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**A BACKWARD MASKING STUDY OF AUDITORY SENSORY MEMORY
DYSFUNCTION IN SCHIZOPHRENIA**

by
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**A dissertation submitted to the Graduate Faculty in Psychology in
partial fulfillment of the requirements for the degree of Doctor of
Philosophy, The City University of New York**

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I. INTRODUCTION

Cognitive deficits in schizophrenia were first noted in the early 1800s (Pinel, 1806; Haslam, 1809; Burrows, 1828) and were described in detail a century later by Bleuler (1924) and Kraepelin (1950). An important avenue for linking together the biological and social aspects of the illness, the examination of cognitive dysfunction in schizophrenia has taken a number of different forms over the past fifty years. The initial emphasis was on comparing Kraepelinian schizophrenia subtypes, particularly paranoid versus nonparanoid, to determine whether there were differences in their cognitive deficits. Dimensions such as premorbid adjustment and chronicity were examined, with prominent researchers Silverman (1967) and Venebles (1964) contending that paranoid and nonparanoid schizophrenics had fundamentally different cognitive styles. They also posited that cognitive symptoms are tempered by premorbid adjustment and that cognitive styles change over the course of the illness, possibly as an adaptive process.

While the subtype, premorbid and chronicity constructs led to useful hypotheses, by the 1980s, with lack of support from longitudinal data, interest in these constructs had waned. The focus turned instead to differentiating between positive and negative symptoms in schizophrenia. The former encompass symptoms such as hallucinations, delusions, formal thought disorder and bizarre

behavior. The latter include symptoms such as social withdrawal, flattening of affect, alogia and apathy.

Crow (1980) proposed that there are two distinct forms of schizophrenia. Type I is characterized by positive symptomatology and is presumed to be caused by reversible neurotransmitter abnormalities. Type II is marked by the presence of cognitive deficits and negative symptoms and is presumed to be linked to structural brain abnormalities. More recent factor analyses (Liddle, 1992), however, have shown that cognitive dysfunction, along with thought disorder, is a symptom cluster distinct from positive and negative symptoms. There has accordingly been an increasing tendency to move from the mainly descriptive research in Type I and Type II studies to examining specific cognitive deficits in depth and testing hypotheses about their mechanisms. Linked with this have been efforts to determine whether cognitive dysfunction in schizophrenia is generalized or whether there are differential deficits in this disorder (Chapman & Chapman, 1978; Blanchard & Neale, 1994), i.e. are schizophrenics relatively impaired in all aspects of cognitive functioning or are there specific, perhaps lateralized, impairments?

Researchers have used a wide variety of psychometric methodologies linked to physiological studies in pursuing these questions. While such research is still in the comparatively early stages, it has become increasingly clear that certain cognitive

deficits may be trait-linked markers of schizophrenia (Neuchterlein & Dawson, 1994). Among such deficits, and of major importance in the daily functioning of schizophrenic patients, is working memory dysfunction.

Working memory is a term used for part of what was formally more commonly called short-term memory. Defined most simply, it is the brain's ability to simultaneously store and manipulate information. The focus of this study, auditory sensory memory, the brief, automatic memory for acoustical stimuli, is a subset and very simple level of working memory. Building on previous work by Strous & Javitt (1995) and Javitt & Strous (1997) which demonstrated a deficit in auditory sensory memory in schizophrenia, the present study is a test of Strous & Javitt's hypothesis that the dysfunction of auditory sensory memory in schizophrenia is the result of imprecise processing of auditory stimuli, as opposed to either an auditory discrimination deficit or a greater fragility of memory trace.

To test for an auditory discrimination deficit, this study employs a minimal delay and delay tone matching for pitch paradigm using schizophrenic and normal control subjects. The same methodology was used by Strous & Javitt but in this study more difficult discrimination levels are used, thus allowing for a more thorough test of auditory discrimination ability. To test for a greater fragility of memory trace in schizophrenia, an auditory backward masking paradigm was added, the masking being done at

subjects' threshold levels of delay tone matching.

This is the first auditory backward masking study in schizophrenia, a trait-linked deficit in visual backward masking having already been demonstrated in schizophrenia and mania (Green & Nuechterlein et. al., 1994a, 1994b). While there have been many auditory backward masking studies done with normal populations, this is the first one done with a psychiatric population. The present study thus addresses a corollary question in testing Strous and Javitt's imprecision hypothesis, namely do schizophrenics have a deficit in auditory backward masking?

Working Memory

Evolved from Broadbent's (1958) concept of a unified short-term memory in which sensory input is mediated by a single, limited capacity channel, working memory is currently hypothesized to involve automatic processes which are distinct from processes demanding conscious attention (Posner, 1978; Shiffrin & Schneider, 1977). There are thought to be two different types of information processing mechanisms in humans: attention-dependent storage and attention-independent storage.

The first of these, attention-dependent mechanisms, are regulated by the central executive and require effort on the part of the subject. Attention-independent storage, by contrast, is driven primarily by external stimuli and holds information in a vivid accessible form for several seconds following cessation of

stimulation (Baddeley, 1986; Cowan, 1988).

In line with Kraepelin (1950), who proposed that active attention is disturbed in schizophrenia while sensory registration is normal, schizophrenia working memory studies have primarily focused on attention-dependent mechanisms. These information processing mechanisms, which can encode complex attributes of stimuli, are thought to reside in heteromodal association cortices of the prefrontal and posterior parietal regions (Goldman-Rakic, 1990). They are used to influence the entry of information into temporary storage, to prolong the presence of useful information in storage, and to retrieve it as needed for tasks at hand.

In recent years, evidence has accumulated that schizophrenics have impaired attention-dependent working memory and that schizophrenics show many of the same deficits as patients with frontal lobe lesions. For example, it has been shown in numerous studies that schizophrenics perform in the “brain-damaged” range of the Wisconsin Card Sorting Test, a test of pre-frontal working memory (Malmo, 1974; Kolb & Wishaw, 1983). Coincident with this lowered dorsolateral regional cerebral blood flow has been demonstrated (Weinberger, et. al. 1986). Schizophrenics also show dramatic and robust deficits on numerous span of apprehension tasks (Asarnow et. al., 1991) and severe deficits in learning and memory (Saykin et. al., 1991) that correspond to a prefrontal pattern (Goldberg et. al., 1989; Schwartz et. al., 1991). They perform poorly on the Stroop Color-Word Test (Asarnow et. al., 1977) and more

recently have been shown to perform poorly on a memory guided spatial working memory task (Park & Holzman, 1992).

In sum, there is ample evidence that attention-dependent working memory is impaired in schizophrenia. What has remained unclear, however, is whether attention-independent processing is disturbed as well. Recent studies involving auditory sensory memory suggest that it is (Strous & Javitt, 1995, 1997)

Auditory Sensory Memory

Auditory sensory memory refers to the brain's ability to maintain transient representations of relatively "primitive" aspects of simple auditory stimuli such as pitch, duration, timbre, and volume. The specific focus of this study is sensory memory for pitch in schizophrenia.

Pitch is the "lowness" or "highness" of a complex sound, such as a tone, and is dependent primarily on frequency. Pitch is detected by humans via the cochlea of the inner ear. The cochlea has approximately 15,000 tiny hairs with delicate nerve fibers located at their base. These nerve fibers respond to the stimulation of the cochlea's hairs by sound waves and carry their impulses to the auditory nerve, which in turn transmits its message, via parts of the brain stem, to the auditory center in the temporal lobe of the cerebrum.

The system underlying pitch perception in humans is highly structured and precisely organized. The human ear can detect sounds from as low as 16 cycles per second to frequencies as high as 25,000 cycles per second, with greatest sensitivity to the range from about 1,000 to 4,000 cycles per second.

In a series of studies, Deutsch (1974) showed that humans code tonal pitch along a monotonic dimension of "tone height" and that this continuum is organized logarithmically with respect to waveform frequency. Supporting this, physiological studies on single units in the auditory pathway have demonstrated an orderly topographic distribution of neural elements that correspond to the frequency of sound (Harris, 1972).

The investigation of auditory sensory memory goes back to the nineteenth century. Then as now, the most parsimonious method by which to behaviorally index auditory sensory memory has been through tone matching for pitch. In the tone matching for pitch paradigm, a psychophysical method sometimes called a "delayed paired comparison", two tones are presented separated by an interstimulus interval (ISI). The subject is then asked to make a judgement about the relationship in pitch between the two tones. The premise is that a representation of the first stimulus must be available at the time of the presentation of the second stimulus in order to compare the two tones correctly. Tone matching for pitch is thus a task that implicitly requires working memory, i.e. the simultaneous retention and manipulation of information.

The first researchers in the field of auditory sensory memory, Wolfe (1886) and Bachem (1954), found that pitch discrimination usually decreases as the ISI is increased. In other words, auditory sensory memory decays as a function of time. While Wolfe and Bachem's finding has held up, their methodology has since been revised. Wolfe and Bachem asked subjects to make a fairly difficult discrimination: whether the second tone was higher or lower than the first. Later studies have focused on a more basic discrimination, "same" or "different."

The first such study was by Wickelgren (1966). Wickelgren had normal subjects listen to a standard tone for 2, 4 or 8 s, followed by an interference tone lasting 2, 4 or 8 s, then followed by a comparison tone lasting 2 s. Subjects were asked to say whether the standard and comparison tones were the same or different. Wickelgren's finding was that accuracy increased with longer duration of the standard tone and decreased with longer duration of the interference tone. The implication was that trace strength can be consolidated by increasing stimulus duration and that trace memory itself decays fairly rapidly.

To look at auditory sensory memory at its purest, researchers since Wickelgren have generally employed a blank ISI. Contrary to Broadbent who assumed that the presence of other stimuli would not effect the degree of memory loss, Massaro (1970b) found that tones or noise in the ISI produce more forgetting than a blank ISI. This, he

reasoned, was due to the filled ISI causing interference in the processing of the first tone. Thus to study pure decay effects, he concluded, one must use a blank ISI.

In subsequent blank ISI studies, it has been found that tone matching performance is high at short ISIs and declines dramatically, toward an asymptotically low level, with ISIs beyond 10 seconds. The nature of a subject's silent mental activity during the ISI matters little, indicating the attention-independent nature of the task, while the effects of an intervening sound during the ISI are large (Deutsch, 1970; Massaro, 1970b; Pechman & Mohr, 1992). Further, memory is very good immediately after the acoustic stimulus even for sounds that are unattended at the time of their presentation and is lost steadily and dramatically as the testing delay increases to about 10-20 s (Cowan, 1990).

Concerning the relationship between pitch in music and in speech, Deutsch (1974) proposed that music and speech have separate working memory stores. In an experiment with normal subjects she showed that interpolating tones between two tones to be compared causes considerable memory disruption while spoken numbers, even when subjects were required to recall them, do not. From this Deutsch deduced that humans have a specialized system for the storage of tonal pitch information and that it does not require any substantial amount of central capacity. A recent study by Salame & Baddeley (1989), however, refutes the notion of separate music and

speech working memory stores. Reasoning that if the processing of linguistic items does not interfere with the processing of musical stimuli than the opposite should also be true, Salame & Baddeley investigated the effects of concurrent speech, noise or music on the retention of verbal material. They found that noise had no detrimental effect whereas music did, though not as much as speech itself. Their results suggest that speech and tonal material are processed in "sister" systems, but with the retention of verbal information being more effective than that of fine-grained sensory information (Pechman & Mohr, 1982).

Abstracting from the results of these and other studies using normal subjects, Cowan (1984) has proposed a two stores model of auditory sensory memory. The first store is a "short auditory store" with a duration of 200-300 ms. This duration was determined with gap detection, simultaneity judgement paradigms and backward masking paradigms. Comprised of a 7 ms initial registration plus auditory persistence, short auditory storage mediates the initial recognition of stimulus properties and integrates the perceptual attributes of sound -- pitch, timbre, loudness, etc. At most it is capable of carrying information about one brief sound segment and this information is relatively unanalyzed. Each new sound overwrites the short auditory storage of the previous sound and this interference cannot be disinhibited. The short auditory store contains a spectral average weighted in favor of most recent input and until the short auditory storage has decayed, the subject

believes the stimulus is still present. Short auditory storage is thus experienced as a continuum of sensation and carries with it the experience that the sound is continuing. It progresses from the stimulus onset and continues for a relatively constant time regardless of the stimulus duration.

Long auditory storage, which lasts up to 20 s, is capable of containing information from a sound sequence, including speech sounds, providing there are smooth transitions from one segment to the next. Each new sound only partially interferes with the long auditory storage of the previous sound and whether it does so or not depends on the similarity between stimuli. Such interference is capable of being disinhibited. Further, long storage does not begin to decay until full stimulus resolution and unlike short storage, which is experienced as sensation, long auditory storage is experienced as memory.

In describing the above as separate stores Cowan, it should be noted, is not necessarily endorsing a storage model of auditory sensory memory. Memory generally, he comments, has often been described using a storage metaphor in which information is conceived as flowing from one compartment to another (not necessarily different parts of the brain), being encoded or processed in some way at each transition point. Conversely, there have also been levels of processing models. In these it is hypothesized that the more elaborate the encoding of a stimulus, the more it will be

remembered.

Both metaphors have a long and rich history and continue to have their proponents. What is important finally, contends Cowan, is that data indicate that short auditory storage and long auditory storage function differently and on different time scales. Combining a storage and a levels viewpoint, he posits that a pattern of neural activity can result in processing and storage of auditory information at the same time. The modes and durations of the relevant neural activity patterns, however, do not form a continuum. One type of activity result in short auditory storage and another type results in storage for a time an order of magnitude larger (the second type of activity may require that the first type has occurred). Moreover, not every pattern of neural activity must be simultaneous with an encoding process of some type. Short auditory storage seems to coincide temporally with an encoding process, he concludes, but long auditory storage may not.

A different model of auditory sensory memory, but one nearly identical to Cowan's, is that of Kallman & Masssaro (1979). Their model specifies a centrally located preperceptual auditory store (PAS) and a synthesized auditory memory (SAM). The PAS is hypothesized to store acoustic features while simultaneously transmitting them to SAM. The features stored in the PAS decay in 250-300 ms and are subject to being overwritten. Auditory sensory memory strength in this model is affected not only by the rate of

forgetting but also by the amount of perceptual processing that a sound undergoes.

In their time frames and in their functioning, Cowan's and Kallman & Massaro's models of auditory sensory stores are essentially the same. Both conceptualize two auditory sensory memory stores, with the first holding information about only one brief sound and the second information from a sound sequence. Both also note that while different researchers' paradigms differ in the observed duration of auditory sensory memory storage, this does not mean that memory decays differently in these paradigms. Rather, the paradigms might draw on a common type of storage with task demands modulating the decay observed.

The Location in the Brain of Auditory Sensory Memory

The cortical fields in the temporal lobe responsive to auditory stimulation can be divided into several distinct areas. There is the primary auditory cortex, believed to lie within the Heschel's gyri in humans (Celesia, 1976; Galaburda & Sanides, 1980; Liegeois-Chauvel & Chauvel, 1991) and there are several other auditory fields which surround it. These may receive input not only from the primary auditory cortex but also directly from the mediate geniculate nucleus.

The critical substrates for auditory working memory appear to reside in the primary and association areas of the auditory cortex

(Lu et. al., 1992; Sams et. al., 1993). The evidence for this comes from a number of studies. Colombo et. al. (1990) found that bilateral lesions to the superior temporal gyrus of monkeys, sparing the primary auditory cortex, lead to deficits on a tone matching task. Similar effects were found in humans who had excisions of the same areas (Zattore, 1985), with pitch discrimination remaining intact. Brain regions other than the primary and association auditory cortices, it appears, are active in auditory processing only when the task or the tonal stimuli become more complex. Zatorre & Samson (1991), for example, found that interference in a tone matching study in humans affected those with right prefrontal excisions more than those with lesions in the left temporal lobe. At the same time, their performance in the absence of distractors showed no deficit. Likewise, melodic discrimination is affected in humans with right temporal lobe lesions while tone matching is not effected (Zattore, 1985).

Significantly, the decline of auditory sensory memory with poststimulus time correlates closely with changes in the electrophysiological state of the primary and association areas of the auditory cortex. Peaks in the evoked response waveform occur 200 to 500 ms after the onset of a sound (Squires et. al., 1975) and Abeles et. al (1975) found 200 ms patterns of single cell behavior within the auditory cortex of cats.

Further evidence for the concept of auditory sensory memory

storage comes from studies of mismatch negativity (MMN). MMN is a short latency cognitive event related potential elicited by physically deviant stimuli. It represents the outcome of an automatic, i.e. attention-independent, process that compares each presented stimulus with a mnemonic trace encoding auditory experience over the preceding 10 - 20 s. Its generators have been localized to the vicinity of primary auditory cortex using EEG and MEG dipole mapping in humans (Hari et. al., 1984; Scherg et. al., 1989) and intercortical readings in monkeys (Javitt & Schroeder et. al., 1994). Significantly MMN has a similar duration as short auditory storage and is similarly effected by ISI. It thus may serve as an index of the operation of auditory sensory memory in the brain.

Auditory Sensory Working Memory in Schizophrenia

In what has been the only research thus far to examine auditory sensory working memory in schizophrenia using tone-matching for pitch, Strous & Javitt (1995, 1997) conducted two separate studies. Their results showed: 1) that schizophrenics have impaired auditory sensory working memory and, they contend, 2) that this impairment is the result of imprecise processing of auditory information rather than a faster rate of memory decay.

In their first study, Strous & Javitt (1995) used a tone matching task in which tone pairs were at two levels of difficulty and with six different ISIs (1 s - 20 s). Subjects were 20 chronic

schizophrenics and 17 controls. In the easy condition, target stimuli (the second in the pair) differed 20% in pitch from the reference stimulus (the first in the pair). Each stimulus sequence contained 12 trials at each ISI. In six of the trials, targets and reference stimuli were the same. In three, targets were increased in pitch by the specified amount (5 or 20%) and in three decreased. The chance performance level was therefore 50%. Across the trials, three different reference stimuli were used (500, 100, and 2000 Hz) in order to minimize subjects learning to recognize the reference stimuli. To assess discrimination ability between tones at the 0 s (minimal delay) interval, 200 ms tones were constructed in which the first half of the tone (100 ms) was at one of the standard frequencies and the second half was either the same, higher or lower in pitch by 5% or 20% with a rise/fall time of 10 ms. Subjects were asked to respond verbally as to whether the composite tone remained the same throughout or whether the end differed in pitch from the beginning. In the delay conditions, the ISI varied in random order during the stimulus sequence and subjects were cued with a visual message ("first tone" or "second tone"). The easy and difficult procedures were then repeated with the introduction of a distraction task in which the subjects were required to read numbers aloud from a computer screen between each member of paired tones when the ISI was 3 s or more. The easy and difficult sequences in the presence or absence of the distraction task were

presented in random order among subjects. All tones were generated using a Neuroscan Stim system and presented free field at an intensity level of 75 dB.

As a control condition, forward and backward digit spans were administered to all subjects with the score for each subject being the greatest number of digits repeated correctly before two successive errors were made at any level.

In considering this experimental design, several points need be noted:

- 1) Both the easy and difficult discrimination conditions were conditions in which ISI dependent memory could properly be said to have been obtained. For as Strous & Javitt point out, if a discrimination is too hard, even a detailed temporary sensory memory trace will not be sufficient to carry out the discrimination well. Conversely, if a discrimination is too easy, a long-term auditory memory record of the trace may be sufficient and thus the task is not truly ISI dependent.

- 2) Long-term auditory memory is to be distinguished from long auditory storage. Long-term auditory memory is that which holds more enduring representations of sound enabling one to, for example, recognize familiar voices or the opening notes of a song heard in one's youth. A stimulus such as a tone may leave a record, if relatively imprecise, in long term memory, (Berliner & Durlach, 1973; Massaro, 1970a). Thus, as noted above, if a tone matching

task is easy enough, long term memory alone may be sufficient to allow for a good performance even after a lengthy time period.

3) As regards excluding those with significant musical training, Pechman & Mohr (1992) found that musicians had superior tone processing in a blank ISI tone matching paradigm. They exhibited no superiority when the ISI was tonal. It is unknown whether musicians' blank ISI performance superiority was due to training or to inborn talent for pitch memory (one reason, perhaps, they became musicians in the first place). Another study, however, a tone identification study, found no effect of musical training (Raz, 1983). Thus the relationship between musical training and auditory sensory memory remains unclear.

4) The visual distracter task was used to minimize the contribution of the "phonological loop system" to the discrimination task. The "phonological loop" is Baddeley's (1992) term for the auditory "slave" system that maintains acoustic or speech based information for 1 to 2 seconds. In Baddeley's model of working memory, slave systems function to preserve incoming perceptual information for as long as necessary for the task in which the subject is involved. The central executive is responsible for monitoring and controlling the smooth functioning of the slave systems and for the distribution of attentional resources if necessary. Two slave systems have been studied in detail by Baddeley: the visuo-spatial sketch pad which holds visuo-spatial information and the phonological loop. The phonological loop

depends on "covert rehearsal" of chunks of information to reactivate items in memory in contrast to auditory sensory memory which maintains representations of stimuli without rehearsal.

Phonological loop memory can therefore be suppressed, Strous & Javitt point out, by having subjects read or repeat irrelevant words as in their study's distracter task. Likewise, digit span was tested in subjects because it is a measure of phonological loop memory. It also served to assess potential nonspecific contributions to overall performance such as effort, cooperation and concentration.

The results of Strous & Javitt's first study were interesting on a number of counts. One was the finding that there was no significant across-group difference in accuracy of performance when there was minimal delay between tones for either the easy or hard discrimination. As expected, both groups showed substantial decrements of performance as a result of ISI and task difficulty. However, the performance fall off was significantly greater for the schizophrenics than for the controls ($p < .0001$). In both the easy and difficult conditions, performance curves diverged markedly such that between-group differences were apparent even at the shortest ISI tested (1s). There were no significant effects of distraction and no significant distraction by group interactions. There was a significant distraction by time interaction but only at the longest ISI (20s). Finally, there was no significant difference in digit span between schizophrenics and controls.

The deficit in the schizophrenics' performance was clearly a working memory deficit, Strous & Javitt conclude, as they performed as well as controls in the minimal delay condition. Whether this deficit reflected imprecise processing, however, or a memory trace that is more fragile, i.e. that has a faster rate of decay, remained unclear. To clarify this point, contrast analyses were performed to analyze whether the significant time and group by time effects were due to differential between-group decay in performance accuracy between 0 and 1 s or to differential decay between 1 and 20 s. The former would suggest imprecise initial processing, the latter premature decay of the memory trace. What was found was a highly significant between-group differential in performance between 0 and 1 s ($p < .0001$) with no further decrement between 1 and 20 s. A closer look at performance curves indicated that given a similar level of initial performance, performance decayed at a similar rate in both schizophrenics and controls. Schizophrenics were as functional in terms of comparison abilities at 20% difference in tone frequency as controls were at 5% difference and the decay of tonal information was almost equivalent in the two cases. This equivalence suggests, say Strous & Javitt, that when the difficulty of the tone comparison is equated across groups, there is no group difference in the rate of automatic decay of auditory sensory memory. In addition it was found that under conditions when controls and schizophrenics showed comparable

levels of performance accuracy, they also showed similar numbers of "same" and "different" responses. Thus the performance decrement in schizophrenia, they reason, was due to increased task difficulty rather than a nonspecific increase in random responding.

From the above evidence, Strous & Javitt hypothesize that imprecise processing of auditory stimuli is responsible for schizophrenics' poor performance in tone matching tasks. This conclusion was further supported by analysis of individual responses. Both groups showed a significant increase in the number of non-identical pairs that were misidentified as being the same as the discrimination was made more difficult, suggesting that both groups used a similar strategy of identifying pairs as the same unless they could be definitively differentiated. In the easy discrimination condition, schizophrenics not only showed a level of correct performance that was statistically indistinguishable from that of controls performing difficult discriminations, but they also misidentified a similar number of non-identical pairs as being the same in the easy condition as controls did in the difficult discrimination condition. This substantiates, say Strous & Javitt, their theory that tone stimuli are defectively represented in a "grosser" form in schizophrenia, making it relatively more difficult for schizophrenics to perceive subtle distinctions between tones.

A recent study done by Holcomb et. al. (1995) supports this view. Using a tone discrimination methodology in which subjects were asked to distinguish two tones from each other (high frequency vs.

low frequency), Holcomb et. al. found that schizophrenics show a significant decrement in accuracy relative to normal controls when the frequency difference between two tones and the presentation level (volume) of tones were degraded (both well established signal degradation maneuvers). Reductions in the signal-to-noise ratio thus had a differentially greater impact on the schizophrenic subjects. This finding supports the hypothesis that schizophrenics represent tones in a less precise form, as one would expect that the more accurate a representation of a tone, the lower the fall in discrimination ability would be caused by a given increase of noise.

In a follow-up study, Strous & Javitt (1997) again utilized tone matching for pitch to study auditory sensory memory functioning in schizophrenics relative to normal controls. There were, however, two changes from the design of the first study. In the delay condition, all the trials were done with a 300 ms ISI (vs. 1-20 s in the first) and in both the minimal delay and delay conditions, an intermediate level of difficulty (10% between-tone pitch separation) was added.

The choice of 300 ms as the delay condition ISI was an effort to examine more closely what happened in the between 0 and 1 s ISI time points during which between-group differential decrement in performance was greatest in the first study. 300 ms was a logical choice as that is the shortest ISI that is possible without two tones perceptually fusing together. In addition, a 300 ms ISI has the

benefit of insuring that the effects of directed attention during the ISI are negligible. For as Strous & Javitt point out in their discussion of their first study, the possibility that attention-dependent mechanisms contribute to encoding cannot be entirely excluded. Massaro & Kahn (1973) and Massaro & Warner (1977) found that the rate of increase in test-tone recognition as a function of ISI was poorer with attention divided between auditory and visual tasks than with attention focused on the target tone. However, the difference in recognition was on average only 10 percentage points while the difference between schizophrenics' and normals' performance in Strous & Javitt's first study was extremely large. Thus that difference, Strous & Javitt argue, cannot be attributed to the effect of attention on tone encoding.

The results of Strous & Javitt's second study were consistent with those of the first study. Schizophrenics and normals showed similar high performance levels in the minimal delay condition, while in the delay condition schizophrenics performed much less accurately than normals in all levels of pitch separation. Repeated measures ANOVA showed a highly significant main effect of diagnostic group ($p < 0.0001$) and a significant group by difficulty interactive effect ($p < 0.001$) with effect sizes (f) all being greater than 0.75, indicating an extremely large between group difference (Borenstein & Cohen, 1988). Schizophrenics showed no difference from normals in overall number of "same" and "different" responses

in any of the discrimination conditions. Further, when six of the schizophrenic subjects were retested after 3-6 months in the difficult discrimination 300 ms ISI condition, there was no difference in their number of correct responses. For normals, Strous & Javitt conclude, the critical factor regulating performance was tone discrimination ability whereas schizophrenics were significantly more effected by adding a delay between tones than by altering the between-tone pitch separation.

In summary, Strous & Javitt's studies are strong evidence that working memory is impaired in schizophrenia even at the level of the auditory sensory cortex. This conclusion is further supported by studies which have demonstrated impaired mis-match negativity (MMN) generation in schizophrenia (Javitt, et. al., 1993; Javitt & Schroeder, et. al. 1994; Shelley et. al., 1991). Importantly too, Strous and Javitt's effect sizes are larger than those that have been reported for far more complex cognitive tasks (Blanchard & Neale, 1994). Strous & Javitt thus raise the interesting possibility that imprecise processing rather than a deficit in retention may underlie schizophrenics' impaired performance on tasks requiring more complex, attention-dependent components of working memory.

While Strous & Javitt's studies are well thought out and their hypotheses compelling, there are several limitations in their methodologies. The first is that performance of both the schizophrenics and normals in the minimal delay condition were at near ceiling levels. The question is thus left open whether tone

discrimination ability in schizophrenics is entirely normal. Strous & Javitt argue that there is a sufficient range of values in the delay condition to indicate that the differential performance deficit in schizophrenics cannot be attributed solely to a nonspecific increase in task difficulty. Still, it remains open whether schizophrenics have a deficit in auditory discrimination as well as a deficit in processing precision. Also, and perhaps more significantly, the integrity of pitch encoding cannot be fully examined using tone matching alone. As noted earlier, there is a perceptual fusion of tones at ISI of less than 300 ms. The question thus remains open, what is occurring during sub-300 ms tone intervals? Is there a decay in memory in this time period that would account for the difference in schizophrenics' and normals' performance in delayed tone matching or are Strous & Javitt correct in maintaining that the deficit exhibited by schizophrenics is one of imprecise processing?

These concerns are addressed in the present study. Utilizing a tone matching for pitch paradigm with schizophrenic subjects and normal controls, minimal delay and delay discriminations of a difficulty greater than those used by Strous & Javitt were added. In addition, an experimental paradigm called backward masking was used. With this technique sub-300 ms sensory auditory processing can be examined, thus bringing further data to bear on the question whether the deficit in auditory sensory working memory in schizophrenia is one of imprecise processing or one of increased

susceptibility to disruption, i.e. of accelerated memory decay.

Visual Backward Masking

Backward masking is a neuropsychological procedure in which an informational target stimulus is presented in close temporal succession with a noninformational masking stimulus. The use of a mask allows a researcher to isolate different stages of information processing by a strict control of the time a subject has to process a stimulus. As Crawford (1947) first demonstrated, when one stimulus is followed closely by another, the second stimulus interferes with the processing of the first. Noted Felsten & Wasserman (1980), a mask permits the investigator to do something that can be done by no other means, namely to deliver information to the brain with precise control over the duration of the information delivered.

In schizophrenia research, all backward masking studies to date have involved the visual system. Typically in visual backward masking, a tachistoscope or computer is used to deliver the stimuli. A suprathreshold exposure of the target, typically the letter "A" or "T", is determined for most subjects or individually, and this identifiable stimulus is then followed by a noninformational masking stimulus, e.g. an overlapping series of Xs. For normal subjects, the target stimulus "escapes" from the disruption of the mask when the interstimulus interval is in the 60 to 240 ms range

(Cowan, 1984). That is, a target that is not identifiable when followed after 30 ms by a mask becomes so when the mask does not appear until after 60 to 240 milliseconds.

Compared with normals, schizophrenics are particularly vulnerable to the disruptive effect of the mask. The first study that looked at visual backward masking in schizophrenia was by Saccuzzo et. al (1974). They compared chronic and delusional schizophrenic subjects with normals and a heterogeneous mix of nonschizophrenic psychiatric controls. Using four different target-mask intervals (50, 100, 150 and 300 ms) and a no mask control condition, they found that normals and the nonschizophrenic psychiatric patients reached no mask control performance at the 150 millisecond interval. The schizophrenics did not do so until at least the 300 ms interval.

In a follow-up study, Sacuzzo & Miller (1977) showed that this impaired performance by schizophrenics could not be caused by impaired learning. When the critical stimulus-mask interval was determined for normals and schizophrenics on four separate occasions, they showed similar learning curves over the course of the four testings, with the schizophrenics showing a consistent performance deficit throughout.

As to whether schizophrenics' deficit in visual backward masking was a specific deficit or whether it only reflected a generalized task impairment (Chapman & Chapman, 1978), further studies supported the specific deficit hypothesis. Brody et al. (1980) found

that young schizophrenics were impaired in visual backward masking even when compared to the elderly, a group with generalized cognitive deterioration who had previously been shown to have a visual backward masking deficit. Further, Steronko & Woods (1978) found that university students diagnosed schizotypic using the MMPI showed masking deficit when compared to normal controls, suggesting that deficient visual backward masking may be a marker of vulnerability to schizophrenia. This link between a visual backward masking deficit and schizophrenic spectrum disorders was further explored by Sacuzzo & Schubert (1981). They compared hospitalized adolescent schizophrenic patients with match groups of schizotypal and borderline adolescents. Again, the schizophrenics and the schizotypals were shown to have masking deficits. Likewise, Braff (1981) found that nonmedicated, nonpsychotic schizotypal inpatients were just as impaired in backward visual masking as were RDC-diagnosed schizophrenic patients. In other words, the deficit was a trait not state marker.

Having established that a visual backward masking deficit is trait-linked with schizophrenia spectrum disorders, the next area explored was the link between the backward masking deficit and specific schizophrenia symptoms. The major researchers in this area have been Green & Walker (1984,1986). Using a procedure in which they determined critical ISIs for both positive and negative symptom schizophrenics, Green & Walker found that negative

symptom schizophrenics had a poorer backward masking performance. Likewise, when Braff (1989) compared negative, mixed and positive schizophrenic patients, he found an increased masking deficit among the negative symptom patients. Braff's study was particularly notable in that, unlike Green & Walker, he determined individually each subjects critical stimulus duration (the stimulus duration necessary for the subject to identify the target). The negative symptom schizophrenics, like chronic schizophrenics in other non-masking studies, had dramatically higher critical stimulus durations. Thus while they had on average 150 ms more time than positive symptoms schizophrenics to process the target stimulus, they still performed worse on the masking task. Further, as Sacuzzo & Schubert (1981) pointed out, low motivation, a typical negative symptom, would not account for Green & Walker's and Braff's findings as low motivation tends to produce relatively flat masking functions. Both Green & Walker's and Braff's findings then, support Knight's (1984) speculation that negative symptoms in schizophrenia are associated with a perceptual organization deficit and concomitant impaired processing. They also strengthen the theoretical links between negative symptoms and global organic brain impairment

As to the possible effect of antipsychotic medications on masking performance, Spohn et. al (1989) and Goldberg & Weinberger, (1996) reviewed previous studies and found that

antipsychotics generally do not have negative effects on working memory and in fact probably normalize sustained vigilance in schizophrenics. Likewise, Braff & Saccuzzo (1981,1982), Brody et. al. (1980) and Saccuzzo et. al., (1974) found that medication may reverse information processing deficits in schizophrenia. In specific, the study by Braff & Sacuzzo (1982) found that schizophrenic patients who were receiving antipsychotic medication showed less visual backward masking deficits than did those receiving no medication. This was despite the fact that those receiving medication were more symptomatic.

In sum, there is good evidence that there is a trait-linked vulnerability to the effect of a visual backward mask in schizophrenia and that it is linked in particular to negative symptomatology. The evidence is not, however, unequivocal. Rund (1993), the first to look at visual backward masking in chronic versus non-chronic schizophrenics (defined as less than two years of hospitalization), found that the non-chronic schizophrenics performed as well as normal controls, leaving open the possibility that previous studies confounded negative symptom schizophrenics with chronic schizophrenics. Moreover, recent studies (Rund, et. al., 1993; Green & Nuechterlein et. al., 1994b) show that manic patients perform as poorly on visual masking tasks as schizophrenics. This, on the one hand, supports the theory that severe bipolar disorder and schizophrenia, given their strong similarities in cross-sectional symptoms, may be different degrees of expression of the same

underlying disorder (Heston, 1970). On the other hand, it is important to note that manic patients performed significantly worse than schizophrenics when the masking consisted of a location rather than identification task (Green & Nuechterlein et. al., 1994b). The implication, say Green and Nuechterlein et. al., is that the two groups may perform poorly on standard identification tasks for different reasons.

This leads to an important question for this study: why do schizophrenic spectrum subjects perform poorly on visual backward masking tasks? A number of theories have been put forth to answer this question. Among the first was that schizophrenics process information slowly, i.e. that they keep information in an erasable or vulnerable form for excessive lengths of time (Sacuzzo & Braff, 1981; Saccuzzo & Schubert, 1981). Information, in this theory, is thought to be transferred slowly from sensory memory to short-term memory in schizophrenics and/or they are slow to classify stimuli (Green & Walker, 1984). A second hypothesis was that schizophrenics fail to reject mask elements as irrelevant (Knight, 1984), suggesting that the formation and decay of visual sensory memory is the same in schizophrenics and normals (Spaulding et. al., 1980). A third hypothesis was that schizophrenics encode visual information imprecisely (Sacuzzo et. al., 1974).

As researchers considered these possibilities it became apparent that greater clarity was needed on precisely how visual masks work.

Two theoretical positions became prominent: the integrative theory and the disruption theory. Erikson (1980) is a proponent of the integrative theory. He contends that when the mask structurally resembles the target and is presented at a high energy level, an integration of the features of the mask and target occur.

Conversely, the interruption theory contends that a mask could simply interrupt processing of the target, this processing being seen, as Schuck & Lee (1989) point out, as an all-or-none affair. The mask would do so by inhibiting the sustained processing channels in the visual system. The sustained channels have a relatively long response latency and are sensitive to high spatial frequency, e.g. the fine details of a stimulus. The other type of visual pathway by contrast, the transient channels, have a short response latency and are sensitive to low spatial frequency, e.g. the coarse features of a stimulus.

The most recent visual backward masking in schizophrenia studies (Green et. al., 1994a) controlled for the differences between the two types of visual channels. What they found was that a combination of integrative and disruptive processes are at work in visual masking in schizophrenia, and that the interruptive process affected icon formation itself. Schizophrenics, it appears, have abnormalities in transient visual channels stemming from overactive responses of the pathways (Balogh & Merritt, 1987). As a result the onsets of the target and masking stimuli may accumulate,

resulting in impaired icon formation. Visual icons, it thus appears, are not formed instantaneously but rather in waves of neural activity. Hence Spaulding et. al.'s study which only examined sustained channel activity may have been a poor assessment of icon formation. It is the dynamic neural process, say Green et. al. (1994a), that is interrupted by masking, with integration perhaps predominating at very brief stimulus onset asynchronies (SOAs), the interval between the onset of the target and the mask, and interruption at longer SOAs.

Green et. al. (1994b) concluded that backward visual masking procedures can be viewed as a special condition of a more general sensory gating deficit. The concept of sensory gating dates back to McGhie & Chapman (1961) who first hypothesized that schizophrenics might have a deficit in "gating" or screening out irrelevant stimuli. They stressed the need of organisms to organize sensory data and to provide a degree of perceptual constancy via reduction of what would otherwise be a chaotic flow of information. Similarly Venebles (1964) hypothesized that schizophrenics are flooded by sensory data, that they lack adequate selection and inhibition processes. This results, he concluded, in secondary cognitive fragmentation, leading to the typical signs and symptoms of schizophrenia.

In the decades following McGhee & Chapman's and Venables' theories, a large number of studies have examined stimuli screening in schizophrenia and found a sensory gating deficit. It has been

shown, for example, that many schizophrenics lack prepulse inhibition of the startle response (Braff et. al., 1992). When a strong stimulus that elicits a startle response in most normals is preceded 30 to 500 ms by a weak prestimulus, the startle response is normally inhibited. Interestingly, attenuation in normals is highest when the ISI between the prepulse and the blink-eliciting stimulus is around 60-120 ms, an interval comparable to the time course of visual backward masking effects. Among schizophrenics, however, there frequently is no prepulse inhibition of the startle response. Likewise, when two rapid click stimuli are separated by 500 ms, the P50 event related potential (ERP), which is an electrophysiological response to novelty, is always large to the first click but is attenuated to the second click in normals. In schizophrenics, by contrast, whether they are medicated or not, this inhibitory process is lost (Adler et. al., 1982).

A sensory gating deficit perspective on the visual backward masking deficit in schizophrenia thus argues against the slow speed of information processing viewpoint, the transient components of normals' and schizophrenics' vision being different according to this model. Instead visual backward masking deficits are seen as a failure to attenuate the disruptive effects of the mask.

Auditory Backward Masking

It is the premise of this study that information about the depth and fundamental nature of cognitive dysfunction in schizophrenia might be gained by determining the simplest level at which the information processing of schizophrenics is impaired. Following from this, there are several reasons why the auditory system may be a better modality for study than the visual system. First, the core deficit in schizophrenia may involve the auditory information processing system. The evidence is that while improvement in clinical state correlates with more normal visual P300 responses, the P300 being a positive brain wave that occurs about 300 ms after stimulus delivery, auditory P300 responses remain abnormal (Duncan, 1988). Second, while the properties of sensory storage in vision and audition appear to be generally similar, the auditory system is more sensitive temporally (Penney, 1975). Thus studies involving the auditory system should provide a better index of the sequencing of memory functions. Third, all visual backward masking tests are by nature attention-dependent and as all to date have been identification tasks, they inherently rely on long-term memory. For both these reasons they are poor tests of sensory memory as compared with tone matching for pitch. Finally, visual tasks by their very nature require higher level processing insofar as they involve symbolic material such as letters or numbers. A pure tone, by contrast, rarely has non-task related meaning for a subject. The processing of such material is therefore necessarily less complex.

To date, all auditory backward masking research has been with nonpsychiatric populations. The form of this research has been similar to that of visual backward masking. Typically one auditory stimulus is followed by a silent ISI of at least 300 ms and then a masking sound, generally either a pure tone or a complex tone. The subject is asked to determine the quality of the stimulus, e.g. is it high or low, or alternatively, long or short (simple tone recognition). Or in a slightly different version of auditory backward masking, two stimuli, separated by an ISI as in tone matching, are followed by another ISI and then the mask. The subject is then asked to make a comparison between the first two stimuli, e.g. are they the same or different, or alternatively, is the second sound higher or lower than the first (two interval forced choice). In either case, the subject is required to recognise an attribute of the stimulus, not simply to detect the stimulus itself as in signal detection paradigms. The mask in this paradigm does not interfere with the registration of the auditory stimulus it follows but rather affects only the registration of the tone's quality.

Auditory backward masking studies with nonpsychiatric populations have repeatedly found that performance is very poor at short ISIs (near chance) and rises to an asymptotic level at about 250 ms (Massaro, 1970b, 1972, 1975, 1976). This is true with ipsilateral, binaural and contralateral presentation of target and mask, although the masking effect is somewhat smaller with contralateral presentation (Leshowitz & Cudahy, 1973; Hawkins &

Preston, 1977; Yost et. al., 1976). Hawkins & Preston (1977) propose that this ear effect occurs because listeners can “tune out” contralateral masks under certain conditions, with presentation ear-effects diminishing or disappearing altogether when the frequency of the mask is varied randomly from trial to trial. Further, while the auditory backward masking effect is somewhat lower using well-practiced subjects, it does not depend on the use of unpracticed subjects (Kallman & Brown, 1986), an important point if backward masking is to be taken as an index of short-term auditory storage.

The attention-independent nature of auditory backward masking is revealed by electrophysiological studies showing that the amplitude of mismatch negativity (MMN) strongly correlates with subjects' performance in a masking-recognition task (Winkler et. al., 1992; Winkler et. al., 1993) . MMN can occur as early as 150 ms following stimulus presentation but MMN amplitude increases to a 470 ms intertone interval, a length of time consistent with performance-based estimates of trace formation time (Winkler et. al., 1993). This is further evidence that MMN may be an index of auditory sensory memory.

As noted earlier, the results of auditory backward masking research have been taken by Cowan (1984) as evidence of a short auditory store of approximately 250 ms. It should be pointed out, however, that different masks differentially affect different stages

of auditory sensory memory. When the mask is acoustically dissimilar to the target it affects short auditory storage; when it is similar it affects the synthesized auditory memory trace in long storage (Loeb & Holding, 1975; Sparks, 1976). This finding is in line with Deutsch's (1974) finding that the interference in tone memory depends on the similarity of the interfering stimulus to the test items held in memory. It also explains why tone masking can still be evident after 250 ms when properties of the target and the mask have some overlap.

To explain more precisely how auditory backward masking works, both interruption and integration theories have been put forth. Masaro (1970a, 1970b, 1972, 1975, 1976), who did much of the early work in auditory backward masking, proposes an interruption model. In his schema, the backward mask disrupts perception of a target by replacing the target in preperceptual auditory storage (PAS), consequently terminating the readout of the target sounds features from PAS. In other words, the information stored in PAS is overwritten before synthesized auditory memory (SAM) receives a complete representation of the stimulus. Masking in this model does not reduce the amount of information obtained before the occurrence of the mask but it does preclude further processing.

Another conceptualization is in terms of temporal summation on the basis of integration in the auditory sensory system (Cowan, 1984; Zwislowski, 1969). According to this view, neural activity is

largest at stimulus onset and decreases to an asymptotic level by about 200 ms. The neural activity is integrated across time, with the most recent activity weighted most heavily in terms of sensory representation. Thus backward masking is explained by an integration of the target and masking tone, with a greater contribution of the mask at shorter ISI.

More recently, research has focused on the question of whether short auditory storage is single channel or multichannel. Massaro's is a single channel model, i.e. one in which different stimulus features such as pitch, timbre, loudness, location and duration are centrally stored in a single cluster. In this model, recognition of different features should be equally degraded by the same mask. Subsequent studies, however, have shown that this is not the case. Kallman & Brown (1986), for example, found that while white noise does not act as an effective mask for pitch it does for duration and that white noise is a less effective interfering stimulus than a complex tone (sinusoid) (Kallman & Brown, 1986). Similarly, Shilling & Sondquist (1990) found that pitch and lateralization recognition were not equally affected by a tonal mask and Semal & Demany (1991) found that pitch is processed separately from timbre. Kallman & Brown (1986) and Shilling & Sondquist (1990) have thus concluded that short auditory storage is not single channel but multichannel.

In the multichannel model the mask is seen as diverting auditory processors from the processing of the target sound. Within the

limited number of "processors" available for the processing of auditory stimuli, some might be specific to processing pitch, and others might extract loudness information, others duration, etc. Thus, according to this model, white noise does not effectively mask pitch because having no discernible pitch it is not likely to activate the relevant pitch processors. It does, however, mask duration because duration is a quality of all audible sounds.

This model clearly resembles that used to explain visual backward masking in terms of transient vs. sustained channels. Future research will perhaps clarify the issue of channels in the auditory system and in particular, if there is a separate channel for pitch and perhaps even for separate frequencies. Likewise, the issue of how, precisely, auditory backward masks work, whether it is by interruption or integration or most likely, a combination of the two, remains to be clarified.

In all the models of auditory backward masking described above, differences in asymptote for backward masking of tone matching for pitch can be explained in five ways. They can be the result of differences in auditory sensitivity, in forming the proper representation of the target tones, of maintaining that representation, of comparing the target tone with the memory representation of the first tone, and of holding a fairly constant decision criterion. Any or all of these differences could conceivably lead to asymptotic differences in performance.

Based on their finding that schizophrenics perform as well as normal controls in no-delay tone matching, Strous & Javitt conclude that schizophrenics do not have a difference in auditory sensitivity. Further, they argue persuasively that since schizophrenics showed the same response criterion as normals, it can be implied that schizophrenics hold a fairly constant decision criteria.

The question then remains, do schizophrenics fail to form a proper representation of tones, do they fail in maintaining that representation, or does their deficit lie in the comparison process? The latter cannot be tested using present technology and so remains purely hypothetical. Of the former two, Strous & Javitt clearly favor the hypothesis that schizophrenics process auditory stimuli imprecisely. It is this hypothesis that is put to a test in the present study.

This study combines tone matching for pitch with auditory backward masking using a dissimilar mask -- a complex tone. All subjects performed the backward masking task at their tone matching 80% threshold. Added were more difficult discrimination levels than in Strous & Javitt's studies in order to more clearly determine whether or not schizophrenics have an auditory discrimination deficit. By adding backward masking to tone matching for pitch, this study was able to examine the integrity of short store auditory sensory memory processing in schizophrenia, given overall equivalence of tone matching performance. If in fact, schizophrenics have imprecise auditory processing, they should

show no impairment in auditory backward masking relative to controls, their memory representations for pitch being, according to Strous & Javitt, just as strong as that of normals only less precise. Conversely, if they have a deficit in maintaining memory representations for pitch, i.e., if these memory representation are more susceptible to disruption, they should show a backward masking deficit.

II. METHOD

Subjects

Informed consent (see Appendix A) was obtained from 14 chronic schizophrenic inpatients and 16 normal control subjects. Groups did not differ for age (patients: 39.6 +- 8.9 yrs; controls: 39.2 +- 7.0 yrs) and all subjects were under age 60. Subjects with significant musical training were excluded and all were of normal hearing by self-report. Schizophrenic subjects were diagnosed according to DSM-III-R (1994) criteria by a board-certified attending research psychiatrist using a semi-structured clinical interview (DSM-111-R checklist), and other clinical materials as needed. Schizophrenic subjects were recruited from Bronx Psychiatric Center and their chronicity was measured by the actual duration of the illness (as marked by first hospitalization), with five years duration as the cut-off point. Subjects with DSM-III-R diagnoses other than schizophrenia, including alcoholism or substance abuse, were excluded from the study. All patients were on antipsychotic medication at the time of testing. In addition, 4 subjects were receiving treatment with anticholinergics, 2 were receiving valproate, 1 was receiving lithium, and 1 was receiving fluoxetine. Subjects on lithium or anticonvulsant medication were excluded

from the study. Control subjects were recruited by personal contact from among faculty, trainees and staff at Bronx Psychiatric Center. The schizophrenic and control groups differed significantly in sex distribution, with more women among the controls (6 M, 10 F) than among the patients (12 M, 2 F). The controls were also significantly higher than patients in IQ as measured by the Quick Test (Ammons & Ammons, 1962) (patients: 96.9 ± 10.2 ; controls: 110.7 ± 14.4 , $t=2.9$, $df=26$, $p<.01$) (see Appendix B). All subjects received a small honorarium (\$10) for their participation.

Procedure

Tone matching ability was assessed first without and then with a between-tone delay. All tones in the study were generated using Neuroscan (Herdon, VA) STIM system implemented on a PC and delivered through earphones at 75 dB SPL nominal intensity.

For minimal delay testing, tones consisted of 200 ms composites made up of an initial 100 ms segment of one pitch and a final 100 ms segment of either the same or a different pitch. A taper (10 ms rise/fall) was applied to the composite stimulus. Blocks of 20 stimuli were presented. In each block the degree of pitch deviance was held constant. For half the stimuli within each block, the initial and final segments were identical ("same" trials). For the remaining half, the final segment differed by a fixed percentage from the initial segment ("different" trials). After each stimulus,

the subject was asked to respond verbally as to whether the stimulus sounded like one long tone of invariant pitch ("same") or whether the pitch appeared to change in the middle ("different"). For each block, total correct responses, number of false positive responses (responding "same" when the pitch changed) and number of false negative responses (responding "different" when the pitch stayed the same) were recorded. Testing was initiated at the easiest level and proceeded to progressively more difficult levels until the subject was no longer able to achieve a score of 80% (16/20) correct responses. Level of task difficulty was determined by the pitch difference (Δf) between the initial and final segment of each stimulus. For all stimuli, the initial segment consisted of a 1000 Hz tone. Levels of difficulty were 40%, 20%, 10%, 7.5%, 2.5%, 2% and 1%, corresponding to final segments of 1400, 1200, 1100, 1075, 1025, 1020 and 1010 Hz. Delayed tone matching was assessed using a similar procedure except that tapers (10 ms rise/fall) were applied to each 100 ms segment individually, and the two segments were separated by a 500 ms silent interval. For both the minimal delay and 500 ms delay testing, intertrial interval was 5 s.

Once threshold had been determined for each subject, effects of backward masking were assessed. The backward masking stimulus consisted of a composite tone constructed by superimposing the 1000, 1020, 1025, 1050, 1075, 1100, 1200 and 1400 Hz stimuli used for threshold discrimination. Backward masking for each

subject was tested at that subject's individually determined threshold. For assessment of backward masking, stimuli were presented in four blocks containing 28 trials each. Each trial consisted of reference and test tones separated by 500 ms, followed by the backward masker presented at a variable interval following the test tone. In one-half of trials, the reference and the test tones were the same; in the remaining half they differed by the fixed level of Δf . 7 levels of test tone - mask interval were employed (0, 20, 40, 80, 160, 250, 500 ms). Test tone - mask interval varied in pseudo-random order within and across each of the four blocks. The number of correct vs. incorrect responses were recorded at each delay interval, and incorrect responses were further subdivided into false positives (responding "same" when reference and test stimuli were different) and false negatives (responding "different" when reference and test stimuli were the same).

III. STATISTICAL ANALYSES

Between group differences in performance on the minimal delay, delay and backward masking procedures were analyzed using repeated measures ANOVA (SPSS for Windows, SPSS, Inc., Chicago, IL) with a within-group factor of ISI (0, 40, 80, 160, 250, 500) and a between-group factor of diagnostic group (control vs. schizophrenic). Because of concern about homogeneity of variance across groups, multivariate F-tests equivalent to Wilkes' lambda were used to assess repeated-measures effects (Harris, 1985). Signal detection indices were calculated as per Grier (1971).

IV. RESULTS

Schizophrenic subjects were severely impaired in their ability to match tones across both the minimal delay and 500 ms delay conditions ($F_{1,28}=25.9, p<.0001$). There was an expected highly significant across-group effect of delay such that both schizophrenics and controls performed with lower accuracy in the the 500 ms than in the minimal delay condition ($F_{1,28}=24.8, p<.0001$). The group x delay interaction, in contrast, was not significant ($F_{1,28}=1.5, p<.2$), reflecting the fact that schizophrenic subjects were no more affected than controls during the transition from a minimal delay to a 500 ms delay condition. Tone matching thresholds were significantly greater for schizophrenic than control subjects in both the minimal delay ($F_{1,28}=13.5, p<.005$) and 500 ms delay ($F_{1,28}=25.4, p<.001$) conditions. In the 500 ms delay condition, schizophrenic subjects required an approximately 20% difference in pitch (Δf) to perform as accurately as controls performed at a 5% level of pitch difference (Figure 1). Using a 10% f threshold, it was possible to correctly categorize 14 of 16 schizophrenic subjects (88%) and 10 of 14 controls (71%, Fisher exact test $p=<.004$).

Susceptibility to backward masking was assessed with each subject performing at an individually determined level of Δf . Masking was tested at 7 different levels of ISI. Across subjects, there was a highly significant effect of ISI ($F_{6,23}=10.3, p<.001$),

indicating progressively greater effectiveness of the mask as ISI was decreased from 500 to 0 ms. There was, however, no significant between-group difference ($F_{1,28}=0.5, p=.5$) and no significant group x ISI interaction ($F_{6,23}=0.6, p=0.8$) (Figure 2). Further, there were no significant between-group differences in performance at any of the 7 levels of ISI considered individually. Thus, despite the effectiveness of the mask, schizophrenic subjects were no more susceptible to backward masking than controls.

Schizophrenics and controls also did not differ in the number of false positives or false negative responses considered separately, indicating similar strategies across groups. Finally, mean sensitivity (a') and bias measures were not different across groups. Although the groups differed in gender composition and IQ, there were no significant correlations between those variables and either tone matching threshold or performance during backward masking. Further, covariation for gender and IQ did not significantly affect the statistical results of the study. Subjects receiving anticholinergics performed somewhat better than those not receiving anticholinergics ($t=2.07, p=0.06$). However, the between-group difference in minimal-delay ($F_{1,24}=18.0, p<.0001$) and 500 ms delay ($F_{1,24}=30.4, p<.0001$) tone matching performance remained highly significant even when subjects on anticholinergics were excluded and the group X delay interaction remained non-significant ($F_{6,19}=0.4, p<0.9$).

In order to exclude the possibility of tone-discrimination threshold shifts during the testing session due, potentially, to fatigue, the final 17 subjects (9 controls, 8 schizophrenic) were retested for threshold following the conclusion of the backward masking trials. Subjects showed the same level of performance following completion of the the backward masking testing as they had during the initial testing.

V. DISCUSSION

There are two major findings of this study: first, that auditory sensory memory performance is severely impaired in schizophrenia; and second, that when adjustment is made for the difference in delayed tone matching performance between schizophrenics and normals, schizophrenic subjects are no more susceptible to auditory backward masking than are controls.

The first finding, of a significant auditory sensory memory deficit in schizophrenia as seen in impaired tone matching for pitch, is in agreement with Strous & Javitt's findings. Importantly, a complication of Strous & Javitt's work was avoided in this study. In both of their studies, the degree of schizophrenics' deficit was so large that levels of Δf that led to psychometrically valid levels of performance in controls led to floor-level performance in schizophrenic subjects. Conversely, levels of Δf that led to psychometrically valid performance in schizophrenic subjects led to ceiling level performance in controls. For the present study, a staircase procedure was used to prevent floor/ceiling effects. Subjects started at a fixed level of Δf and task difficulty was progressively adjusted in accordance with ongoing performance. Using this approach, a highly robust deficit was again observed in auditory sensory memory performance, such that 80% of subjects could be correctly identified based upon delayed tone-matching

ability alone. Further, and in contrast to Strous & Javitt's studies, schizophrenic subjects had significant levels of deficit in the minimal delay and 500 ms delay conditions. This indicates that schizophrenic subjects are impaired whenever they need to utilize a mnemonic representation to solve a task or problem, i.e. that theirs is a deficit in basic auditory processing rather than a deficit in maintaining the sensory memory trace.

It cannot, however, be ruled out that schizophrenics have, perhaps in addition, an auditory discrimination deficit. This reflects a real limitation in the minimal delay condition as a test of auditory discrimination. We do not know, and have no way of finding out, if schizophrenics could perform a pitch discrimination task as well as controls if tones were presented simultaneously rather than sequentially. This approach can be used in the visual system where, for example, two pictures can be presented side-by-side. Unfortunately however, in the auditory system simultaneously presented tones are not processed as distinct elements but rather as one composite sound. Thus there is no way to determine if simultaneously presented tones are processed equivalently in controls and schizophrenics. Likewise, it cannot be ruled out that schizophrenics have a deficit in the process of comparing the target tone with the memory representation of the reference tone. For while the present study and Strous & Javitt's studies showed that schizophrenics held a fairly constant decision criteria and one not

statistically different from normals, a deficit in the comparison process, as noted earlier, would be impossible to detect with current technology.

Three other limitations must also be noted as regards the design of this study. First, like Strous & Javitt's two studies and like so many other studies of cognitive functioning in schizophrenia, it used only hospitalized schizophrenic subjects whose condition is chronic. Hospitalized chronic patients are most often acutely ill and further have relatively low levels of baseline functioning despite extensive treatment with medication. Thus chronic and acute schizophrenia are conflated in this study, making it difficult to tease out what might be the by-product of psychosis itself versus a relatively stable deficit. Further, ratings of levels of positive and negative symptomatology were not made at the time of testing. It thus remains unclear whether these subjects' auditory sensory memory deficit is linked to a particular symptom pattern and whether the deficit is truly trait-linked. It also remains unknown whether other diagnostic groups have the same or similar deficit, i.e. is the deficit specific to schizophrenia or not and further, is it specific to chronic schizophrenia in particular.

The second limitation is that the present study, and again like Strous and Javitts' studies, examines only one facet of auditory sensory memory -- memory for pitch. Recent studies, however, suggest that auditory sensory memory is multichannel rather than single channel. In a single channel model such as Massarro's,

different stimulus features such as pitch, timbre, loudness, location and duration are centrally stored on a single cluster. In this model, recognition of different features should be degraded by the same mask. Work subsequent to his has shown that this is not the case. As noted earlier, Kallman & Brown (1986) found that while white noise does not act as an effective mask for pitch, it does for duration and that white noise is a less effective masking stimulus than a composite tone. Similarly, Shilling & Sondquist (1990) found that pitch and lateralization were not equally affected by a tonal mask and Semal & Demany (1991) found that pitch is processed separately from timbre. Given these findings, a good argument can be made that within the limited number of "processors" available for the processing of auditory stimuli, some might be specific to processing pitch, others might extract loudness information and still others duration, etc. Thus it remains unclear whether schizophrenics' auditory sensory memory deficit is confined to pitch and if they do in fact have sensory memory deficits in other acoustic dimensions, whether they are of the same nature.

Finally, all schizophrenic subjects in the present study were receiving antipsychotic medication and several were receiving anticholinergic medication, compared to none of the controls. It is possible, therefore, that the deficit in tone matching performance is due to medication effect even though antipsychotics do not appear to have marked negative or positive effect on working memory

(Goldberg & Weinberger, 1996). Anticholinergics, on the other hand, do not appear to have been a factor, since subjects on anticholinergics, if anything, performed better than those not on anticholinergics.

The second finding of this study is that when tone matching performance is equated, schizophrenics are no more susceptible to auditory backward masking than are controls. This finding supports Strous & Javitt's imprecision of processing hypothesis. In both schizophrenics and normals, the masking stimulus produced a monotonically decreasing level of performance with decreasing ISI. Moreover, over the interval of 0 to 500 ms, performance in both groups ranged from near chance to a level similar to that observed in the no-mask condition. Thus the absence of a deficit cannot be attributed to psychometric insufficiency on the part of the masking stimulus.

The finding that auditory backward masking performance is not impaired in schizophrenia indicates that storage within the short stage of auditory sensory memory is no more labile in schizophrenic subjects than in controls. Further, as this study demonstrates in examining sub-300 ms processing, the deficit in processing within long storage reflected by schizophrenic subject's impaired no-mask performance, cannot be attributed to dysfunction within a prior stage. A significant finding in Strous & Javitt's prior study of auditory memory performance was that, when corrected for overall

precision of processing, retention of information within the long store of auditory sensory processing was equivalent in schizophrenic subjects and controls. Thus, it is likely that the primary deficit in auditory processing in schizophrenia relates to the precision with which sensory features such as pitch can be represented, rather than the duration such information can be retained.

The findings regarding normal auditory backward masking in schizophrenia contrasts sharply with the extensive body of literature demonstrating increased susceptibility to visual backward masking. Several potential explanations can be considered. First, as noted previously, it is possible that non-medicated patients would show auditory backward masking deficits but that such deficits were normalized by medication. All schizophrenic subjects in the present study were receiving antipsychotic medication.

Second, it may be that the differential results reflect differential architectures of the visual and auditory systems. It has been postulated that impaired visual backward masking in schizophrenia reflects impaired interaction between transient and sustained channels in the brain (Braff, 1993; Green, Nuechterlain & Mintz, 1994b). Because the neural substrates of the transient and sustained channels of visual processing have not yet been identified, it is impossible to determine whether neural correlates of these channels are present also for the auditory system. Primate brains

contain a far greater number of visual than auditory regions. Thus, if the interaction between transient and sustained channels corresponds to interactions between separate sensory regions, it is likely that the substrates responsible for the visual backward masking deficit in schizophrenia are not present within the cortical auditory system. Thus the possible absence in the auditory system of separate channels, and specifically, the absence of a transient channel, would prevent excessive activation within the transient from interfering with information retained in the sustained processing system. However, it has been suggested that deficits in prepulse inhibition of auditory startle response in schizophrenics reflects impaired processing within distinct fast and slow auditory pathways (Braff, 1993). To the extent that distinct fast and slow auditory pathways correspond to transient and sustained visual pathways, this model would predict impaired auditory as well as visual backward masking. In addition, it has been suggested that transient channel deficits, of themselves, are not sufficient to account for the observed visual backward masking deficit in schizophrenia (Weiss, Chapman, Strauss & Gilmore, 1992), leaving open the possibility that there are as yet unknown physiological factors in the visual system affecting backward masking which may or may not be present in the auditory system.

A third possible potential explanation for the lack of susceptibility of schizophrenic subjects to auditory as compared to

visual backward masking, is that visual processing is far more attention-dependent than auditory processing. Thus if the deficit in visual backward masking reflects, primarily, a deficit in sustained attention, visual backward masking would be expected to be disturbed in schizophrenia to a far greater extent than auditory backward masking.

An alternative explanation is that the differential finding regarding auditory and visual backward masking reflects differences in the method with which the two processes were evaluated. In most studies of visual backward masking, it is difficult to equate no-mask performance and thus to compensate for generally poorer no-mask performance in schizophrenia. In contrast, in the present study the two groups were explicitly matched for no-mask performance and their continued equivalence of performance was verified at the conclusion of the study. Had backward masking been measured at the same level of Δf for both schizophrenic and control subjects in the present study, schizophrenic subjects would undoubtedly have performed worse at all masking intervals, since their level of performance in the no-mask condition would have been far lower than that of controls. It has been proposed that schizophrenia is associated with impaired visual processing organization and that deficits in visual backward masking performance in schizophrenia reflect impaired stimulus classification (Knight, Elliot & Freedman, 1985; Schuck & Lee, 1989;

Weiss, Chapman, Strauss & Gilmore, 1992). It is possible therefore that if stimuli were manipulated to produce equivalent no-mask performance, visual backward masking susceptibility would be similar in schizophrenic and control subjects. In a recent study, however, correcting for critical stimulus duration did not normalize backward masking susceptibility in schizophrenic subjects (Saccuzzo et al., 1996), indicating that no-mask performance per se is not the only critical factor in determining backward masking susceptibility. It remains possible, though, that other types of manipulations might have both corrected no-mask performance deficits in schizophrenia while simultaneously "normalizing" susceptibility to backward masking.

Because of the novelty of the finding, no definitive explanation can be given at present to account for the relative preservation of auditory backward masking performance in schizophrenia. A major implication of the present study, however, is that neural models of information processing dysfunction in schizophrenia must be able to account for the impairment of some perceptual processes (e.g. tone discrimination, prepulse inhibition, visual backward masking) and the relative preservation of others. Whatever the underlying mechanisms, the present findings are not compatible with a "general deficit" model of information processing dysfunction in schizophrenia as described by Chapman and Chapman (1978). In such a model, schizophrenic subjects would be postulated to show impairment both in precision of processing and retention of

information. In contrast, in the present study as well as in prior studies, processing precision was impaired while information retention was preserved.

Interestingly, as regards the factor of intelligence, the IQ level of the schizophrenic subjects was lower than that of the controls but there were no IQ correlations for either tone matching threshold or backward masking. Only a very weak relationship between intelligence and sensory-perceptual processing has previously been found (Jenson & Munro, 1979; Smith & Stanley, 1980; Smith & Barron, 1981) but it has been contended that IQ and auditory backward masking performance are correlated (Raz, 1983). In this regard it is worth noting that auditory backward masking performance has previously been evaluated in another group with lower IQ, the aging (Newman & Spitzer, 1983). Elderly subjects had similar levels of performance when the tone-mask interval was long, but performed less accurately than young subjects at intervals below 360 ms, reflecting an age-associated slowing of auditory processing time. Auditory processing impairments in schizophrenia are thus substantially different from those observed as a consequence of aging. The fact that increased susceptibility to auditory backward masking can be observed in some clinical situations indicates that the paradigm is sensitive to some forms of brain dysfunction. The fact that a deficit was not observed in schizophrenia supports the concept that auditory processing speed is

not slowed, but rather precision is impaired.

In summary, despite extensive literature on susceptibility to visual backward masking in schizophrenia, susceptibility to auditory backward masking has not previously been evaluated. This was the first such study and it confirmed Strous & Javitt's finding that schizophrenic subjects require a far larger pitch difference than controls in order to differentiate two tones presented with a short intervening delay and, once floor/ceiling effects were removed, that schizophrenics are impaired in tone matching in a minimal delay condition as well. However, schizophrenic subjects were no more susceptible to auditory backward masking than controls when tested at levels of between-tone pitch difference that yielded equivalent performance in the absence of a mask. These findings thus support Strous & Javitt's contention that whereas precision of processing within the auditory system is impaired, retention of information within the short and long-term auditory stores is relatively unaffected by the disorder.

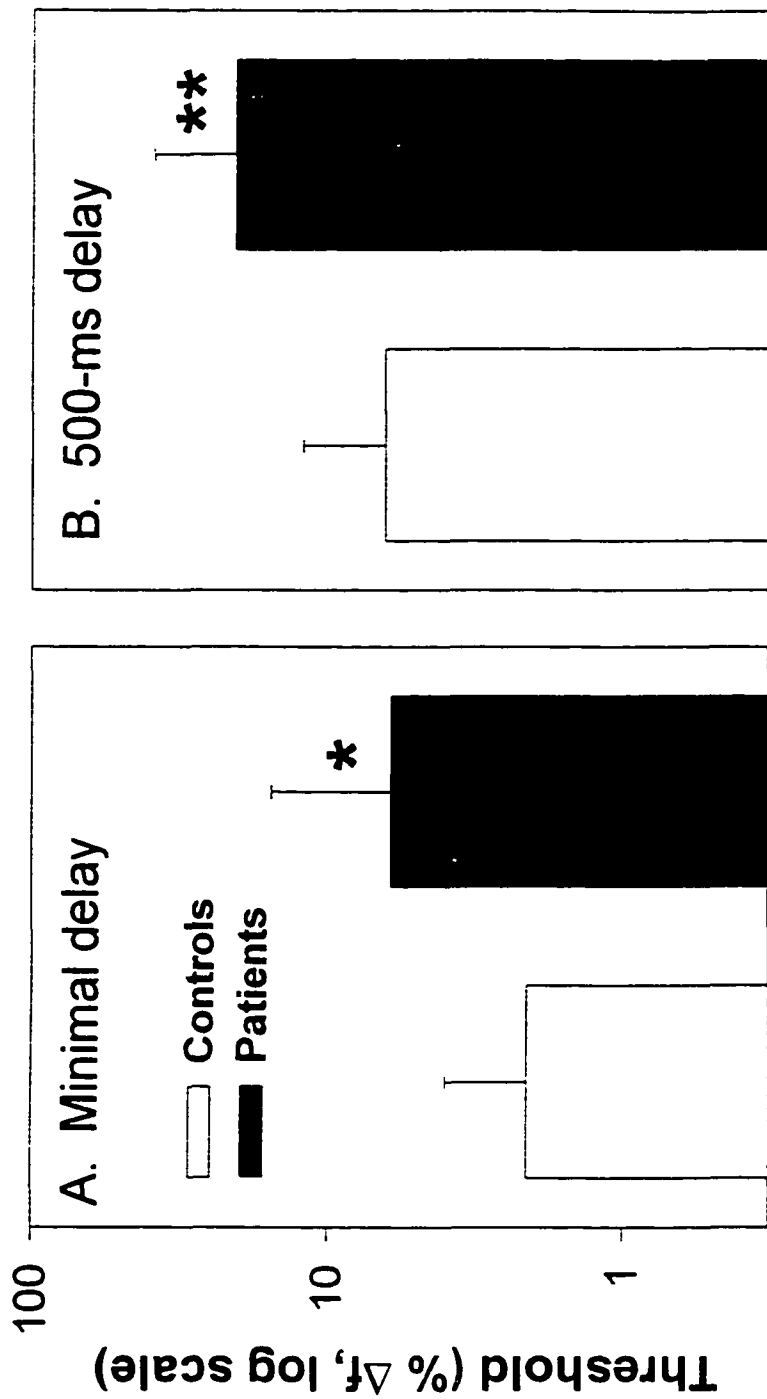


Figure 1

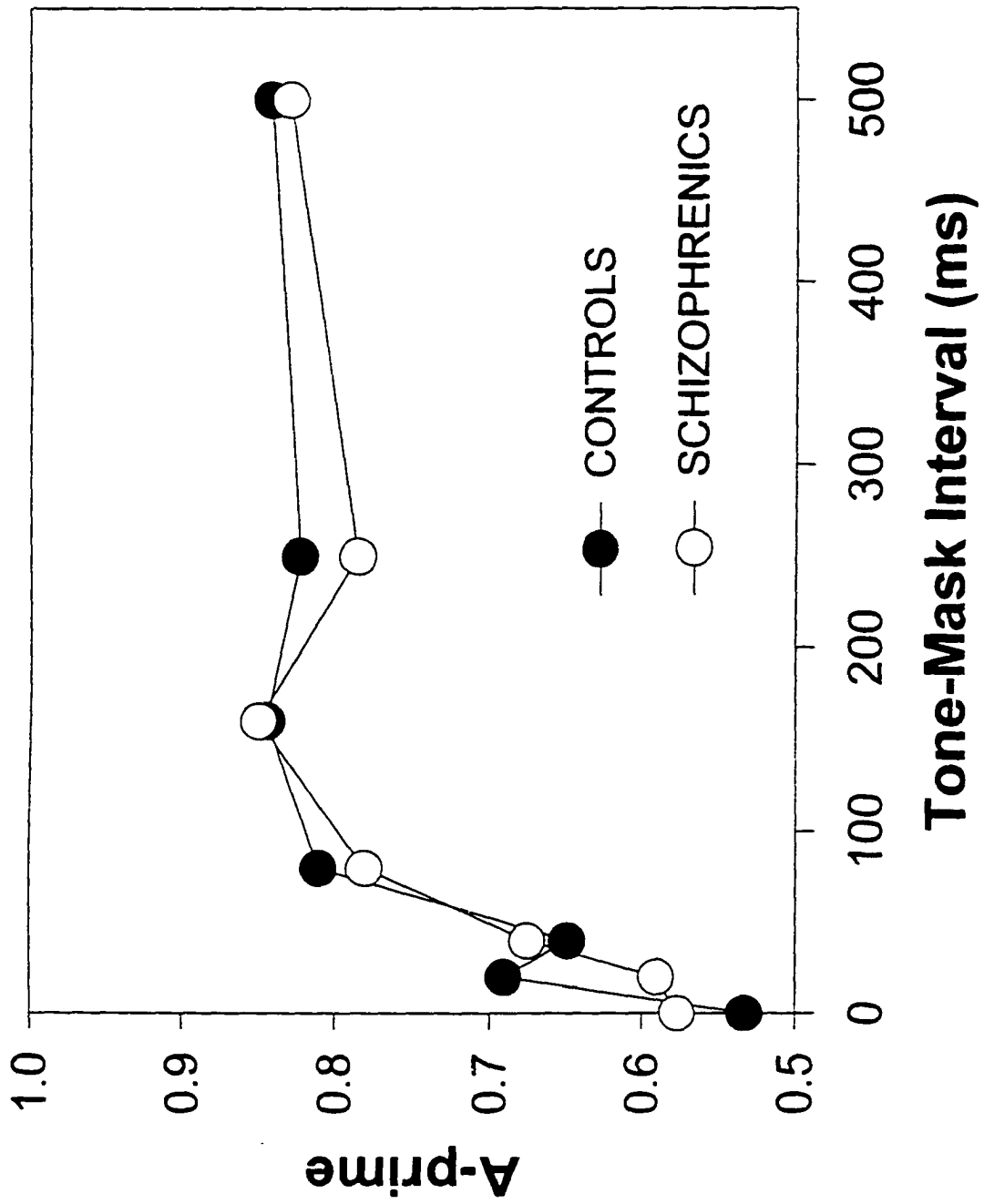


Figure 2

APPENDIX A

BRONX PSYCHIATRIC CENTER/
ALBERT EINSTEIN COLLEGE OF MEDICINE
FORM FOR INFORMED CONSENT

Name of researcher: Daniel C. Javitt, M.D., Ph.D.

Title: The impairment of working memory in schizophrenia

Purpose of research: To study working memory in schizophrenic patients as compared with normal, healthy volunteers in order to gain further understanding of the abnormalities of mental process contributing to the illness.

Procedures:

You have been asked to participate in research aimed at investigating memory functions in mentally ill patients. The research will involve your doing a number of tasks. You will be asked to: (1) watch a computer screen and press a button when you see specific shapes; (2) listen to simple noises through earphones and say if they are the same or different; and (3) categorize small objects that will be placed in your hand according to different features, such as weight, texture, and length. Each session will take approximately two hours. Breaks will be provided automatically.

every 20 minutes and you will be allowed to take additional breaks whenever you ask. If you are a patient, you will also be asked a series of questions about your illness and to participate in psychological tests that may take 1-1/2 hours to complete. You will be paid \$5.00 for each session. If you are a patient, this money will be deposited either with the cashier's office or with the commissary located on Ward 17 of BPC.

Possible risks:

The procedures are without risk.

Benefits:

If you are a patient, it is not expected that the procedures will have any immediate effect on your nervous condition or treatment plan. However, gaining information about memory difficulties associated with mental illness may allow for more effective treatments to become available in the future.

Alternative procedures:

Your participation in this study is completely voluntary. You do not have to take part if you do not want to and you can change your mind and withdraw at any time. If you are a patient your treatment at the Bronx Psychiatric Center will not be effected by declining to participate or by later withdrawal.

All the information that you provide will be stored in a locked filing

cabinet and will be kept strictly confidential. The only people allowed access to the information will be the research staff, the staff who are treating you, the Institutional Research Review Board for the Protection of Subjects, The Committee on Clinical Investigations at the Albert Einstein College of Medicine and the National Institute of Mental Health. When the results of the research are presented, your name or any other information which could be used to identify you will not be used.

Your legal rights regarding the liability of the investigator or the sponsor are not waived.

If you have any questions about this study, contact Dr. Daniel C. Javitt at (718) 931-0600, extension 2327. If you have any questions about your rights as a participant in this study, contact the Chairperson on the Institutional Review Board, Dr. Alvin Pam at (718) 931-0600, extension 2345.

Attestation

By signing this form, I have agreed to participate as a subject in a medical research study entitled: The impairment of working memory in schizophrenia, to be carried out under the supervision of Dr. Daniel C. Javitt, Department of Psychiatry, Albert Einstein College of Medicine and Bronx Psychiatric Center, telephone number (718)

931-0600, extension 2327.

I have been told by the doctor or other persons performing the research that I may be a subject only if I wish, and that I may withdraw from the study at any time. I have also been assured, if I am a patient, that my treatment by doctors and staff at the Albert Einstein College of Medicine or the Bronx Psychiatric Center, now and in the future, will not be effected in any way if I refuse to participate or if I enter the program and withdraw later.

"I _____, agree to participate in the research described above."

Signature of SUBJECT	Date	Signature of WITNESS	Date
Name of person providing this information _____			
Signature and date of information provider _____			

I hereby certify that participation in the research protocol entitled "The impairment of working memory in schizophrenia" does not conflict with this patient's treatment plan.

Signature- _____

member of treatment team

Name

Date

APPENDIX B

Designed for practical, quick testing of verbal-perceptual intelligence, the Quick Test is a 50-item individually administered test in which subjects match vocabulary items spoken by the tester with items in a picture. It requires no special training to use and requires no reading, writing or speaking on the part of subjects, all advantages in the testing of low-income mentally ill persons. Norms for both children and adults are based on a total sample of 458 white children and adults (up to age 45), quota controlled for age, sex, grade in school, and father's, husband's or own occupation. It correlates highly (high .60s into the .90s) with its parent instrument, the Full Range Picture Vocabulary Test. Studies of the criterion-validity of the Quick test provide independent evidence that it is a valid test of intelligence, with positive and significant correlations found between Quick I.Q. scores and standardized measures of academic achievement as well as measures of memory performance. Reliability studies of equivalent forms produced correlations that ranged from .60 to .96 (Keyser & Sweetland, 1984). The mean I.Q. is set at 100 with a standard deviation of 15.

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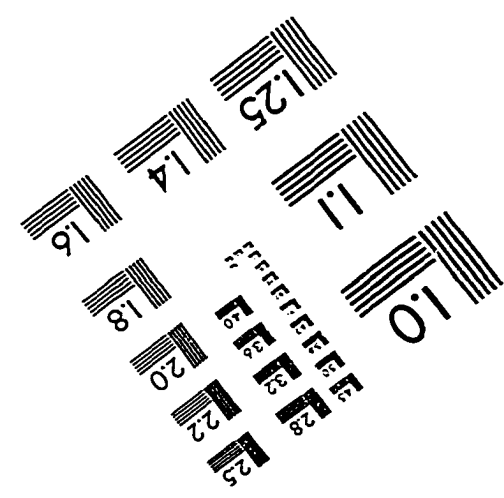
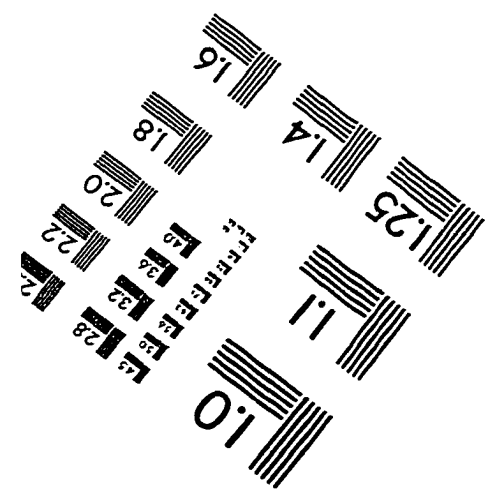
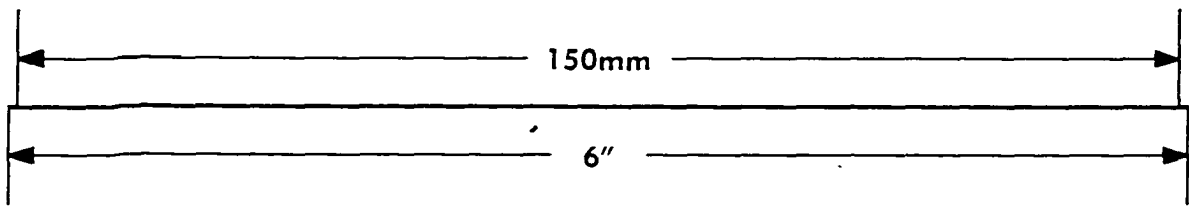
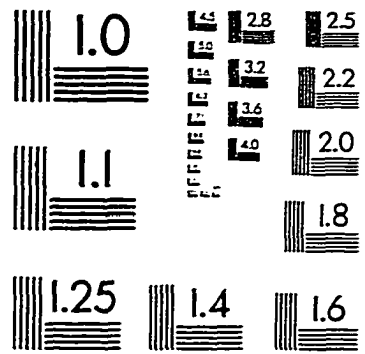
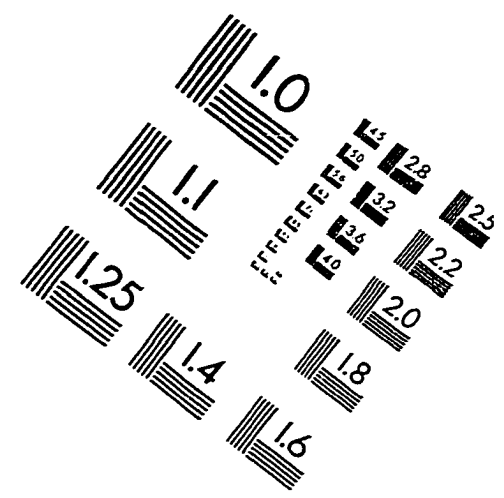
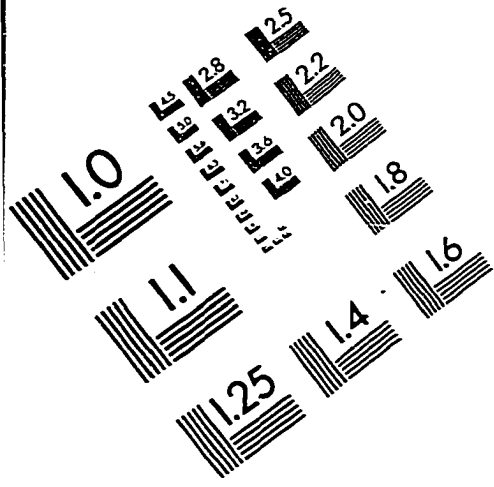
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IMAGE EVALUATION TEST TARGET (QA-3)



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