To the Editor:

Animal Models of Obsessive-Compulsive Disorder

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bsessive-compulsive disorder (OCD) is a condition char-
acterized 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), spe-
cifically 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. Al-
though 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-com-
pulsive-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 stereotypies 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 disor-
ders 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 An-
dersen 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 obses-
sional fear. Again, the psychiatric nomenclature clearly defines
obsessions in OCD as recurrent, persistent, intrusive, and un-
wanted 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
ture 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 pro-
vides additional evidence of the ambiguity in this model by Ander-
sen et al.; does it model depression or OCD or does it simply model
general (nonspecific) distress?

Anomalies in corticostriatal circuits as well as memory impair-
ments 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 observa-
vations might simply illustrate the phenotypic and neurobiological
correlates of clomipramine-induced overstimulation of the sero-
tonin and associated neurotransmitter systems.

Finally, Andersen et al. include hoarding behavior as one of the
“heterogeneous symptoms of OCD” evident in their putative ani-
mal model. Hoarding behavior, however, is known to be a nonspe-
cific response to stressors in rats and other rodents (10,11). More-
over, 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 disor-
ders), 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-com-
pulsive-like symptoms of the findings of Andersen et al. Given that the cardinal symptoms of OCD involve intrusive un-
wanted 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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