Apathy in Schizophrenia: Reduced Frontal Lobe Volume and Neuropsychological Deficits

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Objective: Apathy is a common negative symptom in schizophrenia. The authors investigated neuropsychological performance and regional brain volumes in schizophrenia patients with high versus low levels of apathy.

Method: Schizophrenia patients with low apathy levels (N=18) and high apathy levels (N=20) and 12 healthy comparison subjects completed neuropsychological testing as well as magnetic resonance imaging scanning to obtain lobar volumes after total intracranial volume was controlled.

Results: The high apathy group scored lower than comparison subjects on rapid visuomotor sequencing and verbal learning/recall. The high apathy group had lower performance IQ scores than the low apathy and comparison groups. Only the high apathy group showed significantly reduced bilateral frontal lobe volumes relative to comparison subjects; both schizophrenia patient groups showed bilateral temporal lobe volume reductions.

Conclusions: The present findings are consistent with studies in other disorders showing frontal lobe involvement in apathy.

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and 15 men, three women), or chlorpromazine equivalents (mean=496.3 [SD=351.7] and 421.6 mg [SD=293.5]). They also had similar BPRS total scores (mean=44.5 [SD=11.2] and 47.2 [SD=6.6]) and BPRS depression scores (mean=1.9 [SD=1.3] and 1.8 [SD=1.3]). The high apathy group had higher scores than did the low apathy group on the SAPS (mean=10.5 [SD=3.3] versus 7.0 [SD=4.6]; t=2.69, df=36, p=0.01) and SANS (mean=12.3 [SD=3.0] versus 5.8 [SD=3.3]; t=6.38, df=36, p=0.001). Healthy subjects were comparable in age (mean=31.7, SD=8.7), WRAT reading score (mean=102.4, SD=12.5), handedness (all were right-handed) and sex (11 men, one woman).

A MANOVA that included all neuropsychological test scores was significant (F=1.80, df=24, 72, p=0.03). Further analyses revealed that the high apathy group scored lower than comparison subjects on Trail Making Test Part A (F=4.10, df=2, 47, p=0.02) and Part B (F=3.97, df=2, 47, p=0.03) as well as the California Verbal Learning Test measures of learning (F=5.95, df=2, 47, p=0.005) and delayed recall (F=3.59, df=2, 47, p=0.04). The high apathy group also had a lower performance IQ score than the low apathy and comparison groups (F=3.26, df=2, 47, p=0.04).

The high but not low apathy group showed significantly reduced adjusted volumes relative to the healthy comparison subjects in the right frontal lobe (high apathy group: mean=195.7 [SD=19.6]; comparison subjects: mean=215.8 [SD=17.8]) (F=5.53, df=2, 47, p=0.007) and left frontal lobe (high apathy group: mean=184.8 [SD=19.9]; comparison subjects: mean=200.4 [SD=16.2]) (F=3.48, df=2, 47, p=0.04) (Figure 1). The high apathy and low apathy schizophrenia patient groups both had significantly smaller adjusted volumes than did the comparison subjects in the right temporal lobe (mean=107.5 [SD=6.0] and 111.7 [SD=6.2] versus 118.5 [SD=6.5], respectively; F=11.71, df=2, 47, p=0.001) and left temporal lobe (mean=107.2 [SD=5.6] and 109.2 [SD=8.3] versus 118.8 [SD=8.0]; F=10.20, df=2, 47, p=0.001). A similar but nonsignificant difference was noted for adjusted left and right parietal lobe volumes. SAPS score did not correlate with any of the dependent measures in the combined patient group.

Discussion

In this study, schizophrenia patients with high levels of apathy had poorer visuomotor sequencing and verbal learning and memory, lower performance IQ, and bilateral frontal lobe volume reductions. In contrast, both patient groups performed more poorly than comparison subjects on psychomotor speed and naming, had lower verbal and full-scale IQ scores, and showed bilateral temporal lobe volume reduction, consistent with other studies of schizophrenia (13). Lack of effort during testing is unlikely to account for these findings, since a generalized cognitive deficit was not found in the high relative to low apathy group. Findings were unrelated to level of depression or overall severity of psychopathology. However, we cannot rule out the possibility that differences in overall negative and positive effects of apathy are relevant to different cognitive domains.
symptom severity may have contributed to the present findings. With this caveat, findings are generally consistent with studies of neurological disorders showing frontal-subcortical or right hemisphere involvement in apathy (2).

Impaired sequencing ability in our high apathy group is consistent with prefrontal-thalamus-basal ganglia circuitry involvement in sequencing (14), the finding of reduced frontal lobe volume in this group, and neuroimaging evidence of disruption of this circuitry in patients with schizophrenia with prominent negative symptoms (10, 15). The lower performance IQ in the high apathy patients is consistent with studies showing a relationship between right hemisphere integrity and negative symptoms in schizophrenia (15, 16). The specific cognitive processes through which frontal-subcortical or right hemisphere dysfunction may lead to apathy in schizophrenia remain to be elucidated. Studies of neurological patients have implicated impaired allocation of attention to novel stimuli (17, 18) or disruption of the ability to create internal references that permit selection of appropriate responses to incoming stimuli (19) as the basis for apathy. Studies of these cognitive processes in relation to apathy in schizophrenia would likely be informative.

In conclusion, results of this preliminary study suggest that apathy in schizophrenia is associated with a frontal-subcortical or right hemisphere abnormality. Further studies with larger sample sizes and more comprehensive neuropsychological test batteries would be helpful in determining the generalizability of these findings. Finally, further evaluation of the structural integrity of frontal lobe subregions may be informative, given that the cingulate gyrus has been particularly associated with apathy in other populations.

References


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