Neuroscience Research 102 (2016) 39–46

Contents lists available at ScienceDirect

Neuroscience Research

journal homepage: www.elsevier.com/locate/neures

Review Article

The course of neuropsychological impairment and brain structure abnormalities in psychotic disorders

Neil D. Woodward *

Department of Psychiatry, Vanderbilt University School of Medicine, Nashville, TN, United States

ARTICLE INFO

Article history:
Received 15 April 2014
Received in revised form 7 August 2014
Accepted 13 August 2014
Available online 22 August 2014

Keywords:
Schizophrenia
Psychotic bipolar disorder
Trajectory
Neuropsychology
Neuroimaging

ABSTRACT

Neuropsychological impairment and abnormalities in brain structure are commonly observed in psychotic disorders, including schizophrenia and bipolar disorder. Shared deficits in neuropsychological functioning and abnormalities in brain structure suggest overlapping neuropathology between schizophrenia and bipolar disorder which has important implications for psychiatric nosology, treatment, and our understanding of the etiology of psychotic illnesses. However, the emergence and trajectory of brain dysfunction in psychotic disorders is less well understood. Differences in the course and progression of neuropsychological impairment and brain abnormalities among psychotic disorders may point to unique neuropathological processes. This article reviews the course of neuropsychological impairment and brain structure abnormalities in schizophrenia and bipolar disorder.

Contents

1. Introduction

Psychotic disorders, including schizophrenia (SCZ) and bipolar disorder (BD) with psychotic features (i.e. psychotic BD), are often chronic, debilitating illnesses that result in lifelong limitations in psychosocial functioning, significant caregiver burden, and substantial economic costs (Wu et al., 2005; Meltzer, 1999; Hegarty et al., 1994; Green et al., 2000; Conus et al., 2014; Sanchez-Moreno et al., 2009). In addition to similarities in clinical symptoms and functional outcome, there is also considerable overlap between SCZ and BD in cognitive impairment, brain structure abnormalities, and genetic vulnerability (Maier et al., 2006). However, emerging evidence indicates there are also differences between disorders in the severity and course of brain dysfunction (Lewandowski et al., 2011). Uncovering similarities and differences between disorders will have important implications for psychiatric nosology, clinical

* Correspondence to: Psychotic Disorders Program & Center for Cognitive Medicine, Vanderbilt Psychiatric Hospital, Suite 3057, 1601 23rd Ave. S., Nashville, TN 37212, United States. Tel.: +1 615 322 8361; fax: +1 615 936 3563.
E-mail address: neil.woodward@vanderbilt.edu

http://dx.doi.org/10.1016/j.neures.2014.08.006
0168-0102/

management and treatment, and our understanding of the etiology of psychotic illnesses.

This article reviews the trajectories of neuropsychological impairment and brain structure abnormalities in SCZ and BD, primarily psychotic BD whenever possible, focusing in particular on the pre-morbid, early stage, and chronic stages of the disorders. Particular attention is paid to seminal papers and relevant meta-analyses and qualitative reviews. The article begins with a brief overview of normal cognitive and brain development, focusing primarily on the development of cognitive abilities disrupted in psychotic illnesses and macro-level changes in brain structure.

2. Typical neuropsychological and brain development

2.1. Defining neuropsychological phenotypes

The terms "cognition" and "neuropsychology" subsume a diverse array of constructs and abilities that are measured to varying degrees of precision using a wide range of tests. Before reviewing the development of neuropsychological functioning, it is necessary to define the scope of our review by organizing the spectrum of cognitive abilities that are typically assessed in clinical neuropsychology. Even within the field of clinical neuropsychology, it can be challenging to come up with a parsimonious way of classifying the large number of commonly used tests. Quantitative factor analytic methods have a rich history in psychology and have proven very useful for grouping tests into empirically derived cognitive domains. For example, in the first step toward developing a common set of clinical neuropsychological tests to assess cognitive change in treatment trials in SCZ, the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) initiative reviewed all empirical factor analysis studies of cognitive function in SCZ (Nuechterlein et al., 2004). The results of this effort revealed seven domains of cognitive function that included Verbal Comprehension, Processing Speed, Attention/Vigilance, Working Memory, Verbal Learning and Memory, Visual Learning and Memory, and Reasoning and Problem Solving. We focus our review on these cognitive domains. It should be noted however that most domains of cognitive function identified in factor analysis studies are not completely independent as they correlate with one another to some extent and are usually related to overall intellectual abilities to some degree (August et al., 2012; Tulsky and Price, 2003). For example, verbal comprehension, working memory, and processing speed, although separate factors, are often subsumed under intellectual abilities (Wechsler, 1997). While the multifactorial nature of many neuropsychological tests compared to experimental cognitive approaches, which focus on isolating relatively specific cognitive abilities, is a drawback, the rigorous standardization they have undergone and abundant data on the developmental trajectories of these constructs in healthy subjects are distinct advantages.

2.2. Developmental neuropsychology

Global cognitive functioning, as measured using standardized tests of intelligence for example, continues to develop well into adulthood (Wechsler, 1997). However, there are marked differences in the development, and subsequent decline with aging, of the various factors comprising intelligence (Wechsler, 1997). For instance, so-called "crystallized" abilities reflecting general knowledge and verbal comprehension show a protracted development, peaking in middle age, and remaining relatively stable into old age. In contrast, fluid reasoning and mental processing speed peak relatively early, in adolescence, and decline in a linear fashion throughout adulthood and into old age (Tulsky et al., 2003). Similarly, new learning and memory for verbal and visual material peaks in late childhood/early adolescence, then decreases linearly from early adulthood through old age (Tulsky et al., 2003).

The developmental course of executive cognitive abilities, including working memory, has attracted considerable attention given the prominent role these abilities play in shaping behavior and psychopathology (Salloway et al., 2001). The term 'executive functioning' is a general descriptor that subsumes a number of conceptually complicated processes such as volition, planning and reasoning, and goal-directed behavior (Lezak, 1995). Measuring these abilities with standardized tests is challenging as these concepts can be difficult to operationally define and many tests of executive functioning are multifactorial. That is, they assess more than one ability. Attempts to fractionate executive functions have generally revealed several dissociable factors, including working memory, inhibition/resistance to distraction, and mental set shifting (Miyake et al., 2000). The development of these abilities is protracted. Mental set-shifting, as commonly assessed with the Wisconsin Card Sorting test for example, continues to improve until about age 20 and remains relatively stable until about the sixth decade of life (Heaton et al., 1993). Working memory on the other hand, reaches adult levels in adolescence then, starting in the third decade of life, begins to decline with the decline accelerating around the 7th decade of life (Tulsky et al., 2003).

2.3. Brain development

Brain development has received considerable attention in the neuroimaging community. Several key findings, focusing on studies from early childhood through adulthood are reviewed here. During normal brain development, total brain volume (TBV) increases rapidly in the first 5–6 years of life in parallel with intracranial volume (ICV) (Kamdar et al., 2009; Sgouros et al., 1999). Then, starting around age 12, TBV and ICV begin to diverge; TBV gradually declines throughout adulthood and ICV remains relatively static (Courchesne et al., 2000; Lenroot et al., 2007). This divergence may have important implications for understanding pathological processes and, possibly, the timing of the onset of neuropathological abnormalities. Specifically, ICV can be considered a proxy of early brain development and discrepancies between TBV and ICV an indicator of later neurodegenerative changes and age-related atrophy (Davis and Wright, 1977). The developmental trajectories of the two tissue classes comprising TBV, gray and white matter, vary. Gray matter volume increases rapidly, peaking between 8 and 12 years of age, then gradually declines over time (Lenroot et al., 2007; Good et al., 2001). White matter on the other hand increases from childhood throughout early adulthood and remains relatively stable thereafter (Lenroot et al., 2007; Good et al., 2001).

Just as the trajectories of overall tissue volumes differ, the developmental trajectories of specific brain structures also varies. Frontal, including anterior cingulate cortex and dorsolateral prefrontal cortex (PFC), and temporal lobes are the last to reach adult levels when it comes to gray matter volume and cortical thickness, which is consistent with evidence that synaptic pruning in these regions extends into early adulthood (Giedd, 2004; Shaw et al., 2008). Frontal lobe white matter is also the last to reach full maturity (Reiss et al., 1996). The prolonged development of the frontal lobes presumably reflects the extended development of the 'higher' cognitive functions supported by this region (Lourenco and Casey, 2013).

3. Neuropsychological impairment in psychotic disorders

Neuropsychological impairment is well-established in psychotic illnesses (Heinrichs and Zakzanis, 1998). However, the