Several lines of evidence suggest that cognitive control deficits may be regarded as a connecting link between reported impairments in different cognitive domains of schizophrenia. However, the precise interplay within the fronto-cingulo-thalamic network known to be involved in cognitive control processes and its structural correlates has only been sparsely investigated in schizophrenia. The present multimodal study was therefore designed to model cognitive control processes within the fronto-cingulo-thalamic network. A disruption in effective connectivity in patients in association with abnormal white matter (WM) structure in this network was hypothesized. 36 patients with schizophrenia and 36 healthy subjects participated in the present study. Using functional magnetic resonance imaging (fMRI) a Stroop task was applied in an event-related design. For modeling effective connectivity dynamic causal modeling (DCM) was used. Voxel-based morphometry (VBM) was employed to study WM abnormalities. In the fMRI analysis, the patients demonstrated a significantly decreased BOLD signal in the fronto-cingulo-thalamic network. In the DCM analysis, a significantly decreased bilateral endogenous connectivity between the mediodorsal thalamus (MD) and the anterior
cingulate cortex (ACC) was detected in patients in comparison to healthy controls, which was negatively correlated with the Stroop interference score. Furthermore, an increased endogenous connectivity between the right DLPFC and the right MD was observed in the patients. WM volume decreases were observed in the patients in the MD and the frontal cortex. The present results provide strong evidence for the notion that an abnormal fronto-cingulo-thalamic effective connectivity may represent the basis of cognitive control deficits in schizophrenia. Moreover, the data indicate that disrupted white matter connectivity in the mediodorsal thalamus and in the fronto-cingulo-thalamic network may constitute the determining cause of fronto-cingulo-thalamic dysconnectivity.