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AKTUALITY

SVANTE PÄABO – LAUREÁT NOBELOVY CENY ZA FYZIOLOGII A LÉKAŘSTVÍ V ROCE 2022

Kristýna Brzobohatá

Oddělení genetiky a molekulární biologie – Přírodovědecká fakulta, Masarykovy Univerzity Brno

Laureáti Nobelovy ceny, nejvyššího možného ocenění za vědecký přínos, jsou každoročně vyhlašováni v průběhu října. O jejím udělení rozhoduje komise složená z vědců z Karolinska institut, členové Švédské akademie věd a v případě Nobelovy ceny míru norský parlament. Slavnostní ceremoniál spojený s jejich předáním probíhá tradičně 10. prosince, v den výročí úmrtí jejího zakladatele Alfreda Nobela, a kromě oceněných vědců se ho účastní i švédská královská rodina. První Nobelovy ceny byly uděleny v roce 1901 a byly rozděleny do pěti kategorií: Nobelova míru, Nobelova cena lékařství a fyziologii, Nobelova cena za chemii, Nobelova cena fyziku, Nobelova cena za literaturu Nobelova cena za ekonomii.

V roce 2022 byla Nobelova cena za fyziologii a lékařství udělena švédskému evolučnímu biologovi Svante Pääbemu, působícímu na Max Planck Institute for Evolutionary Anthropology v Lipsku. Svante Pääbo zasvětil svůj profesní život výzkumu evoluce, zejména evoluce člověka pomocí analýzy starobylé DNA (ancient DNA, aDNA). Dosud v historii udělování Nobelových cen nebyl oceněn výzkum, který by tak úzce souvisel s antropologií, jako práce Svante Pääba a proto o něm a jeho práci přinášíme krátký medailonek.

Svante Pääbo se narodil v roce 1955 ve Stockholmu estonské chemičce Karin Pääbo. Jeho otcem je švédský biochemik, taktéž nositel Nobelovy ceny, Sune Bergström (1916–2004). Jednalo se však o aféru a svého otce nikdy blíže nepoznal. Svante Pääbo se nejdříve zajímal o studium jazyků, vystudoval ale medicínu na univerzitě v Uppsale. Pokračoval zde také jako postgraduální student, ve své disertaci, kterou obhájil v roce 1986, se zabýval adenoviry.

Souběžně s prací na doktorátu začal také s experimenty, jejichž cílem bylo prokázat, že DNA perzistuje v historických tkáních tisíce let, a to i po dlouhé době deponace a je možné ji analyzovat podobně jako DNA ze současných vzorků (Pääbo, 1984; Pääbo, 1985).

Po získání doktorátu v roce 1986 působil v Kalifornii, na Kalifornské univerzitě v Bercley a od roku 1990 učil také na Mnichovské univerzitě. Pääbo v Německu zůstal a roce 1997 založil Institute for Evolutionary Anthropology na Max Planck Institutu a zformoval tak nový obor – paleogenetiku, eventuelně archeogenetiku. Tým pod jeho vedení zavedl kompletní metodiku práce s aDNA a zásady analýz z historických tkání (Pääbo, 1987; Pääbo, 1989, Pääbo *et al.*, 1989; Höss *et* Pääbo 1993).

K jeho průlomovým objevům patří sekvenování genomů vyhynulých hominidů (Krings *et al.,* 1997; Noonan *et al.*, 2006; Green *et al.*, 2006; Green *et al.*, 2008) a jejich komparace s genomem šimpanze (Ebersberger *et al.*, 2002; Kitano *et al.*, 2003; Cheng *et al.*, 2005), anatomicky moderního člověka a archaického člověka (Krause *et al.*, 2010). Díky nim víme, jak se od sebe tyto druhy, či poddruhy geneticky lišily, které geny jsou specifické pouze pro anatomicky moderního člověka či neandrtálce (Enard *et al.*, 2002). Odhalil také, že neandrtálec zanechal s anatomicky moderním člověkem potomky, kteří osídlili planetu Zemi, kromě Afriky (Reich *et al.*, 2011; Sankararaman *et al.*, 2012; Hajdinjak *et al.,* 2021). Každý z nás v sobě dosud nese asi 2 % DNA neandrtálce s geny, které nám velkou měrou pomohly přežít nehostinné glaciály. Díky analýze aDNA se Pääbemu také podařilo objevit zcela nový poddruh *Homo sapiens*, který v paleolitu obýval Asii – Denisovana (Krause *et al.*, 2010; Reich *et al.*, 2010; Meyer *et al*. 2012; Zhang *et al*., 2020). Vzpomínky na svou kariéru, začátku a rozvoj paleogenetiky s nahlédnutím do soukromého života, poutavě shrnul v knize *Neanderthal Man: In Search of Lost Genomes* (2014). Kniha byla velmi dobře přijata i kritiky. V roce 2007 navštívil Brno, kde v rámci série přednášek Mendel Lectures přednesl příspěvek o výzkumu genu FOXP2, který je zodpovědný za lidskou schopnost řeči.

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PŮVODNÍ PRÁCE

ANTROPOMETRICKÉ CHARAKTERISTIKY A INDEXY TELESNEJ PROPORCIONALITY AKO PREDIKTORY OBEZITY U ŽIEN VO VEKU 18–25 ROKOV

Anthropometric characteristics and body proportionality indices as predictors of obesity in women aged 18–25 years

Miriama Šlebodová, Soňa Mačeková, Hedviga Vašková, Soňa Kalafutová, Jana Gaľová, Jarmila Bernasovská, Michaela Zigová

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Abstract

Various simple anthropometric parameters and indices can be used to assess body composition and determine the prevalence of overweight or obesity. We aimed to compare the ability of anthropometric indices (BMI, WHR and WHtR) and waist circumference measurements to determine the prevalence of overweight and obesity in young women. In our study group, 25,3 % of women were overweight/obese according to BMI. The WHtR index had the highest prevalence of abdominal obesity (16 %) and waist circumference had the lowest (7,3 %). In addition to commonly used indices, we used newer indices assessing either the prevalence of abdominal obesity or indices reflecting the amount of body fat. In our study, we aimed to compare the mean values of BAI, CI, BRI and AVI indices according to BMI categorization and to find statistically significant differences in the categories. We observed statistically significant differences in mean values among the BMI categories for BAI, CI and BRI indices ($p < 0{,}05$) except for ABSI index, which was not statistically significant.

Key words: *obesity, BMI, anthropometric indices*

Úvod

Obezita predstavuje komplexné multifaktoriálne ochorenie, ktoré je definované abnormálnym množstvom tukového tkaniva, ktoré je lokalizované subkutánne alebo viscerálne. Na definovanie obezity sa používa množstvo techník a meraní (Panuganti, Nguyen, & Kshirsagar, 2022). Antropometrické merania predstavujú neinvazívne kvantitatívne merania, ktoré nám umožňujú cenné hodnotenie stavu výživy u detí a dospelých (Fryar, Ogden, & Flegal, 2016). Ide o jednoduché meranie, ktoré je lacné a nevyžaduje si vysokú úroveň technických zručností. Antropometrické merania sa široko využívajú v klinických a rozsiahlych epidemiologických štúdiách (Kuriyan, 2018). Antropometria stanovuje telesnú hmotnosť, telesnú výšku, obvody tela na posúdenie adipozity a hrúbku kožných rias. Antropometrickými meraniami sa dá posúdiť telesná kompozícia a takisto výskyt nadhmotnosti alebo obezity. So stanovením telesnej výšky a telesnej hmotnosti úzko súvisí BMI (body mass index). BMI predstavuje meradlo nadhmotnosti a obezity na úrovni populácie, pretože je rovnaké pre obe pohlavia a pre všetky vekové kategórie dospelých (Braunerová & Hainer, 2010). Medzi ďalšie antropometrické metódy patrí meranie telesných obvodov pomocou pásovej miery, pričom dĺžka jednotlivých telesných obvodov charakterizuje rozloženie tuku (Kunešová et al. 2016). Najpoužívanejšie je meranie obvodu pása (WC), index WHR (waist to hip ratio) a WHtR (waist to height ratio). Okrem zaužívaných indexov na posúdenie miery nadhmotnosti a obezity sa používajú aj novšie indexy, ktoré hodnotia abdominálnu obezitu resp. množstvo tukového tkaniva, ako napríklad index ABSI (body shape index), index BAI (body adiposity index), index CI (conicity index), index BRI (body roundness index) a index AVI (abdominal volume index). Index tvaru tela (ABSI) je index abdominálnej obezity vyvinutý na základe epidemiologických štatistík a navrhnutý tak, aby minimálne koreloval s indexom telesnej hmotnosti (BMI) (Nagayama et al., 2022). Vysoký index ABSI naznačuje, že WC je vyšší ako sa očakáva pri danej telesnej výške a hmotnosti, a zodpovedá centrálnejšej koncentrácii tukového tkaniva (Dhana et al., 2016). Index telesnej adipozity (BAI) bol navrhnutý ako rovnica na predpovedanie množstva telesného tuku (Lichtash et al., 2013). Index CI (index kuželovitosti) bol vyvinutý ako ukazovateľ obezity a rozloženia telesného tuku, tento index je dôležitým klinickým nástrojom, ktorý sa používa na určenie rizika KVO (kardiovaskulárnych ochorení) v populácii (Andrade et al., 2016). Index zaoblenosti (BRI) tela determinuje viscerálne tukové tkanivo (VAT) a percento telesného tuku. Index CI a BRI boli stanovené ako ukazovatele rozloženia telesného tuku a ich hodnoty sa zvyšujú v závislosti od nahromadenia viscerálneho tukového tkaniva. Index AVI – index objemu brucha sa taktiež používa na determináciu abdominánej (centrálnej) obezity (Thomas et al., 2013).

Cieľ

Našim cieľom bolo pomocou antropometrických charakteristík a indexov hodnotiť telesnú proporcionalitu a určiť prevalenciu nadhmotnosti a obezity u mladých žien. Na posúdenie prevalencie nadhmotnosti a obezity sme aplikovali indexy BMI, WHR a WHtR a ako antropometrické meradlo sme použili obvod pása. Obvod pása a indexy WHR a WHtR slúžia na posúdenie abdominálnej (centrálnej) obezity. Na posúdenie telesnej proporcionality sme použili aj indexy ABSI, BAI, CI, BRI a AVI. Na základe kategorizácie podľa BMI sme porovnávali priemerné hodnoty vybraných parametrov a indexov v každej z BMI kategórii. Nakoľko obezita súvisí s výskytom mnohých chronických ochorení, je potrebné pre jej skríning využívať viacero antropometrických indexov, pretože ich kombináciou dosiahneme objektívnejšie a spoľahlivejšie výsledky.

Metodika

Sledovaný súbor tvorilo 150 žien vo veku 18–25 rokov. Vyšetrované ženy boli študentkami Prešovskej univerzity v Prešove. Výskum prebiehal počas celého roka 2021. Výber sledovaného súboru bol náhodný podľa záujmu oslovených študentiek. Kritériom zaradenia do štúdie bolo ženské pohlavie a vek od 18–25 rokov, pričom probandky boli oboznámené s cieľom a priebehom testovania a podpísali informovaný súhlas.

Meranie prebehlo jednorázovo v laboratórnych priestoroch Katedry biológie, FHPV, Prešovskej univerzity v Prešove.

Každá probandka podstúpila antropometrické merania, ktoré zahŕňali viacero parametrov:

- telesná výška bola meraná pomocou antropometra s presnosťou na 0,1 cm
- telesná hmotnosť bola meraná pomocou digitálnej osobnej váhy Sencor SBS 5050BK s presnosťou na 100 g
- obvodové miery sme získavali meraním pomocou pásovej miery s presnosťou na 0,1 cm. Obvod hrudníka bol meraný mezosternálne, obvod pása sme merali v najužšej časti nad pupkom, obvod bokov sme merali v mieste najsilnejšie rozvinutého gluteálneho svalstva, obvod stehna bol meraný v polovičnej vzdialenosti medzi trochanterom a vonkajším epikondylom femuru, obvod paže bol meraný v najširšom mieste paže a obvod krku sme merali v polovici krku.

Následne sme zo získaných antropometrických údajov vypočítali indexy BMI, WHR a WHtR. Klasifikáciu obezity na základe hodnôt BMI sme robili podľa WHO (2022) a kategorizáciu podľa indexov WHR, WHtR a obvodu pása podľa WHO (2008). U dospelých osôb WHO definuje nadhmotnosť ako BMI od 25,0 do 29,9 kg/m^2 a obezitu ako BMI ≥ 30,0 kg/m^2. Obezita je ďalej klasifikovaná do troch stupňov závažnosti: I. trieda (BMI 30,0–34,9 kg/m^2), II. trieda (BMI 35,0–39,9 kg/m^2) a III. trieda (BMI ≥ 40,0 kg/m^2) (Poirier et al., 2006). Centrálna obezita bola definovaná ako WC > 102 cm u mužov a > 88 cm u žien, hodnota indexu WHR u mužov > 0,9, u žien > 0,85 a hodnota indexu WHtR > 0,5 (Kobel, Kirsten a Kelso 2022). Z novších indexov sme použili indexy ABSI, BAI, BRI, CI a AVI, ktoré sme vypočítali pomocou vzorcov:

$$\text{ABSI} = \frac{\text{obvod pása (m)}}{\text{BMI}^{\frac{2}{3}} \times \text{telesná výška (m)}^{\frac{1}{2}}};$$

$$\text{BAI} = \frac{\text{obvod bokov (cm)}}{\text{telesná výška (m)}^{1,5}} - 18;$$

$$\text{CI} = 0{,}109^{-1} \times \text{obvod pása (m)} \times \left[\frac{\text{telesná hmotnosť (kg)}}{\text{telesná výška (m)}^{-2}}\right]^{\frac{1}{2}};$$

$$\text{BRI} = 364{,}2 - 365{,}5 \times [1 - \pi^{-2} \times \text{obvod pása (m)}^2 \times \text{telesná výška (m)}^{-2}]^{\frac{1}{2}};$$

$$\text{AVI} = [2 \times \text{obvod pása (cm)}^2 + 0{,}7 \times (\text{obvod pása (cm)} - \text{obvod bokov (cm)}^2]/1000$$

(Wang et. al., 2017).

Štatistické spracovanie dát

Dáta boli prevedené do programu Microsoft Office Excel 2013 a následne štatisticky spracované v programe SPSS pre Windows verzia 19.0. Pre štatistické porovanie kontinuálnych dát boli použité parametrické testy (T-test a Anova) podľa potreby. Štatistickú významnosť prevedených testov sme hodnotili na 5 % hladine ($p < 0{,}05$). Pre jednoduchšiu orientáciu a prehľadnejšiu formu prezentácie výsledkov sme zvolili použitie tabuliek, kde sú výsledky uvedené ako priemerná hodnota (M), smerodajná odchýlka (SD), minimum (Min), maximum (Max), medián (Med) či počet (n) alebo percentá (%).

Výsledky

Základná deskriptívna charakteristika sledovaného súboru na základe antropometrických parametrov a indexov proporcionality je uvedená v tabuľke 1. Priemerný vek probandiek v čase merania bol 21,7 ± 2,32 rokov, telesná hmotnosť probandiek sa pohybovala od 45,1 kg do 128,9 kg, pričom priemerná telesná hmotnosť bola 66,08 ± 11,89 kg. Priemerná telesná výška žien bola 167,1 ± 6,06 cm. Priemerný obvod hrudníka bol 92,01 ± 8,42 cm, pása 75,28 ± 8,87 cm, bokov 97,29 ± 8,43 cm, bicepsu 27 ± 2,97 cm, stehna 53,92 ± 5,33 cm a krku 31,53 ± 1,61 cm. Priemerná hodnota BMI bola 21,65 ± 4,06 kg/m^2. Podľa kategorizácie WHO priemerná hodnota BMI v našom sledovanom súbore spadala do kategórie normálnej telesnej hmotnosti. Priemerná hodnota indexu WHR bola 0,77 ± 0,05. Podľa WHO táto hodnota WHR spadá do kategórie normálnej telesnej hmotnosti, pretože až hodnoty WHR nad 0,85 u žien indikujú abdominálnu obezitu. Priemerná hodnota WHtR bola 0,45 ± 0,06. Podľa WHO bola v nami sledovanom súbore priemerná hodnota WHtR v norme, nakoľko až hodnoty nad 0,5 u žien znamenajú centrálnu obezitu.

Tabuľka 1 *Deskriptívna charakteristika antropometrických parametrov a indexov proporcionality u mladých žien (n = 150)*

Parameter	M	SD	Min	Max	Med
Vek	21,7	2,32	18	25	22
Telesná hmotnosť (kg)	66,08	11,89	45,1	128,9	64,45
Telesná výška (cm)	167,1	6,06	152,6	180,0	166,8
Hrudník (cm)	92,01	8,42	78	133	91
Pás (cm)	75,28	8,87	60	127	74
Boky (cm)	97,29	8,43	81	145	97
Biceps (cm)	27	2,97	20	40	27
Stehno (cm)	53,92	5,33	44	80	53
Krk (cm)	31,53	1,61	28	37	31
BMI (kg/m^2)	21,65	4,06	16,79	43,27	23,28
WHR	0,77	0,05	0,68	0,96	0,77
WHtR	0,45	0,06	0,35	0,73	0,44
ABSI	0,07	0,00	0,06	0,08	0,07
BAI	27,1	4,25	19,6	45,9	26,7
CI	1,1	0,06	0,96	1,34	1,1
BRI	2,55	1,05	1,02	8,87	2,34
AVI	11,85	2,96	7,64	32,48	11,46

Poznámka: M = priemer, SD = smerodajná odchýlka, Min = minimum, Max = maximum, Med = medián, n = početnosť, BMI = index telesnej hmotnosti, WHR = pomer pás/boky, WHtR = pomer pás/telesná výška, ABSI = index tvaru tela, BAI = index adipozity, CI = index kuželovitosti, BRI = index zaoblenosti tela, AVI = index objemu brucha

Frekvenčné zastúpenie prevalencie obezity a centrálnej obezity podľa vybraných antropometrických parametrov a indexov uvádza tabuľka 2. Podľa BMI malo v našom cieľovom súbore 7 žien (4,7 %) podhmotnosť, 105 žien (70 %) normálnu telesnú hmotnosť, 29 žien (19,3 %) nadhmotnosť a 9 žien (6 %) obezitu. Podľa obvodu pása spadalo 139 žien (92,7 %) do normy a 11 žien (7,3 %) malo obvod pása vyšší ako 88 cm, čo sa klasifikuje ako abdominálna obezita. Podľa indexu WHR (pomer obvodu pása k obvodu bokov) spadalo 137 žien (91,3 %) do normy a 13 žien (8,7 %) malo index WHR vyšší ako 0,85, čo determinuje centrálnu obezitu. Podľa indexu WHtR (pomer pás/výška) spadalo 126 žien (84 %) do normy a 24 žien (16 %) malo index WHtR vyšší ako 0,5, čo asociuje s výskytom abdominálnej obezity.

Porovnanie priemerných hodnôt vybraných antropometrických parametrov a indexov podľa kategórií BMI uvádza tabuľka 3. Podľa BMI sme rozdelili ženy na štyri kategórie, a to na kategóriu podhmotnosť (BMI < 18,5 kg/m^2), normálna telesná hmotnosť (BMI 18,5–24,99 kg/m^2), nadhmotnosť (BMI 25,0–29,99 kg/m^2) a obezita (BMI ≥ 30,0 kg/m^2). Štatisticky významné rozdiely v priemerných hodnotách medzi jednotlivými kategóriami sme zaznamenali u všetkých sledovaných parametrov ($p < 0{,}05$) s výnimkou telesnej výšky a indexu ABSI. Priemerná hodnota obvodu pása u žien s podhmotnosťou bola o 32,47 cm nižšia ako u žien s obezitou. Priemerný obvod krku bol v skupine žien s obezitou o 3,46 cm vyšší ako u žien s normálnou telesnou hmotnosťou. WHR index bol v skupine obéznych žien priemerne 0,83 ± 0,05, až hodnota WHR nad 0,85 je klasifikovaná ako obezita, to znamená, že nie všetky ženy, ktoré majú podľa BMI obezitu ju majú aj podľa indexu WHR. Index WHtR bol u žien s obezitou priemerne 0,59 ± 0,07, narozdiel od žien s podhmotnosťou kde bol priemer 0,38 ± 0,02. Normálne hodnoty WHtR sú podľa WHO do 0,5 cm, vyššie hodnoty znamenajú abdominálnu obezitu. Index ABSI mal priemerné hodnoty rovnaké vo všetkých sledovaných kategóriách a nezaznamenali sme žiadny štatisticky významný rozdiel. Priemerné hodnoty indexov BAI, CI, BRI a AVI sa zvyšovali s rastúcím indexom telesnej hmotnosti.

***Tabuľka 2** Prevalencia obezity a centrálnej obezity u mladých žien (n = 150)*

Parameter	Kategória	n (%)
BMI (kg/m^2)	Podhmotnosť	7 (4,7 %)
	Normálna hmotnosť	105 (70 %)
	Nadhmotnosť	29 (19,3 %)
	Obezita	9 (6 %)
WC (cm)	Norma	139 (92,7 %)
	Centrálna obezita	11 (7,3 %)
WHR	Norma	137 (91,3 %)
	Centrálna obezita	13 (8,7 %)
WHtR	Norma	126 (84 %)
	Centrálna obezita	24 (16 %)

Poznámka: n = početnosť, BMI = index telesnej hmotnosti, WHR = pomer pás/boky, WHtR = pomer pás/telesná výška

***Tabuľka 3** Porovnanie priemerných hodnôt vybraných parametrov a indexov podľa BMI kategórii u mladých žien (n = 150)*

	Podhmotnosť n/(%) = 7/(4,7)	Norma n/(%) = 105/(70)	Nadhmotnosť n/(%) = 29/(19,3)	Obezita n/(%) = 9/(6)	p < 0,05
Parameter	M ± SD	M ± SD	M ± SD	M ± SD	
Telesná hm. (kg)	50,59 ± 3,2	62,26 ± 6,7	74,34 ± 6,8	96,04 ± 14,1	$2*10^{-16}$
Telesná výška (cm)	169,2 ± 4,7	167,2 ± 6,1	166,9 ± 5,8	165,1 ± 6,1	0,22
Hrudník (cm)	81,71 ± 2,1	89,4 ± 5,5	98 ± 5,47	111,2 ± 9,2	$2*10^{-16}$
WC (cm)	64,86 ± 2,9	72,43 ± 4,9	81,28 ± 4,8	97,33 ± 12,8	$2*10^{-16}$
Boky (cm)	87,86 ± 2,9	94,65 ± 5,2	103 ± 4,3	117,2 ± 12,3	$2*10^{-16}$
Biceps (cm)	23,0 ± 1,5	26,22 ± 1,8	28,45 ± 2,01	34,56 ± 3,1	$2*10^{-16}$
Stehno (cm)	46,57 ± 2,1	52,3 ± 2,9	57,76 ± 4,4	66,1 ± 6,1	$2*10^{-16}$
Krk (cm)	29,86 ± 1,5	31,1 ± 1,1	32,6 ± 1,4	34,56 ± 1,4	$3{,}84*10^{-16}$
BMI (kg/m^2)	17,65 ± 0,6	22,23 ± 1,7	26,64 ± 1,2	35,21 ± 4,5	$2*10^{-16}$
WHR	0,74 ± 0,03	0,76 ± 0,04	0,79 ± 0,04	0,83 ± 0,05	$2*10^{-5}$
WHtR	0,38 ± 0,02	0,43 ± 0,03	0,48 ± 0,03	0,59 ± 0,07	$2*10^{-16}$
ABSI	0,07 ± 0,01	0,07 ± 0,01	0,07 ± 0,01	0,07 ± 0,01	0,26
BAI	21,93 ± 1,32	25,81 ± 2,5	29,81 ± 2,1	37,41 ± 6,5	$2*10^{-16}$
CI	1,09 ± 0,04	1,09 ± 0,05	1,12 ± 0,06	1,17 ± 0,07	0.000472
BRI	1,44 ± 0,24	2,22 ± 0,51	3,15 ± 0,61	5,3 ± 1,7	$2*10^{-16}$
AVI	8,81 ± 0,71	10,9 ± 1,39	13,6 ± 1,5	19,6 ± 5,3	$2*10^{-16}$

Poznámka: n = početnosť, M = priemer, SD = smerodajná odchýlka , BMI = index telesnej hmotnosti, WHR = pomer pás/boky, WHtR = pomer pás/telesná výška, ABSI = index tvaru tela, BAI = index adipozity, CI = index kuželovitosti, BRI = index zaoblenosti tela, AVI = index objemu brucha, p = štatistická významnosť

Diskusia

Antropometrické merania sú základným nástrojom populačného skríningu na posúdenie zloženia tela a obezity. V dôsledku nesprávnych stravovacích návykov a nedostatočnej fyzickej aktivity dochádza k rozvoju mnohých civilizačných ochorení, ku ktorým nepochybne patrí aj obezita. WHO definuje obezitu ako stav nadmerného množstva telesného tuku, ktorý negatívne ovplyvňuje naše zdravie a celkovú pohodu (WHO, 2021). S ohľadom na obezitu, vo väčšine prípadov je najjednoduchším spôsobom jej odhadu zmeranie telesnej výšky a telesnej hmotnosti vyšetrovanej osoby. My sme okrem zaužívaných antropometrických parametrov a indexov (BMI, obvod pása, WHR a WHtR) použili aj novšie indexy posudzujúce telesnú kompozíciu (ABSI, BAI, CI, BRI a index AVI). Dosiahnuté výsledky v našej štúdii sme porovnávali s inými štúdiami rôznych domácich ale aj zahraničných autorov. Pri hodnotení prevalencie nadhmotnosti a obezity sme zistili, že v našom sledovanom súbore malo podľa BMI 25,3 % žien nadhmotnosť alebo obezitu a najvyšším ukazovateľom centrálnej obezity bol index WHtR (16 %). Následne sme zisťovali priemerné hodnoty vybraných antropometrických indexov vo všetkých kategóriách podľa BMI.

V štúdii Matejovičová, Špániková a Schlarmannová (2019) autorky analyzovali telesné zloženie slovenských vysokoškoláčiek. Priemerný vek žien bol v čase výskumu 21,63 ± 2,19 rokov, priemerný index telesnej hmotnosti 22,0 ± 4,78 kg/m^2 a priemerný index WHR 0,87 ± 0,06. Priemerné hodnoty sledovaných parametrov v našom súbore žien boli podobné (priemerný vek 21,7 ± 2,32 rokov, BMI 21,65 ± 4,06 kg/m^2 a priemerný index WHR 0,77 ± 0,05).

V štúdii Stříbrná, Kopecký, Matejovičová a Charamza (2017) sa autori venovali indexu BMI a image tela u českých a slovenských vysokoškoláčiek. Do štúdie bolo zapojených 429 žien s priemerným BMI 22,66 ± 4,03 kg/m^2. Na základe BMI malo 8,86 % žien podhmotnosť, 68,76 % žien normálnu telesnú hmotnosť, 17,48 % žien nadhmotnosť a 4,9 % žien malo obezitu. V nami sledovanej skupine žien malo 4,7 % žien podhmotnosť, 70 % normálnu telesnú hmotnosť, 19,3 % nadhmotnosť a 6 % žien malo obezitu. Z uvedených výsledkov vyplýva, že u vysokoškolských žien je výskyt nadhmotnosti a obezity nižší, čo možno pripísať faktu, že mladé ženy majú všeobecne väčšiu snahu mať svoju telesnú hmotnosť pod kontrolou a snažia sa dodržiavať zdravú životosprávu.

V štúdii Gažárová, Bihari, Lorková, Lenártová a Habánová (2022) sa podobne ako v našej štúdii venovali rôznym antropometrickým indexom na hodnotenie telesnej kompozície mladých žien v súvislosti s výskytom obezity. Štúdie sa zúčastnilo 303 mladých žien s priemerným vekom 21,73 ± 2,10 rokov. Ich priemerná telesná hmotnosť bola 62,27 ± 10,48 kg, telesná výška 167,4 ± 6,01 cm a index BMI 22,21 ± 3,38 kg/m^2. Priemerné hodnoty týchto parametrov v našom sledovanom súbore boli podobné (priemerný vek 21,7 ± 2,32 rokov, telesná hmotnosť 66,08 ± 11,89 kg, telesná výška 167,1 ± 6,06 cm a BMI 21,65 ± 4,06 kg/m^2). Priemerný obvod pása bol v štúdii Gažárová et. al., (2022) o 5,05 cm vyšší ako v našom sledovanom súbore žien. Priemerné hodnoty indexu ABSI sa pohybovali v rozdmedzi 0,078–0,079 podobne ako v našej sledovanej vzorke.

V štúdii Mardali et. al. (2022) sa autori zaoberali prediktormi centrálnej a všeobecnej obezity u detí, pričom skúmali rôzne antropometrické ukazovatele, ktoré možno použiť ako skríningový nástroj obezíty. Deti boli rozdelené podľa BMI na dve skupiny: normálna telesná hmotnosť a nadhmotnosť/obezita. V skupine obéznych dievčat boli priemerné hodnoty indexov WHR (0,82 ± 0,06), WHtR (0,51 ± 0,05), BAI (26,1 ± 5,7) a CI (1,12 ± 0,09). V našej skupine obéznych žien boli priemerné hodnoty indexov WHR (0,83 ± 0,05), WHtR (0,59 ± 0,07), BAI (37,41 ± 6,5) a CI (1,17 ± 0,07).

V štúdii Nagyama et. al. (2022) sa autori venovali indexom ABSI a CI v kontexte obezity. Do štúdie bolo zapojených 26 037 žien so strednou hodnotou veku (medián) 45 rokov, pričom stredná hodnota indexu BMI bola 20,8 kg/m^2 (v našom súbore bol medián BMI 23,28 kg/m^2. Stredné hodnoty indexov boli v ich sledovanom súbore žien nasledujúce: index ABSI (0,0791) a index CI (1,21). V našom sledovanom súbore žien boli stredné hodnoty týchto indexov (ABSI–0,071 a CI–1,098).

V štúdii Christakoudi et. al. (2020) autori porovnávali rôzne antropometrické indexy podľa kategorizácie BMI. Štúdie sa zúčastnilo 232 070 žien s priemerným vekom 51,2 rokov a boli rozdelené podľa BMI na 5 kategórii (BMI < 18,5 kg/m^2, BMI od 18,5 do 24,99 kg/m^2, BMI od 25 do 29,99 kg/m^2, BMI od 30 do 34,99 kg/m^2 a BMI ≥ 35 kg/m^2). Ženy (n = 3967) v kategórii podľa BMI v podhmotnosti mali priemerné hodnoty indexov: BMI (17,7 ± 0,7 kg/m^2), WHR (0,74 ± 0,05), WHtR (0,39 ± 0,03), ABSI (0,074 ± 0,005), CI (1,1 ± 0,07), BRI (1,6 ± 0,4) a AVI (8,7 ± 1,1). V našej skupine žien podľa BMI s podhmotnosťou boli priemerné hodnoty týchto indexov: BMI (17,65 ± 0,6 kg/m^2), WHR (0,74 ± 0,03), WHtR (0,38 ± 0,02), ABSI (0,07 ± 0,01), CI (1,09 ± 0,04), BRI (1,44 ± 0,24) a AVI (8,81 ± 0,71). Môžeme konštatovať, že z vybraných antropometrických indexov boli priemerné hodnoty v skupine žien podľa BMI s podhmotnosťou veľmi podobné ako v prezentovanej štúdii a najväčší rozdiel v našom súbore žien a v súbore žien podľa Christakoudi et. al. (2020) bol zistený pri indexe BRI. Čo sa týka žien zaradených podľa BMI do kategórie normálnej telesnej hmotnosti (n = 119 270) v štúdii Christakoudi et. al. (2020) boli priemerné hodnoty vybraných antropometrických indexov podobné ako v našej skupine žien v kategórii BMI normálnej telesnej hmotnosti. Môžeme konštatovať, že s rastúcim BMI sa priamo úmerne zvyšovali aj indexy WHR, WHtR, CI, BRI a AVI. Index ABSI vykazoval najmenší rast vzhľadom na zvyšujúce sa BMI.

Vyššie BMI neznamená vždy aj zvýšený obsah telesného tuku, pretože nadhmotnosť podľa BMI môže byť spôsobená aj zvýšenou svalovou hmotou, na ktorú má vplyv viacero faktorov (pohlavie, vek, genetika, pohybová aktivita a etnický pôvod) (Gallagher et. al. 1998), preto je dôležité aplikovať pre skríning nadhmotnosti/obezity aj iné indexy, vyjadrujúce percento telesného tuku. Bergman et. al. (2011) uviedli, že index BAI silno koreluje s adipozitou a na rozdiel od BMI je BAI rovnako dobrý pre obe pohlavia a pre rôzne etniká. V štúdii Geliebter, Atalayer, Flancbaum a Gibson (2013) autori porovnávali index telesnej adipozity (BAI) a BMI u ťažko obéznych žien. Ich štúdie sa zúčastnilo 19 morbídne obéznych žien s priemerným BMI (46,5 ± 9,0 kg/m^2), priemerný index WHR bol 0,9 ± 0,1, priemerný WC 124,8 ± 16,1 cm a priemerný index BAI u týchto žien bol 48,9 ± 9,6. V našom sledovanom súbore obéznych žien bol priemerný index BMI 35,21 ± 4,5, WHR 0,83 ± 0,05, WC 0,83 ± 0,05 cm a index BAI 37,41 ± 6,5.

Záver

Obezita súvisí s výskytom mnohých chronických ochorení, preto je potrebné pre jej skríning využívať viacero antropometrických indexov, ktoré odzrkadľujú výskyt patologického množstva tukového tkaniva. V súčasnosti sa na predikciu obezity a centrálnej obezity používajú okrem zaužívaných indexov (BMI, WHR a WHtR) aj novšie indexy ako ABSI, BAI, BRI, CI a AVI. Index telesnej hmotnosti založený na meraní telesnej výšky a telesnej hmotnosti je užitočným a praktickým meradlom výskytu nadhmotnosti a obezity, no napriek tomu nerozlišuje medzi tukovou a beztukovou zložkou tela. Podľa BMI malo v našom sledovanom súbore žien 4,7 % podhmotnosť, 70 % normálnu telesnú hmotnosť, 19,3 % nadhmotnosť a 6 % žien malo obezitu. Podľa obvodu pása spadalo 92,7 % do normy a 7,3 % žien malo podľa obvodu pása abdominálnu (centrálnu) obezitu. Podľa indexu WHR spadalo 91,3 % žien do normy a 8,7 % žien malo centrálnu obezitu. Podľa indexu WHtR spadalo 84 % do normy a 16 % malo abdominálnu obezitu. Pri porovnávaní priemerných hodnôt vybraných antropometrických parametrov a indexov v jednotlivých BMI kategóriách sme zistili štatisticky významné rozdiely medzi všetkými sledovanými údajmi s výnimkou telesnej výšky a indexu ABSI, čo potvrdzuje fakt, že index ABSI je navrhnutý tak, aby minimálne koreloval s BMI. Priemerné hodnoty indexov BAI, CI, BRI a AVI sa zvyšovali s rastúcim indexom telesnej hmotnosti. Pri skríningu obezity je potrebné zohľadňovať nie len index telesnej hmotnosti, ale zakomponovať do meraní aj novšie indexy, ktoré zohľadňujú množstvo telesného tuku a výskyt centrálnej obezity pomocou ľahko dostupných antropometrických meraní.

Poďakovanie

Poďakovanie patrí všetkým probandom, ktorí sa dobrovoľne zapojili do výskumu a poskytli potrebné antropometrické parametre nevyhnutné pre výpočet skúmaných indexov.

Súhrn

V sledovanej skupine mladých žien bolo podľa BMI kategorizácie 19,3 % žien s nadhmotnosťou a 6 % s obezitou. Z indexov, ktoré determinujú abdominálnu obezitu mal najvyššiu záchytnosť index WHtR (16 % žien malo centrálnu obezitu podľa WHtR). Čo sa týka novších indexov, ktoré sme použili na predikciu centrálnej obezity a stanovanie množstva telesného tuku, index ABSI mal priemerné hodnoty rovnaké vo všetkých sledovaných kategóriách podľa BMI a nezaznamenali sme žiadny štatisticky významný rozdiel. Priemerné hodnoty indexov BAI, CI, BRI a AVI sa zvyšovali s rastúcim indexom telesnej hmotnosti a zaznamenali sme štatisticky významné rozdiely medzi všetkými kategóriami BMI.

Kľúčové slová: *obezita, BMI, antropometrické indexy*

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CREATION OF TRAINING MODELS FOR ESTABLISHING INTRAOSSEOUS ACCESS WITH USE OF 3D PRINT – FOLLOWING STUDY

Tvorba modelů pro trénink zavedení intraoseálního vstupu – navazující studie

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Abstract

3D printing technology and simulation medicine have been both experiencing big boom recently. In this work we would like to demonstrate process of creation of training task models for establishing intraosseous access at several locations.

We used 3D scanner and anatomical preparations (humerus and tibia) for creation of the models in the form of .stl file. The models were 3D printed. Students´ feedback was assessed with use of structured questionnaire.

Anatomical structures that are necessary for identification of the place of establishing intraosseous access are well-palpable in all models. When part of each model simulating cortical layer of bone was drilled through a significant feeling of give appeared as a sign of entrance into trabecular part of the bone. Several physicians working either in the field of emergency or anesthesiology confirmed fidelity of our models. Most of the students (88.97 %) reported that our models correspond better to real bones when compared to commercially available models.

The models we created are realistic, easy to reproduce and very cheap. Simulation medicine and medical education may benefit from use of 3D printing technology.

Key words: *simulation medicine, 3D print, intraosseous access, benefit, students*

Introduction

Simulation, in its many guises, is now widespread in many fields of human endeavor and its history stretches back over centuries (Bradley, 2006). For example, the first flight trainer named "Blue Box" was developed by Edwin Link in 1929 (Rosen, 2008). Even though the history of simulation medicine dates back into ancient times (Meller, 1997), the real boom of simulation-based medical education (SBME) developed just over several past decades (McGaghie, Issenberg, Petrusa & Scalese, 2010). The variety of medical simulators ranges from simple task trainers (e.g. suturing, inserting an endotracheal tube, establishing intraosseous access etc.) to highly sophisticated mannequins which provide a possibility of simulating fidelitous clinical scenarios such as myocardial infarction, stroke, pneumothorax etc. (Kunkler, 2006; Sova et al., 2019)

Vascular access is of paramount importance in the care of critically ill patient (Luck, Haines, & Mull, 2010). Obtaining emergency intravascular access in critically ill (especially pediatric) patients can be extremely difficult, time consuming, and at times impossible since the peripheral veins are often collapsed, central lines carry risks, and cutdowns can take considerable amount of time (Anson, 2014; Rosetti, Thompson, Miller, Mateer, & Aprahamian, 1985). On the other hand, vessels in red bone marrow do not collapse during shock (Orlowski, Porembka, Gallagher, Lockrem & VanLente, 1990). Drinker, Drinker, & Lund (1922) and Doan (1922) were the first to independently reveal that bone marrow may serve as a transfusion route. The technique was used frequently during World War II and experienced decrease in its use afterwards (Heinild, Sondergaard, & Tudvad, 1947; Fiser, 1990). Its renaissance started in 1980s (Anson, 2014; Fiser, 1990). There have been several studies conducted on comparison of pharmacokinetics and effectiveness in establishment of intravenous and intraosseous access. These studies confirmed that intraosseous access is at least as beneficial as intravenous access, maybe even better (Johnson et al., 2015; Lewis & Wright, 2015; Reades, Studnek, Vandeventer, & Garrett, 2011; Von Hoff, Kuhn, Burris, & Miller, 2008). Nowadays, intraosseous access is an approved alternative route of administration of drugs included in resuscitation guidelines. It is efficiently used for administration of drugs in advanced life support of both pediatric (Maconochie et al., 2015) and adult (Soar et al., 2015) patients until central venous catheter is inserted (Buck, Wiggins, & Sesler, 2007; Hoskins, do Nascimento Jr, Lima, Espana-Tenorio, & Kramer, 2012).

Vast amount of work has been done in the field of 3D printing since Charles W. Hull (Hull, 1986) patented the first stereolitograph – a predecessor of modern 3D printers. In the past years, 3D printers became cheap and widespread. 3D printing is a rapidly expanding method of manufacturing that already found numerous applications in healthcare, automotive, aerospace and defense industries and in many other areas (Berman, 2012, Dodziuk, 2016). There is a wide range of applications in medicine including dentistry, tissue engineering and regenerative medicine, engineered tissue models, medical devices, anatomical models and drug formulation (Liaw & Guvendiren, 2017; Shafiee & Atala 2016; Tack, Victor, Gemmel, & Annemans; 2016).

In our previous study we tested the possibility of making a simple model of proximal tibia for training of establishing intraosseous access with use of 3D printing technology (Snehota, Kikalova, Kapral, Vachutka, & Plhak, 2019). The model we created was realistic, cheap and easily reproducible. Therefore, we decided to carry on and further improve our model, create models of other places that are typical for establishment of intraosseous access and present the models to students.

Aim

The main goal of this work is to further significantly extend our previous study. In this work we identify proper hardness of the model, create more anatomically accurate medullar cavity, design models of other places that are typical for establishment of intraosseous access and we also conduct a study monitoring students´ response to our and commercially available models when compared to real bones.

Methods

Anatomical preparation

Bones from the collection of the Department of Anatomy of the Faculty of Medicine and Dentistry of the Palacký University in Olomouc were used as models for 3D scanning. The bones in the collection of the Department of Anatomy come from donors who gave a written consent to provide their bodies for teaching and research purposes of students and researchers. At the end of the topographic-anatomical autopsy, which is part of general medical education, the bones were prepared using wet preparation technique. Firstly, we put the bones into boiling water. Then we used sharp tools to remove soft tissue. Subsequently we dried the bones. Lastly, the bones were marked and properly recorded. The bones come from 3 different cadavers. Bone preparation is a time and mentally demanding task and is performed by autopsy technicians.

Hardness of the model

To approach ideal hardness of the material of models (hard enough to remind of the hardness of the bone and provide a feeling of a give when drilling through the cortical layer) several small testing cubes were created. A 1x1x1 cm cube was designed using www.tinkercad.com (Autodesk, San Rafael, California, USA) and exported in .stl format. Using Slic3r software (Prusa Research, Prague, Czech Republic) .gcode files of cubes of different densities of cubic infill were created. The printing was performed with the same equipment, parameters and under the same conditions as the final models of bones described below. Then, an intraosseous drill EZ-IO® G3 and intraosseous needle EZ-IO® 25 mm 15 ga (Teleflex Incorporated, Wayne, Pennsylvania, USA) were used to test the hardness of cubes. We asked the head physician of Centre for Emergency Medicine in University Hospital Olomouc to test infill densities of 50 – 100% with 10% step and determine which one is closest to real situation. Densities below 50% were too soft. Testing of the hardness of cubes was blinded for the head physician.

3D scan

The bones were scanned using a desktop 3D scanner 3D EinScan-SE (Shining 3D, Hangzhou, China) based on structured light technology. The software used to operate the scanner was EinScan-SE series_v2.7.0.8 (Shining 3D, Hangzhou, China). The scanner was calibrated using a procedure recommended by the manufacturer prior to scanning of the bones. Dual-camera HDR regime involving a turntable (15° steps) was used to scan each bone from different angles. Moreover, after the scanning cycle was finished each bone was repositioned twice to scan parts which could not be captured previously. After each repositioning the bone was scanned again using dual-camera HDR regime involving a turntable (15° steps). After finishing the scan, a high detailed water-tight model was created and exported in the .stl format. Simplification ratio was used to encode the object with use of less than 250000 triangles which is a limit for uploading .stl file to online environment for creation and adjustment of 3D objects www.tinkercad.com (Autodesk, San Rafael, California, USA). No significant visual change of the model was observed after applying the simplification ratio. We scanned proximal part of left humerus, proximal part of left tibia and distal part of left tibia.

Adjustment of the model

Anatomical preparations of tibia and humerus were cut lengthwise to visualize trabecular (medullar) part of the bone. The cavity corresponding to trabecular part of the bone was created in each of our models. In Blender (Blender, Amsterdam, Netherlands) we used lattice deformation technique and smoothening, scraping and flattening functions to sculpt the shape of cavity corresponding to medullar cavity. Consequently, Boolean operators, rotation and slight scaling functions were used to optimize the model for printing purposes in www.tinkercad.com (Autodesk, San Rafael, California, USA). Then, the model was exported in the .stl format and transferred to Slic3r software (Prusa Research, Prague, Czech Republic) to create .gcode file containing printing information. A pre-set for printing from PLA material was selected (extruder temperature was set to 215 °C, bed temperature was set to 60 °C and layer height was set to 0.15 mm). Speed of printing was reduced to 80%. Supports were auto-generated only from the printer bed.

Models of soft tissues

Models of soft tissues were created using www.tinkercad.com (Autodesk, San Rafael, California, USA). Boolean operators and previously acquired .stl files of the bones were used to model soft tissue of the desired region. Consequently, Blender (Blender, Amsterdam, Netherlands) software was used to smoothen the surface of the models of soft tissue. Then, the models were exported in the .stl format and transferred to Slic3r software to create .gcode file. A pre-set for printing from FLEX material was selected (extruder temperature was set to 240 °C, bed temperature was set to 50 °C and layer height was set to 0.15 mm). No supports were generated. 0% infill was used in case of the model of tibia at both regions (proximal and distal) since the thickness of soft tissue in these regions is small and use of any infill density resulted in significant increase in toughness of the model. 25% concentric infill was used in case of the model of humerus since the thickness of soft tissue at this region is bigger (especially due to presence of deltoid muscle) when compared to previous ones. The model presented with suitable flexibility when this infill was used.

3D print and creation of the models

Each model of the bone was printed using FDM (= fused deposition modelling) 3D printer Original Prusa i3 MK3 (Prusa Research, Prague, Czech Republic) and PLA plastic filament for 3D printers, 1.75 mm diameter, white colour (Gembird, Almere, Netherlands). Each model of soft tissue was printed using 3D printer Original Prusa i3 MK3 (Prusa Research, Prague, Czech Republic) and Flexfill 98A* filament for 3D printers, 1.75 mm diameter, powder beige (Prusa Research, Prague, Czech Republic). Speed of printing was reduced to 80% in both cases. Models of the bones and corresponding soft tissue were glued together using Mamut glue (Den Braven, Oosterhout, Netherlands).

Comparison of our and commercially available models with real bones by students and statistical analysis

In order to evaluate students´ response to using the models for training of intraosseous access, we introduced a structured questionnaire to 145 students of 5th year of General Medicine. All students completed the survey at voluntary basis. For purposes of the survey, the models were anonymized and labelled as models A – our 3D printed models – and models B – commercially available EZ IO training bone models (Teleflex Incorporated, Wayne, Pennsylvania, USA). We compared 3 parameters of our models and commercially available models: palpation for identification of proper position of intraosseous drill, hardness of the models and feeling of a give as a sign of entering into medullar cavity in comparison to corresponding real formalin-fixed bone without soft tissue. All students tried out corresponding models A, B and real bone. The questions and possible answers are available in Table 1 together with obtained results. The results were statistically analyzed by chi-square test at level of significance P < 0.05. All calculations were performed by GraphPad Prism 6.0 software (GraphPad, San Diego, California, USA). Moreover, we asked students if they considered the models for training of establishment of intraosseous access for application of drugs useful and which models (our 3D printed models or commercially available models) they preferred in general. We also added a question: "Do you have any other comments or suggestions?" with free answer to the questionnaire.

Results

Density of 60% of cubic infill was determined by the head physician to be optimal for creation of the models. This density provided suitable hardness and sufficient feeling of the give when drilling through the cortical layer of the models.

Fig 1. Anatomical preparations which were 3D scanned: a) proximal humerus, b) tibia (proximal part was scanned) and c) distal tibia.

Figure 1 displays the anatomical preparations which were 3D scanned.

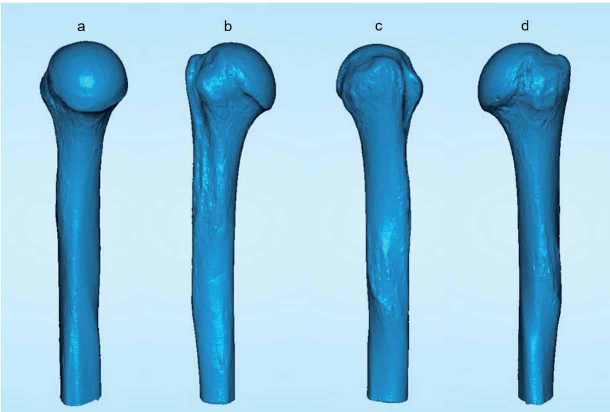

Fig 2. Different points of view of a model created from 3D scan of humerus: a) medial, b) ventral, c) lateral and d) dorsal.

Figure 2 shows water-tight model created from scan of proximal humerus from different points of view.

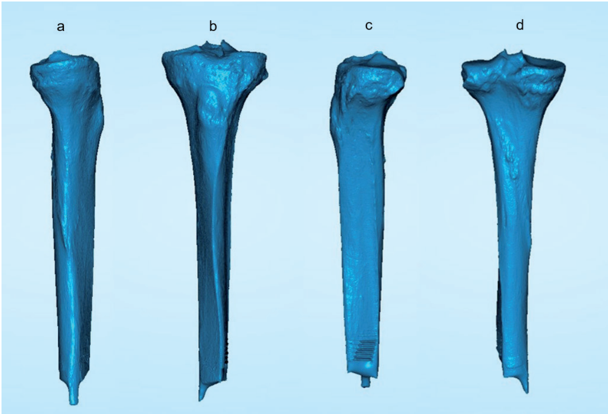

Fig 3. Different points of view of a model created from 3D scan of proximal tibia: a) medial, b) ventral, c) lateral and d) dorsal.

Figure 3 shows water-tight model created from scan of proximal tibia from different points of view.

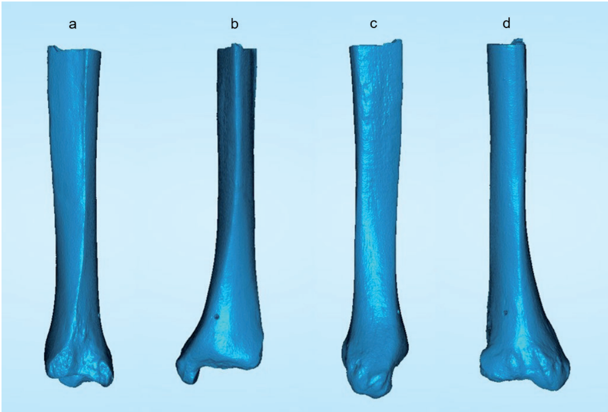

Fig 4. Different points of view of a model created from 3D scan of distal tibia: a) lateral, b) ventral, c) medial and d) dorsal.

Figure 4 shows water-tight model created from scan of distal tibia from different points of view.

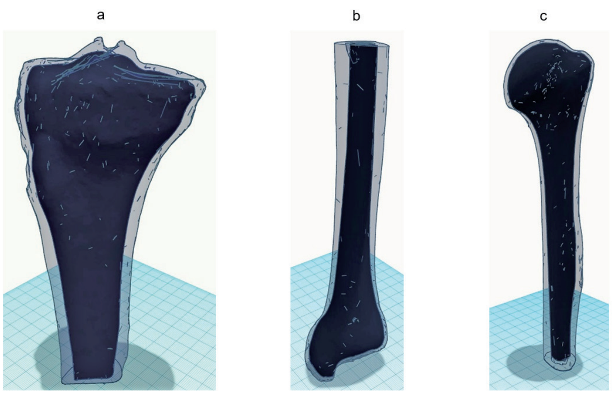

Fig 5. Representations of the cavities created using Blender and www.tinkercad.com. Solid parts of the models are transparent, black parts correspond to the cavities: a) distal tibia, b) proximal tibia and c) proximal humerus.

Figure 5 shows the models of the bones created using www.tinkercad.com. Solid parts of the models are transparent. Black parts correspond to the cavities representing medullar cavity and trabecular part of particular bones. When entering the black parts with the drill a significant give was felt in all cases. All models were mirrored to create the models of bones of contralateral side since right-handed people are in majority in the population and it is better to hold the models in left hand and intraosseous drill in right hand. Moreover, the models of proximal tibia and of proximal humerus were turned upside down as this configuration is spatially more suitable for 3D printing.

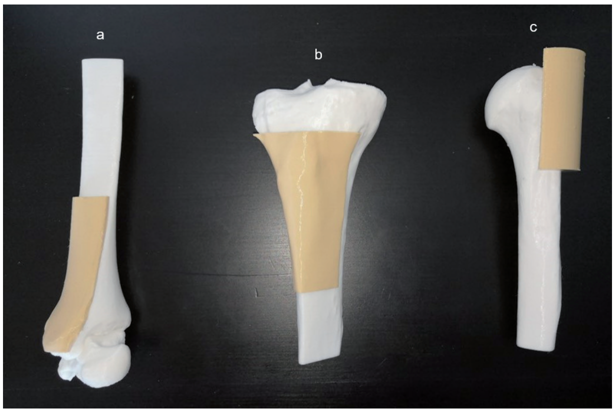

Fig 6. Final models for training of intraosseous access: a) distal tibia (with talus), b) proximal tibia and c) proximal humerus.

Figure 6 shows final models for training of intraosseous access.

Students´ feedback to the models

Vast majority of students (136/142 (95.77%)) generally considered the models for training of establishment of intraosseous access for application of drugs to be useful. The evaluation of selected parameters of our and commercially available models with comparison to corresponding real bones is summarized in contingency table (see Table 1). Statistically more students preferred our models in terms of palpability of anatomical structures which are necessary for proper identification of the position of the drill (P = 0.0011). Moreover, according to students´ responses, the hardness of our models as well as the felling of give as a sign of entering into medullar cavity in comparison to commercially available models were significantly closer to corresponding real bones (P < 0.0001 for both parameters). Finally, most of the students who answered question: "Which of the two models is better for training of establishment of intraosseous access for application of drugs?" (121/136 (88.97%)) preferred our models over commercially available models.

Table 1: *Comparison of parameters of our and commercially available models according to students´ opinion. Results show numbers (and percentage) of obtained answers for particular questions.*

		models created by 3D printer	commercially available models	statistical significance
How well do you feel anatomical structures necessary for identification of proper position of intraosseous drill during palpation?	I feel the structures very well.	102 (70.34%)	74 (51.75%)	*** P = 0.0011
	I am not sure I found particular anatomical structures.	43 (29.66%)	64 (44.76%)	
	I did not find anatomical structures.	0 (0.00%)	5 (3.50%)	
How hard are the models when compared to real bones?	The models are comparable to real bone.	82 (56.5 %)	25 (17.36%)	**** P < 0.0001
	The models are slightly softer.	55 (38.73%)	61 (42.36%)	
	The models are significantly softer.	5 (3.52%)	58 (40.28%)	
How significant is the feeling of give when drilling through the cortical layer (as a sign of entering into medullar cavity) of models when compared to real bones?	The feeling of give is significant.	111 (77.08%)	78 (53.79%)	**** P < 0.0001
	The feeling of give is not significant that much.	33 (22.92%)	55 (38.73%)	
	I did not feel the give.	0 (0.00%)	12 (8.28%)	

20 students left a commentary in the last question ("Do you have any other comments or suggestions?"). 10 students emphasized that our models correspond better to real bone in terms of hardness and feeling of a give. 7 students pointed out that our models of soft tissue should be more realistic and thicker. On the other hand, statistically more students preferred our models in terms of palpability of anatomical structures (see Table 1). 3 students praised us for the activity.

Discussion

Simulation medicine has experienced big boom in the past few decades. It provides students with the possibility of training and practicing skills which are usually highly specific and the possibility of their safe training in the hospital is limited. In case of complicated and specific procedures it is good to practice the procedure prior to performing it directly in a living patient. Thus, unwanted harm can be reduced. Makary & Daniel (2016) estimated that medical error (defined as unintended act or one that does not achieve its intended outcome, the failure of a planned action to be completed as intended, the use of a wrong plan to achieve an aim, or a deviation from the process of care that may or may not cause harm to the patient) is the third biggest cause of death in the US. Not all of the iatrogenic harm can be absolutely eliminated and in certain situations the physician has to consider the risk/benefit ratio (e.g. in case of side effects of drugs or use of imaging techniques based on ionizing radiation). However, using models and simulators prior to acquiring skills in clinical environment may prevent some of the harm (Ziv, Wolpe, Small, & Glick, 2003). In our humble view the simulation medicine is not meant to replace clinically acquired skills. We rather identify with the opinion that the role of simulation medicine is to serve as a valuable bridge between theoretical knowledge and real situations and clinical skills acquired in the hospital (Akaike et al., 2012; Susan Galloway, 2009; Morgan, Cleave-Hogg, Desousa, & Lam-McCulloch, 2006). Simulation based medical education can be a valuable tool for better clinical practice. It provides a safe, controlled environment in which problem-based learning is developed and competences are practiced in high standards (Jones, Passos-Neto, & Braghiroli, 2015). A trainee can make mistakes and learn from them without the fear of harming the patient (Al-Elq, 2010).

Using 3D scanner, 3D printer and several software programs we have demonstrated that 3D printing technology can be used for creation of the models for medical education. All models presented with well-palpable anatomical structures which are necessary for identification of the proper position of intraosseous drill (and needle respectively) – humeral caput, tibial tuberosity, anteromedial face of the tibia and medial malleolus. Significant feeling of a give appeared when we drilled through the cortical layer of the models and entered the cavity simulating trabecular part of the bone.

We decided to print the models using PLA filament because we expect to use a few kilograms of filament each year. PLA filament is made of corn starch and thus, it is biodegradable (Jang, Shin, Lee, & Narayan, 2007; Sudesh & Iwata, 2008) and environmentally friendly (Nampoothiri, Nair, & John, 2010; Vink, Rabago, Glassner, & Gruber, 2003).

The models for training of intraosseous access we created are highly realistic and easy to reproduce. After creation of the .gcode file the reproduction of model is a question of pressing of a few buttons. Moreover, our models are very cheap. Material for production of any model presented in this work costs much less than commercial models. Indeed, the material used for production of our model of proximal tibia costs 9.8%, of distal tibia 6.5% and of humerus 10.4% of the price of commercially available model. Exact prices are displayed in Table 2. Establishing an intraosseous access is a procedure relatively easy to learn (Petitpas et al., 2016). A short training including a lecture and practical use of plastic model significantly increases success rate (Gazin et al., 2011). However, when educating vast amount of medical students use of such commercially available plastic models may become economically exhaustive. Traditional manufacturing methods are still cheaper for large scale production however, the cost of 3D printing is becoming competitive for smaller production runs (Schubert, Van Langeveld, & Donoso, 2014).

Table 2: Comparison of price of our and commercial model.

	3D printed model	Commercial model	Price 3D / price commercial
Model of proximal tibia	£ 2.54	£ 25.94	9.8%
Model of distal tibia	£ 1.52	£ 23.47	6.5%
Model of proximal humerus	£ 2.44	£ 23.47	10.4%

Another advantage additive manufacturing provides is the possibility of customizing of the models (for example scaling the models or mirroring the models to the models of contralateral side). Other research teams also report similar benefits of using 3D printing technology for creation of the models for medical education (Lichtenberger et al., 2018; McMenamin, Quayle, McHenry, & Adams, 2014).

There is a certain amount of literature describing undisputable advantages of the models created by 3D printer with monitoring of students´ opinion (Hochman et al., 2015; Lim, Loo, Goldie, Adams, & McMenamin, 2016). However, according to the best of our knowledge, the models presented in this work have not been 3D printed so far as well as students´ feedback to these models has not been monitored yet. The vast majority (95.77 %) of interviewed pregradual students of 5th year of General Medicine agreed that using of the models for training intraosseous access is useful. In general, the majority of students (88.97 %) preferred our models. Moreover, according to students´ opinions, our models correspond better to real bones than commercially available model in all tested parameters (palpation for identification of proper position of intraosseous drill, hardness of the models and feeling of a give as a sign of entering into medullar cavity).

Students of General Medicine systematically encounter practical training of establishment of intraosseous access for the first time in the 5th year of their studies. Therefore, we also presented the models to 3 skilled physicians working either in the field of emergency or anesthesiology and resuscitation. All 3 physicians confirmed that our models correspond to real situation well in all 3 characteristics of the models (palpability of anatomical structures, hardness and feeling of a give). They also confirmed that our models are suitable for training purpose. All 3 physicians preferred our models over commercial ones.

Limitations of the Study

Even though we used real anatomical preparations in this study the final model was 3D printed. Models of soft tissue are not made from any kind of biological material but from flexible plastic material. Thus, the perceptions during palpation and identification of proper anatomical structures inevitably differ from the real situation.

Also, we used one hardness of the model. However, in real patients bone hardness is rather Gaussian distributed than being just one specific. The interindividual variability of bone hardness is determined by age, sex, ethnicity, presence of diseases (e.g. osteoporosis) etc. Thus, the feeling of a give and pressure which needs to be applied to intraosseous drill will differ in different patients.

Since the students completed the survey at voluntary basis our study may be influenced by selection bias to certain degree. Thus, even though the sample size was sufficient, the data acquired may not completely reflect the overall opinion of all students from 5th year.

Conclusion

Using 3D printing technology, we have created highly realistic models for training of intraosseous access which has been confirmed by students´ opinion. The cost of the models is negligible when compared to commercially available models. 3D printing technology has a potential to become valuable tool significantly enriching the field of simulation medicine.

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Souhrn

Hlavním cílem této práce bylo rozšířit naši původní práci (Sněhota, Kikalová, Kaprál, Vachutka, & Plhák, 2019), tzn. určit optimální tvrdost modelu, vytvořit modely pro trénink intraoseálního vstupu pro další lokalizace (distální tibie, proximální humerus) a zhodnotit reakci studentů na prezentované modely. Metodika byla obdobná předchozí studii. Byly naskenovány anatomické preparáty, tyto modely byly následně upraveny pomocí softwarů www.tinkercad.com a Blender, které byly použity

k vytvoření dutiny uvnitř modelů a modely byly následně vytištěny na 3D tiskárně. Reakce studentů byla zhodnocena pomocí strukturovaného dotazníku, kdy studenti porovnávali naše a komerčně dostupné modely s reálnými anatomickými preparáty. Na všech modelech byly hmatné anatomické struktury nezbytné pro správnou lokalizaci místa zavedení intraoseálního vstupu. Při prostupu intraoseální jehly do spongiózní části kosti byla u všech modelů citelná ztráta odporu. Dotazníkové šetření ukázalo, že statisticky významná část studentů preferuje naše modely oproti komerčním. Provedená studie ukazuje možné přínosy 3D tisku v oblasti vzdělávání studentů medicíny.

Klíčová slova: *simulační medicína, 3D tisk, intraoseální vstup*

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Poznámka úvodem

V průběhu historie druhu Homo sapiens naši předci neustále řešili, jak se co nejlépe přizpůsobit prostředí a jeho změnám a zároveň profitovat a rozšiřovat svůj druh. Člověk se rodí jako nevyvinuté mládě zcela odkázané na péči matky. V dospělosti je pak nucen řešit kompenzaci nedokonalých orgánů a smyslů. Dvojice autorů Ramos a Čuta v článku „SCULPTORS OF OUR HUMANITY. Anthropotechnics: the improvement of the human being from Biotechnology shrnují příklady „vylepšení člověka“ v evoluci a historii druhu jak biologickými, tak kulturními a technologickými adaptacemi. Dále se také zamýšlejí nad budoucností, která se pojí především s aplikací nových biotechnologií a umělé inteligence (artificial inteligence, AI). Termín „enhacement“, který je v této souvislosti v textu používán, nemá přesný český ekvivalent. Překlad jako „zdokonalení“ či „vylepšení“ člověka může být vnímán i s poměrně negativním nádechem, což je dáno především událostmi druhé poloviny 19. století a první poloviny 20. století. V roce 1871 byla publikována kniha O původu člověka a pohlavním výběru Charlese Darwina, kde svou evoluční teorii aplikuje také na náš druh. Myšlenky se však brzy ujali také sociální darwinisté a přetavili ji v eugeniku, myšlenku, že děti by měli mít pouze lidé zdraví, inteligentní, krásní a nadaní. Odtud byl už pouze krůček k rasismu a antisemitismu. Hrůzy druhé světové války pak celému lidstvu ukázali nutnost regulace „vylepšování“ člověka a lidstva.

Druhá vlna „vylepšování“ člověka přichází spolu s novým miléniem, kdy došlo k prudkému rozvoji biotechnologií jako je rychlá a dostupná sekvenace kompletních genomů nebo editace genomu metodou CRISPR/Cas9. Autoři Ramos a Čuta ve svém příspěvku především upozorňují na článek vydaný v časopise Science v roce 2022, který se zabývá jednak zmiňovanou aplikací biotechnologií na člověka, ale především morálními a etickými dopady tohoto počínání. Dvojice autorů Yasemin J. Erden a Philip A. E. Brey University of Twente v Enschede v Nizozemí řeší také otázku budoucnosti člověka jako individua, ale i celého lidstva včetně dopadů enviromentálních změn i zapojení AI.

Svět se rychle mění, biotechnologie se stávají součástí našich každodenních životů. Jak napovídá název článku, už i samotný obor antropologie fúzoval s technologiemi do termínu „antropotechnology“. Pokud máte zájem aktualizovat si své znalosti o tomto tématu, doporučuji se začíst do článku SCULPTORS OF OUR HUMANITY. Anthropotechnics: the improvement of the human being, ale také do zmiňované publikace Ethics guidelines for human enhancement R&D.

Kristýna Brzobohatá

Proč předkládáme tuto diplomovou práci k publikování?

Úpravy a zlepšování lidského těla a jeho funkcí je neoddiskutovatelnou součástí historických i současných dějů, kterými naše společnost tvaruje svou identitu a vlastní koncept humanity. Cílem této přehledové práce je především poskytnout konceptuální vymezení termínu „human enhancement“ z pohledu jeho evoluční kontinuity a historického trvání. Zlepšování našich schopností s jejich pozitivním i negativními aspekty je jedním ze základních atributů lidství, a snaha o jeho potlačení by popírala samotnou podstatu naší existence. Tato počáteční analýza nás přivádí k zřejmé symbióze, která existuje dnes mezi zlepšováním našich schopností a technologickými postupy, ať už v oblasti mechaniky, genetiky nebo farmakologie. Tento vztah je nahlížen z Heideggerovské perspektivy, a umožní nám najít jasné propojení mezi dvěma pohledy na zmiňovaná vylepšení – pohled antropologický a biotechnologický. Tyto pohledy čtenáře přivedou ke konceptu antropotechniky a k současné debatě ohledně využití biotechnologií.

Druhá část této studie zkoumá koncept antropotechniky s cílem objasnit vazby mezi antropologií a biotechnologií a analyzovat současné problémy vyvolané kolem konceptu „human enhancement“. Nakonec jsou předloženy návrhy, které mají do této debaty přispět, zvláště v podobě vymezení pojmů, přijetí nevyhroceného interdisciplinárního přístupu a porozumění všech pro a proti na různých úrovních rozlišení. Nezbytné jsou právní a profesní regulace v procesu biotechnologického výzkumu a uplatnění poznatků v každodenním životě.

Tato přehledová studie si zasluhuje pozornost a publikování v plném rozsahu z několika důvodů. Zaprvé, přináší nový pohled na koncept úprav a zlepšování lidského těla a jeho funkcí a jeho historickou a evoluční kontinuitu, což přispívá k hlubšímu porozumění této problematice. Za druhé, zdůrazňuje významné propojení mezi technologiemi na různých úrovních a lidským zlepšováním, což je zásadní otázka v současném vědeckém a sociálním kontextu.

Martin Čuta

SCULPTORS OF OUR HUMANITY

Anthropotechnics – the improvement of the human being from Biotechnology

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Abstract

The present article aims, first and foremost, to provide a conceptual delimitation of the term "human enhancement" from the perspective of its evolutionary continuity and historical persistence. It is concluded that human enhancement is an inherent process in human beings, making it highly challenging to stop or prohibit it, as it would negate our very essence. This initial analysis leads us to the evident symbiosis that exists today between human enhancement and technology, whether mechanical, genetic, or pharmacological in nature. Therefore, an analogy is drawn between technology and human enhancement, examining this circumstance from a Heideggerian perspective on technique. From these findings, we can deduce an approach to the concept of human enhancement, which clearly links two areas of study: anthropology and biotechnology.

The second part of the dossier explores the concept of *anthropotechnic* in order to elucidate the connections between anthropology and biotechnology, with the aim of analyzing the current issues generated around human enhancement. Finally, proposals are put forward to shed light on the debate surrounding human enhancement: adopting a serene attitude by studying the pros and cons of human enhancement and technology; interdisciplinarity (BASTES) as an approach to addressing life improvement; the use of calculative thinking and meditative thinking in the biotechnological process addressing human enhancement; the necessary legal and professional regulation in the biotechnological research process and the application of human enhancement in everyday life.

Human enhancement as an evolutionary constant in our hominization process (first conceptual framework)

Human enhancement has been a constant factor in the evolutionary process of the human species. Man is the product of a history of self-improvement. He emerges in the world through a successive series of events that refine his status within nature, distinguishing him from other primates. The process of hominization spans a long period of time during which our ancestors evolve and adapt to their environment. The modern human being is the outcome of this process, which is characterized by significant biological changes that form the foundation of human construction.

Paleontology has not yet been able to definitively determine the origin of the *Homo* genus, but it has identified certain aspects that have shaped our biological form. Reconstructing the past is not an easy task, and new data emerges that aligns with new theories as new fossils are discovered. It is understood that from the early hominids to modern humans, there has been an improvement in the purest biological sense: more resilient and complex organs, an immune system with greater defensive capacity, increased longevity, among other features. There has also been an evolutionary improvement, with more qualities to adapt to the environment in which they live, including advancements in cognitive and social development. Humans have acquired qualities that enable them to perform sequential, systematic, and complex activities.

Considering these fields of improvement, it can be observed that from the earliest hypothetical hominids such as *Sahelanthropus tchadensis,* which lived 6-7 million years ago (based on the jaw and teeth found in Chad), or *Ardipithecus*, which existed 5.8-4.4 million years ago, to "the first hominin in which there is total consensus, *Australopithecus anamensis*, which lived 4.2 million years ago in Ethiopia" (Rosas, 2015:40), it is considered in this study that an improvement took place.

This improvement of the hominid continues to manifest itself in *Homo ergaster*, *Homo antecessor*, *Homo rhodesiensis*, until reaching *Homo sapiens*. Just as evolution is not a linear and simple process, neither is the improvement of hominids. Both evolution and improvement give rise to a wide diversity of individuals, multiple species, yet to be discovered and studied. Understanding this past and realizing that the concept of human enhancement is inherent to our own humanity, which does not make sense without considering our relationship with nature; this is essential. Not only to comprehend our current humanity but also to recognize that human enhancement cannot be limited, constrained, or mutilated, even if it involves a diverse process of evolution.

> *(...) human evolution, far from being a linear and simple process, is a complex network from which multiple species and ways of relating to nature have emerged. We must understand that the current humanity is just one of the many possibilities that have existed. (Rosas, 2002:370)*

However, this human enhancement is not exclusively biological or evolutionary; it is also cognitive-social. That is why it gives rise to "multiple species (biology and evolution) and ways of relating to nature (social)." Biology relies on the confluence with the environment in which it develops and with culture, encompassing technical, creative, productive, and collective aspects transmitted from generation to generation. This *endoculturation* (transmission of a group's culture to its children, shaping part of our identity), along with biology and intelligence, gave rise to the human lineage and will possibly shape various types of humanity.

> *But this was not simply the straightforward product of physis, but also of intelligence, which was already notable and efficient since the earliest life forms (if we understand intelligence as the ability to live in harmony with the environment) and had given rise to hunting primates, with the additional benefit of prolonged infancy that allowed for training and "endoculturation." We are acknowledging that neither intelligence nor hunting originated with human beings but rather that it was precisely these developments that enabled the emergence of this lineage. (Ossa Londoño, 2003:16)*

Only within this biological-cultural framework can human anatomy, and therefore human enhancement, be defined. This means that there is a close relationship between the techniques employed by hominids, as well as the use of tools or utensils, and the process of hominization and human enhancement itself. Thus, any physical, anatomical, or biological change, as we will see, entails changes in the use of instruments, which in turn result in anatomical-physiological changes, leading to better adaptation to the environment and increased survival, i.e., the

Darwinian selective outcome. This is known as the "Baldwin effect": "mutations whose effects mimic those of the acquired trait. If the trait in question has a selective advantage, the mutant can spread, thus creating the impression of Lamarckian inheritance" (Klopfer, 1976:26). The concept of human enhancement, from the origin of humankind, is therefore contingent upon biology and culture, arising from the adaptive modifications of the body and from the most frequently repeated actions.

> *The Americans Baldwin, Osborn, and Lloyd Morgan, and later the Frenchman Hovasse (1950), have advocated that evolutionary variation would occur in two stages: the more frequently repeated adaptive modifications of the "soma" would eventually be "copied" by certain mutations, which would then be selected and replace them. (Templado, 1974:106)*

The evolution of the life cycle is studied through life-history strategies, which include not only the chronology of growth periods, gestation, sexual maturation, and longevity but also other variables such as adult size, evolution of dentition, which in turn can determine nutrition and the morphology of the digestive system. The pelvic structure of women, derived from bipedalism, and the size of the brain are also factors that determine growth, the life cycle, and life-history strategies, and likewise shape human evolution and enhancement. These life-history strategies develop within an environment and entail specific relationships with it. It could be, as proposed by Lovejoy (2000), that upright posture and bipedalism were a consequence of a transformation in social behavior related to sexual selection. This adaptive change constitutes one of the early improvements in the process of humanization (specific to humans, although it also has its disadvantages, such as reduced agility in movement). Bipedalism enables the use of hands for tool use and fabrication, which facilitated their lives, as well as for actively extracting hidden food sources (dietary change). These factors influence mutations in our bodies and also our relationships with others and the environment. Lovejoy explains that females chose mates who could provide food for the nest to ensure reproductive success. Females did not demand violent males who would fight over them. They sought provisioning of fatty and protein-rich foods that would enable them to breastfeed their offspring, and they also desired protection for them. To engage in this activity, an upright posture was necessary, allowing them to have their hands free.

Following this event, San Martín and Lovejoy explain another life-history strategy that occurred after bipedalism: *concealed* ovulation, "the masking of ovulation due to upright posture, or the hiding of estrus" (San Martín, 2022:324). Estrus is no longer a stimulus for the male, who requires other resources for copulation and sexual reproduction. The mechanism of agonistic relationships and combat, where males fight over females, is left behind. A cooperative relational strategy emerges, focused on the care of offspring, which possibly gives rise to the social structure of stable and monogamous families. This cooperative behavior led to the reduction of pointed canines in reproductive-age males, as they no longer needed them for competing over females, and this modification also influenced dietary and feeding processes.

Bipedalism changed the pelvic structure in females, leading to a new adaptation: babies have to be born less developed, otherwise the skull would not be able to pass through the birth canal. Therefore, in order to reach adult brain dimensions, a period of postnatal growth is necessary. This type of birth makes us vulnerable and deficient compared to other beings in nature. Some of these deficiencies are retained into adulthood, which is why humans require a technical process of improvement to overcome these limitations.

Throughout these lines, we can observe how the human being is the product of continuous improvement, derived from a perpetual interaction between the environment, others, culture, and biology. Understanding human enhancement as the capacity to overcome difficulties, adapt and interact with the environment, develop qualities, and achieve advancements that make the life cycle more comfortable and prolonged.

Lastly, we will briefly mention the process of encephalization, which allowed for the establishment of optimal neural connections for the development of intellectual potential, and where a synergy between culture, interactions with the environment, and biology takes place. The brain is the most representative organ of human enhancement because, although it remains largely unknown and we are far from fully understanding its functioning, it is the architect of intelligence. Moreover, it is shaped as a product of biological evolution, ethology, and the technology of the *Homo* genus. Its complexity is intertwined with the continuous modifications influenced by social factors and extrasomatic adaptation through the tools we design and produce with our hands.

Research conducted by Dean Falk (2012) demonstrates that cranial fontanels partially fused following the adoption of bipedalism. This suggests that the transformation of the narrower pelvis influenced the evolution, development, and improvement of the brain, which, as mentioned before, grows after the infant has exited the mother's womb. The human brain currently weighs about 1500 cc, which is approximately 2 percent of the total body weight, and consumes about 20 percent of the basal metabolism.

> *The evolution of the Homo genus through different species, culminating in a phylogenetic tree where only our branch remains, represented by Homo sapiens, raises evolutionary questions about the size and social use of the brain and the future of our species. The brains of hominids within our genus have increased from an average of 500 cubic centimeters in the Pliocene, approximately 3 million years ago in the African savannah, to the brain size of Homo neanderthalensis (1600 cc) and Homo sapiens (around 1500 cc). With the exception of Homo floresiensis, with a brain capacity of 350 cubic centimeters, which is considered an epiphenomenon, the increase in brain size has been crucial for our social development. (Carbonell, 2007).*

The use of hands plays an active role in the evolution of the brain. The development of an opposable thumb was not only a powerful biomechanical tool for precise tool-making but also may have had a direct relationship with the neuronal activity in the frontal area of the brain, which is closely associated with higher cognitive functions such as problem-solving, attention, abstract thinking, and decision-making. The use of the opposable thumb, in particular, and the upper limbs, in general, trigger actions in the cerebral areas, allowing for more precise movements. According to Carbonell (2007), this "neuromechanical feedback" is responsible for the morphology and structure of our brain. In other words, tools and the brain have endowed us with capabilities that set us apart from other animals. Similarly, in modern times, we can say the same about technology and the brain.

Ramón y Cajal coined the famous phrase "every human being, if they set their mind to it, can be the sculptor of their own brain" (2011:53). The eminent physician was trying to explain the remarkable neuronal plasticity: the activities we engage in contribute to enhancing our brain development. Research studies have confirmed this idea, such as the work of Eleanor Maguire (2000), who found that taxi drivers had a larger hippocampus, and this growth was related to their professional activity. Elbert, on the other hand, confirmed that musicians who play string instruments have a greater cortical representation of the fingers of their left hand, leading to the conclusion that,

> *The amount of cortical reorganization in the representation of the fingering digits was correlated with the age at which the person had begun to play. These results suggest that the representation of different parts of the body in the primary somatosensory cortex of humans depends on use and changes to conform to the current needs and experiences of the individual. (1995:305)*

The activities we engage in on a daily basis bring about changes in our brain that shape our evolution and improvement as human beings. The tools and utensils we use serve as stimulating elements that help sculpt our brains. Akos Ghosh investigated the cortical potential stimulated by the practice of touchscreens using the index finger and thumb:

> *Remarkably, the thumb tip was sensitive to the day-to-day fluctuations in phone use: the shorter the time elapsed from an episode of intense phone use, the larger the cortical potential associated with it. Our results suggest that repetitive movements on the smooth touchscreen reshaped sensory processing from the hand and that the thumb representation was updated daily depending on its use. (2015:109-116)*

And it is not only limited to manual activities. In 2004, Andrea Mechelli conducted a study on the influence of bilingualism on the brain. The study concluded that bilingual individuals increase the density of gray matter in the parietal area of the brain, which is involved in language. A distinction is made between bilinguals who learn the second language between the ages of 10 and 15, and those who do so before the age of 5, with the latter showing the greatest increase in gray matter in brain scans. Subsequent studies have further expanded upon these initial findings.

It is a reality that the use of upper limbs, tool production, and language represent adaptive capacities whose association allows us to glimpse how the human brain has been positively selected and how improvement has occurred, shaping our lineage into a social brain.

All of this, as we have mentioned, is due to the brain's plasticity, which has been extensively studied by Pascual-Leone (2005). His research has established results indicating that neuronal variation is not only achieved through manual and factual activity but also through thought processes. In an experiment, half of a group of volunteers were taught to play a piano piece using all five fingers. It was observed that with continuous training, the corresponding region in the motor cortex responsible for moving those fingers expanded. This finding demonstrated neuroplasticity, as other researchers had previously shown. However, what was particularly interesting was what happened with the other half of the participants in the experiment. They were asked to imagine playing the piece without physically performing the movements. It was observed that the mental simulation of actual movements activated the regions of the motor cortex required for executing those movements. Mental practice alone was sufficient to promote neuroplasticity.

Pascual-Leone states that these changes exist and are supported by new neuronal connections through dendritic growth and branching. However, he is not certain that this mechanism cannot become a cause of pathologies in the present day. In other words, he does not associate current brain development solely with human improvement, as random variables can also lead to the emergence of pathologies. Therefore, he proposes the modulation of plasticity mechanisms to achieve the best behavioral outcome for a specific individual. This raises one of the current questions regarding human enhancement, prompting reflection within the fields of biotechnology and anthropology.

> *Such rapid, ongoing changes may be followed by the establishment of new connections through dendritic growth and arborization. However, they harbor the danger that the evolving pattern of neural activation may in itself lead to abnormal behavior. Plasticity is the mechanism for development and learning, as much as a cause of pathology. The challenge we face is to learn enough about the mechanisms of plasticity to modulate them to achieve the best behavioral outcome for a given subject. (2005:377)*

This present study argues that there is a strong connection between evolution and human improvement in order to demonstrate that the concept of human enhancement is a regularity, even though it has not been linear or systematic and has sometimes been influenced by evolutionary chance. It is proposed that this regularity is evident in the process of hominization and in the humanization of our species – we are the sculptors of our own humanity. This conceptual assertion is supported by evidence of positive selection found in various fields of study. As an illustrative example of this claim, the genetic evolution of the brain is often cited.

The brain underwent not only a change in size, as explained in the previous lines, but also a transformation in its organizational and functional structures, which involved genes and protein sequences that left their mark on those affected. The primary focus of genetic research, particularly concerning the process of encephalization, has been the identification of genes that have exhibited positive selection compared to other species. These studies have identified genes such as *forkhead box P2 (FOXP2*), which is related to language, and mutations in this gene (positive selection) may have played a role in the emergence of this capability in humans. Additionally, many other genes have been identified that show this positive selection, with the prodynorphin gene being particularly notable for its strong demonstration of positive selection.

> *The prodynorphin gene (PDYN) encodes for a precursor of a 262 opioid neuropeptide involved in various neural processes. An upstream cis-regulatory element of this gene shows a rapid rate of sequence changes in the human lineage after the divergence from chimpanzees, demonstrating the effects of positive selection (Rosales-Reynoso, 2018:261-262).*

The latest scientific discovery in the present year reveals that our evolution is not solely driven by the emergence of new genes or mutations within them. As Steven Reilly, one of the researchers involved in the project, asserts, the absence of certain DNA fragments is just as significant as their presence in shaping our evolution.

> *The elimination of just one or two DNA bases could suppress a repressor sequence, leading to an increase in gene expression, or the deletion of a base that does not fit well with an activator could result in enhanced gene expression. Surprisingly, we observe this in 30% of cases, where a deletion increases gene activity instead of suppressing it (Criado, 2023).*

Indeed, the absence of these genetic filaments specifically affects brain functions, as expressed by scientists in the journal *Science*,

> *These short (average 2.56 base pairs) deletions are enriched for human brain functions across genetic, epigenomic, and transcriptomic datasets. Using massively parallel reporter assays in six cell types, we discovered 800 hCONDELs conferring significant differences in regulatory activity, half of which enhance rather than disrupt regulatory function. We highlight several hCONDELs with putative human-specific effects on brain development, including HDAC5, CPEB4, and PPP2CA. Reverting an hCONDEL to the ancestral sequence alters the*

expression of LOXL2 and developmental genes involved in myelination and synaptic function (Xue, J.R. et alt. 2023)

Genetic deletions serve as a reminder, once again, that evolution is not a linear process. They also reflect that our humanity arises from a "molecular blur," as highlighted by Irene Gallego, a researcher involved in the Zoonomia Project responsible for the mentioned discovery. Gallego states, "But the fact that both mutations and deletions contribute to the phenotypes that characterize us as a species adds a certain degree of humility to what we think of ourselves. Some of the things we value so much are a consequence of a molecular blut!" (Criado, 2023).

Biotechnology has provided numerous insights that, combined with anthropological discoveries, allow us to take advantage of the benefits of human enhancement. Building upon the evolutionary perspective with which we initiated this work, the problems that were previously addressed by positive selection are now being solved. Today, there is a focus on cultural selection that regulates and guides technological advancements. These advancements can stimulate human improvement while avoiding uncertain, pathological, or anomalous outcomes.

Currently, knowledge can replace the randomness of adaptation, and every human being can not only shape their own brain but also, immersed in science and technology, hold the fate of the species and the planet in their hands. This conscious progress can only be directed towards true human enhancement through a reflective and cautious attitude.

These remarks are imprecise unless a theoretical-historical demarcation is made to define how human enhancement is approached today. Therefore, we proceed to provide a brief historical overview that allows us to better understand the concept from which the issue of human enhancement is addressed today.

Human enhancement: a constant in the history of humanity (Second conceptual framework)

Prehistory

The pursuit of human enhancement has been a constant in the history of humanity and is closely linked to the idea of progress, of a better and more fulfilling life. Fire, the wheel, the lever, daggers, and knives are evidence of this desire to advance and become better. The Neolithic revolution became a transformative event in human life, providing enrichment to existence that directly contributed to human development. Domestication was one of the processes carried out during this revolution and can illustrate the capacity for change that living beings possess, facilitated by an interaction between the environment (including human management) and genetics. Domestication is "the process by which an animal population adapts to humans and the captive environment through a combination of genetic changes occurring over generations and evolutionary events induced by the environment, which are repeated in each generation" (Price, 1984:3). The interaction of the components that underpin improvement, not only human but also that of life in general, can already be observed: genetics, environment, and human management. This human management should be guided by respectful behavior, understanding that human life is nothing without the lives of other living beings. We are what we are because other creatures, inhabitants of the same space, make life possible, both ours and that of others. This connection with nature should not be one of dominance and arrogance, but one of collaboration and respect, recognizing that humans are nothing without the ecosystem in which they exist.

Later, the next milestone that would shape our history of human enhancement was writing, an activity that introduced a new way of relating to others, capable of connecting the world and transforming the human self.

Ancient age

Human enhancement is linked to the idea of more perfect and superior beings that can achieve anything, and domestication can serve as an example. Thus, we find numerous myths that emphasize this dominance over the rest of the world, such as the myth of Prometheus, in which the theft of fire from Zeus would enable the improvement of the human condition and their power over other living beings. The artistic expressions of the Greeks and Romans, with a display of ideal proportions embodied in Greek sculptures, or the qualities for war evident in Roman exhibits, yearn for human perfection and greatness compared to other living beings. They became standards of beauty or ideal models for warfare.

Nutrition, potions, and elixirs have, since the dawn of humanity, driven therapeutic improvement and the prolongation of life, in a constant quest for means that generate more strength, more wisdom, and greater resilience, in other words, the enhancement of human capabilities.

Plato would establish a selection of the best individuals to govern the polis, to protect others, in his texts of *The Republic*. These individuals possessed superior qualities by birth, but they developed them through one of the means of human enhancement used since Antiquity: education. Physical and intellectual instruction, provided in the Academy, ensured the increase of capabilities and the superiority of some human beings over others. This means of human enhancement has persisted throughout the centuries, as it is considered crucial for the development of human capacities and is currently regarded as a right and a duty.

Education, as an external agent, has propelled the advancement of individuals. Simultaneously, it has built progress upon a foundation of knowledge. This knowledge has been centered around thought, giving rise to science, literature, arts, and technology. These disciplines would be an illusion if this means of human enhancement had not existed. Learning (an internal agent), executed through education (an external agent), leads to personal human improvement. One of its great exponers is Helen Keller, a deaf, mute, and blind woman born in Alabama in 1880, who writes in her autobiography: "This is how my friends have made the story of my life. In a thousand different ways, they have transformed my physical imperfections into marvelous privileges and have enabled me to walk calmly and happily through the dark night that surrounds me." (1904:166) The process of educating this child bears some resemblance to the process of domestication established during the Neolithic revolution, involving three key interacting factors: genetics, environment, and human intervention. The learning of habits, such as sitting down to eat, picking up a spoon, which is vividly described in the movie *The Miracle Worker* (1962), directed by Arthur Penn, is the means used by the teacher, Anne Sullivan, to "domesticate" Helen. It is the preliminary and essential step for the child to uncover the possibility of understanding the world and interpreting reality. It can be said that learning is an instrument that increases and stimulates neural connections, provoking changes in the brain, related to its plasticity and the use of utensils or tools described in the previous section.

Aristotle, on the other hand, speaks to us of a virtuous person who must seek perfection. "Human good turns out to be the soul's activity that expresses virtue, and if there are more than one virtue, then in accordance with the best and most complete one. Moreover, it must be in a complete life" (Aristotle, 1999: 1098a, 9). Through this pursuit, one attains happiness, which is the ultimate good. However, this achievement is only possible within the social sphere, where human beings interact and develop their abilities.

The virtuous and non-virtuous individuals mentioned by Aristotle emerged in different parts of the world, such as China, Greece, and Persia, during ancient times through ascetic practices. These practices were a set of techniques exercised by individuals, allowing them to excel above others and become moral virtuosos. This meant being superior to others because, through systematic, repeated, and methodical exercise, they transformed themselves and adapted their lives to a specific system of rule. "Sloterdijk notes that the birth of ascetic practices caused a revolution that forever marked anthropogenesis, as it divided humans into two categories: the virtuous and the non-virtuous" (Castro-Gómez, 2012:70).

Man discovers that it is possible to immunize oneself against suffering and protect oneself from despair, not through social technologies that help overcome the material difficulties inherent to human weakness, but through individual technologies that allow distancing from the world, acquiring mental and spiritual strength that brings satisfaction, happiness, even in the midst of all difficulties. Asceticism requires effort, dedication, and discipline, which will become the means of constructing ourselves over the following centuries, of becoming sculptors of our own humanity, leading to a meritocracy, characteristic of our present days, far removed from the uplifting overcoming of the human being from which it started.

Middle ages

The ascetic practices were resumed in monasteries with the purpose of fully realizing the design of oneself (as previously seen in Ramón y Cajal's statement "every human being, if they set their mind to it, can be the sculptor of their own brain") and as we will see again in the Cyborg Foundation's motto "Design yourself.") The emphasis of the monks was not so much on human enhancement, but on the practice itself: the daily routines of rising, praying, attending mass, tending to the garden, eating, reading, and writing manuscripts. These routines served to create immunity against the contingencies of existence. They helped us accept and possibly overcome the afflictions of the "infinite wound" (Esquirol, 2021:61), as "The infinite wound has four afflictions: the affliction of life, the affliction of death, the affliction of the gift of the other, and the affliction of the wonder of the world" (*Ibid*). It is a way to be prepared to face any problem, achieving a homeostatic balance that aligns with circadian rhythms, generating well-synchronized biological clocks. The self-improvement is not solely achieved through biomedical or instrumental techniques; the human being, through self-examination, meditation, and the practice of stable routines, can enhance and expand their capacities. "Philosophy can also be considered as an 'exercise' that can contribute to making us better, which shows that it is also possible to speak of human enhancement in non-biomedical terms" (Galparsoro, 2019:66). Philosophers, ascetics, and monks embodied that imperative of human improvement expressed in the title of Sloterdijk's book, *You Must Change Your Life*

Modern ages

Despite the succession of novelties, commercial advancements, social changes, transportation developments, and new technologies in construction and communication, there was not a significant breakthrough regarding human enhancement, therapy, or eugenics until the end of the Modern Era. It was during this time that sociopolitical revolutions such as the bourgeois, French, and American revolutions, as well as scientific and industrial revolutions, brought about a profound shift on the planet. Humanity embarked on a new era flooded with rapid progress, which eventually led to the current scientific and technological upheaval.

> *We did not give you, oh Adam, a fixed place, a specific appearance, or a particular occupation, so that you may freely choose and possess the position, appearance, and occupations that you desire. The limited nature of other things has been constrained by the laws that we have prescribed. You, free from narrow constraints, shall define yourself according to your own judgment, which I have entrusted to you. I have placed you in the midst of the world so that you may look around more easily and see everything that is in it. We have not made you celestial or earthly, mortal or immortal, so that, almost free and sovereign, you may shape and sculpt yourself in whatever form you prefer. You may degenerate into the lower forms where the gross people or by your will, you may regenerate into the higher forms where the divine resides. (Pico della Mirandola, 2006:5).*

All the utopias throughout history imply a narrative of human improvement: *The City of the Sun*, by Campanella, Tomás Moro's island of *Utopia*, and Bacon's *New Atlantis.* The desire for prosperity as human beings leads us to imagine the ultimate development of humanity in any of its aspects. First, through utopias, and later through science fiction, imagining works like Huxley's *Brave New World*, which already raises the controversy between progress and the potential loss of humanity as it is understood today, or the disjunction between the human being constructed through biotechnological applications and the human being exposed to their own humanity without possibilities of improvement.

In the 17th century, Bacon, in *Novum Organum*, extols the power of science to achieve whatever is within the reach of the scientist.

> *The unassisted hand and the understanding left to itself possess but little power. Effects are roduced by the means of instruments and helps, whixh the understanding requires no less than the hand; and as instruments either promote or regulate the motionof the habd, so those that are applied to the mind promt or protect the understanding. (…) knowledge and human power are synonymous, since the ignorance of the cause frustrates the effect. (1620, 11)*

Power and science go hand in hand to control and transform nature, with the purpose of obtaining useful elements in the pursuit of improving the human condition.

Contemporary age

In the 19th century, Darwin presents his research on evolution, "The Origin of Species," stating that humanity is just one among many possible species. We are in a phase of evolution, and humanity is not the end; we will continue evolving into other biological forms. Thus, an unstoppable process of human improvement is presented, driven by natural selection. The 21st century brings forth another significant problem not considered by Darwin: natural selection dominated by humans themselves, in a scientific and organized manner, rather than leaving it to chance. It combines the freedom to shape ourselves, as presented by Pico de la Mirandola, with the power of science to enhance humanity from within, a concept advocated by Bacon. Mankind confronts natural selection and seeks to exert positive selection that triggers rapid and essential human transformation. It is Galton who initiates this dangerous challenge, which, combined with the ambitions of the most powerful countries, leads to a series of self-destructive practices capable of annihilating humanity.

Galton presented a discipline called eugenics. He proposed using any necessary practices to increase the genetic quality of the human species, stating that the offspring of "superior strains or races" would produce individuals of a high class without genetic flaws (Yanes, 2018). Although Galton based his ideas on Darwinian theories, certain aspects were overlooked, such as Darwin's explanation of environmental influence through pangenesis or the concept of non-gradual evolution. At the time, eugenics was widely accepted, particularly in the United States and Germany. However, after the atrocities committed in its name, a portion of the scientific community labeled it as pseudoscience, citing the reasons mentioned earlier, as well as the manipulation of the discipline for political, ideological, or religious reasons. In the 20th century, the rise of genetics would restore the role of the environment in gene expression, considering that maintaining strict hereditary determinism is not accurate, as the expression of the genotype largely depends on the organism's environment.

Eugenics was presented as a contribution to the common good and proposed two possibilities: negative eugenics, practiced in the United States, where in 1907, the first law was passed in Indiana aimed at "preventing the procreation of confirmed criminals, idiots, imbeciles, and rapists" (*Ibid.*). A campaign of sterilizations was initiated, targeting mentally ill individuals, disabled individuals, alcoholics, homosexuals, sex offenders, and criminals. American society embraced this ideology, and competitions were held to reward the "most fit families." Eugenics found success at fairs, where posters displayed slogans such as "Some people are born to be a burden to others" (*Ibid.*).

The second type of eugenics was classified as positive and relied on the reproduction of individuals considered healthy with good genetics. This positive concept also included practices aimed at improving health, such as physical exercise, a balanced diet, good lifestyle habits, sexual health, and proper nutrition for each individual. This type of eugenics was implemented in other European countries such as France and the United Kingdom.

The 20th century began with the prevalence of eugenic proposals in their most negative sense, intertwined with the concept of the Nietzschean Übermensch, which seeks self-transcendence and the overcoming of one's own nature by constructing a system of values to solidify one's life project. This idea gave rise to numerous interpretations. Nietzsche proposed human improvement arising from the freedom to choose, individuality, and the capacity to struggle to surpass oneself and sustain one's own lifestyle. At the same time, the philosopher affirmed, "The last thing I would want is to 'improve' humanity" (1992:16). He believed that the pursuit of such improvement harbors the belief that we are gods and, as such, capable of controlling the world through artificial selection, a notion that can lead us to self-destruction.

This fusion of arguments, theories, and thoughts (eugenics and the Übermensch, which had been proposed on an individual level) was put into practice on a global scale, leading to the largest ethnic cleansing in history: the Nazi genocide. Human improvement becomes a dangerous and aberrant weapon that can bring about the end of humanity, especially when directed by governing techniques. These two forms of improvement have been described by Sloterdijk when explaining the concept of anthropotechnics. The globally oriented practice is the improvement of one group of men by another group of men (Fernsteuerung), without any margin of freedom. It is the application of technology to "allow oneself to be operated on" (2009:589). The individually oriented practice is the improvement of men by themselves (Selbststeuerung), personalized, individual, informed, and self-sculpted (as we have mentioned in the previous paragraphs, as proposed by Ramón y Cajal when discussing the brain). It is "self-operation" (*Ibid.*). In both cases, they encompass the concept of anthropotechnics, understood as "a set of techniques developed to modify and optimize human behavior" (Castro-Gómez, 2012:67). According to Sloterdijk, these two forms of human improvement can expand upon Foucault's project on biopolitics and the aesthetics of existence, as explained by Castro-Gómez.

> *This typology of anthropotechnics can be seen as a methodological attempt to expand, based on anthropological foundations, Foucault's project that distinguishes techniques of governing populations (biopolitics) from techniques of governing oneself (aesthetics of existence) (2012:67).*

Scientific proposals for human enhancement, particularly eugenics, were banned until the late 20th century when the debate was reignited with eugenic proposals associated with genetic engineering. These proposals include abortion in cases of fetal malformations, assisted reproduction, preimplantation genetic diagnosis, and genetic diagnosis in adults. In the 21st century, genetics and genomics have advanced in the pursuit of human enhancement. The CRISPR/Cas9 technology has become a molecular tool used to "edit" or "correct" the genome of any cell. It is a genetic revolution that has sparked many discussions about its use and the changes it can generate in human beings. However, science and technology continue on their path. Progress continues, and alongside genetically modified organisms, hybrids and chimeras are also emerging.

Transgenic animals incorporate a gene from another organism into their genome, such as transgenic cows that are engineered with human genes to produce human insulin for diabetic patients. Hybrid animals mix genes from two different species in every cell of their body, as seen in mules, which are natural hybrids resulting from the mating of a female horse (Equus ferus caballus) and a male donkey (Equus africanus asinus). Chimeras have at least two genetically distinct cell lines from two different zygotes in their body. In the case of interspecies chimeras, the cell lines belong to different species. There have been numerous examples of these genetic manipulations in the late 20th century and the present century. The concerns raised within the scientific community about this topic are evident due to its long history and the controversial experiments carried out, such as the work conducted by Juan Carlos Izpisúa's team in Spain and later in China. They successfully created chimeric embryos of pig or cow with human (2017: 473-486), and previously worked with mouse embryos with human cells (2015:216-321). In 2021, they achieved chimeras of Macaca fascicularis (macaque) with human (2021:2020-2032). The objective of these experiments is focused on the development of xenotransplantation, which involves transplanting organs or tissues between different species. All of these research endeavors have raised significant moral concerns, although the recent experiments were guided by ethical advisors,

> *For the studies presented here, ethical consultations and reviews were conducted at both institutional level and through the involvement of independent bioethicists with expertise in state and national bioethics policies related to these issues. This meticulous and detailed process helped guide our experiments, which focused entirely on ex vivo chimeric embryos. Furthermore, we limited our studies to the development of chimeric embryos in early stages. (2021: 2031)*

In this work, human enhancement is understood as an improvement of life. The human being is not, and cannot be, without the existence of other living beings and the environment in which it thrives. The destruction or mistreatment of other living beings, or of our own habitat, entails the ruin of mankind itself. Humans are not superior to the rest of living beings since they depend on them. Humans must be aware of the complementarity they need with the rest of the ecosystem in which they dwell in order to maintain their humanity. Perhaps for this reason, chimeras and hybrids have validity not only in therapeutic matters. They may teach us to understand that we are part of the same world: the connections between us are necessary if we want to develop the empathy and understanding essential for respecting and living in collaboration. This same role of inclusion and understanding was achieved through cultural elements in Greek mythology, through the fictional creation of sphinxes, harpies, or centaurs.

In the 21st century, we need a science that teaches us how to use science, guiding scientific actions from metascience. This new science should bring forth a global reflection on the scientific endeavor. It must consider the improvement of life, not only of human life, but of all living beings. Care for the environment, our planet, is essential, as well as the social channeling and the holistic understanding of human identity, encompassing all its facets and not solely reducing it to the biological aspect.

The researcher immerses themselves in the specific and specialized research they are conducting, which exposes them to losing the global perspective. This global perspective needs to be provided by an interdisciplinary team of professionals, weaving a general regulation that is then implemented by these teams to control each experiment. That is why Diéguez argues that "what needs to be demanded, if we do not want to simply paralyze technological development, is the improvement and enhancement of control mechanisms and regulation" (Diéguez, 2021).

Human enhancement cannot be reduced to eugenics, understood as the pursuit of genetic perfection or the ideal genetic traits. The 20th century is characterized by advancements in human life due to significant scientific discoveries that alleviate suffering caused by illness, promote the fight against adversities, and uphold the concept of human resilience in the face of death. While genetics plays a significant role in human enhancement, chemistry and biochemistry are equally important. Vaccines, both traditional ones like the measles vaccine and mRNA-based ones like those developed for Covid-19, serve as preventive measures for healthy individuals, strengthening our immune system, saving numerous lives, and protecting us from diseases. Other vaccines are designed to activate the immune system after the disease has been contracted, enabling the body to fight the pathogen without additional assistance. These vaccines also utilize mRNA technology to transmit information to proteins, triggering an immune response, with cancer vaccines being the most common example. Antibiotics help combat bacterial infections, analgesics alleviate pain, Sildenafil (Viagra) addresses erectile dysfunction, and medications like Ritalin and Rubifen (central nervous system stimulants similar to amphetamines) aid individuals with ADHD (attention deficit hyperactivity disorder). Unfortunately, in some cases, healthy individuals illegally misuse these medications in an attempt to enhance their cognitive abilities. Anti-libidinal drugs are used to lower libido and address problematic sexual behavior, such as aggression or pedophilia, often employing anti-androgens like flutamide or bicalutamide. Pharmacology as a means of enhancement is an integral part of our daily lives.

We are in the era of ingested substances that begins with medications and extends to other elements such as stimulants like taurine, caffeine, and theine; vitamin supplements that enhance memory, imagination, and concentration; protein shakes that boost muscle strength, dermatological essences that beautify our skin, and illicit substances that provide relief from sorrow. All of these substances have become part of our daily lives and can foster addictions and alter human behavior if used improperly. We are facing a form of human enhancement that relies on chemical substances to amplify our capabilities and make us stronger when used appropriately. However, when used improperly, these substances can lead to pathologies and destruction. This echoes the sentiment expressed by Pascual-Leone regarding brain plasticity. The ingestion of these elements can become a cause of pathologies. Chemistry and biochemistry take the reins of this new form of enhancement, which extends beyond therapy and encompasses various aspects of human life, provided they are used appropriately.

Positive eugenics advocated for a healthy life through physical exercise and balanced nutrition. This notion of improvement became associated with aesthetic beauty, reflecting the idealized canons sculpted in marble by the Greeks. When natural methods of human enhancement fail to yield desired results, recourse is made to science. Technological elements such as liposuction, botulinum toxin injections, and plastic surgery are sought after. These techniques are part of the field of plastic surgery, an emerging discipline in recent decades. Initially, it was intended to address deformities, wounds caused by accidents, the consequences of tumor treatments, or the sequelae of diseases. It focused on reconstructive surgery. Today, it is also applied to anyone seeking to enhance their body image. This represents the other facet of plastic surgery, aesthetic surgery, which has become commonplace in our daily lives,

> *The purpose of aesthetic surgery is to improve the physical appearance of body parts that have lost their youthful appearance over time or to alter certain bodily structures (such as ears, nose, breasts, etc.) in youth, which may be the source of body image acceptance issues. (Serret Estalella, 2008:6)*

As mentioned earlier, human enhancement requires a metascience that guides us on how to use science and put it into practice. In the case of aesthetic improvement, Serret Estalella emphasizes the importance of bioethics, stating that "in aesthetic surgery, the four principles of bioethics, including non-maleficence, beneficence, autonomy, and justice, should be well considered" (*Ibid*.).

In the 21st century, human enhancement as an ideal of self-improvement has expanded through educational processes centered around effort and hard work, seeking perfection in the desired activity and, at times, suppressing the natural talent underlying routine and sacrificial practice. The film Whiplash serves as an extreme example of this pursuit of improvement, of the desire for perfection, where the drummer must bring out the best in himself no matter the cost. It echoes the medieval ascetic practices taken to the extreme, aiming for a profound enhancement of the human being. This sequence of human enhancement leads us into the realm of meritocracy, based on the unlimited acquisition of human competencies that can be attested through diplomas or degrees. Life becomes a race for human improvement, while also becoming a fierce competition with others.

Sports provide a clear example of this phenomenon, where numerous techniques have been used to enhance human performance, often with the sole purpose of improving athletic achievements. The rise of biotechnology and pharmaceutical companies has enabled the use of various substances and practices to be administered to athletes in order to enhance their success. From testosterone to substances considered nutritional supplements such as creatine, as well as medications like Angiogenix, which is based on nicotine and designed to help cardiac patients generate new blood vessels while also increasing muscle capacity, a wide range of substances has been utilized. Well-known hormones like erythropoietin (EPO) and darbepoetin, as well as perfluorocarbon, which can dissolve gases including oxygen to better deliver it to tissues, have also been employed. Actovegin, a derivative of calf serum, is used to increase blood capacity and facilitate the rapid transport of oxygen. Hydroxyethyl starch expands plasma volume and dilutes the concentration of red blood cells. However, the majority of these substances are currently prohibited as they are considered doping, alongside amphetamines, anabolic steroids, and diuretics. The use of these elements can lead to the generation of pathologies due to a lack of information regarding their potential side effects on humans, as neurologist Pascual-Leone has previously explained in the context of cerebral plasticity. Nephrologist Ramón Peces Serrano (2003), recognizing that these enhancements place an additional burden on renal function, responsible for eliminating toxic waste, supports this assertion,

> *Often, new chemical products are used before safety studies have been completed, exposing athletes to significant risks. In many cases, the use of some of these products has already exacted a high toll. It is not uncommon for the media to report on the sudden death of athletes under suspicious circumstances. For instance, the illicit use of erythropoietin by certain athletes, who believe that increasing red blood cell mass can enhance their performance, has led to several cases of sudden death. In these athletes, erythropoietin induces an elevation in red blood cell count and blood viscosity, which, when exacerbated by dehydration during intense exercise, gives rise to fatal thromboembolisms. Another complication recently identified in renal patients is the development of anti-erythropoietin antibodies associated with pure red cell aplasia. Although, thus far, antibodies have primarily been detected in renal patients, it does not exclude the possibility of athletes who illegally employ erythropoietic products to enhance their performance also developing such antibodies. Only time will tell. (Peces, 2003:485).*

The athlete who achieves the best records can also be facilitated by technology through the creation of cybernetic organisms, known as cyborgs, which may give rise to a new humanity in the 21st century. The most well-known case in sports is that of Oscar Pistorius, a South African athlete who was born with fibular hemimelia (congenital absence of the fibula and tibial hypoplasia) and had his legs amputated below the knee at eleven months of age. He competed in the Paralympic Games with transtibial prosthetics constructed from carbon fiber. He achieved world records in several events during the 2004 Athens Paralympic Games. From the early peg legs to the current orthopedic prosthetics, there has been significant improvement that has notably contributed to human development. Pistorius himself offered his perspective on this human enhancement, stating, "You are not disabled by the disabilities you have; you are able by the abilities you have" (Gareth, 2007). Pistorius ushers in a new era, not only for athletes but also for everyday life, as it expands the possibility of enhancing our capabilities, offering a glimpse of a new concept of what is considered natural and a fresh perspective on sports,

> *His case is a snapshot into the future of sport. It is plausible to think that in 50 years, or maybe less, the "natural", able-bodied athletes will just appear anachronistic. As our concept of what is "natural" depends on what we are used to, and evolves with our society and culture, so does our concept of "purity" of sport, and our concept of how an Olympics athlete should look. (Camporesi, 2008:639)*

Technological advancements have caused a true revolution. From conventional prosthetics, hearing aids, glasses, pacemakers, cochlear implants, and contact lenses, we have now transitioned to the cyborgs. Humans are merging with machines to overcome their limitations, improve their lives, and expand their humanity. Technological tools have been used for years, but the rapid and impactful scientific and technical advances of recent decades have not only disrupted the routine of everyday life but have also penetrated the traditional norms, shaking the security to which we were anchored. All of this has raised many doubts and questions about this human enhancement that transports us to a new concept of humanity, hence the terms transhumanity and posthumanity. Perhaps this is because technology is progressing rapidly at this moment, forcefully permeating our daily lives.

In this article, the idea is put forth that possibly, there is not a single type of humanity. Just as evolution, through natural selection, materialized into one type of humanity among the many possible, there may currently exist different forms of being human. The human being is diverse, thus encompassing different ways of being human. Progress and evolution change the concept of all the assumptions upon which we base our idea of reality. We are prepared to adapt to these variations. We can embrace the unstoppable alterations generated by humans, even though the need for security may tempt us to cling to the familiar, to tradition, to what has always been, and thereby attempt to halt this variability. Human enhancement, as we are witnessing, is an inherent characteristic of ours and propels these transformations. As we will see in the following sections, technological advancement is also intrinsic to mankind and, therefore, impels new forms of life. Human diversity and the permanent mutations we generate lead us to believe that there is not only one type of humanity because it fluctuates, with the metamorphoses brought about by human enhancement itself and technological advancements. We may ask ourselves, is there anything that always remains in the concept of humanity? Is there any condition that must be preserved amidst the continuous change in the human being? It is possible, and perhaps we can provide an answer: what remains is that which neither human enhancement nor technology can reach, and therefore, it is the only thing that cannot change.

We must not forget that man is "the most important bioartefact created by humans; and it has been so since the first day of its existence – when it already depended on its tools – until today, when it could not live without its multiple technological prostheses and without the artificial 'supernature' in which it dwells" (Diéguez, 2017:148). And indeed, our connection to smartphones, computers, and a daily life dependent on so many artificial technological elements is evidence of this. This work would not have been possible without the capacity for information storage and the ease of retrieval provided by various digital devices. When these did not exist, bibliographic documentation and access to information were restricted and complicated.

The human enhancement brought about by the new technologies of the 20th and 21st centuries is exemplified by Clynes and Kline. They attempted to find a way for astronauts to cope with a hostile environment, not through a suit, but through an adaptation that would become part of their organism and created by humans, not through inheritance or natural selection. They called it a *cyborg* (cybernetic organism).

The first *cyborg* 1.0 and 2.0 came about through the work of Warwick in 1998. He underwent a surgery to implant a RFID (radio-frequency identification) microchip in his arm. This implant emitted information that was received by a computer, which in turn-controlled Kevin Warwick's movements. It was a success. The English scientist states, "Now several thousand people have this implant. It has already been approved in the United States for medical use, and people with epilepsy or diabetes have their medical information stored there" (Warwick, 2022). In the second phase, in 2002, Warwick underwent another surgical intervention to implant a neural interface consisting of a hundred electrodes connected to the nerves in his arm. These electrodes collected information from the arm and sent it to the brain. Warwick aimed to convert the analog signal from the nerves, generated during arm movements, into a digital signal that could be managed by the computer. It was also successful. Together with Peter Kybed, Warwick connected his arm's nervous system to the Internet and was able to control an artificial arm located in England from New York. Subsequently, the engineer, not content with demonstrating that the body and the brain did not have to be physically connected to communicate, sought to establish direct and remote communication between two human nervous systems. He had a similar system implanted in his wife. Whenever his wife moved her hand, he received that information. Currently, he is working on finding a way to connect two human brains without the need for verbal communication, only by thinking about what we want to say.

> *I believe that as humans, we have evolved in a certain way, which is fine for a human being. But now we live in a technological world, and we can see what technology offers us. The way humans act and think has certain advantages, but also some drawbacks. Artificial intelligence can think much faster than us; it has formidable mathematical capabilities and can comprehend the world in multiple dimensions. However, as humans, we are limited to three dimensions, and we think relatively slowly compared to how computers operate. Since we have this technological advantage, why not improve and enhance who we are and how we act by connecting to that technology? Why can't I have an extra memory boost? It could be dangerous, but it is also extremely exciting and offers us new opportunities (Ibid).*

Rob Spence lost an eye when he was a child. In 2009, he decided to implant a prosthetic eye that included a video camera. His intention was not to regain vision. Influenced by his profession as a film director, the Canadian sought an electronic eye that would incorporate a video camera. This is the Eyeborg project, carried out by ophthalmologist Bowen, engineers Grammatis and Martin Ling, along with manufacturer Rf-links. He does not have it connected to the brain, but if it were to be connected, it could provide a wider or night vision. The brain demonstrates with the prosthesis that it possesses flexibility and adaptation to new situations, and that this potential can continue to develop.

Under the slogan "Design Yourself" (recalling the slogan of Ramón y Cajal mentioned in previous paragraphs, "every human being, if they set their mind to it, can be the sculptor of their own brain"), inspired by Pico della Mirandola's message and the proposition of asceticism, Neil Harbisson and Moon Ribas created the Cyborg Foundation,

> *Cyborgs are the union between cybernetics and organisms. Since both are in exponential evolution, the definition of cyborg is also constantly changing. We define cyborgism as the various types of relationships between technology and organisms. There is a difference between technology that allows you to know things and technology that allows you to feel things. (…) The Cyborg Foundation is an online platform for the research, development, and promotion of projects related to the creation of new senses and perceptions through the application of technology to the human body. Our mission is to help people become cyborgs, promote cyborg art, and advocate for cyborg rights. (Harbisson and Ribas, 2020)*

Neil suffered from achromatopsia, a condition that led him to implant an intracranial antenna in the occipital area. He has a sensor and a chip connected to it. These convert the frequencies of light detected by the sensor into audible frequencies that travel through the bones of the skull. He became the first officially recognized *cyborg* in his documents (ID) by a government, the British government. In order to achieve this recognition, Harbisson argued that his artificial eye was not an addition but already part of his body and that he needed it. He solved his problem and learned to "hear" colors through the antenna, gaining a new sense thanks to technology. This new sense has been integrated by the brain, which, due to its plasticity, has adapted perfectly to the device, incorporating it into the mechanisms of action as if it were something biological. He does not consider himself a *cyborg* because of the union between the electronic eye and the head, but rather because of the connection between the software and the brain.

Moon, on the other hand, wears sensors in the form of earrings that allow her to detect the speed at which people around her are moving. As a choreographer, this new ability to sense movement is an aid to artistic creation. The technology enables them to feel, not just to know.

Neurobiologist Rafael Yuste is the director of the BRAIN Project (Brain Research through Advancing Innovative Neurotechnologies or Brain Activity Map Project). This project investigates the brain through the advancement of innovative neurotechnologies. It aims to map brain activity in order to uncover the keys to the functioning of the human brain and thus help in the cure or prevention of neurological diseases such as Alzheimer's or Parkinson's. Yuste argues that, just as we currently carry smartphones, in a few years we will use a sensor that allows us to think in a language and the sensor will translate our thoughts and express them in words. It is an interface between neurons and processors that, initially, will have a non-invasive implementation by placing the device in glasses, headbands, caps, or earrings. Later on, these sensors will become part of our brain. Thus, there will be humans augmented by technology and others not augmented, potentially creating social inequalities due to different levels of capacity development and, as is the case now, different access to information.

In this regard, Elon Musk, CEO of Tesla, is also working in this direction. He has already presented a chip for mind reading and it has been successfully implanted in the brain of a monkey. Yuste sees issues of brain protection, thought privacy, and individual privacy in this biotechnological link. That's why he is fighting for neurorights to become a reality and be included in the *United Nations Charter*. Human Rights should encompass neurorights if we want an international legal framework to protect brain activity and data. Chile has become the first country in the world to modify its *Magna Carta* by including an article on neurorights in the constitution. Subsequently, a law will be enacted to regulate the requirements, conditions, and restrictions for the use of scientific and technological advancements in individuals, with a special focus on protecting brain activity and the information derived from it. Spain also has the *Charter of Digital Rights* (2021), which recognizes the new challenges in the application and interpretation of rights in the digital environment. Article 26 of the charter states that the conditions, limits, and guarantees for the implementation and use of neurotechnologies in individuals can be regulated by law.

> *To ensure the dignity of individuals, equality, and non-discrimination, and in accordance, where applicable, with international treaties and conventions, the law may regulate those cases and conditions regarding the use of neurotechnologies that, beyond their therapeutic application, aim to enhance cognitive abilities or stimulate and enhance human capabilities. (Government of Spain, 2021:28)*

New technologies and synthetic biology open new perspectives, not only in biomedicine but also in everyday life, as we have seen. In biomedicine, applications such as pharmaceuticals, personalized genomics, gene therapies, tissue repair and regeneration, and cellular reprogramming with stem cells are some examples. In relation to the environment, practices such as bioenergy, biomaterials, bioremediation to prevent ecosystem contamination, genetically modified organisms (GMOs), and biosensors are transforming the world.

Although the concept of *anthropotechnics* proposed by Sloterdijk at the end of the last century has already been mentioned in previous lines and will be further developed in the following sections, it is necessary to explain it here. According to Sloterdijk, this concept not only represents "a set of techniques developed to modify and optimize human behavior" (Castro-Gómez, 2012:67), but also implies that human modification generated by these techniques is justified due to the role that technology has played in the construction of humanity,

> *If there is a human being, it is because technology has made them evolve from the prehuman state; thus, technology becomes the true producer of human beings or the plane on which they can exist. Consequently, humans do not encounter anything new when they expose themselves to subsequent creation and manipulation, and they do nothing perverse if they change themselves through self-technologization. (Sloterdijk, 2001:23; Sibilia, 2005:160)*

If there is a historical continuity, as we have pointed out with the events described in the previous pages, Paula Sibilia then wonders, "Wouldn't teleinformatics and biotechnologies represent just one more step in that millennial trajectory traced by cultural evolution?" (Sibilia, 2005:160).

It is possible, although we lack evidence to state it with precision. However, this continuity does not prevent the need for intervention in various aspects, as we will see below. Sibilia also asks, "Why do the contributions of the most recent technoscience present themselves as a radical break with the past?" From these pages, as previously mentioned, the reasons are considered to be the speed of advancements, their intrusion into everyday life, and the insecurity generated by witnessing the shaking of principles and paradigms that have been upheld in our cultural and scientific tradition for decades. These are the reasons why certain adaptive measures are deemed necessary, which will be outlined in the following sections and represent a new way of approaching research, as well as the integration of human enhancement in various aspects of our existence: interdisciplinary collaboration in laboratories (BASTEC); reflective and creative thinking (*poiesis*) alongside calculative thinking; dissemination of information on the potential consequences and all aspects entailed by proposed biotechnology for humans (science communication and opening up the scientific community to the world); personalization of biotechnology applied to each individual; international regulation that applies equally to all within the framework of human rights, as advocated by Rafael Yuste with neuro-rights, and its implementation tailored to each country's local laws and its own idiosyncrasies.

Human enhancement has been a constant throughout human history. In this dossier, selected events from each era have been deemed important in establishing the conceptual framework of the term. These events serve as illustrations to demonstrate the exponential development of human enhancement, which not only affects certain social groups but also extends beyond medical aspects. Human enhancement has permeated everyday life, encompassing all that we do, becoming an imposition from which, it is difficult to escape.

The way in which young people are educated (enculturation) can also lead to irreversible biological changes, as we have seen in the first section of this work when discussing the brain, which can be transmitted to future generations. As Savulescu aptly points out, "if we consider it morally right to enhance people's well-being through environmental factors such as education and diet, we should equally consider direct genetic means that have the same purpose" (Savulescu, 2012: 272-273).

The expansion of technology has led to the convergence of NBIC technologies (Nanotechnology, Biotechnology, Information Technology, and Cognitive Sciences), which have already begun to cause what Kurzweil refers to as "*technological singularity, a future time in which the pace of technological change will be so rapid and its impact so profound that human life will be irreversibly altered*" (2012: 48).

As we have mentioned earlier, this is based on an exponential, non-linear advancement of technology that gives rise to a profound change in the concept of humanity. Hence, the term "posthumanity" is used. Underlying this concept is the idea of directed evolution, as outlined in the preceding paragraphs. Humans will be capable of guiding their own evolutionary process through the manipulation of the germ line, as asserted by some authors such as Mehlman (2009).

The issue, as we can see, arises from the rapid and impactful technical, scientific, and technological advancements that have occurred in recent times, shaking the foundations of our principles, traditions, and routines, generating insecurity and a potential danger to certain moral aspects. This is why human enhancement is a topic of debate, polarizing opinions between those who are in favor and those who are against it. At this point, we lean towards presenting a more balanced judgment, adopted by some thinkers, as in this essay, which acknowledges both the yes and the no of human enhancement, the yes and the no of technology as already discussed by Heidegger in his essay *The Question Concerning Technology.*

The yes and no of human improvement, the yes and no of technology

From the Heideggerian perspective, technology is "an act of the human being" (Heidegger, 1993:96). As we have seen with human enhancement, it is something inherent to human beings. Human enhancement finds an analogy with technology because it is also a "mode of human activity" directed towards other human beings and oneself (F*ernsteuerung*, "being operated upon" and S*elbststeuerung*, "self-operation") (Sloterdijk, 2009: 589), as previously explained. Moreover, in the contemporary world, human enhancement and technology go hand in hand, and I believe it is this fusion that generates the entire current debate and questioning. These reasons have led me to undertake this reflection based on Heideggerian analysis.

What does this "mode of human activity" imply? This "mode of human activity" allows us to reveal what is hidden, to reach what is there but not seen—it is what Heidegger calls *revealing*. In order to find what is hidden, human beings engage in a process of creation (creation is found in artistic activities and, to a great extent, in technological and scientific activities—the researcher creates, reveal, through the investigations carried out), discovery, revealing, which leads us to exercise the art of production. Therefore, we can say that technology is a mode of human activity; it is creation, it is revealing, it is *production*. Similarly, current human enhancement encompasses all of these possibilities.

The art of *production* is an act of symbiosis between humans and matter, aimed at *revealing* the hidden, bringing forth truth. It is also an act of care (*Sorge*) because *Being-in-the-world* involves caring for what is intramundane, with intentional practical and useful activity, recognizing that everything that constitutes our environment, whether produced by technology or not, is essential to our relationship with the world. "Being-in-the-world is about serving, manufacturing, addressing business, taking possession of something, preventing or protecting from damage," as cited by Heidegger (Chillón, 2017: 119). Heidegger questions whether technology is improving or worsening our way of caring for the world. Human enhancement gets into the questions raised throughout the preceding pages regarding the deviation that sometimes occurs due to chance and unknown variables, giving rise to pathologies or unexpected effects. Therefore, we express the same doubt as the German thinker.

To *reveal* is to care, to *be-in-the-world* with a commitment. This commitment entails recognizing that everything in the world is essential to our relationship with it. It leads us to not devalue anything that exists in our environment. It compels us to care for our planet and nature. It guides us to treat living beings with the respect and care that *being-in-the-world* entails, with the awareness that human beings are not the owners of everything. We cannot manipulate every element at our whim. Our relationship with the world, our very existence, depends on this knowing how to *be-in-the-world*. This applies equally to human enhancement that expands through technological means, and this *being-in-the-world* is what makes us contemplate the concept of life improvement, rather than just human enhancement, as the latter is meaningless without the former: we exist because others exist.

To *reveal* is what results from the act of thinking, "because the thinker is the one who discovers, reveals realities never seen before by anyone" (Ortega y Gasset, 2002:122). Therefore, we cannot equate *revealing* with the current sense of producing, that is, with accumulating manufactured objects or industrial transformations. It must be identified with thinking in the sense of *revealing*. If not done so, the creative process, the *poiesis*, is nullified, and man loses the essence of technology, becoming subjected to it. This is where the first risk of technology emerges, to distance oneself from the creative action, from revealing, discovering, creating, and instead getting lost in the fabrication of objects. Similarly, human enhancement cannot dissolve into that mode of production that strays from the creative process. By distancing ourselves, we can no longer sculpt ourselves, design ourselves. Instead, we submit ourselves to pure and calculating technology, to the reality of the laboratory wrapped in technical and economic structures that prevent us from seeing life as it is, the human being as it is, because it distances us from both. Life and the human being then become manipulable objects to be used and discarded.

By distancing ourselves from *poiesis,* "the *revealing* of modern technology appears as a provocation that imposes on nature the demand to release and supply its internal structure to be rationalized, and then used, stored, and exploited" (Alsina Calvés, 2021). We exploit nature in favor of technical actions and human enhancement itself, turning *revealing* into a *provocation*. We impose, demand, aggress, and shape nature to fit human needs, without understanding that we are a part of it. The same applies to human enhancement: we demand, exploit its possibilities, whether through technology-related enhancement or cultural enhancement. An example of the exploitation of the latter is the aforementioned film, *Whiplash*. The calculating thinking of the scientist takes precedence over reflective thinking. The race towards achievement is deemed more powerful than reflection on what is happening.

Life becomes technified, as we have seen in the previous paragraphs when discussing human enhancement. This implies that man distances himself from nature, moves away from *poiesis*. Everything turns into pure instrumentalization. The care for our surroundings is forgotten, restricted to the accuracy of experiments and calculative thinking. The creative process that drives the researcher is abandoned, leaving behind the meditative thinking that regulates our actions.

This change in human life, brought about by technology, makes man feel powerful. The same applies to human enhancement. Man feels powerful because this technified relationship with the world makes us believe that we dominate everything, even our own body, our brain. All improvement becomes about the continuous and upward domination of the human being. Thus, we strut around as lords of the Earth, distancing ourselves from our own selves to submit to technology. This is where the second risk of technology arises. Everything that exists has value to the extent that it can be used or technically transformed, including the human being itself.

Human enhancement, as we have mentioned, is currently linked to technology (biotechnology), and precisely for this reason, it faces the same risks that Heidegger explains in his essay *The Question Concerning Technology*. In this article, the issue that has sparked much debate is raised: the fusion that has been established between technology and human enhancement.

However, the risks presented by technology are, for Heidegger, merely a possibility to rethink our situation in the modern technological world, without rejecting technology, but rather seeking a new attitude, a different way of establishing relationships between Science, Technology, and Society. This aspect also applies to human enhancement; neither can be eliminated or mutilated because if man is man, it is because "a technique has caused him to emerge from the prehuman" (Sloterdijk, 2001: 86). This means that man is linked to technology. Technology is not separate from man. It is out of place to try to separate these two elements (man and technology) and morally condemn attempts to apply technology to man (an operation manifested in the term "anthropotechnics").

These risks are an opportunity to think about technology and human enhancement. They should never be taken as a means to reject them because, being inherent to human beings, we would be rejecting our own humanity.

The solution proposed by Heidegger is to adopt a new attitude, serenity, knowing when to say yes and no to technology, yes and no to human enhancement,

> *I would like to designate this attitude that simultaneously says 'yes' and 'no' to the technological world with an ancient word: Serenity (Gelassenheit) towards things [...] We can say 'yes' to the inevitable use of technical objects, and at the same time, we can say 'no' to them insofar as we refuse to let them require us in such an exclusive manner, to bend us, confuse us, and ultimately devastate our essence (Heidegger, 2002:28).*

An approach to the definition of human enhancement

The concept of human enhancement has given rise to multiple interpretations. Perhaps because its definition is broad, changing, and specific to particular contexts depending on the here and now in which it is discussed. From the time Julian Huxley, biologist and first director of UNESCO, introduced the concept of transhumanism, to Robert Ettinger's development of the idea of cryonics in his book T*he Prospect of Immortality* as a means to escape death, a period of latency has been experienced. Since Ettinger's book, the concept of transhumanism has gained momentum and continues to evolve to this day. It is defined by the World Transhumanist Association as follows,

> *The intellectual and cultural movement that affirms the possibility and fundamental desirability of enhancing the human condition through applied reason, particularly by extensively applying and making accessible technologies that eliminate aging and significantly improve intellectual, physical, and psychological human capabilities. (2003)*

As we can see from this explanation, one of the central concepts is the enhancement of the human condition, focused on certain aspects. Our concept is much broader, encompassing a temporal or permanent overcoming of the limitations of the human body through natural or artificial means, which can be highly diverse and tailored to each particular case.

In this work, we agree with Bostrom (2005) that transhumanist enhancements or modifications are related to extending healthy life, eradicating diseases, eliminating suffering, and enhancing intellectual, physical, and emotional capacities. However, we also emphasize the importance of improving life in our environment, while recognizing that none of these improvements should result in the annihilation of humanity, life itself, or the natural world. Without this premise, which serves as a natural limit to the pursuit of life improvement, human enhancement could lead to self-destruction. This perspective differs from Pearce (2019) in that transhumanism cannot solely aim for superintelligence, super-longevity, and super-well-being for all of humanity. This article proposes a more homeostatic achievement that includes improving life and our *being-in-the-world*, with a commitment to caring (*sorge*) for our surroundings and, consequently, for ourselves.

Therefore, in this essay, in this particular context and time, we aim to clarify an evolutionary and historical conceptual framework from which we will extract certain characteristics that define what is meant by human enhancement. Thus,

- It is considered an inherent constant in human beings, based on evolution, the process of hominization, adaptation to the environment, and positive selection. Furthermore, it is a constant throughout human history.
- It is described as a symbiosis of biology and culture.
- It is shaped by the relationship with the environment and others. Human enhancement is not conceived outside of social relationships and the surrounding context.
- Tools, techniques, and technology are integrated aspects of culture that not only play a role in the process of humanization but are also essential elements in human enhancement, due to the feedback that occurs between their use and human development.
- Technique, technology, and human enhancement are analogous human activities that have followed parallel paths and pose similar issues.
- From this initial conceptual outline, it is already evident that denying or mutilating the process of human enhancement would imply denying or mutilating human beings and their own humanization. This does not mean that the existing problems and questions surrounding this issue are denied, but presenting the denial or mutilation of human enhancement as a solution is not viable.
- Human enhancement is a broad concept that encompasses not only the optimization of human capacities but also those of other living beings and the environment in which they exist. Human beings are interconnected with others, and the concept of enhancement implies well-being for humans, the environment, and other living beings, regardless of their species. This requires a balance among all these elements.
- Human enhancement can originate from the environment (such as education), from the individual themselves (asceticism), or from the interaction of both (including all technological applications related to genetics, bionic elements, substance intake, plastic surgery, etc.). In any of these cases, since human enhancement is understood as the improvement of life, it is interpreted as an interaction between biology, culture, and all social aspects. Consequently, some variables cannot currently be controlled, and due to this inherent randomness in each person, the applications of research may vary, potentially leading to unintended pathologies.
- Human enhancement will be individual, personal, and specialized, following established protocols that include prior information about the causes, consequences, risks, and application of the process.
- It can be therapeutic or eugenic in nature.
- Human enhancement in research should not be limited or mutilated, but it should be regulated. It should be carried out by interdisciplinary teams that include professionals from the humanities.
- Applied human enhancement should be limited to cases where its application does not pose risks to the individual. In cases of uncertainty regarding potential outcomes, the most beneficial option should be chosen, determined by the interdisciplinary team and justified with evidence.
- The individual who undergoes human enhancement should make decisions freely (as proposed by Pico de la Mirandola), based on the information provided by the professional team(s).

Biotechnology and anthropology in human enhancement

Throughout the previous pages, it has been observed how different disciplines of knowledge participate, determine, and guide the way we shape our humanity. The dialogue and convergence among them are not always accurate and smooth, just as collaborative work is not. Anthropology and biotechnology constitute an important foundation in human enhancement: the former addresses the question of what it means to be human, while the latter applies technology to life, not only human life but life on our planet as a whole. When Sloterdijk develops the imperative *You must change your life*, he combines these two disciplines into a single term: anthropotechnology. Human beings and life united through change, transformation. It is from the union of these two fields that human enhancement emerges. Why these fields and not others?

Man is a being born with deficiencies, entering the world prematurely, in a larval state. He undergoes a transformation and experiences a metamorphosis as he becomes an adult. However, this metamorphosis is not complete, as it retains immature aspects from the juvenile stage. This phenomenon is known as neoteny. Neoteny renders us weak because we maintain juvenile, underdeveloped traits. Consequently, humans face difficulties in defending themselves in their environment. Compared to other living beings, humans are more vulnerable. They lack organs for attack, defense, or escape, and they are not adapted to live in the open, nor do they possess the speed or visual acuity of other animals. This lack of specialization in their organs leads humans to create tools and strategies to aid in survival. Humans become cultural beings, and technology complements their deficiencies. They create an artificial habitat that turns them into sculptors of themselves, relatively independent of the organic environment but dependent on the various tools and artifacts they create to protect themselves from adversity. This perspective stems from the concept of humans as *Mängelwesen*, beings with *deficiencies*, as described by Arnold Gehlen (1980:10). From this perspective of human deprivation, human enhancement is justified, and technology is described as a substitute for one of the human organs,

> *It is through this inherent deficiency that humans develop everything that is considered to be the highest aspects of human civilization, such as technology, science, art, politics, philosophy, religion, and culture in general. According to Gehlen, technology, in particular, serves as a "substitute organ" (Holzapfel, 2014:45) to compensate for this fundamental lack.*

Anthropology defines the human being, while biotechnology constitutes that "substitute organ" which is intended to alleviate human shortcomings. Both are interconnected because technology is not an addition to humanity; it is an inherent part of the human animal. Humans need to think and act technically in order to survive and to be human. It is this compensatory ability that allowed us to become *Homo sapiens*.

Biology relies on that artificial environment, on that cultural group that enables it to defend itself. When biology and culture come together, they generate a human enhancement that is passed on to future generations and can lead us to the production of superior cultures. This symbiosis of biology and culture allows us to create an immunological project in which the social group extracts from itself the protection that makes these social relationships possible. This immunological aspect can provide relief for the "infinite wound," with its four afflictions: the affliction of life, the affliction of death, the affliction of the gift of the other, and the affliction of the wonder of the world.

This need for immunological practice is the meaning that Sloterdijk assigns to *anthropotechnics*. *Anthropotechnics* refers to "the set of techniques through which people from different cultures have systematically tried to protect themselves from the blows of fate and the risk of death" (Sloterdijk, 2012: 62). These immunization techniques have been historically developed by humans in two directions that can be complementary and contradictory, which is why they require guidance and regulation. On one hand, there are socio-immunological practices that seek to optimize society in the face of the threat of external aggressors; they have a more global character and can give rise to controversial proposals. On the other hand, there are psycho-immunological techniques that aim to enhance individuals' capacity to confront their own mortality and the contingencies of life.

Biotechnology and all its applications are integral parts of the human being and they join anthropology to form the concept of *anthropotechnics*. It encompasses not only human enhancement but also the protection and implementation of social and individual immunological practices that enable our development.

The impact of biotechnology is defined as "the set of tools that allow the analysis and understanding of the functioning of living organisms at different levels (physiological, tissue, cellular, and molecular) and can be applied in various fields ranging from health to agriculture, industry, or energy sector" (Ruiz Galán et al., 2011:16). Throughout these lines, we have seen the multiple biotechnological applications, but some of the most important ones in current times include biomarkers, regenerative medicine, cellular therapy, gene therapy, genomics, proteomics, metabolomics, and pharmacogenomics.

According to the study conducted by Garcés Castellote and Jiménez Rodríguez (2016), the most impactful biological transhumanist enhancements that will occur in the coming years are as follows, in order of importance: enhanced immunization capacity, response, and treatment for major human diseases such as cancer and infectious diseases; absence of any degenerative diseases of the nervous system; freedom from sequelae caused by cerebral infarctions; freedom from sequelae caused by spinal cord injuries; a cardiovascular system with regenerative capabilities; complete regeneration of tissues damaged by traumas, burns, accidents, or ulcers; full capacity to regenerate bones, cartilage, and tendons; absence of any genetic-based diseases; enhanced cognitive abilities.

The practical materiality of the yes and no of human enhancement

The issue of whether to embrace technology-induced human enhancement already has an answer: yes and no. It is the yes and no of human enhancement. The enhancement of the human being through technological means cannot be rejected because both the enhancement itself and the technology used for it are human endeavors, necessary for the preservation of their own humanity. This is the *yes*.

The *no* is materialized in the actions that we will propose below and that must be implemented in the different fields of knowledge that regulate our lives: legal, educational, formative, and research. The *no* of human enhancements implies refusing "to be so exclusively demanded, to be bent, confused, and ultimately devastated our essence" (Heidegger, 2002:28).

1. *An ethical and legal frame of reference*

the first action involves the establishment of an ethical and legal framework that addresses research activities and the use of technological and biotechnological elements applied to human beings resulting from scientific endeavors. In 1997, UNESCO, aware of this situation, determined to establish the *Universal Declaration on the Human Genome and Human Rights*. This document sparked debate as it was considered restrictive in some aspects. However, that is not the focus of this work. What is important is that it has been the first step in establishing a reference framework. Now, based on this work, it is considered necessary to continue advancing by differentiating the framework for research and its ethical and legal reference from the framework for the application and use of such research, along with its ethical and legal boundaries.

In 2005, the *Universal Declaration on Bioethics and Human Rights* was presented, also promoted by UNESCO, involving governments and different sectors of society, addressing both scientific activity and its personalized use.

The European Union, as part of the *Horizon Europe* project, has published an ethical framework for human enhancement in the journal *Science*. This document, led by Philip Brey (2022), will regulate research aimed at enhancing the physical, cognitive, moral, cosmetic, or longevity capabilities of individuals through emerging technologies. It includes aspects of Artificial Intelligence, genomics, and all technologies that contribute to human enhancement. This is the first step in implementing systematic ethical oversight of R&D, from a global perspective, bringing together the perspectives of transhumanists and bioconservatives, philosophers of science, and scientists, allowing for coherent and rational concretization in scientific activity. Five categories of human enhancement applications are defined: physical, cognitive, moral, cosmetic, and longevity, with six key values. The first three values are related to the individual, focusing on individual well-being, autonomy, and informed consent. These values ensure that individuals receiving these enhancements, especially irreversible ones, are aware of the benefits and potential issues in both the short and long term. The next three values focus on the social aspect, emphasizing equality, justice, and moral and social responsibility, aiming to "avoid perpetuating or exacerbating existing inequities or inequalities among groups and communities" (Brey and Erden, 2022: 836). These inequalities refer to social discriminations that may arise from the social division between those who can afford these treatments and those who cannot, between those who have access to human enhancement and those who do not, or in the case of genetically modified babies.

These general frameworks are also slowly being implemented in different countries. In previous sections, we have seen how Chile has included neurorights, a part of human enhancement, in its Constitution, and Spain has developed the *Charter of Digital Rights* in 2021, which includes some aspects related to human enhancement. Rafael Yuste, the driving force behind the BRAIN Initiative, is one of the promoters of establishing neurorights within a general framework and implementing them in different contexts.

We are still far from achieving an orderly and coherent regulation regarding human enhancement, but the process has been initiated and must continue to advance. This includes implementing specific regulations in different countries and establishing even more practical guidelines in research laboratories and centers. Research protocols should not only address experimental techniques but also require a specific ethical framework for each particular research, anticipating the consequences of the use and dissemination of these investigative actions.

Parallel to all these endeavors, it is considered necessary to develop an ethical code that is common to all researchers and scientists, similar to the Hippocratic Oath followed by physicians. In this regard, the European Commission, in 2006, developed a regulation called REACH (Registration, Evaluation, Authorization, and Restriction of Chemicals) and a *Code of Conduct for Responsible Research in the fields of Nanoscience and Nanotechnology*. Although these codes are not born from the research teams themselves, their application is more of an imposition than a self-reflective action. Establishing valid codes entails thinking about science, engaging in metascience that links each research endeavor with reflection on it.

2. Meditative thinking and calculative thinking

human enhancement is characterized by a calculative, strategic, mathematical, scientific, and experimental mindset. This thinking arises from technological actions, from research and scientific endeavors themselves. By itself, it drives activity, but it often unfolds without guidance or orientation, without a connection to the human being. Human enhancement, and I would argue any scientific endeavor, should be accompanied by a meditative, reflective thinking that allows us to conceive life from a less anthropocentric perspective, contemplating the premise that humans are who they are because of their relationships with the environment in which they live, relying on the natural and the social to ensure their existence.

> *We must ask ourselves, as Winner (1987: 34) proposes, what kind of world we are constructing. For this, an educational effort is needed to raise awareness among as many people as possible about the consequences of uncontrolled technology. This effort should highlight that technology does not have merely instrumental value, but it can shape our ways of life. It should contribute to the emergence of a new image of the relationship between humans and nature, based this time on respect rather than domination (Diéguez, 1993: 200).*

This idea hints at the concept of social responsibility that stems from such reflective thinking and is integral to it. As Jonas points out, it is necessary to invoke new imperatives such as "Act in such a way that the effects of your actions are compatible with the continued existence of an authentic human life on Earth," or expressed negatively: "Act in such a way that the effects of your actions are not destructive to the future possibility of that life" (1995: 40).

3. Attitude of serenity

Human enhancement requires not only the practice of meditative thinking but also translating it into attitude. This attitude of serenity involves reflection and action in order to know when to say yes and no to human enhancement. Achieving this requires having information, taking responsibility, and being aware of who we are. Researchers need to be in constant exchange with the values and expectations of the population, which is why the dissemination and interaction between the scientific community and the public through conferences, publications, and other means are necessary.

In recent decades, the techno-scientific community has made great efforts to promote the dissemination of technological endeavors through books, magazines, videos, and other informative materials that bring complex technological activities closer to social groups in a less technical language. This aims to encourage personal development of the inherent human capacity that combines various thoughts, as well as to bring research and innovation closer to the entire population. Based on this, the concept of *Responsible Research and Innovation* (RRI) emerges, which aims to "reduce the gap between the scientific community and society by encouraging different stakeholders (civil society entities, educational community, scientific community, policy makers, business and industrial sectors) to work together throughout the research and innovation process" (Observatory of Bioethics, Law, and RRI, 2022). Although the concept emerged about a decade ago, it has gained more relevance when it was included in the *Science with and for Society* program launched by the European Commission as part of the *Horizon 2020* research plan.

4. Interdisciplinarity: bastes

researchers need to open the doors to reflective thinking and a mindset of serenity every day in order for human enhancement to have true meaning. This can only happen if our teams are based on interdisciplinarity. Interdisciplinarity requires an intertwining of relationships that involve different perspectives and visions regarding the creative power of human enhancement and its impact on the environment. Achieving this intertwining is challenging due to the inherent distancing that exists among the various knowledge domains. The barriers erected between different areas of knowledge must be dismantled, borders must be blurred, and a path of fluid relationships among multiple disciplines must be initiated. It is time to eradicate the "two cultures" referred to by Mitcham and understand that human enhancement necessitates a holistic integration of knowledge and perspectives,

> *The true Grand Challenge of engineering is not simply to transform the world. It is to do so with critical reflection on what it means to be an engineer. In the words of the great Spanish philosopher José Ortega y Gasset, in the first philosophical meditation on technology, to be an engineer and only an engineer is to be potentially everything and actually nothing. Our increasing engineering prowess calls upon us all, engineers and nonengineers alike, to reflect more deeply about who we are and what we really want to become. (2014)*

There are already examples of this interdisciplinarity in the field of Science, Technology, and Society studies, as well as in *Converging Technologies* such as *NBIC Technologies*, **N**anotechnology, **B**iotechnology, **I**nformation Technologies, and **C**ognitive Science, or the *BANG Convergence* (**B**its, **A**toms, **N**eurons, and **G**enes). However, it would be necessary to integrate them into university curricula, as well as in businesses, so that research teams can incorporate a technoscientific perspective alongside a broader understanding of the concept of life as explained in the preceding lines, as well as a knowledge of humanity, which ultimately drives the technological advancements in human enhancement.

The interdisciplinary response presented in this work starts with the ***Bio** (life),* encompassing life in general, not only human life. It then proceeds to the ***Anthropo** (human)*, referring to the design and reception of life enhancement. The ***Socio*** dimension considers the social environment's role in regulating and shaping this human improvement. The ***Tecno*** aspect represents the human capacity to progress and the actions that underlie the optimization of life. ***Ethos,*** condition that guides our work. Lastly, ***Sciencie*** encompasses research, innovation, the system, and the method, embodying the calculated thinking necessary to drive the entire human process.

This interdisciplinary approach requires experts in these fields to work together in all research teams, breaking down barriers, so that human enhancement becomes an optimal reality. It enables us to become satisfied sculptors of our humanity, proud of our work, both today and in the future.

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