Perceptual skill and brain physiology in subgroups of persons with schizophrenia

Persons with schizophrenia (SZ) are often noted to have difficulties making judgments associated with categories or abstractions. It is not routinely appreciated that some people with this syndrome are unable to make simple perceptual classifications. In recent studies by our group,[1,2] the behavioral impact of small frequency differences and the brain response to those differences were studied in volunteers with SZ and healthy normal volunteers (NV). From these investigations, we learned that SZ volunteers are sensitive to small changes in tone frequency in ways that NVs are not. This observation has also been reported and extended by Javitt and his colleagues.[3,4] Some SZ volunteers are unusually sensitive to simple tone frequency differences. This report describes our findings in a group of 18 SZ inpatients. A more detailed discussion of these data has been published elsewhere.[2]

It is not understood why persons with SZ are unable to recognize the physical differences between similar objects or stimuli when they are presented sequentially over time. Deficits in attention and working memory in this group are being extensively explored. One approach to this problem is derived from stimuli that are either extremely similar or extremely different in their psychophysical characteristics. In this investigation, we studied 18 SZ volunteers who were admitted to the Residential Research Unit of the Maryland Psychiatric Research Center. Twelve NVs were recruited from the community by newspaper advertisements. The SZ participants were withdrawn from antipsychotic medication prior to their brain-imaging studies. Both groups were given extensive practice on a "forced-choice" tone recognition task. Briefly, this task consists of recognizing a tone that is presented for a short time interval (100 ms). The volunteer is given 2 s in which to decide

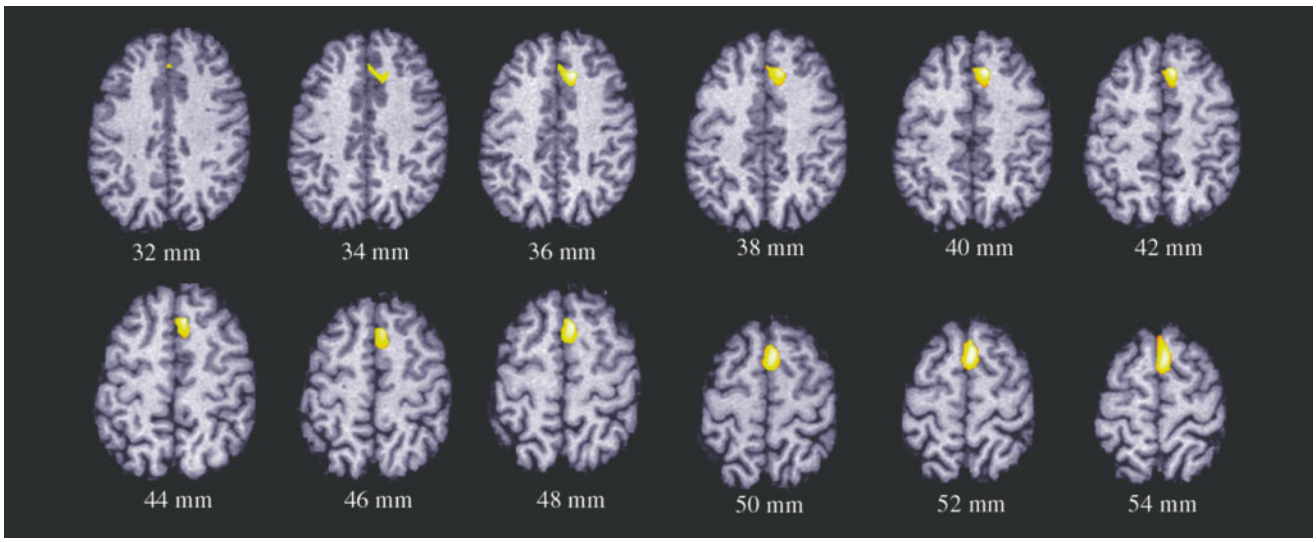

Figure 1. Healthy volunteers minus unmedicated schizophrenia (SZ) patients: tone decision minus motor control at comparable performance. Healthy comparison subjects exhibit significantly greater neural activity in the anterior cingulate cortex when they shift from a low-demand to a high-demand task. The increased likelihood of error is associated with a shift in activity in the group of healthy volunteers (NV), but not in the group with SZ, in spite of the matched performance in the two populations.

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whether the tone is relatively "high" or "low" in frequency with respect to the block of stimuli provided. Only two frequencies are presented within a blocked set of trials. During training, the subjects practiced on blocks of trials in which the tones were far apart in frequency on some occasions and close together in frequency in other sets. Through repetition, all NVs and most SZ participants were able to dramatically improve their accuracy in making difficult distinctions.

Following training on 2000 to 3000 trials, spread out over a 2- to 3-week training phase, the participants engaged in positron emission tomography (PET) studies. Regional cerebral blood flow (using bolus oxygen-15) was measured in participants while engaged in each of three different behavioral conditions: resting, sensory-motor control, and decision. During the resting condition, no tones were presented; during the sensory-motor task, subjects alternated their hands used to press buttons in time with the tones being presented; and during the decision task, subjects were expected to make recognition decisions about the stimuli.

Behavioral results of these studies revealed that SZ persons were extremely diverse in their ability to improve with practice. One third of the SZ participants were unable to increase accuracy or increase speed with practice. That group was also unable to make accurate judgments about tones that were similar. Only if the tones were more than 10% different could they distinguish the differences accurately. In marked contrast, NVs were able to make 80% accurate judgments when stimuli differed by little more than 1%; the majority of the SZ volunteers performed well (80% accuracy) when stimuli were about 2% different.

Physiologically, the SZ participants who were unable to improve with learning exhibited marked cingulate cortex abnormalities *(Figures 1 and 2)*. They were unable to increase cingulate activity when shifting from the sensory-motor task to the decision condition. This impaired SZ group also exhibited significantly reduced activity in the right premotor cortex.

Large differences in tones permitted the highly impaired group to make accurate decisions, but this group was unable to improve with practice. The marked inactivity in this group's anterior cingulate and premotor regions may account for their inability to gain with training. The cingulate appears to be fundamentally important for error recognition and correction.[5-8] The right premotor region is similarly vital for attention and working memory functions.[9-12]

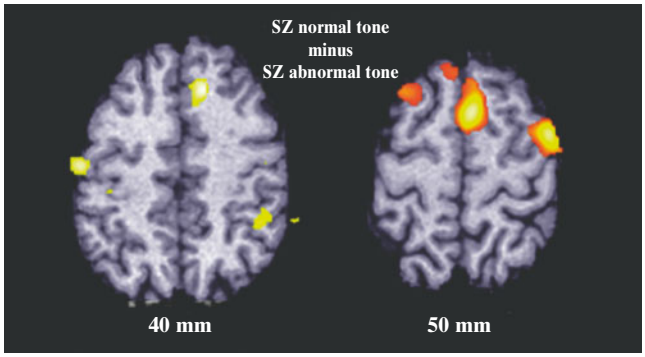

Figure 2. Volunteers with schizophrenia (SZ) able to make tone recognitions only when the difference between stimulus frequencies was greater than 10%, were compared with SZ persons able to make accurate decisions when the stimuli differed by no more than 2%. The group able to perform with more "difficult" tones exhibited greater activity in the cingulate and prefrontal region than those SZ volunteers who needed large tone disparities.

This study emphasizes the cognitive heterogeneity of the SZ group. By providing each subject with an individually determined difficulty level, we were able to make useful observations regarding the presence of an initially unapparent subgroup. This subgroup's inability to make auditory judgments as well as the cohorts with SZ emphasizes the role of cingulate and prefrontal cortex in making simple perceptual decisions. With further work using functional magnetic resonance imaging, it will be possible to identify at what point various affected groups fail to encode sensory information, or fail to make use of that information in their responses.

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