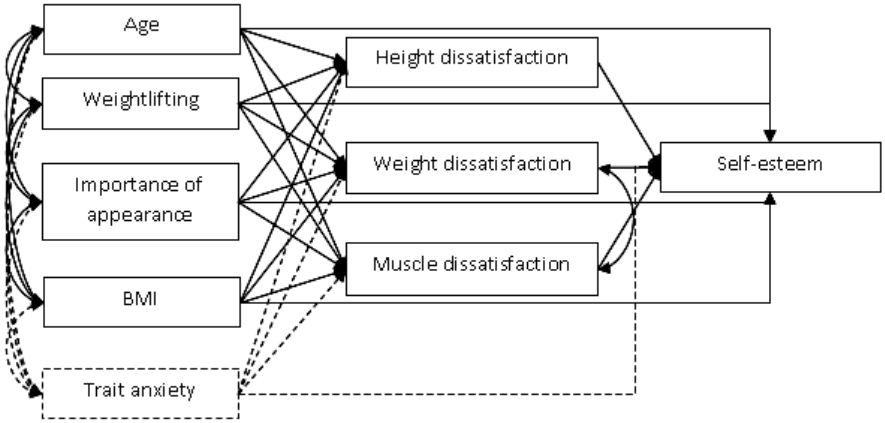

Figure 1. The theoretical models. The first model does not involve trait anxiety.

According to the results of the first model (Figure 2) all three aspects of body dissatisfaction showed significant negative association with self-esteem. Older age predicted greater height dissatisfaction. The perceived importance of body appearance and BMI were positively associated with weight dissatisfaction. Weightlifters were significantly more satisfied with muscularity than their non-weightlifting counterparts. The model explained 20.5% of the variance in self-esteem (χ^2=2.446, *df*=2, *p*=0.294, CFI=0.995, TLI=0.948, RMSEA=0.031 [90% CI: 0.000–0.136], SRMR=0.013).

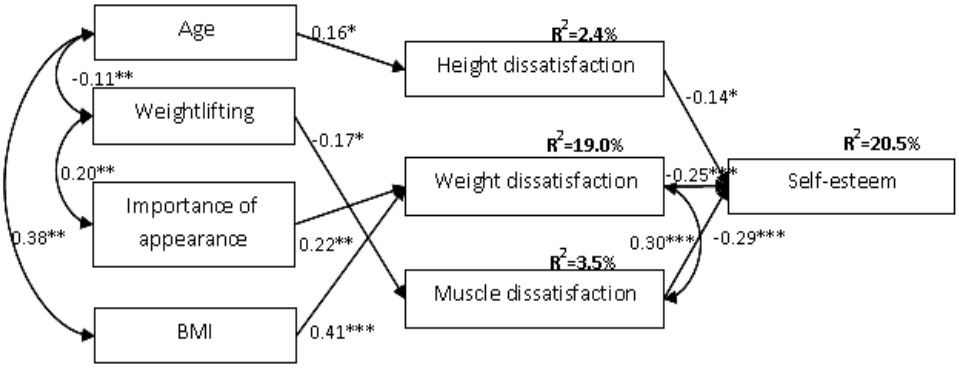

Figure 2. The final Model 1, which contains only significant (p<0.05) standardized path coefficients.

Note. N=239. Arrows: regression weights, double arrows: covariances. Weight-lifting is coded as follows: (0): non weightlifter, (1): weightlifter. R^2: explained variance. * p<0.05, ** p<0.01, *** p<0.001.

According to the results of the second model (Figure 3) greater trait anxiety was associated with greater dissatisfaction with height, weight and muscularity, and with lower self-esteem. In this model only muscle dissatisfaction was significantly associated with self-esteem, and it partially mediated the relationship between trait anxiety and self-esteem (standardized β=-0.04, p=0.049, R^2=0.05). The model explained 54.4% of the variance in self-esteem (χ^2=1.442, df=2, p=0.486, CFI=1.000, TLI=1.029, RMSEA=0.000 [90% CI: 0.000–0.116], SRMR=0.008).

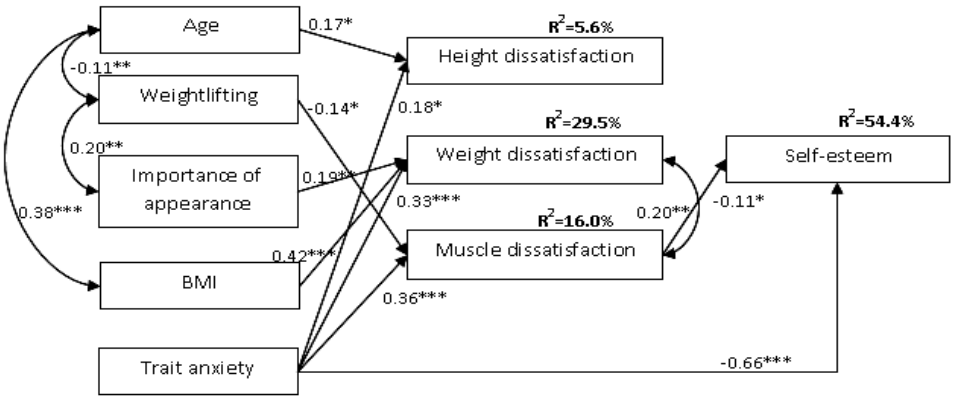

Figure 3. The final Model 2, which contains only significant (p<0.05) standardized path coefficients.

Note. N=239. Arrows: regression weights, double arrows: covariances. Weight-lifting is coded as follows: (0): non weightlifter, (1): weightlifter. R^2: explained variance. * p<0.05, ** p<0.01, *** p<0.001.

Discussion

The aim of this study was to examine the relationships between body dissatisfaction, self-esteem and trait anxiety in male university students. Three aspects of body dissatisfaction were investigated: muscle dissatisfaction, weight dissatisfaction and height dissatisfaction.

The results revealed significant discrepancies between objective weight status and perceived weight status. Based on self-reported height and weight data only 4.0% of the sample was underweight, however, nearly one-third of the participants regarded themselves as thin. This result is consistent with previous studies finding that the number of men rating themselves as underweight is higher than the number of men who would be categorized as underweight by objective standards [2].

We found an association between self-esteem and perceived weight status in our sample. Those who regarded themselves as thin or overweight had lower self-esteem than those who regarded themselves as being about the right weight;

however, we found no difference in self-esteem between those who perceived themselves as thin and those who perceived themselves as overweight. This finding is consistent with a previous study showing that in males' body dissatisfaction resulting from being either under- or overweight has a negative effect on their self-esteem [2].

Results of structural equation modeling suggested that after adjusting for age, BMI, weightlifting activity and the perceived importance of body appearance, greater dissatisfaction with height, weight and muscularity predicted lower self-esteem. The involvement of trait anxiety in the model showed that higher trait anxiety was associated with lower self-esteem and greater dissatisfaction with height, weight and muscularity. Among these aspects of body dissatisfaction only muscle dissatisfaction had a significant relationship with self-esteem. Our results corroborated an earlier report that in multivariate model body height dissatisfaction does not predict self-esteem [8]; however we failed to replicate their finding that body weight dissatisfaction predicted lower self-esteem. It may be explained by methodological differences; the two studies used different instruments and different background variables, and trait anxiety was not measured in the above mentioned study. Our results imply that trait anxiety could be a background factor in the relationship between males' body dissatisfaction and self-esteem. This possibility should be considered when interpreting the results of earlier studies [3,8], and it highlights aspects relevant to intervention, particularly the importance of reducing anxiety in males with considerable body dissatisfaction.

Benetti and Kambouropoulos noted out that trait anxiety is associated with increased negative affect, which is considered a dimension of subjective distress and is often implicated in negative mood states; they found that negative affect mediated the association between trait anxiety and self-esteem [9]. Another study reported an association between negative affect and body dissatisfaction [6]. These results indicate that body image dissatisfaction may mediate the relationship between trait anxiety and self-esteem. In this study of men, the association was partially mediated by muscle dissatisfaction; neither body weight dissatisfaction nor body height dissatisfaction was related to self-esteem. This finding suggests that dissatisfaction with muscularity plays a greater role in men's self-esteem than their dissatisfaction with body weight or height. Men whose self-esteem is dependent on their appearance may engage in maladaptive appearance-improving behaviors (e.g., excessive exercise, rigid diets), and low self-esteem may motivate weightlifting activity. Men may desire a more muscular body because they consider it a way of gaining acceptance or respect from others [4].

Limitations

The limitations of this study must be acknowledged. The main limitation was the use of convenience sampling. We do not have any data from eligible participants who declined to take part in the study. Therefore, the

generalization of the results is restricted. The cross-sectional study design does not allow us to draw conclusions about causality. A variety of alternative models may exist (e.g., low self-esteem may lead to body image disturbance which leads to anxiety, or anxiety may lead to low self-esteem which leads to body image disturbance). In cross-sectional studies, we must address the problems of equivalent models in SEM modeling; therefore, we can make only theoretical assumptions relating to the direction of the effect, but it is not statistically possible to determine the effect direction. Body height dissatisfaction was measured with only one item, albeit one with high face validity. All anthropometric data were self-reported; thus their validity is questionable. It is also important to note that in muscular men, BMI is not an adequate measure of overweight as it does not distinguish between muscle and fat mass. Men with high muscle mass may be incorrectly categorized as overweight or obese on the basis of BMI. Several important dimensions of male body image were not investigated (e.g., head hair, body hair, and penis size). Although we measured the importance of general body appearance, it would also be interesting to explore the perceived importance of individual aspects of male body image, such as muscularity, body height, body weight [5].

Conclusions

Limitations notwithstanding our study contribute to research on male body image by examining the psychological correlates of dissatisfaction with muscularity, weight and height with involvement of weightlifting activity, which has been identified as a risk factor for muscle dysmorphia. Previous studies of the relationship between male body image dissatisfaction and anxiety focused on the fear of negative evaluation [7], and social anxiety about physique [20], whereas a limited number of studies examined trait anxiety [21]. To the best of the authors' knowledge, this study is the first to investigate associations between body dissatisfaction, trait anxiety and self-esteem using structural equation modeling by considering the subjective importance of body appearance. Our results provide evidence that body dissatisfaction in men is associated with some symptoms of psychological disturbance. Our findings confirm that body dissatisfaction is a significant concern for both men and women, it is similarly important that health interventions should include body image improvement strategies. Future research should examine whether our findings can be generalized to different cultures. It would also be valuable to investigate body image in other male populations - such as professional bodybuilders, other sportsmen, obese men or minority groups - using a model of similar complexity to that used in this study.

Conflict of Interest Statement

The authors declare no conflict of interest.

NEZADOVOLJSTVO TELOM, DIMENZIJA ANKSIOZNOSTI, I SAMOPOŠTOVANJE KOD MLADIH MUŠKARACA

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Uvod i cilj: Nezadovoljstvo telesnom shemom nedavno je opisano kao „normativ“ i za muškarce i za žene. Uprkos intenzivnom teorijskom interesovanju za multidimenzionalni model slike muškog tela, sveobuhvatni modeli retko su empirijski potvrđeni. Cilj ove studije bio je, prema tome, da se ispita povezanost između slike tela i samopoštovanja među muškarcima u multivarijantnom modelu. **Metod:** Učesnike ove studije preseka činilo je 239 univerzitetskih studenata muškog pola (prosečna starost: 20,3 godine, SD=2,78 godina, opseg: 18-39 godina). Instrumenti: upitnik o antropometrijskim podacima, aktivnost podizanja tegova, značaj izgleda, procenjen telesni status, satisfakcija telesnom visinom, Upitnik o obliku tela (Body Shape Questionnaire) – kratka forma, Skala o zadovoljstvu izgledom mišića (Muscle Appearance Satisfaction Scale), Rozenbergova skala o sampoštovanju (Rosenberg Self-Esteem Scale) **Rezultati:** Strukturalna jednačina modelovanja pokazala je nakon kontrole varijabli - godine, BMI, aktivnost podizanja tegova, značaj izgleda i dimenzije anksioznosti, nezadovoljstvo mišićima kao prediktor smanjenog samopoštovanja (β =-0,11. p=0.333). Nezadovoljstvo visinom, kao ni nezadovoljstvo težinom, nisu pokazali značajnu povezanost sa samopuzdanjem. Nezadovoljstvo mišićima delimično je posredovano vezom između dimenzije anksioznosti i samopoštovanja (β =-0,04, p=0.049, R2=0.05). Ovaj model objašnjava 50,4% varijanse u samopoštovanju. **Zaključak:** Rezultati naglašavaju da dimenzija anksioznosti može biti varijabla u pozadini veze između nezadovoljstva muškim telom i samopoštovanja, koju treba razmotriti u budućim istraživanjima i tretmanu.

Ključne reči: *muški pol, nezadovoljstvo telom, samopoštovanje, dimenzija anksioznosti, strukturalna jednačina modelovanja*

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WORK-LOAD, BURNOUT AND MENTAL HEALTH OF DUAL-DOCTOR COUPLES. DEPERSONALIZATION AS A COPING MECHANISM?

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Abstract: Background: In line with the feminization of medicine the rate of dual-doctor couples among physicians has increased. The aim of this study is to describe the impact of the special stress-load related to medical profession on the members of these couples. **Methods**: Data in this representative cross-sectional epidemiological study were obtained from online questionnaires completed by 5,607 Hungarian physicians. In the quantitative analysis data of those who lived in a partner relationship were processed: 1,549 physicians with a physician partner versus 3,095 physicians with a non-physician partner. In our descriptive analysis we compared the amount of work-load (number of working hours, workplaces and night shifts), leisure time, and time spent on housework in the two groups. We also analyzed certain indicators of mental health (sleep disorders, signs of depression, psychosomatic symptoms, and perceived stress) and the presence of burnout and role conflict. **Results**: There was no difference in the amount of work-load between the two groups. No differences were detected in case of mental health indicators either; however, medium and high level of depersonalization and high level of role conflict was more prevalent among doctors with physician partner. Multivariate analysis demonstrated that having a physician partner was an important risk factor of depersonalization. **Conclusions**: Developing depersonalization might be a response on the 'double' emotional burden that affects doctors who live in a dual-career partner relationship. Higher prevalence of burnout among dual-physician couples draws the attention to the need for prevention and intervention.

Keywords: *physician-physician couples, work-load, burnout, role conflict, mental health*

Introduction

In the 19th century model of the medical profession the attributes of a physician were associated with the image of a responsible, professionally committed man who optimally had a supportive wife in the background [1]. As large numbers of women entered the field of education and work the 'profile' of the profession has changed. Medicine has become increasingly feminized: in the past decades a dynamic rise in the number of female physicians has been witnessed. Among others, there has been a striking increase in the United States, where the rate of female university students was around 10 percent 50 years ago, while more than half of university students are women nowadays [2]. In the past half century a shift of genders can be seen in medicine, too: while in the 1950s and 1960s far more men graduated from medical universities, and in the 1970s and 1980s the number of male and female medical students were similar, on the turn of the 20th and the 21st century female medical students outnumbered their male counterparts [3,4,5]. Forecasts in the 1990s prognosticated that every third medical doctor would be a woman by 2010; however, it has become clear by now that more than 50 percent of those studying and practicing medicine are women [6,7]. In line with this, the rate of female students exceeds 60 percent at medical universities worldwide [8,9].

As women entered the field of medicine in large numbers, the pattern of the partner relationship of physicians has also changed. In North America and Western Europe doctors' wives were housewives as a rule, but with the increasing number of female physicians the 'dual-earner' and 'dual-career' partner relationship models have become more and more prevalent [7]. In these models the rate of physician-physician couples has also increased [10,11,12]. Nevertheless, it must be noted that the situation in Central-Eastern Europe has been different from the one described above. In the socialist countries labor market was a 'distinguished field' of women's emancipation: men and women were equally important participants of labor market until the 1990s [13]. There have been almost as many female as male physicians in this region since the 1950s [14,15]; therefore, it was not only the 1970s when the number of women physicians started to increase: this trend has already started in the early socialism.

In Hungary, just as in many countries in the region, the opposite of the international trend has been witnessed: medical profession has become less 'isolated' and the rate of physician-physician couples has decreased. While in the 1990s two-fifths of Hungarian doctors had a doctor partner and a further 14% had a spouse working in health care [15], the findings of the representative study of Hungarian physicians in 2013 showed that 38% of respondents had a partner working in the field of health care, which is a decreased rate in comparison with the data obtained from the end of the second Millennium [16].

Relatively few research studies have focused on dual-physician couples. In the beginning of the 1970s Rapaport et al. were the first to describe that dual-manager couples were more likely to face serious difficulties during their effort to reconcile work and family tasks [17]. Based on their findings further studies distinguished dual-earner and dual-career couples. Dual-career means greater commitment and heavier work-load on both members of the couple: in these families women disrupt their working activities less frequently and for shorter periods. The prerequisite of the above described situation is that the traditional division of labor has changed: in line with the masculinization of women's walk of life the 'feminization' of men's walk of life has become inevitable [18]. Beside the extraordinary situation of dual-career couples there has been a further important field of research in the past decades, namely the problematic harmonization of work and family related duties [19,20]. These studies reveal several dimensions when describing the burden on physicians: studies on quality of life, burnout and career options also deal with the issue of possible conflicts between work and family [21,22]. In view of the above mentioned transitions it is of extreme importance to describe how quality of life, stress burden and coping mechanisms of physician-physician couples have changed over time. Due to the special character of medical work dual-physician couples, especially those with small children, are often challenged by difficult situations. Among these are the long and often unpredictable working hours and the difficulties in harmonizing the work-load related to shift work [23,10]. In a study on physician-physician couples' time management it was revealed that among the couples with small children women spent less time with formal professional work while the amount of working hours of their spouses was similar to that of men with non-physician spouses [24,25]. Other studies confirmed that female physicians who had physician partner spent less time with professional work than women whose partner was not a physician [26,27,25,12]. On the other hand, Wang et al. found that having a physician partner decreased the amount of professional working hours in both sexes [28]. Based on these findings, many studies confirmed that physician-physician couples encountered more difficulties in harmonizing work and family related duties than non-physician couples [29,30,26]. Having said all these, the comparison of the mental and physical health status and burnout of members of dual-doctor couples and their colleagues with non-physician partners might be interesting. There are few related studies in the literature: these showed that having a physician partner increased the rate of mental problems of physicians, especially depression and perceived stress [29]. However, qualitative research on physician-physician couples highlighted that physician partners provided each other significantly more emotional and professional support in comparison with non-physician partners of doctors [31,10].

The aims of the present study are to reveal the most important similarities and differences between dual-doctor couples and non-dual doctor couples on a representative sample of Hungarian physicians.

Methods

Study design and data collection

Online survey of Hungarian physicians

Our online quantitative survey took place between May 9 and July 15, 2013 and focused on physicians and dentists who worked in Hungary. A link to an anonymous online self-administered questionnaire was sent to all potential participants, followed by four reminder e-mails (sent every two weeks on average). Potential participants were the registered members of the Hungarian Medical Chamber with valid e-mail address (n = 42,342). Response rate was 16.18% (n = 5,607), which is considered acceptable in comparison with the average response rate of online surveys [32].

Our data were weighted by gender, age and profession (physicians, dentists). After three-dimensional weighting, data regarding the region and type of workplace were compared with the same type of data from the Hungarian Central Statistical Offices. We considered our survey to be representative, because we did not find significant difference according to regions (by counties), nor according to type of workplace (general practice, in-patient and out-patient care).

The survey was performed with the permission of the Hungarian Medical Chamber. Ethical permission was obtained from the Ethical Committee of Semmelweis University, Budapest (No: 60/2013).

Measuring instruments

The following age groups were applied: 24 to 35, 36 to 45, 46 to 55, 56 to 65 years and older than 65 years. Marital status was coded into a two-category variable as ‘living with partner’ (married or cohabiting) or ‘single’ (single, living separately from partner, divorced, or widow) to increase statistical power. Answers to the item regarding the number of children were dichotomized into having or not having children to obtain a proxy measure for parity. The variables of current workplace were categorized into four groups: working in in-patient care; working in out-patient practice; working in a general practice or other (non-governmental organization etc.). We examined the number of weekly working hours (40 or more than 40), and the number of workplaces (one or more than one).We also detected the amount of household related work (hours/week). We examined the amount of weekly shift-work. In case of those who were not single, the partner was coded according to having been a physician or not.

Assessment of burnout

Burnout was measured by the Hungarian version of Maslach Burnout Inventory - Human Services Survey (MBI) [33,34]. The 22-item questionnaire assesses each of the three components of burnout (emotional exhaustion: EE, depersonalization: DP and decreased personal accomplishment: PA) by three different subscales. Responses were rated on a seven-point Likert scale (from 0 = 'never' to 6 = 'every day'). In our study the Cronbach's alpha coefficients for the subscales proved to be 0.909 for EE, 0.767 for DP and 0.818 for PA.

Assessment of work vs. family conflict

Perceived conflict between work and family related duties was assessed by three instruments developed for means of research on physicians' role conflict by Firth, Mellor, Moore, and Loquet [35], and Warde, Allen, and Gelberg [36]. The items were rated on a five-point Likert-scale (from 1 = 'not at all' to 5 = 'very much/extremely often'). The variables of role conflict were dichotomized (1 = never, rarely or sometimes experience role conflict; 2 = often or very often experience role conflict).

The role conflict was measured by the following questions:

"How often do you feel irritated or dissatisfied because of the impression that you cannot balance between your workplace, family, household, or partnership engagements?"

„How often do you experience that family related duties interfere with workplace activities?"

„How often do you feel that workplace engagements disturb family related activities?"

Assessment of mental health disorders

Sleep disorders were assessed by the Hungarian version of the shortened Athens Insomnia Scale (AIS) [37,38]. In our sample the Chronbach's alpha value of the Hungarian version of AIS was 0.874.

We assessed *depression* by the shortened version of Beck Depression Inventory (BDI) [39]. In our study the Cronbach's alpha value of BDI was 0.86.

In the survey we used a modified version of the second question of Paykel's „Suicidal ideation and suicide attempts" questionnaire to assess *suicidal thoughts* [40]. The modified question used for the assessment of suicidal thoughts was the following:"Have you ever been preoccupied with suicidal thoughts?". For the classification of the answers (1 = no suicidal thoughts; 2 = suicidal thoughts in the past year; 3 = suicidal thoughts in the past five

years; 4 = suicidal thoughts for more than five years) we used a dichotomous key (1 = no suicidal ideation; 2 = have had suicidal thoughts).

Psychosomatic symptomatology was assessed by the Patient Health Questionnaire (PHQ) somatic symptom check-list [41,42]. The symptoms were rated according to severity: 0 = did not occur, or not bothered at all; 1 = it occurred and bothered a little; 2 = it occurred and bothered a lot. Based on the total score obtained, four levels of severity were formed: 0-4 = no symptoms; 5-9 = low severity; 10-14 = medium severity; above 15 = high severity). In this analysis this variable was transformed into a dichotomous variable: the cut-off point was 10. The Cronbach's alpha value of the scale was 0.797.

We assessed *perceived stress* by the shortened Perceived Stress Scale (PSS) [43,44,45], which consists of 10 items and assesses the participants' subjective stress level. We used dichotomous categories: score below the mean value = low perceived stress; score above the mean value = high perceived stress. The Chronbach's alpha value of the scale was 0.812.

Statistical analyses

Descriptive statistics were used to determine the prevalence of mental health disorders, work-load, burnout and role conflict among Hungarian physicians. Characteristics of 'dual-doctor partners' (DDP) and the 'physician control group' (PCG) were compared by $\chi 2$ tests. Binary logistic regression analysis was performed to detect the association between socio-demographic and work related variables and burnout. In binary logistic regression analysis we used binary variables of EE, DP and PA as dependent variables, whereas independent variables were gender, age, number of children, type of workplace, working hours/week, number of workplaces, role conflict and having a physician partner.

Results

In the present analysis the rate of respondents with a physician partner (married or cohabiting) was 33.3% (n = 1,549). Rate of doctors with non-physician partner (control group) was 66.6% (n = 3,095). Most important demographic characteristics of the respondents are shown in *Table 1*.

Table 1. Main socio-demographic characteristics of dual-doctor partners (DDP; n = 1,549) and the physician control group (PCG; ***n*** = 3,095)

	PCG	DDS
Age (years)	**%**	**%**
<35	17.9	18.1
36-45	18.5	17.4
46-55	20.5	21.6
56-65	21.2	23.1
>66	22	19.9
Number of children		
0	21.3	14.8
1	18.9	17.7
2	39.5	44.5
3 or more	20.3	23
Type of workplace		
In-patient care	35.3	39.6
Out-patient care	22.8	20.8
General practice	27.1	23.1
others	14.3	16.9

Among those with physician partners 53.4% were men and 46.6% were women. Reverse rates were found in the control group: 43.1% were men, and 56.9% were women. Mean age of respondents with a physician partner was 52.22 years (SD = 15.38), in case of the control group this number was 52.05 years (SD = 15.28). Almost 10 percent of doctors with non-physician partner divorced previously (9.2%), whereas this rate was 3.3% among those with physician partner ($p < 0.000$). Childless were 14.8% of the index group, 17.7%, 44.5% and 23% had one, two, and three or more children, respectively. These rates among those with non-physician partners are the following: 21.3% were childless, 18.9% had one child, 39.5% had two children, and 20.4% had three or more children. The rate of childless physicians was significantly lower in the index group (14.8% vs. 21.3%; $p < 0.000$).

In the index group 39.6%, 20.8%, and 23.1% worked in in-patient and out-patient units, and as a general practitoner, respectively. In the control group these rates were 35.3%, 22.8%, and 27.1%, respectively. In the index group 14.3%, while in the control group 16.9% worked in other types of workplaces (public administration, civil sector, private practice). Higher rate of doctors with physician partners worked in in-patient units ($p < 0.003$).

Doctors in the index group worked 54.6 hours a week on average, and spent further 14.7 hours on average having been on-duty. They spent 2.2

hours a day on average doing housework. In the control group these numbers were 52.4, 14.2, and 2.3 hours (not significant).

No difference was detected in the number of workplaces either: in the index group 46.4%, whereas in the control group 44.1% had more than one workplace. In the index group more doctors had more than one specializations (45.5% vs. 41.8%, respectively; $p < 0.001$)

Our next field of research was development of burnout and the issue of harmonizing work and family related duties (*Table 2* and *Table 3*).

Table 2. MBI subscales among doctors with physician partner (***n*** = 1549)

	EE* %	DP** %	PA*** %
Low level	49.3	56.8	33.9
Moderate level	28	24.8	26.2
High level	22.7	18.4	39.9

*EE: emotional exhaustion subscale
**DP: depersonalization subscale
***PA: personal accomplishment subscale

Table 3. MBI subscales in the physician control group (*n* = 3095)

	EE* %	DP** %	PA*** %
Low level	51.3	64	34.9
Moderate level	26.6	22.5	26.2
High level	22.1	13.5	38.9

*EE: emotional exhaustion subscale
**DP: depersonalization subscale
***PA: personal accomplishment subscale

We found that moderate and high level of emotional exhaustion was similar in the two groups (50.7% vs. 48.7%, respectively), and the same result was found in case of decreased personal accomplishment (66.1% vs. 65.1%, respectively). The prevalence of moderate and high level of depersonalization was significantly higher among doctors with physician partners (43.2% vs. 36%, respectively; $p < 0.035$).

Among doctors with physician partner 44.6% often or very often found it difficult to harmonize work and family related activities, while this ratio was 41.8% in the control group ($p < 0.012$). Family related duties had significantly interfered with work in 12.1% of the index group and 9.5% in the control group ($p < 0.000$), whereas 45.6% of the index group, and 41.1% in the con-

trol group felt to be significantly distracted from family duties by work ($p < 0.028$).The two groups were similarly affected by sleep disorders according to the AIS: rates of high scores were 41.6% vs. 43.7% in the two groups, respectively. Mild and moderate depression was detected by BDI in 7.7% vs. 7.6%, respectively. Higher levels of psychosomatic symptoms and perceived stress were present in the same rate in the two groups of physicians (21.6% vs. 18.4% and 43.2% vs. 43.5%, respectively; data not shown).

Multivariate analysis was performed to examine the factors that had significant impact on the depersonalization dimension of burnout. Significant difference was found between the index and control groups regarding certain dimensions of role conflict. Nevertheless, we made a methodological restriction, because both the presence and the intensity of role conflict were measured by only one item each. Since this might have had an impact on validity and reliability, our further analysis was restricted to the depersonalization dimension of burnout.

The multivariate analysis demonstrated that beside the traditional risk factors having a physician partner was an important contributor to moderate and high levels of depersonalization (OR = 1.218, CI = 1.0183-1.457, *Table 4*)

Table 4. The association between moderate and high level of depersonalization and having a physician partner

Dependent variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Depersonalization	1.144 (1.010-1.96)**	1.218 (1.018-1.457)*

*Adjusted for age, shift-work, gender, number of children, type of workplace, working hours/week, number of workplaces, role conflict and having a physician partner.
**$p < 0.05$

Discussion

We examined the work-load, burnout and mental health of Hungarian physicians living in partner relationship by means of a representative survey conducted in 2013. Respondents who had physician partners were compared to doctors with non-physician partners (n = 1,549 vs. n = 3,095, respectively). In spite of the expectations that were based on the extra difficulties that dual-doctor couples face, our findings showed that they had more children and the rate of previous divorce was lower among them, compared with the control group. In the comparison we found no difference between the two groups according to number of workplaces, hours of night-shifts, and weekly working hours. No difference was found in the amount of leisure time and time spent on doing housework. On the other hand, higher rate of doctors with physician partner than physicians from the control group reported frequent or very frequent role conflicts. Furthermore, we found higher rates of

depersonalization (cynicism) in the index group. No significant difference was found in case of other indicators of mental health and stress burden (sleep disorders, depression, psychosomatic symptoms, and perceived stress) between the two groups of respondents. Multivariate analysis showed that beside the traditional risk factors (amount of working hours, shift-work, having multiple jobs, work-family conflict) having a physician partner was a further risk factor for higher scores obtained at the depersonalization subscale of burnout.

Finding the balance between work and family is crucial in the life of dual-physician couples. According to previous research, when these two fields of life are harmonized, physician-physician couples are in a more advantageous situation both emotionally and professionally [9,46,12]. Almost all studies highlight the importance of time management in the life of double-doctor couples; however, satisfaction with partner relationship greatly depends on how they spend their leisure time. Several studies indicate that it is not the amount but the quality of time spent together that really matters in partner relationship [47,48].

Our survey provides several important new findings in comparison with previous studies. In this Hungarian sample the rate of previous divorce among physician-physician couples was lower compared with their colleagues with non-physician partner (3.3% vs. 9.3%, respectively) or other qualified professionals [49]. According to international data rate of divorce among physicians is between 10-20% which is lower in the general population [50,48]. Additionally, Hungarian dual-physician couples have more children; therefore, it seems plausible that these couples are more 'family-centered'. Presumably, due to the mutual knowledge of each other's profession, members of these couples have deeper understanding toward each other's work-load and commitment. It is possible, that this empathy leads to less unresolved conflicts. A recent research in the US confirmed that rate of divorce among physicians was lower than in the general population. It is interesting, though that higher rate of divorce was found among female doctors than among their male colleagues [51]. On the other hand, almost half of our respondents often encounter difficulties during harmonization of work and family duties. In our previous study we found high level of perfectionism among Hungarian female doctors which had proven to be an important contributor to the development of emotional exhaustion [52]. Therefore, it is plausible that the perfectionist performance both at work and at home leads to more intensive role conflict.

Another unique finding of our study is the difference in level of burnout among physicians with physician partner and doctors with non-physician partner. After controlling for several factors in the dimension of

depersonalization, having a physician partner proved to be an independent risk factor. Depersonalization dimension of burnout manifests through a reserved behavior toward patients, clients and colleagues; furthermore, it means a more impersonal care, cynicism, and lack of emotions [53]. The question is which mechanisms are responsible for the development of depersonalization among the members of dual-physician couples. A doctor faces many difficult, stressful situations during his/her work that might be difficult to cope with. Help from a physician partner can be very useful; however, the emotional burden might be doubled by taking over the problems of the partner. It is conceivable that after some time the members of the physician couples start to keep a distance from these cases to protect themselves, which can lead to depersonalization. This is supported by our result, i.e. in case of physician-physician couples the same level of depersonalization was found among men and women; although, most research outcomes indicate higher prevalence of depersonalization among men [54,55]. It is possible that there is a kind of 'desensitization': the exponential increase in the amount of emotional burden that affects the private life of physician couples may activate mechanisms of self-defense. Thus, keeping distance from problems related to patients and difficult cases becomes more frequent. Nevertheless, further research is needed to explore this issue.

The strength of our study is that we could explore the situation of physician-physician couples based on a representative sample and by using-validated instruments. Furthermore, it was possible to include a representative control group of doctors with non-physician partners. The limitation of our study is that we assessed the direction and intensity of role conflict by only one item each. Further research on the development of role conflict among physician-physician couples and its background factors would prove useful.

Competing interests: All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Abbreviations: MBI: Maslach Burn-out Inventory; EE: Emotional Exhaustion; DP: Depersonalization; PA: Personal Accomplishment, SD: Standard Deviation; OR: Odd's Ratio; Dual Doctors Partners: DDP; Physicians Control Group: PCG

OBIM POSLA, BURNOUT I MENTALNO ZDRAVLJE PARTNERSKIH ODNOSA MEĐU LEKARIMA - DEPERSONALIZACIJA KAO COPING MEHANIZAM?

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Uvod: U skladu sa feminizacijom u medicini, procenat partnerskih odnosa među lekarima je u porastu. Cilj ove studije bio je da se opiše uticaj povišenog stresa povezanog sa medicinskom profesijom među ovim parovima. **Metod:** Podaci u ovoj epidemiološkoj studiji preseka, dobijeni su preko online upitnika popunjenih od strane 5,607 mađarskih lekara. U kvalitatvnoj analizi obrađeni su podaci onih koji žive u partnerskom odnosu: 1,549 parova dvaju lekara, prema 3,095 lekara čiji partner nije lekar. U našoj deskriptivnoj analizi, uporedili smo obim posla (broj radnih sati, radno mesto i noćne smene), slobodno vreme, kao i vreme provedeno u kućnim poslovima u ove dve grupe. Takođe, analizirali smo izvesne indikatore mentalnog zdravlja (poremećaji spavanja, znaci depresije, psihosomatski simptomi i doživljeni stres), prisustvo burnout-a i ulogu konflikta. **Rezultati:** Nije bilo razlike u vrednostima obima posla između dve ispitivane grupe. Takođe, nisu otkrivene razlike u indikatorima mentalnog zdravlja; međutim, srednji i visok nivo depresonalizacije, kao i visok nivo uloge konflikta, bili su više izraženi među doktorima čiji su partneri takođe lekari. Multivarijantna analiza pokazala je da partnerski odnos medju lekarima značajan faktor rizika za depresonalizaciju. **Zaključak:** Depresonalizacija razvijena u toku burnout-a može biti odgovor na „dvostruko“ emocionalno opterećenje koje utiče na doktore koji žive u dualnim, karijera-partner odnosima. Viša prevalencija burnout-a među parovima dvaju lekara, skreće pažnju na potrebu za prevencijom i intervenisanjem.

Ključne reči: *lekar-lekar parovi, obim posla, burnout, uloga konflikta, mentalno zdravlje*

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RANI SKRINING POREMEĆAJA AUTISTIČNOG SPEKTRA KOD DECE UZRASTA 16 DO 30 MESECI

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Apstrakt: Uvod: Prevalenca poremećaja autističnog spektra u svetu je u porastu. Skrining i rana dijagnoza su od izuzetne važnosti, jer pružaju mogućnost rane intervencije. **Ciljevi:** Ovo istraživanje je deo istraživanja koje se sprovodi u Srbiji sa ciljem validacije srpskog prevoda Modifikovanog upitnika za autizam kod male dece (Revidiran, sa kontrolom) – M-CHAT-R/F. Drugi cilj ispitivanja je analiza faktora rizika, koji se dovode u vezu sa pojavom ASD. **Materijal i metode:** Istraživanje je sprovedeno u Domu zdravlja Savski venac i na Institutu za mentalno zdravlje (IMZ). Ispitivana grupa je obuhvatila roditelje zdrave dece uzrasta od 16 do 30 meseci pri poseti pedijatru i roditelje dece upućene na pregled psihijatra u IMZ. Za svrhu istraživanja korišćen je M-CHAT-R/F. **Rezultati:** U istraživanju je učestvovalo ukupno 65 ispitanika. Ispitani u Domu zdravlja su svrstavani u grupu niskog rizika, a ispitanici upućeni u IMZ svrstavani su u grupu visokog rizika. Poređenjem navedenih grupa, nije pronađena statistički značajna razlika u odnosu na uzrast deteta i starost roditelja pri rođenju deteta. Nađena je značajna razlika u odnosu na gestacijsku nedelju u kojoj je dete rođeno, kao i značajno veća učestalost komplikacija u trudnoći u visokorizičnoj grupi. **Zaključak:** Daljim istraživanjem psihometrijske osobine M-CHAT upitnika će biti u potpunosti proučene, međutim i preliminarni nalazi ukazuju da M-CHAT može prepoznati značajan broj slučajeva ASD tokom rutinskog pedijatrijskog pregleda. Pojedini prenatalni i perinatalni faktori kao što su komplikacije u trudnoći i gestacijska starost pri rođenju mogu uticati na povećanje rizika za razvoj ASD.

Ključne reči: *poremećaji autističnog spektra, skrining, M-CHAT, prenatalni faktori*

Uvod

Autistični spektar poremećaja (ASD) je skup neurorazvojnih poremećaja koje karakterišu oštećene socijalne interakcije, komunikacijski deficiti i repetitivna ponašanja, neuobičajena ili ograničena interesovanja. Deca sa ASD ne uspevaju da "pročitaju" ljude, ignorišu ih i često uporno izbegavaju kontakt očima. Tipično, ne traže utehu i ne dele interesovanja drugih. Ne uspevaju da razviju komunikaciju bilo govorom, gestovima ili izrazima lica. Karakteristično je da mala deca ne koriste pogled ili pokazivanje prstom da usmere pažnju svojih roditelja. Mogu imati motorne stereotipije kao što su pokreti prstiju, uvrtanje žice, udaranje po stranicama knjige ili oblizivanje. Repetitivni pokreti čitavog tela uključuju vrtenje i trčanje napred nazad [1].

Trenutna prevalenca ASD se procenjuje na 1 od 68 rođenih [2]. Širom sveta postoji tendencija rasta incidence poremećaja autističnog spektra, a tačni uzroci ovog porasta još nisu sasvim jasni (spominju se biološki faktori ali i poboljšana dijagnostička procedura) [3-7]. Takođe je poznato da rane intervencije mogu voditi ka značajno boljoj prognozi kod dece sa ASD [8-12]. Međutim, još uvek se dijagnoza najčešće postavlja posle navršene treće godine [13] ili kasnije [14]. Mogućnosti intervencije pre uspostavljanja dijagnoze su veoma ograničene, stoga su skrining i rana dijagnoza od izuzetne važnosti [9]. Kod većine obolele dece simptomi autizma se razvijaju postepeno, dok se kod približno 30% uočava regresivni početak obično u uzrastu od 18 do 24 meseca [15-18].

Brojna istraživanja nedvosmisleno ukazuju da je efekat intervencija utoliko veći ukoliko se one ranije započnu. Savremena saznanja u oblasti neuronauka ukazuju da je uticaj ranih iskustava na razvoj neuronskih struktura i veza koje se nalaze u osnovi saznajnih, emocionalnih, govorno-jezičkih i drugih sposobnosti deteta najveći upravo u ranim periodima života.

Ciljevi rane intervencije su da se unapredi zdravlje i razvoj deteta, da se umanji zaostajanje u fizičkom, saznajnom, emocionalnom, govorno-jezičkom i/ili društvenom razvoju deteta, da se spreči funkcionalna onesposobljenost deteta, i da se unapredi socijalna uključenost deteta i porodice. Put ka postizanju ovih ciljeva jeste odstranjivanje ili ublažavanje činilaca koji ometaju ili ugrožavaju razvoj deteta i uvođenje i unapređivanje snaga i činilaca koji pomažu razvoj deteta [10].

Iskustva deteta u tom periodu koja su pozitivna, raznovrsna i obogaćena, mogu mu pomoći da prevaziđe početni zastoj u razvoju motornih, saznajnih i drugih sposobnosti i da razvije sposobnosti komunikacije i rešavanja problema, da uspostavi zdrave odnose sa vršnjacima i sa odraslima i da razvije različite druge sposobnosti koje će mu biti korisne tokom celog života. Dokazano je da pozitivno roditeljstvo i stimulisanje interakcije majka-dete u ranim periodima života može značajno da unapredi kvalitet psihomotornog i psihosocijalnog razvoja deteta. Osnovni principi kojima se treba rukovoditi pri proceni potreba deteta sa sumnjom na ASD su da procena

bude usmerena na dete, da je zasnovana na detetovom individualnom razvoju i na identifikaciji teškoća, ali i postojećih snaga deteta i porodice, da je uključen interagencijski pristup proceni i obezbeđenju usluga, da to bude kontinuirani proces, a ne samo jednokratan događaj, kao i da su u proces procene obavezno aktivno uključeni porodica deteta i samo dete.

Preporučuje se da sva deca budu podvrgnuta skriningu na rane znake ASD u okviru primarne zdravstvene zaštite. Na taj način se ne postavlja dijagnoza ASD već se kod pozitivno označenih podstiče brže upućivanje na referentno kliničko ispitivanje. M-CHAT-R/F (Modified Checklist for Autism in Toddlers, Revised with Follow-up) je specijalno dizajniran upitnik koji se koristi u primarnoj praksi za identifikaciju odojčadi u riziku za ASD. M-CHAT-R/F je najčešće korišćen skrining instrument, a mogu ga popunjavati roditelji u čekaonici [19].

Ovo istraživanje je deo istraživanja koje se aktuelno sprovodi u Srbiji sa ciljem ispitivanja i validacije srpskog prevoda Modifikovanog upitnika za autizam kod male dece (Revidiran, sa kontrolom) u našoj populaciji, s obzirom da u našoj zemlji ne postoje publikovani rezultati o psihometrijskim osobinama i korišćenju ovog instrumenta. Drugi cilj ispitivanja je i analiza dobijenih faktora rizika kod ispitivane grupe dece, a koji se dovode u vezu sa pojavom ASD.

Materijal i metode

Istraživanje je sprovedeno u periodu od sredine decembra 2014. do sredine februara 2015. godine u Domu zdravlja Savski venac i na Institutu za mentalno zdravlje (IMZ). Ispitivana grupa je obuhvatila roditelje zdrave dece uzrasta od 16 do 30 meseci pri poseti pedijatru i roditelje dece upućene na pregled psihijatra u IMZ. Za svrhu istraživanja korišćen je Modifikovani upitnik za autizam kod male dece, revidiran, sa kontrolom (M-CHAT-R/F), prilog I. M-CHAT-R/F predstavlja dvofazni instrument samo-procene namenjen roditeljima dece uzrasta 16 do 30 meseci. Koristi se za ustanovljavanje rizika od ASD i identifikaciju ranih znakova ASD ili zastoja u razvoju [19]. Istraživanje je anonimno. Roditelji koji su učestvovali u istraživanju potpisivali su pisani pristanak sa informacijama i ispunjavali upitnik koji sadrži deo o demografskim podacima ispitanika i M-CHAT-R/F koji se sastoji od 20 pitanja. Na kraju ove faze ispitivač je pregledao odgovore i donosio odluku o potrebi dodatnog razgovora. Očekivano je da kod dece kod koje nije postavljena sumnja na ASD roditelji odgovore sa „da" na sva pitanja osim na 2., 5. i 12. gde je očekivan odgovor „ne". Odgovori koji se uklapaju u očekivane označavani su sa „prolaz" a oni koji odstupaju od očekivanih sa „pad". Daljem ispitivanju podlegli su ispitanici koji su imali od 3 do 7 odogovora označenih kao „pad". Ukoliko je druga faza potrebna, sledio je razgovor u kom se pojašnjavaju i dopunjavaju određeni odgovori dati u prvoj fazi.

Opšta pedijatrijska populacija ispitana u Domu zdravlja je svrstavana u grupu niskog rizika (low-risk), a ispitanici upućeni od strane pedijatra u IMZ pod sumnjom na razvojne probleme svrstavani su u grupu visokog rizika (high-risk). U istraživanju je učestvovalo ukupno 65 ispitanika od toga 32 dečaka (49,2%) i 33 devojčice (50,8%). U grupi niskog rizika bilo je 58 ispitanika od toga 27 dečaka (46,6%) i 31 devojčica (53,4%), a u grupi visokog rizika 7 ispitanika od toga 5 dečaka (71,4%) i 2 devojčice (28,6%). Uzrast pri anketiranju kretao se od 16 do 30 meseci u obe grupe. 54 upitnika (83%) popunile su majke, a 11 (17%) očevi.

Istraživanje je odobreno od strane Etičkog komiteta Instituta za mentalno zdravlje.

Sva statistička izračunavanja su urađena preko računarskog programa SPSS 18. Za obradu podataka su korišćene mere deskriptivne statistike i parametrijske (univarijantna analiza varijanse) i neparametrijkse (Hi-kvadrat test) metode za ispitivanje razlike između dve grupe.

Rezultati

Poređenjem grupa niskog i visokog rizika, nije pronađena značajna razlika u odnosu na uzrast, starost majke pri rođenju deteta kao ni starost oca pri rođenju deteta. (Tabela 1).

Tabela 1. Demografski podaci ispitanika i rezultati analize varijanse pri poređenju razlika između grupa

Varijabla	Grupa	M	SD	minimum	maksimum	F	p
Uzrast	Niskog rizika	23.5	4.0	16	30	.09	.760
	Visokog rizika	24.0	5.9	16	30		
Starost majke	Niskog rizika	31.4	4.5	17	41	1.17	.282
	Visokog rizika	33.3	3.8	26	38		
Starost oca	Niskog rizika	35.7	5.6	26	61	.01	.919
	Visokog rizika	35.4	4.5	30	42		
Gestacijska nedelja	Niskog rizika	38.5	2.1	33	43	**7.8**	**.007**
	Visokog rizika	35.8	3.2	32	40		

M – aritmetička sredina; SD – standardna devijacija; p – nivo značajnosti

Nađena je značajna razlika među posmatranim grupama u odnosu na gestacijsku nedelju u kojoj je dete rođeno. Deca iz grupe visokog rizika

rađala su se u proseku tri nedelje ranije nego deca iz grupe niskog rizika (Tabela 1).

Kod 4 ispitanika anketirana u Domu zdravlja dobijen je rezultat koji je zahtevao sprovođenje druge faze ispitivanja odnosno odgovori na 3 ili više pitanja označeni su kao „pad". Daljim ispitivanjem broj odgovora označenih kao „pad" je smanjen na manje od 2 odnosno odbačena je sumnja na ASD. Svi ispitanici iz grupe visokog rizika kod kojih je upitnikom postavljena sumnja na ASD imali su 7 i više pitanja označenih kao „pad" te nije bilo indikovano sprovođenje druge faze ispitivanja. Broj pitanja na koja su dobijeni odgovori koji su označeni kao „pad" u grupi niskog rizika prosečno je iznosio M=0,6 (SD=0.96), a u grupi visokog rizika M=7.1 (SD=6.8). Broj kritičnih pitanja na koja su dobijeni odgovori koji su označeni kao „pad" u grupi niskog rizika prosečno je iznosio M=0.1 (SD=0.4), a u grupi visokog rizika M=1.0 (SD=0.8).

Poteškoće u održavanju trudnoće prijavljene su kod 7 (13.8%) majki dece iz grupe niskog rizika, dok je taj broj u grupi visokog rizika iznosio 4 (57.1%). Ova razlika bila je statistički značajna (χ^2(1.N=65)=7.798; p<0.01). U grupi niskog rizika navođene su prenesenost, prevremeno skraćenje grlića materice, prevremene kontrakcije, hormonska terapija, hipotireoza, gestacijski dijabetes i hyperemesis gravidarum, dok su u grupi visokog rizika komplikacije bile – placenta previa, hipertenzija i prevremena dilatacija grlića materice. Komplikacije pri porođaju javile su se kod 6 (8.6%) ispitanika iz grupe niskog rizika i kod 2 (28.6%) ispitanika iz grupe visokog rizika. Razlika među grupama po ovom osnovu nije bila značajna.

Diskusija

Korist instrumenta koji detektuje slučajeve ASD ranije nego što bi oni bili prepoznati u okviru kliničke prakse ogleda se u ranijem upućivanju na dijagnostičku evaluaciju i omogućava ranu intervenciju. Upitnici za roditelje su pogodan instrument za procenu simptomatologije i obezbeđuju merenje nad većom populacijom uz smanjenje finansijskih ulaganja i vremena. M-CHAT je razvijen u svrhu rane identifikacije dece pod rizikom za nastanak ASD. Dvofazni M-CHAT skrining specifičan za ASD uz određene modifikacije prilagođene srpskom jeziku ima za cilj efikasniju identifikaciju dece sa potencijalnim ASD.

U našoj studiji psihometrijske osobine M-CHAT upitnika nisu u potpunosti proučene, što se planira u daljem istraživanju, međutim preliminarni nalazi ukazuju da M-CHAT može prepoznati značajan broj slučajeva ASD tokom rutinskog pedijatrijskog pregleda.

Preporučljivo je ispitivati pojedinačne stavke da bi se razlikovala deca pod sumnjom na ASD od druge dece u uzorku. Šest najznačajnih odnosno kritičnih diskriminišućih stavki odnosi se na pažnju (pokazivanje kažiprstom, praćenje pogledom, donošenje stvari roditelju), socijalnu povezanost (interesovanje za drugu decu i imitiranje) i komunikaciju

(odazivanje na zvanje po imenu). Izostajanje navedenih oblika ponašanja je među ranim znacima ASD [21].

U grupi visokog rizika ukupan broj pitanja označenih kao „pad“ kao i broj kritičnih pitanja označenih kao „pad“ je veći u odnosu na iste parametre u grupi niskog rizika, što je u skladu sa drugim studijama gde je primenjivan isti instrument [22, 23, 24].

Ma koliko efikasan upitnik bio, ovakav skrining je baziran isključivo na onome što roditelji prijavljuju. Neki roditelji loše procenjuju ponašanje svog deteta, posebno ako imaju ograničen uvid u ponašanje druge male dece, dok drugi mogu imati poteškoća pri odgovaranju na pismeno postavljena pitanja. Treba imati u vidu da je M-CHAT namenjen isključivo u svrhe inicijalnog skrininga i da nije dijagnostičko sredstvo. Stoga je kod dece koja pokažu odstupanja na ovom upitniku neophodna dalja evaluacija sa ciljem postavljanja dijagnoze i blagovremene intervencije. Ovakav pristup može povećati uspešnost ranog prepoznavanja problema i ranih intervencija.

U literaturi je preko 60 perinatalnih i neonatalnih faktora razmatrano kao faktor rizika za ASD u meta-analizi. Među njima su različite komplikacije u trudnoći poput poremećaja prezentacije ploda, male gestacijske starosti, komplikacija vezanih za pupčanu vrpcu, fetalnog distresa, kongenitalnih malformacija, maternalnog krvarenja, ABO i Rh inkompatibilije i hiperbilirubinemije, ali i komplikacije pri porođaju kao što su porođajne povrede, višestruki porođaji, nizak Apgar skor u petom minutu, aspiracija mekonijuma i druge (mala telesna težina novorođenčeta, teškoće pri hranjenju, neonatalna anemija) [25].

Ova studija našla je značajne razlike u učestalosti komplikacija u trudnoći, koje su se u grupi visokog rizika javile u 57,1% slučajeva, dok je u grupi niskog rizika bilo 13,8% komplikovanih trudnoća. U case-control studiji u Kini sprovedenoj na 286 autistične dece i istom broju zdrave dece pronađeno je da je starost majke preko 30 godina u trenutku rođenja deteta, nizak nivo obrazovanja roditelja, preteći abortus, komplikacije u trudnoći, bolest majke u toku trudnoće, mentalno zdravlje majke, porodična istorija mentalnih bolesti, neonatalna žutica, asfiksija na rođenju, prevremena ruptura plodovih ovojaka i gestacijska starost manja od 37 nedelja značajno češća u grupi obolelih od ASD [26]. Za razliku od navedene naša studija nije pokazala značajne razlike među posmatranim grupama u pogledu starosti majke i starosti oca pri rođenju deteta.

Iako ne postoji dovoljno dokaza koji ukazuju da je ijedan perinatalni ili neonatalni faktor etiološki činilac za razvoj ASD, pojedine studije daju dokaze koji sugerišu da prisustvo višestrukih neonatalnih komplikacija može povećati rizik. Prenatalni činioci najvećeg uticaja su starost roditelja na rođenju deteta, maternalno krvarenje u trudnoći, gestacijski dijabetes, prvorođenost i upotreba medikamenata u trudnoći [27]. Akušerske komplikacije kao značajan faktor za ASD ističu moguću ulogu fetalne i neonatalne asfiksije [28-33].

Iako prevremeno rođenje nije pouzdano povezano sa rizikom od nastanka ASD, postoji značajna heterogenost među studijama. U 5 studija sa širokim dijagostičkim kriterijumima prevremeni porođaj je povezan sa povećanjem rizika za 76%, a u 10 prospektivnih studija prevremenom porođaju pripisano je povećanje rizika za 54% [27].

Naše istraživanje je takođe došlo do statistički značajne razlike u gestacijskoj starosti na rođenju među dvema posmatranim grupama. I u drugim studijama prepoznat je postepen porast rizika za razvoj ASD kod kraće gestacije u odnosu na duže trajanje trudnoće [34]. Primenom istog upitnika u jednoj studiji je 25% odojčadi rođene pre 30. gestacijske nedelje označeno pozitivno [35] dok se u drugoj studiji navodi da je pozitivan skrining rezultat prisutan kod 21% odojčadi rođene pre 28. gestacijske nedelje [36].

Jedno od ograničenja ove studije je što su poređene opšta pedijatrijska populacija i visokorizična grupa dece. Trenutno, veličina uzorka ne dozvoljava analiziranje ovih grupa zasebno. Prikupljanjem većeg broja anketa omogućiće se i ovakva ispitivanja. Drugo ograničenje je što nisu utvrđene senzitivnost i specifičnost instrumenta.

Zaključak

Porast prevalence ASD zahteva unapređivanje ranog prepoznavanja poremećaja i u našoj zemlji, što se može postići masovnom primenom ovog upitnika na redovnom pedijatrijskom pregledu zdrave dece u drugoj godini.

Dalja istraživanja će se kretati u pravcu kompletne validacije upitnika i utvrđivanja specifičnosti i senzitivnosti instrumenta na većem uzorku.

EARLY SCREENING FOR AUTISTIC SPECTRUM DISORDERS IN TODDLERS AGED 16 TO 30 MONTHS

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Abstract: Introduction: Prevalence of autism spectrum disorders (ASD) worldwide shows a significant rise. Screening and early diagnosis are extremely important and provide a possibility for an early intervention. **Objectives:** This study is a part of validation process for a serbian translation of Modified Checklist for Autism in Toddlers, Revised with Follow-up (M-CHAT-R/F). Another aim was to analyse the risk factors which are associated with the development of ASD. **Methods:** The study included parents of toddlers aged 16 to 30 months during a well-child care visits in Dom zdravlja Savski venac and parents of toddlers sent to see a psychiatrist in Institute for mental health (IMH). Children were screened using the M-CHAT-R/F. **Results:** The study included 65 toddlers. The ones screened in Dom zdravlja were placed in a low-risk group, and others who were referred to IMH were classified as high-risk group. Comparing these two groups no statistically significant difference was found in terms of children's age or parents' age at birth. Statistically significant difference was found in terms of gestational week at birth, and significantly higher incidence of pregnancy complications in high-risk group. **Conclusion:** Further investigation should completely examine the psychometric characteristics of M-CHAT, but the preliminary findings show that M-CHAT can detect many cases of ASD during a routine pediatrician examination. Some prenatal and perinatal factors such as pregnancy complications and gestational age at birth can lead to increased risk of developing ASD.

Key words: *autistic spectrum disorders, screening, M-CHAT, prenatal factors*

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Svetomir Bojanin: Četiri eseja o dobroti

Konras, Beograd, 2014.

Prikaz knjige

Knjiga Četiri Eseja o dobroti je delo koje je nastalo postepenim sakupljanjem i ranijim prikazivanjem promišljanja na temu dobrote profesora Svetomira Bojanina koje je objavljivao u časopisima kao što su Filozofski godišnjak filzofskog društva Banja Luka i Zenit, odnosno koje je iznosio na naučnim i stručnim skupovima. Tragajući sam za delima koja bi na najbolji mogući način doprinela razumevanju razvoja dečje psihijatrije i njenog nepredovanja profesor Bojanin je „imao doživljaj da je ljudska dobrota čvrst temelj svim nastojanjima koja oblast dečje psihijatrije čine tako živom i tako potrebnom našoj savremenosti“. Knjiga je kako sam autor navodi nastajala postepeno; čini se da je otkrivanje dobrote razvojni fenomen i da su verovatno decenije potrebne pre nego što se isto objedini u jednom delu. Dobotu je definisao kroz četiri fenomena, na način kroz koji se dobrota prikazuje kao obeležje ljudskog načina postojanja:

1. Preobražaja odnosa prema mentalnom bolesniku i pristup isceliteljskom radu koju je prikazao kroz dobrotu jednog bolničara s psihijatrijskog odeljenja Opšte bolnice Bisetr u Parizu, svim psihijatriima poznata kao bolnica u kojoj su privu put skinuti lanci mentalnim bolesnicima u poslednjoj trećini XVIII veka.
2. Put izrastanja identiteta ljudske ličnosti – kroz prevazilaženje zastoja u razvoju čoveka i njegove slobode i rađanja ljudske odgovornosti za dobrobit drugog; u tom kontekstu dobrotu definiše kao odgovornost za dobrobit bližnjeg, a slobodu kao njen preduslov.
3. Fenomen dobrote definisan u relaciji dete – odrasli; pokušaj razumevanja nesporazuma između onog što deca i mladi u razvoju očekuju od odraslih i onoga što im svet odraslih daje; opisi gušenja dobrote kao rezultanta opisanih sukoba i kriza odrastanja.
4. Opis ljudske dobrote kao rezultat uspostavljanja estetskih i etičkih merila kojima čovek premerava svoje postupke, a koji proističu iz slobodnog izbora ljudskih htenja.

I esej – Mentalna higijena ili „civilna kontrola stručnosti“ u psihijatriji ili van nje

U Institutu za mentalno zdravlje već više od 3 decenije postoji edukacija Mentalna higijena razvojnog doba namenjena lekarima, socijalnim radnicima, psiholozima. U ovom eseju pronalizmo odakle pojam Mentalna higijena – u prvoj deceniji XX veka kada je američki građanin Birs izašao iz psihijatrijske bolnice, u potpunosti oporavljen, ali veoma gnevan zbog ponižavajućeg odnosa osoblja prema pacijentima; o tome je počeo da govori u javnosti i bio je začetnik mentalno-higijenske aktivnosti. Autor navodi da je „problem visoke stručnosti i niskog nivoa vaspitanja u ophođenju s ljudima – problem mentalne higijene ili nehigijene“, a to je i osnov prvog eseja o dobroti.

Osim iskustva građanina Birsa, u ovom eseju je opisan i podvig građanina Pisena, koji je živeo u XVIII veku, i koji je nakon sopstvenog izlečenja tubekuloznog adenita ostao da radi u okviru opšte bolnice Bisetr. Ovaj bolničar se, kako profesor kaže, „drznuo da na svoju ruku, nikome ne govoreći i nikoga ne pitajući, skine lance s jednog bolesnika čiju je patnju razumeo, saosećajući se s njim“. Ova neposlušnost humanog bolničara, moralno hrabrog, autonomnog i odgovornog samom sebi bila je uvod u prvu psihijatrijsku revoluciju; poznati Pinel je bio tihi posmatrač vrednog i moralnog Pisena, koga kasnije i vodi s sobom u psihijatrijsku bolnicu Salpertrije, gde je pisao (radio) novu psihijatrijsku istoriju. Svojim životom i načinom rada Pisen je pokazao praktični metod mentalno-higijenskog delovanja – tiho, nekonfliktno i odgovorno. Profesor o Pisenovom delu piše „saosećanje, razumevanje, dobrota i odgovornost su osnovni fenomeni ljudskog psihizma koje je Pisen, seljak koji je živeo u duhu srednjovekovne tradicije, a bolničar, uveo u praksu savremene psihijatrijske bolnice“.

Čitalac na dalje može da postavi pitanje: zašto se nije nastavilo s skidanjem jednog po jednog okova u narednim decenijama razvoja psihijatrije; gde se delo saosećanje s bližnjima, dobrota, odgovornost; ili kako sam autor navodi „mnogi stručni ljudi, u suštini lepo vaspitani, tokom svog radnog vremena u psihijatrijskoj bolnici, ponašaju se kao da nisu dobili elementarno porodično vaspitanje“. Zaključak ovog eseja bi trebalo da uđe u sve udžbenike koji se bave etičnosti lekara i odnosa lekar-pacijent; autor navodi sledeće kao neophodno kako bi se pacijentu pomoglo i zapravo daje odgovor na pitanje šta pacijenti žele: da budu sigurni u to da ih je neko razumeo, da ih neko poštuje, omogućavajući im slobodu biranja; da im pruži ponašanje usklađeno s vrlinama. Eliot je kazao da je prvi uslov dobrote jeste nešto voleti, a drugi nešto poštovati (1); Bekon smatra da sklonost ka dobroti je utisnuta u ljudsku prirodu i to u tolikoj meri da ukoliko ne očituje prema ljudima, očitavaće se prema drugim živim bićima (2). Hoćemo li da dela budu dobra, mora najpre čovek koji ih čini da bude dobar i smeran, jer odatle gde nema ništa dobro, ne može ništa dobro ni izaći (3).

II esej – Čovekov identitet i naša savremenost

U drugom eseju autor iznosi da nastanak identiteta ličnosti se dešava od primarnog biološkog entiteta, na kojem se kasnije zasniva telesni, porodični i zavičajni identitet na čijim osnovama se kasnije u životu dešavaju viši integrativni procesi koji vode formiranju nacionalnog i religioznog identiteta jedne ličnosti. Sav razvoj počinje tokom detinjstva i adolescencije kroz kako autor navodi „bujanje biološkog sloja", razvoja govora i ostvarivanjem socijalnog sloja koji „odražava čar drugog međuljudskog susretanja".

Dobrota je u ovom eseju prikazana kroz analizu odgovornosti za dobrobit bližnjeg, gde je sloboda njen preduslov – samo slobodom se prevazilaze zastoji u razvoju čoveka (a pod zastojima smatra ljudske navike i bezumlja).

U zaključku ovog eseja autor iznosi svoj sud da kao što su prošlovekovni nasilni režimi nasiljem lišavali čoveka kreativnosti i stvaralaštva, tako saveremeno društvo ugrožava „bitno proces hominizacije i dovodi u pitanje njegov dalji pravolinijski tok".

III esej – Nametanje i odupiranje u ljudskom životu tokom razvojnog doba

Ljudsko postojanje odaje utisak neprestanog odupiranja nečemu što se nameće iz okruženja. U analizi funkcionisanja ljudskog bića profesor spominje tri standardna nivoa – biološki, socijalni i psihološki. „Biološki obrasci odnosa prema stvarnosti omogućavaju čoveku da prepozna sopstvenu radoznalost i čar posedovanja, ono što je novo, nestalnost ili promenljivost sveta i sadašnje vreme u kojem se odvija život svakog od nas." S druge strane „socijalni sloj omogućava čoveku da prepozna doživljaje koji određuju čovekovo postojanje i čine ga tradicija, lični identitet i prošlost kao dimenzija vremen", čime se možda i daje način sagledavanja značaja istorije u razvitku jednog pojedinca. Psihički sloj deifniše kroz fenomen egzistencijalne strepnje – kroz čari posedovanja i potrebe za sigurnošću u cilju održivosti dobrobiti u budućnosti, koja je neizvesna i time nedokučiva ljudskom biću i predstavlja stalni potencijali izvor krize.

Izuzetno značajna je evaluacija i razmatranje radoznalosti kao fenomena neophodnom u rastu i razvoju deteta. Bez radoznalosti dete ima skučen prostor reagovanja i intereagovanja: u najtežim razvojnim poremećajima kao što su poremećaji autističnog spektra upravo ta socijalno izmenjena radoznalost ostavlja dete zaključano u svom svetu socijalno nedokučivih interesovanja. Autor definiše radoznalost kroz stapanje inteligencije i istančane osećajnosti u ljudsku mudrost; kroz otkrivanje etičnosti i otkrivanje bezuslovnog zahteva ljudskog bića, kroz duhovnost.

Dete razvija svoju radoznalost kroz stalno istraživanje svojih mogućnosti od motornih preko saznajnih i emotivnih kontinuiranih iskustava. Kada govori o ulozi nas odraslih u razvoju dečje radoznalosti navodi „deci

treba pomoći da se na prikladan način izlažu naporima saznavanja novog, čije ih savladavanje raduje“. Napominje da je od izuzetne važnosti uključivanje deteta u svakodnevne aktivnosti odraslih omogućavajući ih da nam pomognu, izlažući ih našim modelima ponašanja shodno njihovim potrebama i razvoju. Proces identifikacije s odraslima (učenje po modelu) zbog toga jeste jedini prirodni put vaspitavanja, koje se obavlja s našim znanjem ili bez njega – dete se ne identifikuje s našim rečima, poukama, deklamacijama, popovanjem i sl već načinom na koji se mi ophodimo sa stvarima, svetom koji nas okružuje, među sobom kao odraslima, sa samim detetom. Tertulijan je kazao „Dušu su stvorili roditelji“.

Kao odrasli nedovoljno se bavimo razumevanjem i analizom radoznalosti deteta. Skloni smo da namećemo isključivo sopstvene zahteve i svoja interesovanja, sprečavajući i deformišući prirodnu radoznalost deteta čime vrlo često nesvesno utičemo na spontanu motivaciju dece za učenjem, savladavanjem napora i dr. Zato u nekoliko knjiga, pa i u ovoj, citiranje Komenskog o tome kako bi trebala škola da izgleda – odnosno šta ne treba škola da traži uvek je akutelna (4): škola da ne traži: ništa previše, s obzirom na uzrast deteta; ništa prebrzo u odnosu na njihov ritam primanja i ništa što sama dece ne žele (dodala bih i što sami odrasli ne žele).

U ovom eseju je dotaknut i fenomen jogunstva kod dece koje autor definiše kao odgovor deteta na zahtev koje po njegovom doživljaju ugrožava njegov sopstveni identitet. Autor s pravom i s ogromnim iskustvom i kao dečji psihijatar, i kao terapeut, ali i kao roditelj savetuje „...nemojte lomiti jogunstvo svog deteta“...na bilo kom uzrastu, na bilo kom mestu. On savetuje „prihvatite ga s puno ozbiljnosti; budite otvoreni za razumevanje, strpljivo sačekajte da se ukaže trenutak za razgovor, koji počnite temom izvan konflikta...na nju dođite kada se strasi smire...nastojte da razumete dete i ako se ne slažete s njim“. Ovo je suština vaspitnog procesa – strpljenje, razumevanje, prihvatanje, uvremenjeno reagovanje, „vođenje u pravcu realnih mogućnosti i potreba neposredne stvarnosti“. Zbog svega iznetog ideja da tučemo sopstvenu decu radi njihovog dobra zvuči pervezno. Roditelji od dečjih psihijatara, a vrlo često isto čine i škole, institucije gde deca na žalost borave ne svojom krivicom, lišena roditelja i topline sopstvenog doma, očekuju da decu dovedemo u red nekim magičnim formulama, lekom, hospitalizacijom. Očekuje se da dete bude onakvo kakvim ga roditelj zamišlja, jer ovo što čini, što je sada, nije ono što se zamišlja da treba da bude. Ili kada od adolescenta očekujemo, jer je odrastao, da sve razume, ali da za u inat ne želi, a zaboravljamo da svašta zanju, ali i dalje ništa ne razumeju te da je i tada potrebno naše strpljenje i umeće da ih do toga dovedemo.

U izgradnji sopstvene autonomije, a samo autonomni i samosveni smo korisni i sebi i drugima, svaki vaspitni stav koji je nametnut može dovesti dete u situaciju sopstvenog doživljaja kao „ugroženog subjekta“ čime se odnos dece i odraslih dovodi u fazu opšteg nerazumevanja gde obično

nastrada onaj slabiji. S tim u vezi, autor navodi da „očigledno je da su roditelji nespremni da razumeju svoju decu, kao i da deca nisu naučila bilo koga da razumeju, pa ni svoje roditelje“. I šta se nudi u ovakvoj situaciji? Po autoru, čovek kao biće istinitosti i pravednosti, zahteva negovanje, od najranijih dana „u sebi svoje istine, koje su uvek opšte, stalne i nepromenljive bez obzira na odore u koje ih odevaju“.

I šta predlaže: istina o odbrani života, istina o smislu za kojim tragamo i istina o stvaralačkom radu. „To je način da se čovek odupre nametanju besmisla sopstvenog postojanja kao i da se brani stalnim zahtevom za samousavršvanjem ... duša mi uporno prelazi na stranu dobrote u terapijskom procesu“. Deluje da iskreni čin dobrote može više terapijski učiniti nego bilo koje veštačko, emocionalno kontorlisano stanovište koje često odlikuje „terapija“

IV esej - Psihoterapija kao fenomen helensko-hrišćanske tradicije

U poslednjem eseju autor se bavi istorijiskim razvojem psihoterapije napominjući da je mnogo pre XIX veka upućen prvi psihoterapijski postulat „poznaj sebe“ koji tumači kao poziv čoveku „da rešenje svojih problema čovek ne očekuje od proroštva nego da ga traži u samom sebi“. S tim u vezi psihoterapiju opisuje kao put ka promeni, psihoanalizu kao kulturalni fenomen subjektizovan kroz istoriju zapadne civilizacije; „spoznaj samog sebe“ tumači na način – odvoj se od samog sebe kroz introspekciju sagledavajući sebe i kao subjekta i kao objekat.

Opisujući helensko doba i dijaloški model koji se tada koristio, daje opis dramskog trougla gde je žrtva dobro, viša sila zlo, a gledalac spasilac, te da je ovo doba obogatilo mogućnost psihoterapije sagledavanjem etičkog konflikta u čoveku, podsticanjem odluke da bude moralan i težnjom ka umerenosti u svemu.

Epoha hrišćanstva je donela koncept greha i grešnosti, gde se uvodi koncept da je osoba dobra, a njen postupak loš. Nastajanjem čina pokajanja pred drugim svedoči se o našem postojanju, a „iskrenim ispovedanjem tokom celog života postajemo dostojni da damo obećanje Bogu“ (5).

U rezimeu ovog eseja autor navodi da je u samom čoveku i uzork pada i mogućnost spasenja. Da bi se to postiglo neophodan je specifični tip razgovora s drugim, iskren odnos prema sebi kroz „samoupoznavanje putem razgovora s drugim“, donošenje „odluke pokajanja“ i ostvarivanjem duševnog mira kroz samoodgovorno ponašanja.

Na kraju i sam autor kaže da je knjiga mogla da se nazove Na tragu dobrote. Profesor Bojanin je napisao da svaki čovek ima poneku mudrost, a među mnogim ljudima uvek se javi po neki mudri čovek.

Ovu novu knjigu mudrog i vrednog čoveka preporučujem za čitanje jer mera mentalnog zdravlja je sklonost pronalaženja dobrog u svemu.

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Milica Pejović Milovančević

Kalendar kongres

2016.

6th International Conference of Physical Therapy in Psychiatry and Mental Health
March 09-11, 2016, Madrid, Spain
http://icppmh.org/madrid_home.html

EPA 2016 – 24th European Congress of Psychiatry
March 12-15, 2016, Madrid, Spain
http://www.epa-congress.org/

Treating Depression 2016
March 24, 2016, London, United Kingdom
http://www.mahealthcareevents.co.uk/depression2016
Email: lisa.freeman@markallengroup.com

World Psychiatric Association, Section on Epidemiology & Public Health 2016 Meeting
Co-sponsored by World Psychiatric Association (WPA)
Psychiatric epidemiology meets genetics: the public health consequences
March 29 – April 1, 2016, Munich, Germany
www.wpaepi2016.org

5th Biennial Schizophrenia International Research Society Conference
April 2-6, 2016, Florence, Italy
http://www.schizophreniaconference.org/

8th International Congress of Psychopharmacology & 4th International Symposium on Child and Adolescent Psychopharmacology
April 20-24, 2016, Antalya, Turkey
http://www.psychopharmacology2016.org/Invitation.php

23rd International Symposium about Current Issues and Controversies in Psychiatry (Barcelona & Internet)
April 28-30, 2016, Barcelona, Spain
http://www.controversiasbarcelona.org/en/
Email: secretaria@controversiasbarcelona.org

2nd International Conference on Psychiatry and Psychiatric disorders 2016
May 02-04, 2016, Chicago, United States
http://psychiatry.global-summit.com/
Email: psychiatry@annualcongress.com

IV kongres Društva za dečju i adolescentnu psihijatriju i srodne struke Srbije
12-15. maj 2016, Zlatibor, Srbija.
www.deaps.org

Recent Advances in Neuropsychiatric, Psychological and Social Sciences Annual International Conference of the Association of Psychology and Psychiatry for Adults and Children
May 17-20, 2016, Athens, (Greece)
http://www.appac.gr/displayITM1.asp?ITMID=18&LANG=EN

WPA 2016 International Congress
July 6-10, 2016, Istanbul, Turkey
leventkuey@wpaistanbul2016.org

18th Annual Conference of the International Society for Bipolar Disorders Held Jointly with the 8th Biennial Conference of The International Society for Affective Disorders
July 13-16, 2016, Amsterdam, The Netherlands
http://isbd2016.com/

22nd International Association for Child & Adolescent Psychiatry and Allied Professions
July 16-21, 2016, Calgary, Alberta, Canada
http://htp://www.iacapap2016.org/

11th International Conference on Child and Adolescent Psychopathology
July 18-20, 2016, London, UK
http://www.roehampton.ac.uk/Research-Centres/Centre-for-Applied-Research-and-Assessment-in-Child-and-Adolescent-Wellbeing/Child-and-Adolescent-Psychopathology-Conference/

4th International Congress on Borderline Personality Disorder and Allied Disorders
September 08-10, 2016, Vienna, Austria
http://www.borderline-congress.org/

29th ECNP Congress
September 17-20, 2016, Vienna, Austria
www.ecnp-congress.eu

International Association for Child & Adolescent Psychiatry and Allied Professions World Congress 2016
September 18-22, 2016, Calgary, Canada
http://www.iacapap2016.org/

XV National Congress of the Serbian Psychiatric Association – Pathways and Crossroads of Psychiatry
XV Kongres Udruženja psihijatara Srbije – Putevi i raskršća psihijatrije
kosponzorisan od strane Svetske psihijatrijske asocijacije
12-15. oktobar 2016., Srpska akademija nauka i umetnosti, Beograd, Srbija
http://ups-spa.org/

International Neuroscience and Biological Psychiatry ISBS Symposium "TRANSLATIONAL NEUROSCIENCE OF STRESS"
November 10-11, 2016, San Diego, United States
http://www.scribd.com/doc/274040475
Email: isbs.congress@gmail.com

WPA 2016 – **World Psychiatric Association International Congress**
November 18-22, 2016, Cape Town, South Africa
http://www.wpacapetown2016.org.za
Email: charlene@soafrica.com

2017.

18th World Congress of the World Association for Dynamic Psychiatry WADP, co-sponsored by WPA
"Creative processes in psychotherapy and psychiatry"
April 19-22, 2017, Florence, Italy
www.Wadp2017.org

6th World Congress on ADHD
April 20-23, 2017, Vancouver, Canada
http://www.adhd-congress.org
Email: adhd@cpo-hanser.de

17th International Congress of ESCAP 2017
July 8-12, 2017, Geneva, Switzerland
www.ESCAP2017.eu

30th ECNP Congress
September 2-5, 2017, Paris, France
www.ecnp-congress.eu

WPA XVII World Congress of Psychiatry Berlin 2017
October 8-12, 2017, Berlin, Germany
www.wpaberlin2017.com

UPUTSTVA SARADNICIMA

PSIHIJATRIJA DANAS je zvanični časopis Udruženja psihijatara Srbije. Izlazi dva puta godišnje i objavljuje pregledne i istraživačke radove, prikaze slučajeva, prikaze knjiga i pisma uredniku.

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Prikazi slučaja treba da sadrže zanimljive kliničke izveštaje i opise slučajeva u kojima su primenjeni novi dijagnostički i terapijski metodi. Ne smeju imati više od 1500 reči.

Opšti radovi sadrže stavove o teoriji i praksi psihijatrije, o psihijatrijskim službama, o graničnim oblastima psihijatrije i drugih disciplina, itd. Ne treba da imaju više od 2000 reči.

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Tekst treba podeliti u delove (npr. za istraživačke radove: Uvod, Metod, Rezultati, Diskusija). Rezultate koji se pojavljuju na tabelama ne treba detaljno ponavljati.

Fusnote nisu dozvoljene u člancima.

Tabele, grafikone i slike priložiti na posebnim listovima papira (na kraju fajla), sa odgovarajućim naslovom, arapskim brojem (Tabela 1) i u tekstu označiti njihovo mesto. Izbegavati vertikalne i horizontalne linije u tabelama.

Skraćenice koristiti samo kad je neophodno i za svaku navesti pun termin pri

prvom navođenju u tekstu. Korišćene skraćenice u tabeli i grafikonu treba objasniti u legendi.

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Primeri:

1) Članak u časopisu: Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002;347:284-7.

2) Poglavlje u knjizi: Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93-113.

3) Knjiga: Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

4) Disertacija: Borkowski MM. Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.

5) Neobjavljen materijal (u štampi): Tian D, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. Proc Natl Acad Sci U S A. Forthcoming 2002.

6) Članak iz časopisa u elektronskom obliku: Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [Internet]. 2002 Jun [cited 2002 Aug 12];102(6):[about 1 p.]. Available from: http://www.nursingworld.org/AJN/2002/june/Wawatch.htmArticle.

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Uz štampan tekst, radove dostaviti na disku (CD) koja je Windows kompatibilna. CD treba da sadrži samo fajl koji će biti štampan. Odštampana kopija rada u potpunosti treba da odgovara verziji na CD. Tekst treba da bude napisan u tekst procesoru (Word), u fontu Times New Roman. Tabele, grafikoni i slike često se moraju ponovo uraditi pa treba dostaviti i njihovu odštampanu kopiju.

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Review articles should be written by one author only, unless the second author is not a psychiatrist. They should contain one's own results already published and should not exceed 7500 words.

Research papers must be based on a research protocol and statistical evaluation of the findings is essential. They should not exceed 3000 words.

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Articles must be typewritten, double-spaced on one side of the paper with a margin of at least 3.5 cm. All pages must be numbered, starting with the title page.

Title page should indicates the title of the paper (which should not exceed 12 words), the names and surnames of the authors, their academic titles, institutions where they work, as well as the name, surname, address, telephone number and e-mail address of the author in charge of correspondence.

Abstract (up to 300 words) should be sent on a separate, second page. It should include main facts from the paper, as well as 3-6 key words, selected based on *Medical Subject Headings – MeSH* (http://gateway.nlm.nih.gov).

Text should be divided into sections (e.g., for research papers: Introduction, Method, Results, Discussion). Results ap-

pearing in the tables should not be reported again in detail in the text.

Footnotes are not allowed in articles.

Tables, graphs and figures should be submitted on separate sheets of paper (at the end of the file), with an adequate heading and Arabic enumeration (Table 1). The desired position of the table relative to the text should be indicated in the text. Avoid vertical and horizontal lines in tables.

Abbreviations should only be used when necessary, and the full term for which it stands should precede its first use in the text. Abbreviations in tables and graphs must be explained in the key to abbreviations.

Acknowledgement: List all persons who contributed to the creation of the manuscript, but do not meet the criteria for authorship (e.g. technical help, help in writing etc.). Also list the financial and material support (sponsor, scholarship, equipment, drugs etc.).

References: The list of references should include only the publications cited in the text. They should be identified in the text by Arabic numerals in square brackets in the order in which they are first mentioned in the text (*Vancouver style - http://www.nlm.nih.gov/bsd/uniform_requirements.html*), e.g. Kernberg [1] states that...

Abbreviations of journals should conform to the style used in *Index Medicus* (journal database listed at http://www.ncbi.nlm.nih.gov/nlmcatalog). Journals not indexed there should not be abbreviated. After journal abbreviations use the dot. When citing pages, cite the beginning page. and end page without the repeating number/s (e.g. from 274 p. to 278 p. is written 274-8).

In references with up to six authors, all the authors must be listed. In references with more than six authors, list first six authors and et al.

Examples:

1) *Journal article:* Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002;347:284-7.

2) *Book chapter:* Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93-113.

3) *Book*: Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

4) Dissertation: Borkowski MM. Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.

5) *Unpublished material (in press):* Tian D, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. Proc Natl Acad Sci U S A. Forthcoming 2002.

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