**First evidence of a general disease (“d”) factor, a common factor underlying physical and mental illness**

The links between mental and physical illness are an emerging topic, with the potential to transform research and practice in medicine and psychology1.

Symptoms of mental illness have been found to be underpinned by one single factor explaining the propensity to develop any mental health condition, which has been termed the “p” (for psychopathology) factor2. The “p” factor has been demonstrated not only at the symptom2, but also at the genetic level3, and in overlapping neural correlates across a wide range of psychiatric disorders4.

However, there is evidence of comorbidity not only among mental conditions, but also between mental and physical conditions, as shown by studies pointing to transdiagnostic associations across a wide range of physical and mental disorders1,5. These findings suggest that there may be another factor that accounts for the individuals’ propensity to develop mental as well as physical conditions, that we termed the “d” (for disease) factor6. The existence of this factor would have highly relevant research and clinical implications regarding our understanding and management of mental and physical conditions, as well as for service organization.

We empirically tested the hypothesis of a “d” factor in the 1970 British Cohort Study (BCS), which recruited 19,196 individuals born in a single week of 1970 in England, Scotland and Wales7. We used the biomedical sweep of the BCS7, collected in 2016 from 8,581 participants aged 46-48.

Mental conditions included anxiety, phobia, depression, schizophrenia, obsessive-compulsive disorder, insomnia, and stutter. Physical conditions included chronic fatigue syndrome, migraine, stroke, seizures, asthma, eczema, hay fever, arthritis, back problems (prolapsed disc/pain), ulcer, ulcerative colitis/Crohn’s disease, irritable bowel syndrome, gallstones, kidney/bladder stones, hearing impairments, visual impairments, tinnitus, obesity, diabetes, heart problems, high blood pressure, and cancer. Physical problems were assessed via self-report and/or by asking participants whether the condition had been diagnosed by a physician. Mental health conditions were assessed by one-item self-report questions or questionnaires (see supplementary information).

We ran three hierarchical models, that are typically used to investigate hierarchically structured constructs2 using confirmatory factor analysis, as follows: a) a correlated factors model, assuming that all conditions (mental and physical) would be correlated, b) a unifactor model, assuming that all conditions would be best explained by one underlying factor, and c) a bifactor model, assuming that mental and physical conditions would load on individual factors, but that an underlying disease dimension (“d”) would explain the data best.

Model fit was assessed using weighted least square mean (WLSM) and variance estimator, and compared using chi-square values, the comparative fit index (CFI), the Tucker-Lewis index (TLI), and the root-mean-square error of approximation (RMSEA). Lower RMSEA values indicate better model fit (< 0.06 = good model fit); higher CFI and TLI values indicate better model fit (> 0.95 = good model fit)8. Data analyses were conducted in Mplus v89.

We found that the bifactor model fitted the data best (CFI=0.98, TLI=0.98, RMSEA=0.016). All physical and mental conditions loaded positively onto a common disease factor, with the highest factor loadings for chronic fatigue syndrome (0.71±0.04), heart problems (0.66±0.04), irritable bowel syndrome (0.57±0.03), ulcer (0.56±0.06), and obsessive-compulsive disorder (0.53±0.03). The majority (15/22) of physical conditions loaded significantly on a “physical factor”, apart from cancer, chronic fatigue syndrome, ulcers, gallstones or kidney stones, vision impairments, and seizures. Cardio-metabolic variables (obesity, diabetes, hypertension, heart problems) loaded negatively onto the physical conditions factor. Mental conditions loaded highly positively onto a psychopathology (“p”) factor (see supplementary information).

Therefore, we found that the data were best explained by a bifactor model with a mental conditions factor, a physical conditions factor, and an additional underlying disease dimension, reflecting a general vulnerability to develop any of the included conditions. Therefore, our results support the assumption of the existence of a general “d” factor in adults6.

Although our study does not test underlying mechanisms, several suggestions can be made based on existing literature. First, it is likely that a range of physical and mental conditions share common genetic polymorphisms that generate a vulnerability towards developing a wide range of diseases3. Other possible mechanisms include common lifestyle and socioeconomic factors. For instance, smoking, high alcohol consumptions, disrupted sleep, and lack of exercise are associated with increased cardio-metabolic risk. Unhealthy lifestyle is also associated with immune system dysfunction, which in turn is related to a variety of physical and mental conditions.

Our findings have relevant implications for the conceptualization and classification of mental and physical conditions. Current classification systems have been criticized2 because of the high comorbidity between mental disorders. Our results contribute to this debate by showing the existence of a common dimension, beyond mental health conditions, that includes also physical health conditions. Transdiagnostic research assessing risk and pathways of transmission of diseases might benefit from taking both mental and physical conditions into account. A pertinent question is whether it is still meaningful to differentiate between mental and physical disorders or whether it might be more useful to view them both as health conditions.

The results of this study have also important implications for clinical practice and policy. Our findings stress the need to reduce the gap between physical and mental health care regarding assessment and treatment. Furthermore, our results strongly call for health care policies to promote more integrated health care systems, bridging the current gap between mental and physical health care services that exists across countries and health systems.

Strengths of this study include the large sample size and the broad range of physical conditions that were included. Limitations include the limited number of mental health variables related to thought disorders and externalizing disorders, which is why a three-factor solution (internalizing, externalizing, thought disorder)2 could not be modelled. Additionally, data were limited to a predominantly white, middle-aged British sample, and replications are needed in younger and older samples and in samples from various areas of the world, including low-income countries. Furthermore, the physical conditions were ascertained largely by single self-report items, with no direct assessment of the conditions.

Future studies should use data from health registries around the world with comprehensive mental health assessments, assess the temporal links between mental and physical disorders, evaluate the possibility of a “d” factor across development, and explore possible common genetic and pathophysiological pathways.

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