# In addition to PCOS/PMOS, Neurodevelopmental and Psychiatric Disorders, what other illnesses or disorders that were once thought to involve only 1 bodily system are actually Multi-System Disorders?

## Multi-System Disorders Beyond PCOS and Psychiatric Conditions

Many conditions once framed as single-organ problems are now understood as **multi-system** disorders involving immune, metabolic, cardiovascular, and other systems interacting over time.

### Major Examples of Newly Recognized Multi-System Disorders

#### Neurological and Psychiatric-Adjacent

- **Parkinson's disease** – Formerly a "brain/motor" disease, now seen as multiorgan, with gastrointestinal onset hypotheses, widespread non-motor symptoms, and aging–environment interactions across systems (Costa et al., 2022).
- **Psychosis (including schizophrenia)** – First-episode psychosis shows substantial immune, cardiometabolic, and HPA-axis changes whose magnitude is similar to many brain alterations, supporting a multi-system view even at onset (Pillinger et al., 2018).
- **Bipolar disorder** – Proposed as a **multi-system inflammatory disease**, with early and frequent comorbid cardiovascular, metabolic, autoimmune and inflammatory abnormalities, not just consequences of medication or lifestyle (Leboyer et al., 2012).

#### Classically "Local" Diseases Now Seen as Systemic

| Condition (old view) | New systemic understanding | Citations |
|---|---|---|
| Periodontitis (oral disease) | Acts as a **systemic inflammatory disease**, associated with cardiovascular disease, diabetes, rheumatoid arthritis, respiratory disease and multimorbidity via shared pro-inflammatory and prothrombotic states (Villoria et al., 2024) | (Villoria et al., 2024) |
| NAFLD/MAFLD (liver) | A **multisystem metabolic disease** promoting cardiovascular disease and cancers through a pro-inflammatory, profibrotic, procoagulant milieu (Pipitone et al., 2023) | (Pipitone et al., 2023) |
| Obesity (adipose tissue) | Chronic **multisystem disease** affecting cardiometabolic, malignant, and mental health outcomes; non-metabolic complications increasingly recognized (Sarma et al., 2021) | (Sarma et al., 2021) |
| Sarcopenia (muscle loss in aging) | Multifactorial disorder involving neuromuscular, cardiovascular, endocrine, metabolic, and inflammatory pathways, not just "muscle aging" (Popescu et al., 2026) | (Popescu et al., 2026) |

FIGURE 1 Conditions reclassified from single-organ to multisystem disorders

### Conceptual and Classification Shifts

- **Functional somatic disorders** (e.g., IBS, fibromyalgia clusters) are explicitly framed as **multisystem**, **single-system**, or single-symptom types, reflecting overlapping symptoms across organ systems and shared brain–body mechanisms (Burton et al., 2020).
- Broader frameworks argue that most chronic diseases and toxicities are inherently systemic because inflammation, aging, and organ-to-organ crosstalk link multiple organs in disease progression (Kim et al., 2024; Li et al., 2025; Bennett et al., 2018; Zoccali et al., 2025; Knockaert, 2007; Smirnova et al., 2019).

### Summary

Beyond PCOS and neurodevelopmental/psychiatric disorders, strong examples of conditions re-framed as multi-system include Parkinson's disease, psychosis and bipolar disorder, periodontitis, NAFLD/MAFLD, obesity, and sarcopenia. Across these, shared themes are chronic inflammation, metabolic–immune–endocrine crosstalk, and overlapping comorbidities, challenging organ-by-organ views of disease.



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