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Review

The neurobiology of repetitive behavior: . . .and men

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ABSTRACT

In young, typically developing children, repetitive behavior similar to that in certain neuropsychiatric syndromes is common. Whereas this behavior is adaptive in typical development, in many disorders it forms a core component of symptoms and causes prominent impairment in the daily life of affected individuals. Understanding the neurobiological mechanisms involved repetitive behavior will improve our understanding of the pathogenesis of developmental neuropsychiatric disorders, stimulating novel approaches to these conditions. However, studies on the neurobiology of human repetitive behavior have often been limited to distinct conditions and generalization has been hindered by inconsistent terminology. In this paper, we synthesize the 'disorder-driven' literature, building on findings from fundamental animal research and translational models. These findings suggest a model for classifying repetitive behavior by its neuroanatomical correlates.

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1. Introduction

During early development, children engage in a significant amount of ritualistic, repetitive, and compulsive-like activity that is part of the normal behavioral repertoire (Evans et al., 1997). This developmental phase is characterized by perfectionism, preoccupation with ordering objects just-so, attachment to a favorite object, concerns about dirt and cleanliness, preferred household routines, actions repeated over and over or a specific number of times, rituals for eating, awareness of minute details in the home, hoarding, and bedtime rituals (Boyer and Liénard, 2006). It is thought that such ritualization and compulsions may serve to ward off anxiety (Evans et al., 1997) and may represent a mechanism for organizing, accommodating to and eventually mastering the environment (Gesell et al., 1974). In other words: childhood

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rituals are hypothesized to be a way to calibrate the system (Boyer and Liénard, 2006). As such, early theories of child development include hypotheses of an adaptive role for repetitive behavior (Gesell, 1928; Piaget, 1952). The wide variety of ritualistic, repetitive, stereotyped and compulsive behavior that can be observed in typically developing young children has striking similarities to the ritualistic and compulsive behavior observed in psychiatric disorders such as obsessive–compulsive disorder (OCD), Gilles de la Tourette syndrome and autism spectrum disorders (ASD) (Evans et al., 1997; Boyer and Liénard, 2006). Clearly, the adaptive element of this behavior is lost in such neuropsychiatric conditions, where they cause prominent impairment to the daily life of affected individuals.

Repetitive behavior was recognized as a common characteristic of mental illness from early on. In a historical overview of repetitive behavior in schizophrenia, Frith and Done (1990) quote from 18th century publications: "We see also mad people, in whom phancy reigns, to run upon some action, as reading, or knitting of straws, without variation" (Grew, 1701) and "When lunatics attempt to write, there is a perpetual recurrence of one or two favorite ideas, [...] patients will run their ideas in the very same track for many weeks together..." (Ferrier, 1795). Later, Kahlbaum (1874) described repetitive behavior in his work on catatonia, as did Kraepelin (1899) in his characterization of dementia praecox and Asperger (1944) and Kanner (1943) in the first reports of autism spectrum disorders. In modern-day neuropsychiatry, the term repetitive behavior is an umbrella term, used to refer to broad and often disparate classes of behavior linked by repetition, rigidity, invariance, and inappropriateness and observed in a wide array of developmental, psychiatric and neurological disorders (Turner, 1999). Across disorders, many varieties of behavior are included in this term, including stereotypies, rituals, compulsive and obsessive behavior, circumscribed interests, echolalia, insisting on sameness, tics, perseveration and self-stimulation or self-injury. Even when only one particular disorder, e.g. autism, is considered, there is little consensus in the terminology used among clinicians (Bodfish et al., 2000). Furthermore, it has been argued that the use of categorization such as the often-used subdivision into lower level (motor) and higher level (cognitive) repetitive behavior may further obscure key differences between different forms of repetitive behavior, as such broad categories may oversimplify by grouping together relatively heterogeneous behaviors (Turner, 1999). In other cases, categorization may falsely suggest differentiation between behaviors, for example, when it arises from a clinical need, whereas the distinction may not be so clear behaviorally or biologically (Garner, 2006). In sum, difficulties in classification and quantification complicate systematic research of repetitive behavior in distinct neuropsychiatric disorder.

1.1. Scope of this review

The occurrence of similar repetitive behaviors in diverse neuropsychiatric disorders, as well as in certain phases of typical development, raises a key question: to what extent are these phenomenologically related behaviors mediated by overlapping versus distinct neural substrates? Understanding the neural networks involved in repetitive behavior and related problems will improve insight into the pathogenesis of neuropsychiatric and developmental disorders. This in turn will stimulate novel approaches in thinking about this behavior, encouraging new therapeutic initiatives. In this paper we aim to investigate the neurobiological systems associated with various clinical manifestations of repetitive behavior. The phenomenology and neurobiology of human repetitive behavior has been studied from many different perspectives, but has often been limited to distinct conditions in which these phenomena occur. In this review, we aim to synthesize findings across disparate syndromes, while building on findings from fundamental animal research and translational models that are discussed in a separate review (Langen et al., 2010). We have separated the discussion of animal and human work, as translating findings from animal work to the human field is not easy, complicating comparisons of the neurobiological mechanisms of animal and human repetitive behavior.

In this paper, we do not include cognitive findings or (neuro)psychological models of repetitive behavior. Cognitive models have provided valuable guiding hypotheses for how neurobiological circuitry might be disturbed in repetitive behavior, as well as insights into how different facets of repetitive behavior relate to each other. However, we chose not to include the 'in-between step' of cognitive models to avoid losing focus in this paper, but rather have restricted ourselves to the neurobiological data available.

The structure of this paper is as follows: first we briefly discuss the anatomy of the corticostriatal circuits that are central to repetitive behavior. Next, we discuss neurobiological findings in neurodevelopmental disorders that involve repetitive behavior. Rather than to discuss all clinical conditions where repetitive behavior is seen (e.g. addiction, schizophrenia, trichotillomania, anorexia, hypochondria, body dysmorphic disorder), we have chosen to focus on three neurodevelopmental disorders that include repetitive behavior in their *core* symptoms and have an extensive literature on this topic available: Gilles de la Tourette syndrome (Section 3), obsessive–compulsive disorder (Section 4) and autism spectrum disorders (Section 5). In Section 6, we discuss research on Parkinson's disease (PD) and Huntington's disease (HD). Finally, in Section 7, we synthesize the findings and present a functional and neuroanatomical classification of human repetitive behavior, as well as a suggestion for how these behaviors may group together in symptom clusters as seen in various psychiatric disorders.

2. Anatomy of the corticostriatal circuits

The corticostriatal circuits are multiple parallel, segregated feedback circuits with outputs from striatum targeting primary motor areas, and specific pre-motor and prefrontal cortical areas. They are typically grouped in (1) the sensorimotor circuit, (2) the associative or cognitive circuit and (3) the limbic circuit. These circuits innervate the motor and pre-motor cortex; the dorsolateral prefrontal cortex; and the lateral orbitofrontal and anterior cingulate cortex, respectively. The primary function of the corticostriatal circuits is to control and select goal-directed motor, cognitive and motivational behavior. Disruption of co-ordinated function within the basal ganglia or between striatal and forebrain structures results in changes in behavior, often including repetitive or stereotyped behavior: feedback to frontocortical areas becomes dysfunctional, resulting in inadequate repetition of a behavioral set, inability to switch to other behavior, or facilitation of inappropriate behavioral sets. More detailed information on corticostriatal anatomy and a discussion on how this circuitry is thought to be involved in repetitive behavior in animals is presented in a separate paper (Langen et al., 2010).

3. Gilles de la Tourette syndrome

Gilles de la Tourette syndrome (TS) is a genetically based, childhood-onset neurodevelopmental disorder that is defined by the presence of phonic and motor tics (Makki et al., 2008) (see Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) (American Psychiatric Association, 2000) for diagnostic criteria). These tics characteristically