CORRESPONDENCE

Animal Models of Obsessive-Compulsive Disorder

To the Editor:

Obsessive-compulsive disorder (OCD) is a condition characterized by obsessions and compulsions (1). Andersen *et al.* (2) recently reported that early life clomipramine exposure produced a "behavioral phenotype in adult rats that is consistent with an OCD-like profile in humans" (p. 745), specifically involving enhanced anxiety, marble burying, behavioral inflexibility, working memory impairment, and hoarding. They also reported neurobiological changes, including corticostriatal dysfunction and elevated neurotransmitter receptor activity. Although Andersen *et al.* concluded that their data support a novel animal model of OCD, their findings are open to alternative, equally plausible interpretations. Here, we show that the nature of the phenotype and neurobiological differences they have observed in rats is ambiguous and therefore provides no basis for generalizing the reported findings to OCD or obsessive-compulsive-like behavior.

The psychiatric nomenclature clearly defines compulsions in OCD as repetitive, intentional behaviors or mental acts that the person feels compelled to perform in response to obsessions (1). Empiric research consistently demonstrates that compulsive urges are provoked by obsessions (3). The implication here is that compulsive rituals are therefore distinguishable from other repetitive, stereotypic behaviors, such as sterotypies observed in pervasive developmental disorders, tics observed in Tourette's syndrome, and perseverative behaviors observed in patients who have sustained closed head injuries. It is therefore difficult to determine, on the basis of mere behavioral observations, whether repetitive behaviors constitute true compulsions. That is, although behaviors such as stereotypical movements in developmental disorders and tics share a similar form or topography with compulsive rituals in OCD (i.e., they might all be repetitive and senseless), they have different functions: in OCD, the repetitive behavior is performed in response to an obsession. Accordingly, it is at best unclear whether Andersen *et al.* were actually measuring OCD-like compulsive rituals as opposed to some other form of repetitive behavior.

Andersen *et al.* did observe behavior in their rats that might be consistent with the presence of anxiety. Perhaps the behavior Andersen *et al.* have labeled as OCD-like is a response to this anxiety. This could be the case, yet such "anxiety" is not the same as obsessional fear. Again, the psychiatric nomenclature clearly defines obsessions in OCD as recurrent, persistent, intrusive, and unwanted thoughts, ideas, or images that are not simply excessive worries about life problems and that are subjectively resisted because they provoke marked anxiety or distress (1). It would be nearly impossible to demonstrate whether a rat is experiencing a true obsession versus general anxiety or some other form of distress, which again illustrates the previously raised ambiguity problem.

Interestingly (and consistent with the difficulties we describe here), Andersen *et al.* (4) in 2002 argued that their clomipramine paradigm is an animal model of depression: "postnatal treatment between 8–21 days of age with clomipramine (15 mg/kg, twice daily) produces an animal model that has many of the behavioral hallmarks of depression" (p. 50). So, the same dose of clomipramine for postnatal rats was used by Andersen *et al.* as an animal model for depression in one study and an animal model of OCD in another study. Other investigators have also used neonatal clomipramine administration as an animal model of depression (5–7). This provides additional evidence of the ambiguity in this model by Andersen *et al.*; does it model depression or OCD or does it simply model general (nonspecific) distress?

Anomalies in corticostriatal circuits as well as memory impairments are also not specific to OCD. Abnormal functioning in the orbitofrontal cortex and striatum and cognitive deficits such as memory impairment are present in other psychiatric disorders, such as social anxiety disorder (8,9). This reveals further ambiguity in the Andersen *et al.* data: it is unclear whether their findings reveal anything about the neurobiology of OCD per se. Rather, the observations might simply illustrate the phenotypic and neurobiological correlates of clomipramine-induced overstimulation of the serotonin and associated neurotransmitter systems.

Finally, Andersen *et al.* include hoarding behavior as one of the "heterogeneous symptoms of OCD" evident in their putative animal model. Hoarding behavior, however, is known to be a nonspecific response to stressors in rats and other rodents (10,11). Moreover, although some authors have considered hoarding as a symptom of OCD, research suggests that hoarding is not necessarily OCD-related. Specifically, relative to other obsessive-compulsive symptoms (e.g., washing, checking), hoarding is more strongly related with other sorts of psychopathology (e.g., personality disorders), associated with earlier age of onset, tends to have distinct neural activity patterns and genetic susceptibility loci, and has a weaker response to treatments with demonstrated efficacy for OCD (12,13). Thus, hoarding is now generally considered as distinct from OCD and might become its own disorder in DSM-V (13,14). Taken together, this casts further doubt on the relevance to OCD or obsessive-compulsive-like symptoms of the findings of Andersen *et al.*. Given that the cardinal symptoms of OCD involve intrusive unwanted obsessional thoughts about uniquely human topics (e.g., being responsible for harm or mistakes, religion, morality, the fear of contamination) and compulsive rituals designed to neutralize these types of obsessions, it is difficult to imagine a true animal model of this condition (especially one involving rodents) that avoids the type of ambiguity and anthropomorphism we describe here.

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