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# Thought disorder and nucleus accumbens in childhood: a structural MRI study

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**Abstract**

Thought disorder has been described as a hallmark feature in both adult and childhood-onset schizophrenia. The nucleus accumbens (NAc) has been repeatedly proposed as a critical station for modulating gating of information flow and processing of information within the thalamocortical circuitry. The aim of the present study was to investigate the relationship of thought disorder measures, which were administered to 12 children with schizophrenia and 15 healthy age-matched controls, and NAc volumes obtained from high-resolution volumetric magnetic resonance imaging analyses. The propensity for specific thought disorder features was significantly related to NAc volumes, despite no statistically significant differences in the NAc volumes of children with schizophrenia and normal children. Smaller left NAc volumes were significantly related to poor on-line revision of linguistic errors in word choice, syntax and reference. On the other hand, underuse of on-line repair of errors in planning and organizing thinking was significantly associated with decreased right NAc volumes. The results of this pilot study suggest that the NAc is implicated in specific thought patterns of childhood. They also suggest that subcortical function in the NAc might reflect hemispheric specialization patterns with left lateralization for revision of linguistic errors and right lateralization for repair strategies involved in the organization of thinking.


*Keywords:* Schizophrenia; Thought disorder; Ventral striatum; Childhood; Lateralization; Morphometry; Neuroimaging

## 1. Introduction

Thought disorder is regarded as a core feature of adult schizophrenia (Andreasen and Grove, 1986; Holzman et al., 1986; Docherty et al., 2000; Titone et al., 2000) and childhood-onset schizophrenia (Caplan, 1994; Caplan et al., 2000), yet little is known about its pathophysiology. Children with schizophrenia exhibit illogical thinking and loose associations, impaired use of linguistic devices to connect ideas and to make reference to objects and events (i.e. cohesion), and poor on-

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line monitoring and repair of communication breakdown (Caplan et al., 1996, 2000).

Similar to children with schizophrenia, young normal children have high illogical thinking scores and loose associations, together with underuse (i.e. low frequency) of cohesion and repair devices. In healthy young children these features are part of a normal developmental process. Indeed, whereas loose associations are not found in the conversation of normal children above age 7, normal children use illogical thinking, albeit at significantly lower levels than children with schizophrenia, through age 10 years (Caplan et al., 2000). Similarly, with age, normal children increase their use of cohesion and self-initiated repair devices during conversation (Caplan et al., 1996, 2000; Caplan and Dapretto, 2001).

In addition to schizophrenia, thought disorder has been found in children with a wide variety of neurobehavioral disorders, such as schizotypal personality disorder (Caplan et al., 1990a; Caplan and Guthrie, 1992), attention-deficit hyperactivity disorder (Caplan et al., 2001b), high functioning autism (Arbelle et al., 1995), complex partial seizure disorder (Caplan et al., 2001a, 2002) and primary generalized epilepsy with absence (Caplan et al., 2002). In children with schizophrenia and in children with other neurobehavioral disorders, the younger peers had significantly more thought disorder than the older ones. Thus, thought disorder appears to reflect the impact of these disorders on the on-going acquisition of children's higher-level linguistic skills and their ability to organize and formulate their thoughts.

Structural (Shenton et al., 1992; Rajarethinam et al., 2001; Matsumoto et al., 2001) and functional magnetic resonance imaging (MRI) studies in adult schizophrenia (McGuire et al., 1998; Kircher et al., 2001, 2002) have linked thought disorder with several brain abnormalities, particularly in the superior temporal gyri and the inferior frontal gyri, although there has been some inconsistency across studies. Furthermore, information processing and thought disturbance measured in close temporal proximity provide strong evidence that sensorimotor gating deficits correlate highly with measures of perceptual and reasoning disturbances in adult schizophrenia (Perry et al., 1999). Impaired information processing has also been associated with the clinical manifestations of thought disorder in children with schizophrenia (Caplan et al., 1990b).

The nucleus accumbens (NAc) and its related circuits appear to be specifically implicated in the attentional and cognitive deficits related to dysfunction in the processing of information (Grace, 2000; Heimer, 2000; Ballmaier et al., 2002). The NAc receives glutamatergic afferent input from brain regions presumably involved in the pathogenesis of schizophrenia, including the prefrontal cortex, the hippocampus and the amygdala (Beckstaed, 1979; Sesack et al., 1989; O'Donnell and Grace, 1995). NAc neurons send projections to the ventral pallidum, which in turn sends a major projection to the mediodorsal nucleus of the thalamus, which is interconnected with the prefrontal cortex and regulates its activity (Young et al., 1984; Lavin and Grace, 1994). There is evidence that both hippocampal input and amygdalar input to the NAc affect its capability of processing and transferring information from prefrontal afferents to the ventral pallidum and the thalamocortical system (Grace, 2000).

In the normally functioning brain, the balance of inputs from cortical and medial temporal structures to the NAc is used to prepare, initiate and prevent selected behaviors, as well as maintain a coherent stream of goal-oriented activity (Rolls, 1994). As such, the NAc acts as a subcortical integrative hub, connecting forebrain and limbic structures that control gating of information flow and processing (Swerdlow and Geyer, 1998).

Additionally, there is evidence that prefrontal cortex (Luke et al., 2002; Romanski and Goldman-Rakic, 2002), hippocampus (Holdstock et al., 2002; Shergill et al., 2002) and thalamus (Johnson and Ojemann, 2000; Murdoch, 2001) may play a role in cortical networks related to speech and language processing. Given the extensive anatomic connections between these regions and the NAc, it is not unreasonable to hypothesize that structural abnormalities of the NAc might also contribute to integrating basic and higher level linguistic and cognitive functions involved in coherent and cohesive organization of thinking and processing of discourse.