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Modeling Illnesses of the Mind: Human Uniqueness Among Other Animals

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Human uniqueness among other animals is a philosophical and compelling psychological issue, and included in a Christian understanding of human nature. Theologically, humans are unlike animals because they are created in the 'image of God' (Genesis 1:27). Yet scientifically, against the idea of human uniqueness, there is the authoritative influence of Darwin's finding of no fundamental difference between humans and the higher mammals in their mental faculties. Recent theories, however, have challenged Darwin's analysis on the similarity of animals and humans.

This article proposes an alternative yet complementary approach to human nature: that of animal models of human illnesses involving the mind and brain. In particular, it explores how animal models contribute to psychological and theological ideas about human beings among other animals. There is continuity and resemblance, but the inadequacy of animal models and shortfall in effectiveness serve to highlight the uniqueness of the human.

Human uniqueness among other animals is a philosophical matter (Harrison, 1993; McMullin, 2013; Moritz, 2011) and is now a compelling psychological issue (Gagneux & Gagneux, 2001; Middlebrooks & Sommer, 2012). Uniqueness also features in a Christian understanding of human nature. Theologically, humans are unlike animals because they are created in the "image of God" (van Huyssteen, 2006). This *imago Dei* can be interpreted, for example, as a unique capacity for personal relatedness and preeminence with Jesus (Jeeves, 2011). Or it is understood as the biblical or Hebrew concept of election (Moritz, 2011). Although, some argue against human uniqueness and in favor of "human distinctiveness" (Brown, 2010). Others even extend the imago Dei to all creatures (Muray, 2007). The image of God itself is also the subject of empirical psychological research (Lawrence, 1997; Steenwyk, Atkins, Bedics, & Whitley, 2010; Testoni, Visintin, Capozza, Carlucci, & Shams, 2016).

Yet scientifically, against the notion of human uniqueness, there is the powerful influence of Darwin's finding that "there is no fundamental difference between man and the higher mammals in their mental faculties…the difference in mind between man and the higher animals, great as it is, is certainly one of degree and not of kind" (Darwin, 1871). Recent theories, however, have challenged Darwin's judgment on the similarity of animals and humans, after about 30 years of fixation with animal–human similarity (Premack, 2010). For example, animal abilities are limited adaptations confined to a single goal, whereas human intelligence has a generalist character which blends their independently evolved abilities. Moreover, differences in species are less manifested among young animals than among adults; therefore, species comparisons also require comparisons of developmental routes and an explanation of the species-specific mechanism(s) involved (Shettleworth, 2012). Here for instance, human cognition includes basic modular and domain-general processes in common with other animals, together with cognitive and social developmental processes, which renders adult cognition unique.

This article proposes an alternative yet complementary approach to human nature: that of animal models of human illnesses involving the mind and brain. In particular, it explores how animal models contribute to psychological and theological ideas about human beings among other animals. There is continuity and resemblance, but the inadequacy of animal models and shortfall in effectiveness serve to highlight the uniqueness of humans.

This article is comprised of six main parts. It opens with a brief consideration of the uniqueness of humanity in Christian theology and psychology, especially as being created in the image of God. Secondly, we introduce the context of illness, which is followed in the third part by the concept of animal models and several cases involving the mind. Fourthly, we examine

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the research efforts to develop animal models of mental illnesses and how they support the notion of *resemblance* and *continuity* of humans with animals. In the fifth part, we turn to the human-animal *discontinuity* and the *uniqueness* of the human. This can be surprisingly positive, and differences are helpful, both ethically and conceptually. Nonetheless, as will be seen in the final part, there are serious doubts about animal modeling of human mental illness. Here the exceptionality of the human animal becomes clearly visible. In all, there are important biblical and theological ideas that are reflected in the concepts and empirical research.

Uniqueness, Theology, and Humanity

When compared, the theological and psychological understanding of human persons are somewhat different; however, for Christians they can be integrated (Clinton & Sibcy, 2012). The specialness of humanity begins with the triune God who has revealed a plan to share the communion of trinitarian life with persons created in God's image (International Theological Commission [ITC], 2004). This occurs when humans are conformed to Christ (Rom 8:29) through the gifts of the Holy Spirit (Rom 8:23), and where salvation entails the restoration of the image of God by Christ who is the perfect image of the Father (Col 1:20). The ITC explains how humans are created in the image of God in order to become partakers of the divine nature (2 Pet 1:3-4). The ontological difference between human beings and animals endures because only man and woman are created in the image of God, and God has given them sovereignty over the animal world (Gen 1:26,28; Gen 2: 19-20).

Yet, there is an obligation of stewardship. God appoints humanity as stewards in the manner of the master in the Gospel parables (cf. Luke 19:12). "The only creature willed expressly by God for his own sake occupies a unique place at the summit of visible creation (Gen. 1:26, 2:20; Ps 8:6-7; Wisdom 9:2-3)" (p. 243). This is without forgetting other elements of human nature found in the New Testament: the concept of forgiveness of one human being by another, and repenting and asking for forgiveness; the Pauline notion of the divided self; and the Pauline-Augustinian notion of weakness of will (Roberts, 2012).

In the psychological world, some researchers hold that while modern science has narrowed some of the gap separating human beings from other creatures, it has also demonstrated how fixed and even wide that gap remains (Fisher, 2005). Humans differ from other animals primarily in their cognitive powers (Gregg & Mahadevan, 2014). Take for instance the essential organ of humans and animals, namely, the brain, which makes evolutionary comparisons possible. Neuroscientists ask, "What's human about the human brain?" (Preuss, 2000). Many think that the human brain is not a super ape brain but contains major quantitative and qualitative modifications (Schoenemann, 2006). One explanation of how human brains are characterized as distinct from those of early monkey and ape ancestors sees three main ways (Kaas, 2013). 1. The human brain increased in size, whereby the amount of neocortex constituted 80% of the human brain. 2. Some parts of the neocortex were enlarged much, compared to the remainder of the neocortex. 3. There is evidence that the number of fundamental functional divisions of cortex-cortical areas greatly increased as human brains evolved.

Likewise, consider how the orbitofrontal system and its cortical and subcortical links, known as the "senior executive of the emotional brain," has a regulatory function and is expanded in the right hemisphere (Schore, 2000). These neural structures are dominant in human infancy. Attachment processes are based on right-brain psychobiological interactions and are vital to the growth and adaptive capacities of the infant.

The contrasting portraits of the human in theology and psychology can be further understood as human/animal continuity and uniqueness. To explore this more deeply via an alternative perspective, in the second part we present the context of illness, the concept of animal models, and some relevant examples.

Illness as a Human Context

While it is often assumed that the world's population is healthy and flourishing, illness is a human reality. This harmonizes with biblical thought. In the peaceable kingdom (Isa 11:1-9) and the apocalypse (Rev 22:1-5) there will be fulfilment. But until then, it is as Paul observes: the creation waits in eager expectation for the children of God to be revealed, and the creation was also subjected to frustration (Romans 8:19-20). Through Adam, human beings fell out of favor with God; creation had a "fall" and the earth was cursed due to Adam's sin (Byrne, 2007). It was no longer a garden but a place of sweat and lifelong toil (Gen 3:17-19).

In the studies of the mind, the influence of positive psychology on social, clinical, personality, and developmental psychologies has turned the imagination towards human wellness and development (King & Whitney, 2015). However, mental illness remains a global reality. Therefore, it is an important context for discussion. For most countries, the number of deaths in comparison with 1990 are more than doubled, not only for HIV/AIDS, Alzheimer's disease, and other dementias which are among the top 30 mortality causes, but also for Parkinson's disease and other conditions (GBD, 2013; Mortality and Causes of Death Collaborators, 2015). A study in 2010 based on European data found that the spectrum of disorders of the brain is large, including hundreds of disorders that are listed in the mental or neurological disorder chapters of the established international diagnostic classification systems. The study notes how these disorders involve short- and long-term impairments and disabilities, and consequent financial, emotional, and community burden to the patients, their families, and their social network. The total cost of disorders of the brain was approximated at ∈798 billion in Europe in 2010. It is estimated that each year 38.2% of the European Union population suffers from a mental disorder. Adjusted for age and comorbidity, this corresponds to 164.8 million persons affected.

In the United Kingdom, there was an estimated total of approximately 45 million diagnosed cases of brain disorders, ranging between 26,000 cases of brain tumor and 18 million cases of headache, with a cost of ∈134 billion per annum (Fineberg et al., 2013). There were greater than 5 million cases of anxiety disorder (8,196,000; 18.17% of UK population) and sleep disorder (5,268,000; 11.68%) and greater than one million cases of addiction (1,878,000; 4.16%), mood disorder (i.e., unipolar depression and bipolar disorders; 3,937,000, 8.73%), and somatoform disorder (2,396,000; 5.31%; Wittchen et al., 2010). Internationally, with large numbers of people experiencing the burden of disease, an analysis of human persons in a framework of illnesses and treatments is valid. Some of these maladies are yet to be fully understood and treated. This is where scientists turn to animal models.

Animal Models

Every Nobel Prize in medicine, except two, over the last one hundred years has depended on animal research (Redmond, 2012). Variations of this frequently-repeated statement continue while critics question whether such statements have been formally validated (Matthews, 2008). Nevertheless, the general thrust of the statement is reasonable.

An animal model can be understood as an experimental paradigm developed with the aim of studying a given phenomenon found in humans (Koob & Zimmer, 2012). Animal models of human disease can be classified into spontaneous, induced, negative, and orphan models (Van Dam & De Deyn, 2014). *Spontaneous* models are assumed to develop their condition in the absence of experimental manipulation, although for neurological and psychiatric conditions, few spontaneous models exist. *Induced* models require a pathology to be experimentally induced, e.g., applying physicochemical stimulus. *Negative* models are models in which a specific human disorder does not develop. *Orphan* models express a condition that has never been described in man or other target species.

For many central nervous system (CNS) disorders, for example, stroke and optic nerve injury, animal models have resulted in progress in understanding essential disease mechanisms, although challenges and controversy continue to occur in animal modeling of human CNS diseases (Chesselet & Carmichael, 2012). We present three examples.

Cases

Zebrafish models are becoming a significant resource for advancing neurogenetics and neuroscience, possessing high genetic and physiological homology to humans, sensitive to every major neurotropic drug, and with capabilities to respond to these in similar manner as humans (Kalueff, Stewart, & Gerlai, 2014). It has potential for research into Autism spectrum disorder (ASD), a neurodevelopmental disorder with complex symptoms and uncertain multi-factor pathogenesis (Stewart, Nguyen, Wong, Poudel, & Kalueff, 2014). For instance, social deficits in ASD can be matched in zebrafish by reduced social interaction in a test called a shoaling test, such as less time spent in shoals and increased average inter-fish distance.

Another complex psychopathology is obsessive-compulsive disorder (OCD), an anxiety-spectrum disorder marked by obsessions or persistent intrusive thoughts and compulsions or repetitive actions (Welch et al., 2007). Dysfunction of the brain's circuits known as the cortico-striato-thalamo-cortical circuitry is implicated in OCD. The SAP90/PSD95-associated protein 3 (SAPAP3) is a protein at excitatory synapses that is highly expressed in the striatum of the brain. A study demonstrated that mice with genetic deletion of *Sapap3* display increased anxiety and compulsive grooming behaviors resulting in loss of facial hair and skin lesions. The authors note, "although there are inherent limitations of evaluating thought content in mice, our study further indicates that cortico-striatal synaptic defects may be central to the genesis of OCD-like behaviours" (p. 898). The striatum integrates the various inputs from the brain's cortex and uses this information to choose particular motor and/or cognitive programs. That study and other ones open the possibility that defects in excitatory synaptic transmission in the cortico-striatal circuit may contribute to the pathogenesis of OC-spectrum disorders in humans.

A third case is treatments. There is widespread evidence that exercise training (ET) has positive neurorehabilitative outcomes for motor symptoms in Parkinson's disease (PD; Wang, Guo, Myers, Heintz, & Holschneider, 2015). ET has been proposed to generate brain neuroplasticity, resulting in the recruitment of compensatory circuits or restoration of function of the impaired circuits. In rats with intra-striatal 6-hydroxydopamine (6-OHDA) lesion, there have been reported behavioral improvements and functional brain reorganization induced by using simple running wheels or non-skilled aerobic exercise (NSAE). A study used a complex running wheel with irregularity in spacing of rungs as a tool for skilled aerobic exercise (SAE). It found that skilled aerobic exercise training was successful in alleviating lesion-induced motor deficits in 6-OHDA rats. Furthermore, there was distinct functional brain reorganization compared to NSAE. The results are interpreted as implying that skilled aerobic exercise leads to enhanced compensatory motor control by the prefrontal cortex and the cerebellar–thalamocortical circuit. This greater understanding of the neural substrates of exercise-induced neurorehabilitation in Parkinsonian rats can crucially inform future exercise regimes seeking to maximize cognitive motor control for the treatment of PD.

Overall, the number of brain and mind disorders targeted by researchers, and the complexity and multiplicity of their methods, highlight the merits of animal models. Within these research efforts there is an assumption about the relationship of humans and other animals: the resemblance and continuity of nature. This is explored next in part four.

Continuity and Resemblance

Animal models are founded on the biological continuity of humans evolved from animals, and the numerous common characteristics, which enables models to be conceptually and practically implemented. Take for example amyotrophic lateral sclerosis (ALS) and Huntington's disease (HD), which are incapacitating neurodegenerative conditions for which there are no effective cures. Genetic determinants of the two diseases have been identified, shedding light on the neuropathological mechanisms and possibilities for therapeutic intervention (Islam, Kwak, Jung, & Kee, 2014). Models using mice, zebrafish, worms (C.elegans), and fruitflies (Drosophila) have been developed to study differing aspects of disease progression. Future inventions in genomic engineering technology could result in new and better models of human conditions. All this presumes resemblance and continuity.

Such resemblance is evident in reverse where the animal model responds to human-centered techniques. One is neuroimaging and *in vivo* study of disease models. This enables researchers to study the disease process, compensatory changes arising in response to the disease process, and to design and assess potential therapeutic interventions (Strome & Doudet, 2007). The *in vivo* imaging allows noninvasive studies in the same subjects longitudinally over time, with results that can be translated into the human situation. Positron emission tomography (PET) and/or magnetic resonance imaging (MRI) have been instrumental in basic science research and in the preclinical evaluation of potential therapies for these human disorders. Various dedicated small animal imaging scanners have been developed with high specificity, sensitivity, and resolution (Virdee et al., 2012; Waerzeggers, Monfared, Viel, Winkeler, & Jacobs, 2010).

Animal models for psychiatric diseases appear to have their strengths in modeling single symptoms or clusters of a few symptoms only (or what is termed endophenotypes), instead of the disorder in its full intricacy (Gass & Wotjak, 2013).

Cases include hyperlocomotion in attention deficit hyperactivity disorder (ADHD), anhedonia in depression, and decreased sociability in autism. But each of these may also be a characteristic of a schizophrenia model. This reflects the human context wherein a single symptom is not disease-specific (Gass & Wotjak, 2013). Then again, it is easier to identify the mechanisms beneath endophenotypes and their definition in relation to genetics, neurotransmitters, brain systems, and electrophysiological properties rather than studying a complex syndrome.

Some ask whether it is necessary for the animal mind to be as complex as the human mind due to common and related evolutionary pathways, e.g., behavioral responses to threats in other vertebrates (Van Dam & De Deyn, 2014). It is thought that while some aspects seem to be rather unique to the human brain, other attributes appear to be shared with more species than originally believed, such as the prefrontal cortex.

What does all this mean? The essential foundation is resemblances between animals and humans, offering hope that discoveries in animal models, even if only partial, can be translated into applicable knowledge for human settings and their possible treatments. Yet it could also be argued that the use of animal models partly undermines the case for human uniqueness because the reality of continuity and resemblances reminds humans of their animal lineage.

In another sense, the use of animals expresses our dependence on the animal kingdom. Hence, even if humans are unique, they are not autonomous among other animals. This is consistent with the first creation story, where humans created in the image of God are given dominion of the animal kingdom (Gen 1:26, 28); humans depend on animals for food and worship (Gen 9:3; Lev 11; Deut 14:3-21; Lev 3:1-2; Ex 12:1-27; Luke 2:24; Acts 10:9-16). In contemporary times, humans still depend on animals. Rare and complex illnesses contain uncharted scientific territories, and in certain cases animal models may be the only imaginable pathway to progress, e.g., Tourette syndrome (Cauchi & Tárnok, 2012).

Discontinuity and Uniqueness

Alongside the usefulness of human continuity with animals is the reality of discontinuity, and this has some surprisingly positive implications for human beings. In this fifth part we investigate two benefits: firstly, an ethical feature which upholds the dignity of humanity, and secondly, a feature where the dissimilarity of the human presents opportunities for discoveries.

Ethical Aspects

Inducing diseases and injuries recalls the horrors of Nazi human experimentation. Thus, many clinically relevant neurophysiological parameters can only be assessed through animal experiments, e.g., acute neurological injuries (Goldstein, McKee, & Stanton, 2014). These have disturbing effects across the whole of human life. Neurological injuries modelled include ischemia, subarachnoid hemorrhage, traumatic injury to the brain and spinal cord, and penetrating and blast injuries.

These lines of continuity with animals are reinforced in the human trials phase of the development of new therapies. Primate animal models are an essential step before reaching human clinical research due to anatomical, physiological, genetic, or behavioral similarities between the two species (Ghorayeb, Page, Gaillard, & Jaber, 2011). For genetic disorders and diseases affecting the CNS, animal models, despite the challenges, allow researchers to test the safety and efficacy of novel therapeutic agents in vivo to obtain greater knowledge of mechanisms of action for novel drugs and to gather fundamental data to make progress in therapies for human clinical trials (Gagliardi & Bunnell, 2009; Smith & Samala, 2014). That is, these animal experiments intend that pathology, physiology, and novel phenotypes can be understood in the living environment which is the most relevant setting (Van Dam & De Deyn, 2014).

Dissimilarity is potentially hopeful

Being different to animals may lower the prospects of finding suitable animal models, but it can have advantages. For example, two of the most common and devastating neurodegenerative conditions are Alzheimer's disease (AD) and Parkinson's disease (PD; Raslan & Kee, 2013). Pharmacological strategies aim at alleviating symptoms, and there is no effective cure or treatment. Yet, transgenic animal models are valuable tools in uncovering the molecular bases of neurodegenerative disorders and in understanding the mechanisms of how the diseases progress. In those cases where experiments investigate the absence of some mental conditions in animals, this fact exemplifies the uniqueness of the particular species. It is paradoxical that the scarcity of age-related neurodegenerative diseases in nonhuman animals could return some mechanistic insights into the etiology of the human diseases, e.g., the sources of resistance in nonhuman animals to age-related neurodegeneration (Jucker, 2010).

Similarly, investigators of axon regeneration after spinal cord injury in vivo observe how it is different from studying cancer or many neurodegenerative diseases. This is because axon regeneration is a process that does not happen typically in the adult mammalian CNS (Lee & Lee, 2013). As well as investigating the molecular and cellular processes that support axon regeneration, researchers also have to acquire knowledge of how to detect regenerating axons.

In short, the use of animals, although dissimilar to humans in some characteristics, has dual benefits: it presents opportunities for breakthroughs and supports the unique identity of humanity as it holds up the dignity of human beings. There are experiments that are inhuman and beneath the dignity of human subjects. Furthermore, another indicator of uniqueness is that we seek the causes of mental illnesses, possible cures, and effective treatments. In other words, only humans use reason and their minds to address problems of mind and disordered thinking and behaviors.

Doubts about Models

On the other hand, misgivings about animal models underscore human uniqueness and discontinuities with animals. In the final part, we examine some doubts about models of neurocognitive conditions and then focus on two areas: neurodegeneration and mind disturbances.

Modeling difficulties

The ideal animal model of a disease would parallel the full spectrum of its characteristics and a matching time course in the evolution of changes in patients (Pouladi, Morton, & Hayden, 2013). The model of a neurobehavioral disorder must be decomposed into elemental phenotypes that are observables or elements that can be observed and measured; measurables or elements that can be given quantitative or qualitative attributes; and testables or measurables which can be statistically evaluated to test, confirm, or falsify a hypothesis (van der Staay, Arndt, & Nordquist, 2009). This is a high standard.

Animal models are complicated (Bauer & Norwood, 2013); for example, consider modeling epilepsy in children. Since human epilepsy is understood as the appearance of multiple, spontaneous, and recurrent seizures, models involving the induction of acute seizure activity alone, without subsequent chronic seizures, ought to be viewed as models for seizures rather than epilepsy in particular (Auvin, Pineda, Shin, Gressens, & Mazarati, 2012). Animal models of epilepsy are beneficial to facilitate the study of pathophysiological mechanisms, the development and assessment of novel antiepileptic treatments, and the study of the significance of conditions which may be concomitant with epilepsy, such as cognitive effects and/or comorbidities. Researchers think it probable that no one animal model can authentically recapitulate all characteristics of human epilepsy.

Looking at failures, in attempting to account for unsuccessful animal models of stroke to predict clinical trial results, the most easily remedied outcomes would be if the failure was due to inadequate rigour in experimental design (O'Collins, Donnan, Macleod, & Howells, 2013). But the more challenging case is if the failure was due to deficient resemblance in the physiological processes of different species, maybe associated with scaling and vascular dissimilarities. Alternatively, reasons for slow progress may be methodological, such as a lack of agreement about what constitutes an appropriate animal model of blast traumatic brain injury and how to evaluate the validity of experimental results obtained from these models (Goldstein, McKee, & Stanton, 2014).

Similarly, the modeling of the mechanisms beneath primary headache disorders such as migraines is challenging because of limitations in testing the postulated hypotheses in humans (Erdener & Dalkara, 2014). Animal models of headache and migraine are mere approximations of reality based on the current limited understanding. Indeed, modeling for these disorders is more complex due to their unknown etiology. Likewise, although the human situation can be compared with mouse model results from small animal PET/SPECT and MR scanners, any true "humanized" animal models have yet to be fully developed. Therefore, interventional results obtained from mouse models will not necessarily be translated perfectly to the human realm (Waerzeggers et al., 2010).

The accumulating conceptual doubts and methodological problems invite deeper scrutiny; they point towards human uniqueness, especially when it comes to the human mind.

Translation Difficulties: Neurodegeneration

Age-related neurodegenerative diseases are largely human diseases (Jucker, 2010). Several higher-order animal species and aged nonhuman primates do demonstrate features similar to those of human brain aging; nevertheless, these animals normally do not freely develop the full human neuropathological or clinical phenotypes. Aged mammals, like aged, cognitively normal humans, can develop the neuropathological lesions that define human AD. But traditional laboratory animal species including flies, mice, or worms do not naturally develop the protein aggregates characteristic in AD, partly due to their relatively short life span (Baker & Götz, 2015).

Some disease symptoms, for instance, deficits in language-related functions in Huntington's disease (HD), may be problematic to replicate in animal models (Pouladi et al., 2013). The average age of HD onset is around 40 years old and experiments would require aging animal models for many decades, something impossible for most animal models in light of their short lifespan. At a minimum, animal models are right to reproduce particular characteristics of the disease in attempting to elucidate potential mechanisms and assess proposed therapies.

Foundational Difficulties: Mind disturbances

Modeling psychiatric disorders with collections of symptoms and comorbidity is a problematic, often impossible task (Lawrence & Cryan, 2014). The complex, spectrum nature of neuropsychiatric disorders and pathogenetic connections between varying disordered domains are increasingly recognized. Questions are asked about the unifying "core" pathogenesis that links the two phenotypes/domains together to comprise one, diagnosable and definable clinical disorder (Kalueff & Stewart, 2015). Some argue that existing animal models of psychiatric disease are not valid, that efforts to model syndromes are affected by nosology, that models of symptoms are anthropomorphic, and that models make unjustified presumptions about subjective experience (Rollin & Rollin, 2014).

For instance, the vast range of diagnostic symptoms which define bipolar illness and depression also manifests the problems for researchers to simulate these disorders in the laboratory (Cryan & Slattery, 2007). Moreover, depression and schizophrenia too are challenging to model because they are characterized by particular disturbances in functions which are unique to humans (Dean, 2009; Micale, Kucerova, & Sulcova, 2013). It is also contended that transgenic manipulations in a mouse cannot remake the scope of characteristics approximating schizophrenia or autistic disorders (Ferris, Febo, & Kulkarni, 2013).

There are also conceptual and logical difficulties in linking pathophysiology and animal behavior. Consider rodent marble burying behavior which represents a single-domain of OCD (Stewart & Kalueff, 2015). This model is questioned, as it may also be hampered in the overreaching and maybe erroneous assumption that this activity is underlined by a comparable psychological drive for order, cleanliness, and control which typifies clinical OCD. Furthermore, it is noted that a reduction in this behavior by antidepressants next assumes, correctly or incorrectly, that the neural expressions of clinical OCD and the rodent OCD-like phenotype are shared, and the reduction is caused by direct action on these circuits as opposed to decreasing motivational behavior.

Generally, cognitive and affective dysfunctions are manifested in the mind with symptoms internal and subjective in the sufferer, for example, dysphoria, hallucinations, guilt, and flashbacks (Stewart & Kalueff, 2015). These are humanly unique.

Discussion

Mental illness is a reality, even for Christians (Greene-McCreight, 2015; Weiss, 2011). The experience of sickness can be recognized as part of creation groaning, awaiting the redemption of our bodies (Rom 8:23). The sick are those in whom the works of God and the glory of God are revealed (John 9:3; John 11:4) because of him who took upon himself our infirmities (Matt 8:17). With these scriptures in mind, animal models of human illnesses are an apposite scientific setting to ponder the animal-human relationship. The thesis of evolutionary continuity of animals and humans, arising from Darwin's thinking, is the foundation for trusting in animal model research to further our knowledge of the human brain and mind disorders.

Conversely, there are substantive cases illustrating conceptual and methodological discontinuities which favor the perspective of human uniqueness. This lends support to the biblical account of humans alone being created in the image of God and who are the only creatures God expressly willed for his own sake, occupying a unique place at the apex of visible creation (Gen. 1:26; 2:20; Ps 8:6-7, Wisdom 9:2-3; ITC, 2004). The imago Dei notion counters a perceived imbalance in the integration of psychology and theology which concentrates much on what is wrong with human beings to the neglect of what is right about human beings (Entwistle & Moroney, 2011).

The imago notion is also dynamic. In the later part the twentieth century, the emerging consensus among theologians was that the uniqueness of the imago Dei was preeminently understood via types of relationality rather than static structures. Yet now theological viewpoints are shifting once more (King, 2016). Current trends indicate more expansion than narrowing, with theologians less inclined to restrict the imago Dei to one notion, e.g., relationality, but more likely to involve wider perspectives.

Certainly Jesus made some comparisons of humans with animals, teaching that humans are worth more than many sparrows (Lk 12:6-7) and "how much more valuable is a human being than a sheep" (Matt 12:12). This is evidenced in animal modeling. But uniqueness appears enigmatic. On the one hand, there is an implied uniqueness when experiments are performed on animals which cannot ethically be performed on humans due to the harm to humans that is envisaged. We need animal models to protect human dignity and achieve progress in understanding and treating human diseases. On the other hand, it reveals much-desirable solidarity with animals, based on common evolutionary lineages. We need close biological links for any prospect of success of the models and translation to the human situations.

Some are concerned for animal welfare. In rodent models of human disease, the pathophysiological changes are generally assessed using invasive techniques, often requiring the sacrificing of animals (Van Dam & De Deyn, 2014). Such methods also entail using a large number of animals to reach statistical significance, high costs including labor, and how subsequent or longitudinal studies are impossible in the same animal.

These utilitarian, reductive methodologies are necessary for experimental studies; however, with a biblical-theological outlook, there is also a call for respect for creation and stewardship. Animals have a status on their own. The death of sparrows is known to the Father (Matt 10:29; Lk 12:6), who feeds the birds and clothes the lilies in royal robes greater than Solomon's (Matt 6:26, 28-29). Some theologians go further, arguing that "*individual* animals and birds will be taken up into God" and that "the resurrection promise means a future for individual sparrows and kookaburras" (Edwards, 2006, p. 115 & p. 120; Wintz, 2009).

On the regulatory side, stewardship may not be among criteria for obtaining research ethics approval. But there are standards of care, e.g., animal models of acute neurological injury are challenging to design in a way which minimizes animal distress and pain and attains the experimental outcomes (Schantz, 2009). Protocols have to describe surgical procedures, anesthesia, postoperative care and monitoring, and chronic care of the animals following injury. Elsewhere it is recognized that environmental enrichment ought to be provided. Stimulating the natural environment of captive animals supports their psychological and behavioral well-being, promotes expression of species-specific behaviours, minimizes distress, and decreases the occurrence of abnormal behaviours (Coleman, Weed, & Schapiro, 2013).

Returning to Jesus, notwithstanding an appreciation for the created world, animals are used, eaten, and die while on earth. He gave permission for the legion of unclean spirits to enter about two thousand pigs, which charged down the steep bank into the sea and drowned (Mark 5:9-13). At the sea of Tiberius, after his resurrection Jesus cooks a meal of fish and bread for his disciples (Jn 21:1-14). In fact, Jesus only heals and raises human beings (Mk 5:21-24, 35-43; Jn 11). Some argue that to avoid attributing "higher" characteristics to distantly related animals because it is speciesist and anthropocentric may not be justified (Gosling, 2001). Persons can be thought of as ethical only in relation to a background of morality and values and they can be thought of as artistic only within the context of a cultural aesthetic (p. 70). These are human characteristics.

Conclusions

There is inviting potential in the integration of Christian theology, neurobiology, and psychology (Clinton & Sibcy, 2012). The God whom Jesus describes "does not purpose sickness but health. With whatever models we explain the phenomena of sickness and healing, this affirmation of God's will for human wholeness must stand at the center of a theology of healing informed by the Gospels" (Carroll, 1995, p. 139). This includes psychological health, and animal models make a contribution. The quest for useful models reveals their significance for the study of human beings and what it means to be human and also an animal. Current models are partial because humans are unique, and this includes the mind and its dysfunctions. Nonetheless, human beings are in debt to animal models because sometimes investigations and untried treatments are only ethically possible using animals. Both continuity and dissimilarity with other animals have pioneering potential.

To conclude, we recommend another biblical text apt for an animal models approach to human uniqueness. Traditionally the imago Dei (Gen 1:26) from the first creation account in the book of Genesis (Gen 1-2:4a), and the image of Christ (Rom 8:29), are central scriptural passages. However, there is also the second creation account in the first book of the Bible (Gen 2:4-25), specifically the creation of the man, followed by the animals, and finally the exclusive creation of the woman. Just as there is a "measure of correspondence between the human being and the animals, as both were formed 'from the ground' (cf. 2:7 and 2:19)" (Wilfong, 1988, p. 59), so too there is some human-animal resemblance in animal models.

In Genesis, God brought animals to the man to see what he would call them, but "for the man there was not found a helper fit for him" (Gen 2:20, RSV). The man is forced to "recognize his fundamental difference from the animals-they are not really helpers fit for him" (Naidoff, 1978, p. 5-6). Additionally, contrasting the customary translation of "helper" or "helpmate" suitable for man, an alternative is "a power equal to or corresponding to man" (Freedman, 1983, p. 57); so she may be not his helper, but his partner. We see this translated more recently as, "there was not found a helper as his partner" (Gen 2:20, NRSV).

The sense of the Hebrew word for "suitable" is not that of subservience but of prominence or complementarity (Bergant, 2013). While both man and the animals are of the earth, the animals do not wholly correspond to the man. The narrator of Genesis teaches the equality of the human sexes as "destined companions" (Bledstein, 1977). Naturally, the chapters of Genesis 1-3 can be interpreted variously, for example, as a patriarchal text to be resisted and as an egalitarian text to be recovered from after a long history of distorted reading (Gossai, 2003; Watson, 1992). But an interpretation of human to human relationship is plausible.

Still, the scripture also highlights the inadequacy of the animals named by the man. It requires, "bone of my bones and flesh of my flesh" (Gen 2:23). The human needs another human. All other living creatures, that is, the animals, cannot approach the woman as corresponding to the man. This seems to reflect how there is no perfect animal model, and all models have degrees of applicability in comparison to the human being who is unique.

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