Obesity has limited behavioural overlap with addiction and psychiatric phenotypes

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Obesity is a widespread health condition[1], likely driven by increased availability of inexpensive high-calorie food[2]. People vary in their behavioural response to food plenty. Such variation is likely driven by behavioural styles[3,4], as behaviour accounts for entire food intake[5]. A prominent hypothesis is that people with obesity respond to rewards similarly to people with addictions such as alcohol abuse or smoking[6,7]. For instance, perceived overeating or "Uncontrolled Eating" (UE) is the most common obesity-associated personality trait[8] and resembles the perceived loss of control seen in drug addiction. Likewise, both obesity and addictive behaviours have similar correlations with broad personality domains[3]. Here, we seek to empirically test whether obesity and UE overlap behaviourally with addiction and psychiatric disorders, collectively referred to as phenotypes. We test for behavioural similarity by linking the personality profiles of each phenotype. NEO Personality Inventory (NEO PI-R/3) profiles of 28 phenotypes were extracted from 22 studies, encompassing summary statistics from 18,611 unique participants. Obesity had moderate and UE high behavioural similarity with addictions. UE also overlapped behaviourally with most psychiatric phenotypes, whereas obesity was behaviourally similar with mood disorders and certain personality disorders. Facet-based phenotype profiles provided more information than domain-based profiles.

Vulnerability to drug use and to overeating have been suggested to have a shared behavioural basis [3,6,7]. For instance, drug use and obesity are associated with similar personality questionnaires and cognitive tests[3]. However, the similarities are observational and have not been quantified. Quantifying the behavioural overlap between obesity and addictions has nosological and therapeutic implications, and may reveal underlying behavioural mechanisms and risk factors.

Addictive features may also characterise a commonly identified eating-related phenotype, Uncontrolled Eating (UE). UE is conceptualised as high food reward sensitivity combined with poor self-control [8,], and this trait explains most of the variance in the common eating-related questionnaires measuring emotional eating, food addiction, or binge eating [8,9]. Despite these questionnaires' slightly differing definitions and item content ([reviewed in 10]), UE-related questionnaires demonstrate similar correlations with other variables, such as obesity [8] and personality traits [10]. UE may capture aspects of behaviour that resemble addictions, as one of the UE questionnaires, the Yale Food Addiction Questionnaire, is based on the Diagnostic and Statistical Manual of Mental Disorders' criteria for drug abuse. However, the behavioural similarities between addiction, obesity, and UE have not yet been systematically investigated.

Addictive features likely explain only part of the behavioural repertoire of obesity, as this condition can develop from multiple behavioural paths [11]. Therefore, we also assessed potential behavioural similarities of obesity and UE with other psychiatric conditions. Obesity and the extreme form of UE, binge eating [8], are comorbid with various psychiatric phenotypes, such as autism [12], anxiety [13], mood disorders, including depression and bipolar disorder [14], as well as with avoidant, antisocial, and schizotypal personality disorders [15]. This raises the possibility of an underlying behavioural endophenotype that confers vulnerability to obesity, overeating, and various psychiatric phenotypes. We therefore explored the similarity of the behavioural profiles of obesity and UE with those of several possibly relevant psychiatric phenotypes.

To estimate behavioural similarity, we compared the personality profiles of each phenotype derived from a popular and comprehensive personality test, the NEO PI-R/3 [16,17]. We use the term behavioural similarity only for simplicity as NEO PI-R/3 summarises people's actions, as well as thoughts, feelings, and goals [16]. NEO PI-R/3 has 240 questions, which can be summarised

into 30 facets, which in turn belong to five major personality domains: Neuroticism, a tendency to experience negative affect; Extraversion, a tendency to experience positive affect; Openness, a preference for novelty and intellectual curiosity; Agreeableness, a tendency for altruism; and Conscientiousness, an ability to control impulses that facilitates goal-directed behaviour. A phenotype's personality profile refers to the pattern of associations that this phenotype has with personality traits.

Most profile comparison research has focused on the broad domains level where the phenotypes of interest tend to be behaviourally similar. Several reviews and meta-analyses have shown the tendency for alcohol consumption, smoking, obesity and different psychiatric phenotypes to have a similar underlying personality profile, characterised by high Neuroticism and low Conscientiousness [3,4,18,19] (see also Figure 1, domain section). However, this literature ignores the more fine-grained information contained in the facets that make up each domain. Two phenotypes *seemingly* similar based on high Neuroticism and low Conscientiousness domain scores, may, in fact, be very different in their facet-level personality profiles. This is not a mere hypothetical, as obesity is associated only with specific facets within Neuroticism and Conscientiousness [e.g., 20]. Therefore, obesity might indeed be less similar with addictions based on facet-level behavioural profiles than the domain-based evidence would suggest (compare domain vs facet profiles in Figure 1).

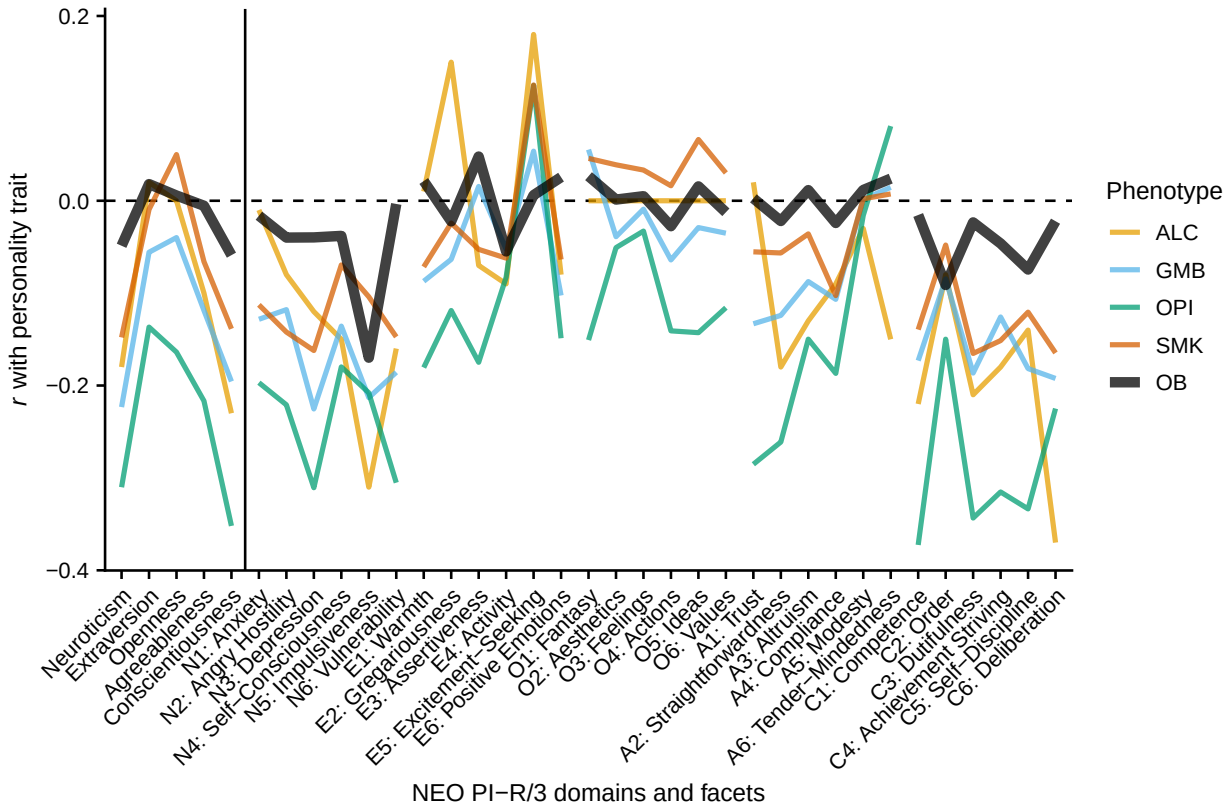

Figure 1. Personality trait profiles of obesity and selected addictions. Neuroticism has been reversed to Emotional Stability to avoid inflation of profile correlations. Solid vertical line separates domains from facets. The horizontal dashed line indicates 0 on y axis. Figure has been conceptually reproduced from Michaud et al. [3]. ALC = Alcohol; GMB = Gambling; OB = Obesity; OPI = Opioid abuse; *r* = correlation; SMK = Smoking

To assess behavioural similarity between obesity, UE, addiction and psychiatric phenotypes, we "upcycled" previously published NEO PI-R/3 domain and facet profiles of each phenotype (Supplementary Table 1). The personality profiles were obtained either by comparing mean NEO PI-R/3 scores of people with a diagnosis (e.g., depression) to those of a control group, or correlating the NEO PI-R/3 facet scores with a continuous trait, such as body mass index (BMI) or a self-report questionnaire score. An example set of profiles is presented in Figure 1. We then

formally assessed behavioural similarity of the phenotypes by correlating the personality profiles, obtaining *personality correlations (r_p)* between them. For most analysis, we present the domain-based results along with the facet-based results, to compare their informativeness.

Inspecting personality correlations revealed an overall similarity in all phenotypes, but also some notable clusters among them. See Supplementary Figure 1 for domain-based personality correlations and Supplementary Figure 2 for facet-based personality correlations. The mean absolute personality correlations were stronger within the domain-based analysis (mean r_p = .54, 95% CI [.51, .56]) than facet-based analysis (mean r_p = .45, 95% CI [.42, .47], as confirmed by paired two-tailed *t*-test: $t(377) = 9.55$, $p < .001$, $d = .49$, 95% CI [.35, .64]. This suggests that facet-level profiles demonstrate behavioural differences between phenotypes that are not evident from domain-based profiles. In other words, facets allow for greater discriminant validity among the phenotypes.

We next sought to formally assess the extent to which our target phenotypes, obesity and UE had behavioural similarities with addiction and psychiatric phenotypes. As an effect size baseline, our analysis also included education and gender to provide a "null hypothesis" for the associations. As maximum expected effect size, we considered the correlations that addiction/psychiatric phenotypes had with each other.

At the domain level, phenotypes varied in the personality correlations they had with addictions ($F(4, 34) = 11.26$, $p < .001$, $\eta_p^2 = .57$, 95% CI [.27, .68]). This is illustrated in Figures 2a and 2c, where obesity (mean r_p = .73, 95% CI [.52, .94]) and UE (mean r_p = .67, 95% CI [.48, .86]) seemed to have considerably stronger personality correlations with addictions than gender (mean r_p = .42, 95% CI [.23, .61]) or education (mean r_p = .48, 95% CI [.26, .69]) . At the same time,

there was considerable behavioural similarity between UE, obesity, and addictions, as personality correlations that UE or obesity had with addictions were of similar magnitude as those between the different addictive phenotypes (mean r_p = .85, 95% CI [.78, .92], Figure 2c). To statistically test the differences between the mean values in personality correlations with addictions, we repeated the ANOVA as a regression model where phenotype category predicted personality correlation strength with addictions, setting obesity or UE as a reference category (full model adjusted R^2 = .52, 95% CI [.31,.79], $F(4,34) = 11.26$, $p < .001$). We then extracted the contrasts comparing OB and UE with other phenotypes and corrected p-values across these contrasts with Holm correction. Education had lower personality correlations with addictions than obesity (b = -.38, 95% CI [-.57 -.18], p = .003) and than UE (b = -.28, 95% CI [-.47 -.08], p = .03). Similarly, gender had lower personality correlations with addictions compared to obesity (b = -.43, 95% CI [-.63 -.23], p = .001) and to UE (b = -.33, 95% CI [-.53 -.13], p = .009). At the same time, there were no statistical differences between addiction-related personality correlations of obesity and UE (b = -.1, 95% CI [-.3 .1], p = .652), between obesity and addictions (b = 0, 95% CI [-.16 0.17], p = .989), and between UE and addictions (b = .1, 95% CI [-.06 .27], p = .652). All reported statistical comparisons are also reported in Supplementary Table 2.

A more nuanced result emerged from facet-level analyses (Figures 2b and 2d). The five groups were better separable in the personality correlations they had with addictions, as suggested by higher effect size ($F(4, 34) = 40.82$, $p < .001$, η_p^2 = .83, 95% CI [.67, .87]). Figure 2d revealed a gradient of similarities with addictions, where education (mean r_p = .21, 95% CI [.06, .37]) and gender (mean r_p = .18, 95% CI [.11, .24]) were the lowest, followed by obesity (mean r_p = .36, 95% CI [.23, .49]), which was followed by UE (mean r_p = .51, 95% CI [.36, .66]), and then by

addictions (mean r_p = .73, 95% CI [.67, .8]). The gradient was confirmed when comparing differences in personality correlation estimates from the regression model (adjusted R^2 = .81, 95% CI [.73,.9], $F(4,34) = 40.82$, $p < .001$.) Regarding baseline phenotypes, gender had weaker personality correlations with addictions than obesity (b = -.22, 95% CI [-.36 -.09], p = .006) and than UE (b = -.4, 95% CI [-.54 -.27], p <.001). Similarly, education had weaker personality correlations with addictions compared to obesity (b = -.22, 95% CI [-.36 -.09], p = .006) and (UE -.4, 95% CI [-.54 -.27], p <.001). Intriguingly, UE had higher similarity to addictions than obesity (b = .18, 95% CI [.04 .31], p = .019). Further, addictions had even higher similarities with each other than with UE (b = .15, 95% CI [.04 .26], p = .019) and with obesity (b = .33, 95% CI [.22 .44], p <.001).

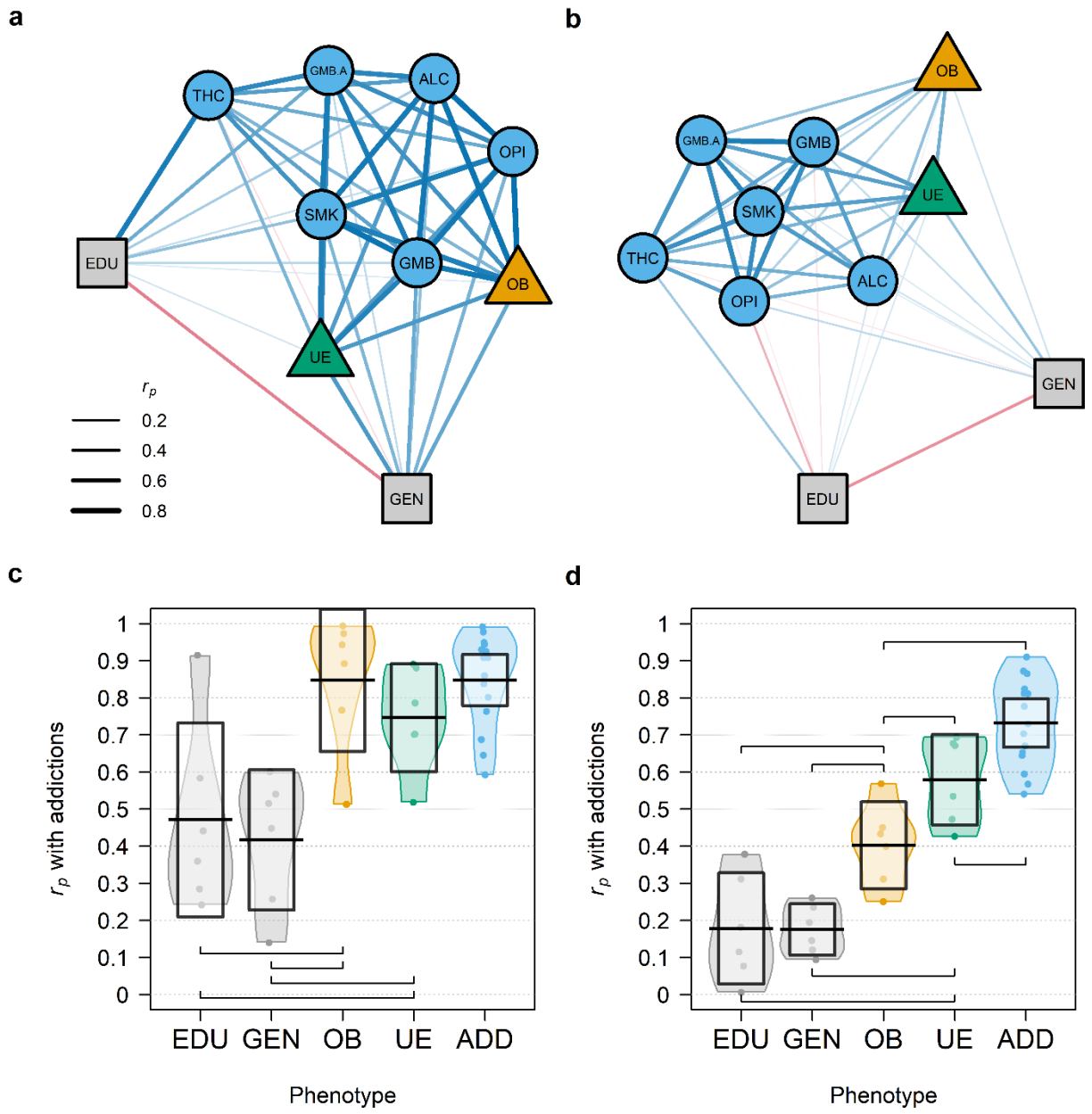

Figure 2. Personality correlations (r_p) with addiction phenotypes. A and B: Spring-embedded network graph based on domains (A) or facets (B), using Fruchterman-Reingold algorithm. Circles mark addiction phenotypes, triangles mark targets of the behavioural similarity analysis, rectangles mark baseline phenotypes. Blue edges mark positive correlations, red edges mark negative correlations. C and D: Same data as in panels A and B based on domains (C) or facets (D). Correlations are in absolute values, organised by analysis targets. Points represent individual

personality correlations, thick lines represent mean values, beans represent smoothed densities, and the rectangles represent 95% confidence intervals. EDU, GEN, OB, UE have 6 personality correlations, ADD has 15 personality correlations. Horizontal brackets indicate significant differences in two phenotypes regarding their mean personality correlation with addiction phenotypes. Differences were detected with multiple regression, using Holm corrected p value < .05. Full statistics are reported in Supplementary Table 2. ADD = Addictions; ALC = Alcohol; EDU = Education; GEN = Gender; GMB = Gambling; GMB.A = Gambling with attention deficit hyperactivity disorder; OB = Obesity; OPI = Opioid abuse; SMK = Smoking; THC = Cannabis; UE = Uncontrolled Eating.

We repeated the analytic approach with psychiatric phenotypes other than addiction. In the domain-based analysis, the five groups differed little in their behavioural similarities with psychiatric condition (Figures 3a and 3c; $F(4, 220) = 3.30$, $p = .012$, $\eta_p^2 = .06$, 95% CI [0, .11]). Reanalysis with the regression model ($R^2 = .04$, 95% CI [0,.12], $F(4,220) = 3.3$, $p = .012$) revealed that there were no significant differences between obesity (mean $r_p = .46$, 95% CI [.35, .57]), gender (mean $r_p = .49$, 95% CI [.34, .65]), and psychiatric conditions (mean $r_p = .54$, 95% CI [.5, .58]) , apart from UE (mean $r_p = .64$, 95% CI [.51, .78]) being more similar to psychiatric conditions than education (mean $r_p = .37$, 95% CI [.25, .48]; -.31, 95% CI [-.48 -.13], $p = .007$). The non-significant contrasts were: obesity-education: $b = -.1$, 95% CI [-.28 .08], $p = .63$; obesity-gender: $b = .04$, 95% CI [-.14 .22], $p = .665$; obesity-UE: $b = .21$, 95% CI [.03 .39], $p = .135$; obesity-psychiatric conditions: $b = .09$, 95% CI [-.05 .22], $p = .63$;

UE-gender: b = -.17, 95% CI [-.35 .01], p = .319; UE-psychiatric conditions: b = -.12, 95% CI [-.26 .01], p = .319, see also Supplementary Table 3.

However, facet-based analyses once again revealed more differences between obesity and UE in their personality correlations with psychiatric conditions (Figures 3b and 3d, $F(4, 220) = 9.42$, $p < .001$, $\eta_p^2 = .15$, 95% CI [.06, .22]). Regression analysis of personality correlations ($R^2 = .13$, 95% CI [.07,.21], $F(4,220) = 9.42$, $p < .001$) revealed that obesity had generally low similarity with psychiatric conditions (mean $r_p = .24$, 95% CI [.17, .31]). Namely, obesity had similar personality correlations with psychiatric conditions like the two baseline phenotypes of gender (mean $r_p = .32$, 95% CI [.23, .42]); b = .09, 95% CI [-.07 .25], p = .794 and education (mean $r_p = .27$, 95% CI [.2, .34]); b = .03, 95% CI [-.13 .19], p = 1, and correlations among psychiatric phenotypes were considerably higher than obesity's personality correlations with them (b = .27, 95% CI [.15 .39], p <.001). UE (mean $r_p = .49$, 95% CI [.38, .6]) had higher similarity with psychiatric conditions than obesity b = .28, 95% CI [.12 .44], p = .004 or education b = -.25, 95% CI [-.41 -.09], p = .013, but not gender b = -.19, 95% CI [-.35 -.03], p = .085. UE had similar personality correlations with psychiatric conditions to the personality correlations between psychiatric conditions (mean $r_p = .5$, 95% CI [.46, .54]); b = -.01, 95% CI [-.13 .11], p = 1 (Supplementary Table 3). This suggests that there was considerable behavioral overlap between UE and many psychiatric phenotypes but obesity had generally lower similarities.

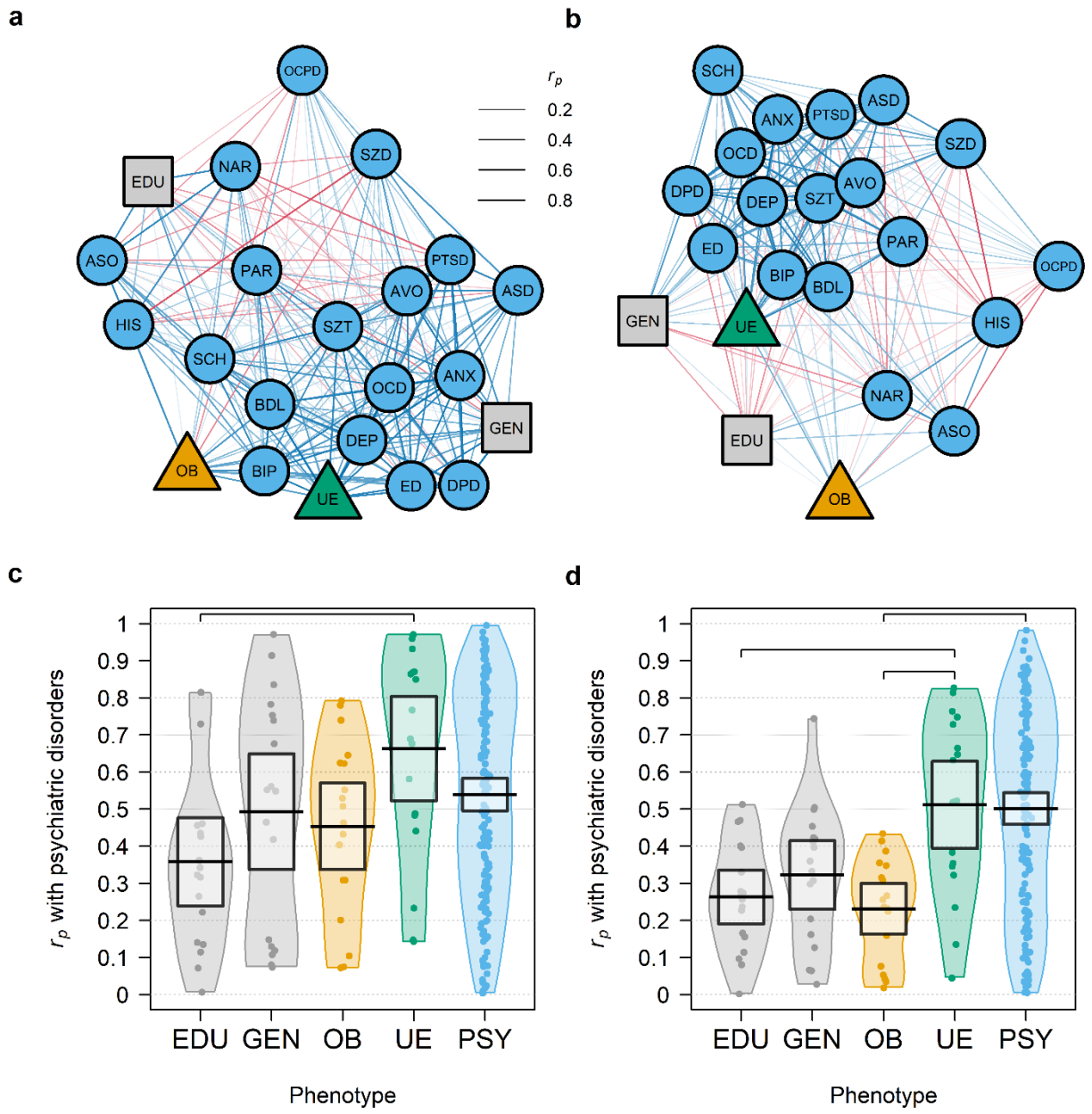

Figure 3. Personality correlations (r_p) with psychiatric phenotypes. A and B: Spring-embedded network graph based on domains (A) or facets (B), using Fruchterman-Reingold algorithm. Circles mark psychiatric phenotypes, triangles mark targets of the behavioural similarity analysis, rectangles mark baseline phenotypes. Blue edges mark positive correlations, red edges mark negative correlations. C and D: Same data as in panels A and B based on domains (C) or facets (D). Correlations are in absolute values, organised by analysis targets. Points represent

individual correlations, thick lines represent mean values, beans represent smoothed densities, and the rectangles represent 95% confidence intervals. EDU, GEN, OB, UE have 18 data points, PSY has 153 data points. Horizontal brackets indicate significant differences in two phenotypes regarding their mean personality correlation with psychiatric phenotypes. Differences were detected with multiple regression, using Holm corrected p value < .05. Full statistics are reported in Supplementary Table 3. ANX = Anxiety disorders; ASD = Autism; ASO = Antisocial; AVO = Avoidant; BDL = Borderline; BI*p* = Bipolar; DE*p* = Depression; DPD = Dependent; ED = Non-anorexic eating disorders; EDU = Education; GEN = Gender; HIS = Histrionic; NAR = Narcissistic; OB = Obesity; OCD = Obsessive compulsive disorder; OCPD = Obsessive compulsive personality disorder; PAR = Paranoid; PSY = Psychiatric phenotypes; PTSD = Post traumatic stress disorder; SCH = Schizophrenia; SZD = Schizoid; SZT = Schizotypal; UE = Uncontrolled Eating.

As exploratory analysis, we described psychiatric phenotypes whose personality correlation with obesity was observed of similar magnitude like between obesity and addictions (r_p = .46, Figure 4c). A systematic review by Gerlach et al [15] suggested that cluster C personality disorders related to anxiety and fearfulness may have higher overlap with obesity than other two other personality clusters (cluster A “odd-eccentric” and cluster B “dramatic-emotional”). However, only obsessive-compulsive personality disorder from cluster C had a negative association with obesity in our quantitative analysis (Figures 3b, 4f, and Supplementary Figure 2). Other correlations of similar magnitude implicated behavioural similarities between obesity and mood disorders (bipolar and borderline) and cluster B personality disorders (antisocial disorder, narcissistic disorder, histrionic disorder) (Figures 3b, 4d, and 4e, and Supplementary Figure 2).

To understand which facets from the NEO PI-R/3 tended to account for the behavioral similarities of addictions, obesity and UE, we plotted the facet-based behavioural profile correlations. UE's similarity with addictions (Figure 4a) was characterised by high scores on Neuroticism and no associations with Openness. In contrast, obesity's similarity with addictions (Figure 4c) was mostly driven by certain specific facets: N5: Impulsiveness, C2: Order, and C5: Self-discipline. Perhaps su*rp*risingly, the E5: Excitement-Seeking facet was an outlier as it was associated with addictions, but not with UE or obesity.

Similarly, the association between UE and psychiatric phenotypes was again driven by high associations with Neuroticism and generally no associations with Openness (Figure 4b). Because the behavioural similarity between obesity and psychiatric phenotypes was generally low, we inspected the few psychiatric phenotypes that had a relatively higher behavioural similarity with obesity (Figures 4d-f). Again, similarity in associations with specific facets, such as N5: Impulsiveness, C2: Order, and C5: Self-discipline was prominent. Interestingly, obesity's association with cluster B personality disorders also highlighted that these phenotypes were similar in having association with E3: Assertiveness (Figure 4d).

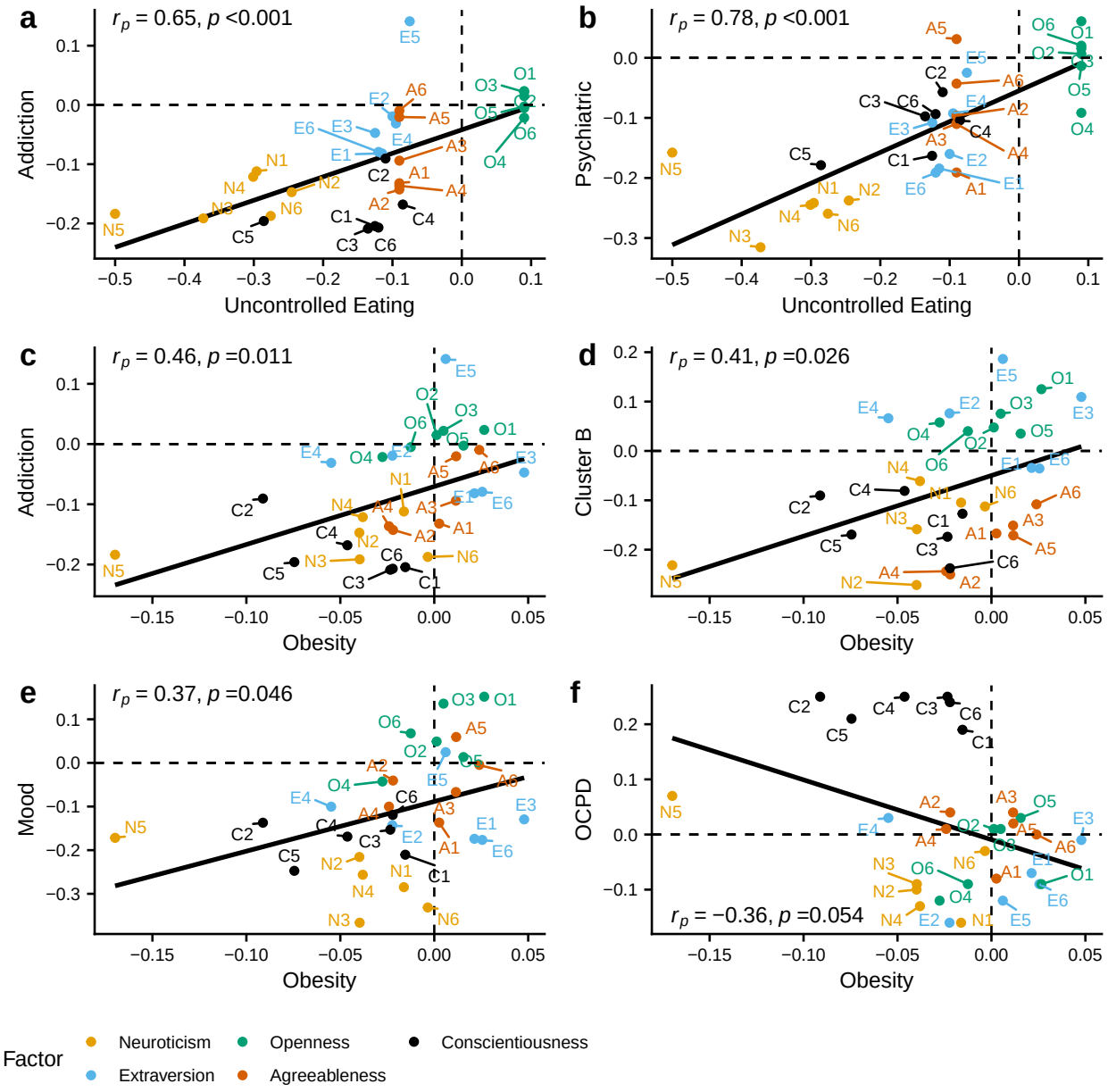

Figure 4. Scatterplots of personality correlations (r_p) between profiles of Uncontrolled Eating and obesity and addiction and psychiatric phenotypes. Associations for Neuroticism were inverted to avoid inflation of profile correlations as Neuroticism is keyed to the socially undesirable direction, as opposed to the other four domains. X and y values represent correlations of phenotypes with individual facets of NEO PI-R/3. Profiles on y axis in plots A-E have been aggregated across several profiles, See Figure1, Figure2, and Supplementary Table 1 for

classification. Data points represent individual personality facets, colour-coded by domain. OCPD = Obsessive-compulsive personality disorder.

The current analysis provides a quantitative estimation of behavioural similarities between obesity, UE, and addictions. This was achieved by employing the personality profile comparison approach. Although the similarity was highly uniform based on five broad personality domains, higher-resolution facet-based analysis revealed that behavioural overlap between obesity and addiction was smaller than those of UE and addictions or among addictions themselves. Facet-based behavioural similarity analyses further revealed that UE had considerable behavioural similarity with most psychiatric phenotype tested, whereas obesity's behavioural similarity pertained to mood disorders, cluster B personality disorders and obsessive-compulsive personality disorder.

The moderate behavioural similarity between obesity and addictions provides empirical support for comparing these phenotypes in more detail [3]. Specifically, we also highlighted the personality facets possibly characterising both obesity and addictions. The similarity was mostly driven by high N5: Impulsiveness and low Conscientiousness. This is in accordance with previous evidence [18] and suggests that similar self-regulation therapeutic approaches can be developed for both obesity and addictions [21]. But unlike addictions, obesity does not have a consistent association with sensation-seeking [3,18] , here measured by the E5: Excitement-seeking facet of the NEO PI-R/3, which characterises craving excitement and stimulation. Therefore, sensation-seeking aspects of addictions might not translate to obesity.

Intriguingly, UE had more similarity with addictions than obesity. UE may therefore be considered as a useful phenotype to summarise addiction-like behaviours potentially contributing to obesity. It is important to note that the UE profile was derived from questionnaires that were not based on the "food addiction" concept [22]. Therefore, we suggest that creating and using a food addiction-specific questionnaire is not crucial to understand the common substrate between addictions and overeating or UE [e.g., 23]. In the current study, the behavioural similarity between UE and addictions was driven by Neuroticism, a tendency towards negative mood states and anxiety driven behaviours. Several mechanisms are possible: either traits encompassed by Neuroticism could be common causes contributing to overeating and addictive behaviours, or overeating and addictive behaviours contribute to a person focusing on the negative aspects of these behaviours, leading to higher Neuroticism scores [10,24].

As obesity is less addiction-centred than UE, we explored whether the behavioural profile of obesity could be similar to profiles of other psychiatric phenotypes. Only a handful psychiatric phenotypes seemed to have behavioural similarity with obesity with an effect size close to the association between obesity and addictions. Note that the similarities were descriptive and not statistically tested. These were mood disorders, cluster B personality disorders, and obsessive-compulsive personality disorder. Their overlap with obesity was driven by associations with N5: Impulsiveness and Conscientiousness. As a novel finding, similarities with cluster B personality disorders was further driven by the positive association between obesity and the E3: Assertiveness facet of Extraversion. While assertiveness (or dominance) has been implicated in previous NEO PI-R/3 studies of obesity [e.g., 20], it has not been considered in behavioural models of obesity. Individuals with Cluster B personality disorders, particularly individuals with narcissism are known to have an exaggerated sense of superiority[25], which may explain their higher scores

in E3: Assertiveness. At first, it is hard to imagine most people with obesity having a heightened sense of superiority, as people with obesity typically have lower self-esteem[26] . However, it could be speculated that low self-esteem in obesity is a response to the increased status-driven individualism[27], which may be indexed by higher E3: Assertiveness. Alternatively, higher E3: Assertiveness may index increased reward sensitivity in people with obesity[3]. Future focused analysis will have to disentangle this association.

A caveat is that each personality correlation was based on 5 domains or 30 facets. At the same time, the "scores" for domain or facets were not single-participant data points, but average scores of at least 52 participants – at times even thousands of participants. While each correlation had only 3 or 28 degrees of freedom, it borrowed power from the studies that the average facet scores were based on. Future methodological developments are required to properly assess the role of sample sizes that correlation profiles are based on, providing more accurate standard errors and *p* values for personality correlations. Until then, less emphasis should be put on their *p* values than on their relative magnitudes. In addition, profiles based on smaller sample sizes may provide noisier estimates which lowers the personality correlations. However, there was no statistically detectable association between profiles ranked by sample size and by profiles' average of absolute personality correlations (domains: *rho* = -.14, 95% CI [-.57, .35], $n = 18$, $p = .59$; facets: *rho* = -.31, 95% CI [-.68, .18], $n = 18$, $p = .21$).

Another caveat is that the personality profile of phenotypes may vary depending on the diagnostic instrument as well as the personality trait measure used [28]. This is not a major concern for BMI, whose behavioural profile correlates $r_p = .96$ -.99 with other measures of adiposity [20]. Regarding the personality measure, current analysis was mostly limited to the NEO PI-R/3, which is intended for use in normal populations. For now, we find that these limitations are

offset by the NEO PI-R/3 profiles' wide availability. Future research of this kind may benefit from operationalising behavioural profiles using more numerous and more specific personality characteristics, possibly operationalised as single test items (nuances) [29]. Indeed, as recently reviewed [30,31], there is a considerable amount of reliable information present in the 240 NEO PI-R/3 items that is lost when the single items are aggregated into the 30 facets and, especially, the five domain scores. Therefore, researchers should make their data available at the item level, enabling more sophisticated profile comparison based on hundreds of specific behavioural characteristics. Until these more detailed profiles become widespread, researchers are forced to work with the 30 NEO PI-R/3 facets, which "are not likely to be the ideal specification of lower level traits, but for now they are a serviceable one, with known reliability, validity, and utility." [32]

Even at the facet level, as used here, the behavioural similarity analysis can bring novel insights into similarities between phenotypes. Currently, we focused on addiction and psychiatric phenotypes as there was a priori theoretical and empirical evidence for potential overlap. In the explorations, obesity and UE can be related to any other phenotype for which a NEO PI-R/3 profile has been published. This "upcycling" approach is more cost-effective than measuring all the phenotypes and obesity in a single study. Once behavioural similarity is established, the analysis on the particular facets driving the similarity can provide insights into how the behavioural similarity emerges. These insights can inform study design when obesity and the behaviourally similar phenotypes are finally included in the same study. For instance, current results suggest that obesity, personality disorders, and E3: Assertiveness-related behaviours should be studied together in greater detail.

In summary, obesity has behavioural similarity with addictions. The main overeating-related trait, UE is even more addiction-related, suggesting that UE is a useful summary of food-related

addictive behaviours. However, obesity cannot only be explained by a propensity to addictive behaviours. Comparison with psychiatric phenotypes highlighted that cluster B personality disorders might bring additional insight into understanding the behavioural profile of obesity. Our study provides a general framework for quantifying the behavioural similarity across many phenotypes.

Methods

Justification for NEO PI-R/3. We chose to conduct behavioural profiling based on the 30 personality traits forming the facets of the five-factor model as operationalised in the NEO PI-R/3 [16,17]. The 30 NEO PI-R/3 facets are designed to comprehensively sample aspects of behaviour related to the Five-Factor Model of personality (or the Big Five) [33], and the questionnaire has been related to a wide range of phenotypes. While the questions are designed to be used in normal populations [34], the NEO PI-R/3 performs su*rp*risingly well in subpopulations with addiction or psychiatric phenotypes – theoretical factor structure can be recovered, the questionnaire has test-retest reliability, and the questionnaire is also responsive to treatment of a psychiatric condition [35–37]. Here we analyse the personality domain and facet profiles of phenotypes of interest based on previously published associations.

Finding papers. Studies profiling obesity, UE, addiction, and psychiatric phenotypes with the NEO PI-R/3 were searched for in Google Scholar by entering "NEO PI-R/3" together with phenotype names, such as obesity, smoking, gambling, drug use, and other phenotypes listed in Supplementary Table 1. The goal of the search was not to be exhaustive, but to find a broad set of addiction and psychiatric phenotypes. When several papers were available on the phenotype, the effect sizes were either merged (see below), or previously calculated meta-analytic estimates were preferred over individual studies. Only papers reporting NEO PI-R/3 facet-based

associations were included. 21 empirical papers [20,35,38–56] were kept in the analysis, which analysed data from 19 different samples (Supplementary Table 1). We also included results from one meta-analysis summarising 16 different empirical studies analyzing 18 independent samples [28]. Altogether, the analysis is based on the summary statistics from 18,611 unique participants. Besides the phenotypes outlined in the introduction, we also included personality profiles of education and gender. As true null association between profiles cannot be expected, we provide education and gender as reference effect sizes for inter*p*reting the effect sizes of obesity and UE. We further use personality correlations among addiction/psychiatric themselves as maximum expected correlations.

Data extraction, transformation, aggregation. Our goal was to present all associations between personality traits and phenotypes in a common metric – correlation. Correlation or another measure of effect size was readily available in fewer than half of the empirical papers [20,38–44]. In other papers, correlations were obtained in the following way. Most papers reported NEO PI-R/3 facet T-score means and standard errors / standard deviations (*SD*) for one or more study group (s) and control group. For some of the traits, multiple groups were available, for instance smokers, never smokers, and former smokers [50] or underweight, normal weight, overweight, and obese [51]. In these cases, we focused on the phenotype group vs control group, for instance smokers vs never smokers; normal weight vs obese. We excluded former drug users, as for instance former smokers have a different personality than current and never smokers [55]. We extracted the mean, *SD*, and sample size for study groups [psychiatric, current users, obese (body mass index BMI $\geq$ 30 kg/m^2)], and control group [never users, normal weight (BMI between 18.5 and 24.9 kg/m^2). Using control group data from the included studies was preferred, as this approach reduces cross-cultural differences that may occur when the study and control

groups come from different countries or regions [38]. However, when control group data was not available, the NEO PI-R/3-R US normative sample (mean = 50, *SD* = 10, *n* = 1000)[16] was used. US normative sample data was also used in cases where the control group consisted of participants with psychiatric disorders [52]. In one case, findings were available for two time points; these measurement were aggregated [35]. When *SD* was not available [35,45], it was calculated from standard error, or assumed to be 10, as per the NEO PI-R/3-R manual [16].

The mean difference between the study group and the control group in a personality trait was converted into a correlation in the following way. First, a summarised *t*-test was performed between the control group and the study group for each domain and facet, using the extracted means, *SD*-s and sample sizes. Unequal variances were used as per previous recommendations [57]. The procedure was conducted using tsum.test() from the R package BSDA [58]. The *t*-test was two-sided with a *p*-value of .05. However, the *p*-values were not used in the further effect size conversion process. Obtained effect sizes were converted to a correlation coefficient using conversion formulas implemented in the compute.es R package, which first convert the *t*-test values into Cohen's *d*, which is then converted into a correlation, using standard formulas [59,60]. We tested the effect size conversion procedure using data from a paper [20] that provided both trait mean and *SD* for both groups that had either normal weight or obesity, as well as continuous trait-BMI correlations [20]. The trait-obesity correlations reported in that paper [20] were almost identical to the trait-obesity status correlations calculated from contrasting the group having normal weight with the group having obesity (r_p = .99).

When several papers were available, the correlations were aggregated using meta-analytic random effects aggregation. Random effects aggregation accounts for variation in study methodology between different study sites [61]. Before meta-analysing, correlations were

transformed based on Fischer's *r*-to-*z* transformation (from Pearson-*r* to normal distribution *z*-score), which is a recommended approach as *r* is not normally distributed [61]. These steps were conducted by the metacor() function of the meta R package [62,63]. We also aggregated data for conceptually similar smaller samples, for instance phobias and anxiety disorders. There, the sample size weight was the size of the study group (see phenotype group column in Supplementary Table 1). Since many eating-related traits are highly similar [8,9], we also aggregated emotional and external eating [39] into UE. Some papers omitted facets with small effect size; missing facets were then replaced with domain level effect sizes. Two papers [38,54] omitted domain-outcome correlations. We then used the other 26 profiles to train a model that predicted each domain-outcome correlation from the facet-outcome correlations belonging to that domain. 5-fold cross-validation within the 26 profiles revealed that mean absolute error ranged from $r = .03$ to $r = .04$ for different domains. Only self-reported profiles were used [e.g., 43]. Data sources and meta-analytic aggregations are summarised in Supplementary Table 1.

Data analysis. Profile similarity was assessed by shape similarity, which is computed with Pearson correlations between profiles [64]. We focus on similarity based on profile shape, as shape is the most fundamental element for personality profile comparison and drives other similarities [64]. We inverted the scores of Neuroticism, to avoid inflation of profile correlations due to Neuroticism being keyed to the socially undesirable direction, while the other four domains are keyed in the socially desirable direction. For an initial presentation (Supplementary Figures S1 and S2), the resulting correlation matrix was clustered with the "wa*rp*.d2" method [65]. We conducted separate analysis for addiction and psychiatric phenotypes. Subsets of the main correlation matrix were visualised with a network with spring-embedded layout [66] that creates clusters of more strongly related variables (Figures 1a, 1b, 2a, and 2b).

We first sought to establish, if there were any differences in how addiction/psychiatric phenotypes related to baseline, target, and other addiction/psychiatric phenotypes. Therefore, personality correlations of addiction/psychiatric phenotypes were organised into five groups: correlations with 1) education, 2) gender, 3) obesity, 4) UE, and 5) other addiction/psychiatric phenotypes. Those groups were used as predictors of absolute personality correlation in a one-way ANOVA model. Post-hoc tests were run in a linear regression model where target phenotype (obesity or UE) was the reference category, whose absolute correlations with addiction/psychiatric phenotypes were compared with the correlations that variables within four other variable sets had with the same phenotypes (Supplementary Tables S2 and S3). *p* values of post-hoc comparisons of interest were two-sided and corrected for multiple comparison with Holm method.

To understand which facets of NEO PI-R/3 drive the correlations, scatter*rp*lots between the profile correlations were inspected. To limit the number of scatter*rp*lots, the profiles of addiction or psychiatric phenotypes were aggregated by the categories outlined in Supplementary Table 1, using meta-analytic principles, but keeping the sample sizes equal (e.g. $n = 100$), as we wanted each phenotype to contribute equally to the aggregated profile.

All analysis was conducted in Microsoft R Open 3.5.1 [62] using the August 2018 version of several addon packages [58,59,63,67–77]. Analysis code is available as described in code availability section.

Data availability

The correlation profiles of phenotypes used in the analysis are available at https://osf.io/zfsxd/ and also as Supplementary Data and part of Supplementary Software.

Code availability

The analysis script used to generate results based on the correlation profiles is available at https://osf.io/zfsxd/ and also as Supplementary Software

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Competing interests

The authors declare no competing interests

Author contributions.

All authors read and contributed significantly to the manuscript and approved the submitted version.

U.V: collected data, analysed data, wrote the paper.

B.M: contributed to data analysis

Y.Z.: contributed to data analysis methods

A.M.: contributed to inter*p*retation

R.M.: contributed to data analysis methods and inter*p*retation

A.D.: contributed to data analysis methods and inter*p*retation

Figure legends

Figure 1. Personality trait profiles of obesity and selected addictions. Neuroticism has been reversed to Emotional Stability to avoid inflation of profile correlations. Solid vertical line separates domains from facets. Figure has been conceptually reproduced from Michaud et al. 3. ALC = Alcohol; GMB = Gambling; OB = Obesity; OPI = Opioid abuse; *r* = correlation; SMK = Smoking

Figure 2. Personality correlations (r_p) with addiction phenotypes. A and B: Spring-embedded network graph based on domains (A) or facets (B), using Fruchterman-Reingold algorithm. Circles mark addiction phenotypes, triangles mark targets of the behavioural similarity analysis, rectangles mark baseline phenotypes. Blue edges mark positive correlations, red edges mark negative correlations. C and D: Same data as in panels A and B based on domains (C) or facets (D). Correlations are in absolute values, organised by analysis targets. Points represent individual personality correlations, thick lines represent mean values, beans represent smoothed densities, and the rectangles represent 95% confidence intervals. EDU, GEN, OB, UE have 6 personality correlations, ADD has 15 personality correlations. Horizontal brackets indicate significant differences in two phenotypes regarding their mean personality correlation with addiction phenotypes. Differences were detected with multiple regression, using Holm corrected *p* value < .05. Full statistics are reported in Supplementary Table 2. ADD = Addictions; ALC = Alcohol; EDU = Education; GEN = Gender; GMB = Gambling; GMB.A = Gambling with attention deficit hyperactivity disorder; OB = Obesity; OPI = Opioid abuse; SMK = Smoking; THC = Cannabis; UE = Uncontrolled Eating.

Figure 3. Personality correlations (r_p) with psychiatric phenotypes. A and B: Spring-embedded network graph based on domains (A) or facets (B), using Fruchterman-Reingold algorithm. Circles mark psychiatric phenotypes, triangles mark targets of the behavioural similarity analysis, rectangles mark baseline phenotypes. Blue edges mark positive correlations, red edges mark negative correlations. C and D: Same data as in panels A and B based on domains (C) or facets (D). Correlations are in absolute values, organised by analysis targets. Points represent individual correlations, thick lines represent mean values, beans represent smoothed densities, and the rectangles represent 95% confidence intervals. EDU, GEN, OB, UE have 18 data points, PSY has 153 data points. Horizontal brackets indicate significant differences in two phenotypes regarding their mean personality correlation with psychiatric phenotypes. Differences were detected with multiple regression, using Holm corrected p value < .05. Full statistics are reported in Supplementary Table 3. ANX = Anxiety disorders; ASD = Autism; ASO = Antisocial; AVO = Avoidant; BDL = Borderline; BIP = Bipolar; DEP = Depression; DPD = Dependent; ED = Non-anorexic eating disorders; EDU = Education; GEN = Gender; HIS = Histrionic; NAR = Narcissistic; OB = Obesity; OCD = Obsessive compulsive disorder; OCPD = Obsessive compulsive personality disorder; PAR = Paranoid; PSY = Psychiatric phenotypes; PTSD = Post traumatic stress disorder; SCH = Schizophrenia; SZD = Schizoid; SZT = Schizotypal; UE = Uncontrolled Eating.

Figure 4. Scatter*rp*lots of personality correlations (r_p) between profiles of Uncontrolled Eating and obesity and addiction and psychiatric phenotypes. Associations for Neuroticism were inverted to avoid inflation of profile correlations as Neuroticism is keyed to the socially undesirable direction, as opposed to the other four domains. X and y values represent correlations of phenotypes with individual facets of NEO PI-R/3. Profiles on y axis in plots A-E

have been aggregated across several profiles, See Figure1, Figure2, and Supplementary Table 1 for classification. Data points represent individual personality facets, colour-coded by domain. OCPD = Obsessive-compulsive personality disorder.