Sensory Gating and Inhibitory Function in Late-Life Schizophrenia

by Joan M. McDowd, Diane L. Filion, M. Jackuelyn Harris, and David L. Braff

Abstract

Although similarities between the cognitive deficits observed in schizophrenia and those observed in aging have been recognized for over 50 years, little work has been done to directly examine these similarities or their implications for late-life schizophrenia. We review studies of prepulse inhibition, habituation, latent inhibition, and negative priming that indicate marked similarities in the patterns of deficits observed in schizophrenia and in aging. We also present new data from preliminary studies of prepulse inhibition and negative priming in which we compared young normal controls, older adult normal controls, and late-life schizophrenia patients. For both measures, both schizophrenia patients and older adults showed an inhibitory deficit relative to young controls. In the case of negative priming, older schizophrenia patients showed evidence of greater inhibitory dysfunction than did normal older adults, suggesting that older schizophrenia patients suffer a deficit resulting from the combined effects of schizophrenia and aging. The implications of these results and directions for future research are discussed.

Information-processing and attentional dysfunctions have long been identified as fundamental cognitive deficits in early-onset schizophrenia patients (e.g., Gjerde 1983; Mirsky and Duncan 1986; Anscombe 1987). It is interesting to note that strikingly similar dysfunctions have been reported in association with normal aging (e.g., Plude and Hoyer 1985; McDowd and Birren 1990); that is, both schizophrenia and aging are characterized by deficits in the efficiency with which information is encoded and processed. In both populations, these deficits may result in slowed processing, increased distractibility, and inefficient allocation of attentional resources. Saccuzzo observed these similarities in 1977. Echoing Cameron’s (1939) proposal, he suggested that much could be learned about the cognitive deficits specific to schizophrenia from a systematic study of both states, schizophrenia and normal aging. According to Saccuzzo, what Cameron and perhaps others since then failed to realize, however, [is] the potential value of systematically determining at what point the similarity between schizophrenia patients and the elderly ends. By determining the ways in which schizophrenia patients and the elderly are similar and those in which they are not, researchers can separate those experimental tasks uniquely related to schizophrenia from those that are related to other forms of pathology and deterioration. [Saccuzzo 1977, p. 597]

Saccuzzo’s point is well taken in any analysis comparing cognitive function in schizophrenia patients and older adults. Although the two groups appear similar on some variables, they are obviously very different on others. Schizophrenia is an acute or chronic psychopathological disorder that is associated with a variable course. Aging is inevitably a chronic process that is part of normal devel-

Reprint requests should be sent to Dr. J.M. McDowd, Dept. of Psychology, Pomona College, 550 N. Harvard Ave., Claremont, CA 91711.
The neurobiological mechanisms underlying the similar alterations in cognitive function in the two groups may or may not be the same. Although the question of the commonality of underlying neurobiological deficits is an important one to consider as we attempt to understand the combined effects of schizophrenia and aging, the present review focuses on two other issues: (1) Is there a common process underlying the cognitive deficits observed in both schizophrenia and normal aging? (2) How do schizophrenia-related deficits in late-life schizophrenics interact with normal age-related cognitive changes?

Niederehe and Rusin (1987) asked similar questions in their review of schizophrenia, aging, and information processing. They concluded that the information processing literature sheds little light on the cognitive status of aging schizophrenics. The available data do not permit inferences about what is likely to change from an information processing viewpoint as a schizophrenic individual ages. We cannot gauge whether the aging changes are likely to add to the schizophrenic deficits, to have little further effect, or in some way to counterbalance the cognitive deficits seen earlier. [p. 178]

The present article addresses these questions in the context of specific attentional deficits involving sensory gating and inhibitory function. A brief review of the data relevant to these issues is presented, and a framework that may provide a link between the cognitive deficits seen in schizophrenia and those seen in normal aging is proposed. In addition, we present some interesting new data that bear on the questions raised here.

One key to understanding schizophrenia- and age-linked cognitive dysfunctions may be found by examining the role of inhibitory processes in selective attention and efficient information processing. Inhibition of irrelevant stimuli is a vital component of all information-processing stages, ranging from automatic sensory gating and habituation to the more voluntary processes of stimulus selection and focused attention. Declines in the integrity of inhibitory function may produce the deficits in selective attention commonly observed in older adults. More severe inhibitory failures may result in a vulnerability to cognitive fragmentation and the formation of psychotic symptoms (Braff et al. 1992). Thus, efficient inhibitory function is critical to the ability of humans to maintain their cognitive functional integrity.

Interest in the role of inhibitory processes in schizophrenia can be traced back to Venables (1960), who hypothesized that schizophrenia patients are "flooded" by sensory overstimulation, as well as to McGhie and Chapman (1961), who discussed a schizophrenia-related inability to provide organization for, and a reduction of, "the otherwise chaotic flow of information reaching consciousness." Consistent with the views of these early theorists, several lines of evidence now exist that suggest schizophrenia-related inhibitory deficits.

Inhibitory function in cognition and aging has recently enjoyed a resurgence as a focus of research (see Birren 1959; Jerome 1959 for earlier discussions). It has been postulated that with aging there is a greater deficit in inhibitory than in facilitatory processes, which disrupts the balance in attention and reduces behavioral efficiency. There are a variety of behavioral data to support the hypothesis that older adults have weakened inhibitory control relative to young adults. For example, decreased inhibitory function may be responsible for patterns of data such as the increased intrusion errors seen in older adults in free-recall tasks (e.g., Fuld et al. 1982; Stine and Wingfield 1987), increased Stroop color-word interference (Comalli 1962; Cohn et al. 1984), less accurate frequency judgment (Kausler and Hakami 1982), and less efficient problem-solving (Hoyer et al. 1979). In Hasher and Zacks' (1988) theoretical framework, an age-related decline in inhibitory function is central to their account of age differences in working memory capacity.

Thus, strikingly similar information-processing deficits have been observed in schizophrenia and aging. Unfortunately, to date few studies have been carried out that directly compare sensory-gating and inhibitory function in schizophrenia patients and older adults. However, the separate literatures contain some overlap in experimental paradigms and dependent measures. In the following sections, we will review evidence for sensory gating and inhibitory deficits in both schizophrenia and aging, focusing on those measures for which there are parallel studies for each population of interest. We will conclude the review with new data from experiments using two of these paradigms.

It is important to note that although each of the experimental paradigms we review was designed to measure inhibitory function, at this stage of our knowledge we cannot say whether each paradigm measures exactly the same centrally mediated inhibitory
function. At a basic level of information processing, inhibition of irrelevant stimulation occurs as a process termed “sensory gating.” This process regulates sensory input, filters irrelevant information, and allows the early stages of processing of relevant information to occur without disruption (Braff and Geyer 1990). Sensory gating provides a buffer for incoming information, allows selective stimulus processing, and prevents sensory overload. However, in addition to sensory gating, it is likely that inhibitory processes are involved in many other information-processing tasks, and perhaps the neurobiological mechanisms responsible for inhibition in each of these tasks differ. The following review includes one paradigm that is believed to provide a relatively direct measure of sensory gating (prepulse inhibition [PPI]) and several other paradigms (habituation, latent inhibition [LI], and negative priming) that are likely to reflect inhibitory processes occurring later in the flow of information processing in addition to sensory-gating processes. Regardless of whether the tasks reviewed here measure a common inhibitory mechanism or various forms of inhibitory processes, they provide a useful foundation for comparing inhibitory function in schizophrenia patients and older adults. The data reviewed here point the direction for future research on the interacting effects of schizophrenia and aging to provide a better understanding of their combined effects in late-life schizophrenia.

**PPI**

One measure of sensory gating used in schizophrenia research is PPI of the eyeblink component of the startle reflex. The startle eyeblink is part of a general automatic, involuntary, brainstem-mediated (Davis 1984) reflex that is reliably elicited by relatively strong stimuli with abrupt onsets. PPI of the startle reflex occurs when a relatively weak nonstartling stimulus (prepulse) precedes the onset of a startle-eliciting stimulus by a “lead interval” of approximately 500 ms or less. In such cases, the magnitude of the elicited startle reflex is significantly reduced and sometimes even completely suppressed (see Graham 1975; Hoffman and Ison 1980; Anthony 1985 for reviews). The PPI effect occurs across species, is quite robust, and is evident even during sleep.

It has been hypothesized that PPI acts in humans to protect early stimulus processing (Graham 1980; Hoffman and Ison 1980). According to this view, when a prepulse is detected and processed, a gating process is also initiated that momentarily decreases or buffers other sensory stimulation until the processing of the prepulse has been completed. This attenuation serves to protect the processing of the prepulse stimulus from disruption. Consistent with this view, recent research has shown that the PPI effect in humans is increased when subjects are instructed to focus their attention on the prepulse (Delpezzo and Hoffman 1980; Hackley and Graham 1987; Hackley et al. 1987; Acocella and Blumenthal 1990; Filion et al. 1993). Thus, attention directed to a task-relevant or significant prepulse may act to increase the level of protection provided to the processing of that prepulse.

**Schizophrenia.** In a number of studies that have examined PPI in schizophrenia, a no-task paradigm has been used to assess automatic sensory gating (Braff et al. 1978, 1992; Grillon et al. 1992). In these studies, groups of chronic schizophrenia inpatients and matched control subjects were presented with a series of startle-eliciting noise bursts, some of which were preceded by a nonstartling prepulse. In the first study (Braff et al. 1978), 12 schizophrenia patients and 20 matched controls were tested with these procedures; prepulses were presented at lead intervals of 30, 60, 120, and 240 ms. The schizophrenia subjects showed significantly less PPI than did the controls at the 60-ms lead interval. Braff et al. (1992) extended this finding. They examined 39 schizophrenia patients and 37 control subjects, using lead intervals of 60, 120, and 240 ms, and found that the schizophrenia patients exhibited significantly less PPI than did the controls at all three intervals. In a third study, Grillon et al. (1992) found that schizophrenia patients showed abnormally reduced PPI across a range of prepulse intensities 5 to 20 decibels (dB) above the background noise. These results strongly suggest that chronic schizophrenia is associated with a fundamental deficit in the ability to automatically filter sensory stimulation.

In a fourth study, Dawson et al. (in press) employed an “attention to prepulse” paradigm to examine more voluntary attentional effects on PPI. In this study, a group of 15 young recent-onset remitted schizophrenia patients and a group of 14 matched control subjects were presented with two prepulse types, high-pitched and low-pitched tones, and instructed to attend to one type and ignore the other. The attended and ignored...
prepulses were presented at lead intervals of 60, 120, and 240 ms. Schizophrenia and control subjects exhibited comparable levels of PPI to the ignored prepulse. However, while the control subjects showed significantly greater PPI during the attended prepulse than during the ignored prepulse, the schizophrenia subjects showed equivalent levels of PPI to both prepulses. These results suggest an inability on the part of the young, remitted schizophrenia subjects to increase the level of protection provided to the processing of task-relevant stimuli. Together with the results of Braff et al. (1978, 1992), these data suggest differing levels of inhibitory deficits for young remitted and older chronic schizophrenia patients. Whereas the chronic schizophrenia patients displayed deficits in automatic sensory gating, the young remitted schizophrenia subjects exhibited a PPI deficit only under an attentional load. These findings are consistent with Callaway and Naghdi’s (1982) suggestion that at least some schizophrenia patients may be deficient primarily in the more voluntary aspects of selective attention.

Normal Aging. The first study to examine age effects on sensory gating (Harbin and Berg 1983) involved a no-task paradigm similar to that used by Braff et al. (1978); it revealed that groups of young (college age) and older (over 65 years) subjects exhibited equivalent levels of PPI. The second study (Harbin and Berg 1986) included a no-task trial block as well as a trial block in which subjects were required to perform a task. Although the task was unrelated to the startle-eliciting stimuli and prepulses, it did serve to focus attention on the sensory modality of the prepulse stimuli. The results revealed no age differences in PPI in the no-task block, but there were group differences in the task phase. Whereas the young subjects displayed a significant increase in PPI during the task phase, the older adults showed no such increase.

Filion and McDowd (1991) recently conducted a third study to examine PPI and its attentional modulation in groups of normal young and older adults. The methodology used in that study was essentially identical to the procedures of Dawson et al. (in press), with the exception that the startle-eliciting stimulus was an air puff presented to the suprasternal notch. While the young subjects (mean age = 18.8) showed significantly greater PPI to the attended than to the ignored prepulse, the older adults (mean age = 73.7) showed equivalent levels of PPI to the two prepulse types, a pattern of results similar to that found with young remitted schizophrenia patients in the Dawson et al. (in press) study. The finding that their PPI deficit was observed only under an attentional load suggests an inability on the part of the older adults to mobilize volitional attentional resources, thereby increasing the level of protection provided to the processing of task-relevant stimuli.

Together, the patterns of data for schizophrenia subjects and normal older adults indicate some similar deficits and suggest that the PPI paradigm is a useful one for identifying similarities and differences in inhibitory function in the two subject groups.

Habituation

Habituation, often referred to as “the simplest form of learning,” is operationally defined as the exponential decrement in response that occurs when the same initially novel stimulus is presented repeatedly at rates too slow to produce sensory adaptation or effector fatigue. Habituation is a critical component of information processing in which individuals learn to rapidly inhibit processing of irrelevant stimuli (Hernandez-Peon 1969; Groves and Thompson 1970; Cheal et al. 1982; Siddle 1983). Habituation is similar to PPI in that it has been described as a “gating mechanism subserving selective attention” (Waters et al. 1977, p. 228).

Schizophrenia. The most commonly employed measure in studies of habituation in schizophrenia is the skin conductance orienting response (OR) to mild stimuli. Current information-processing models of orienting hold that elicitation of the OR is associated with the allocation of attention (e.g., Kahneman 1973; Ohman 1979; Posner 1980; Dawson et al. 1989). In an extension of this view, habituation of the OR may be interpreted as reflecting the inhibition of the allocation of attention to irrelevant stimuli. Thus, if an individual’s inhibitory processes are compromised, that individual should demonstrate less control over the allocation of attention and should be slower to habituate to irrelevant stimuli. Although the literature on skin conductance habituation in schizophrenia is complex, there is general agreement that at least some schizophrenia subjects exhibit decreased levels of OR habituation (Gruzelier and Venables 1972; Spohn and Patterson 1979; Bernstein 1987).

A second response system used to examine habituation in schizo-
phrenia is the startle response. Geyer and Braff (1982) reported that a group of schizophrenia patients exhibited impaired habituation of the startle blink reflex compared with normal or patient controls in a paradigm in which 121 presentations of acoustic stimuli were presented. Whereas normals and patient controls exhibited a decrement of approximately 70 percent in response amplitude across trials, schizophrenia subjects showed a reduction of less than 50 percent. A trend in the direction of schizophrenia-linked startle habituation deficits \((p = 0.056)\) was also observed by Braff et al. (1992) in a paradigm that was less optimal for measuring habituation relative to PPI.

**Normal Aging.** A small number of studies have examined habituation in younger and older organisms. For example, Gakkel and Zinina (1953) reported that behavioral orienting is slower to habituate in older dogs, Levine et al. (1987) found older cats slower to habituate than younger cats, and Brennan et al. (1984) found older rats slower to habituate than young rats. In humans, three studies have employed the skin conductance OR to examine age effects on habituation. The data of Rogozea and Florea-Ciocoiu (1988) indicate that adult humans over 45 years of age require more trials to habituate to a repetitive auditory stimulus than do young adults. Similarly, Eisenstein et al. (1990) reported that the best predictor of OR habituation rates among males ages 18–39 years was age, concluding that “the younger the subjects the faster the habituation rate, the older the subject the slower the habituation rate” (p. 169). Finally, McDowd and Filion (1992) reported a study in which young adults were observed to habituate relatively rapidly to stimuli designated as irrelevant, whereas older adults continued to orient to both relevant and irrelevant stimuli across the trial sequence, showing very little habituation. These data give further credence to the hypothesis of an age-related deficit in the ability to inhibit the processing of distracting or irrelevant information. In addition, these studies in which habituation was used as an index of inhibitory function indicate that schizophrenia patients and older adults show a similar alteration in the efficiency of inhibitory processes.

**LI**

LI is believed to be a measure of a basic, automatic inhibitory function. LI is “the detrimental effect of passive, non-reinforced preexposure of a stimulus on the subsequent ability of an organism to form new associations to that stimulus” (Lubow 1989, p. 1). Much of the work on this phenomenon has been done with animals. In the LI paradigm, one group of animals is preexposed to a certain stimulus and a comparison group is given no such preexposure. In a subsequent test phase, animals in both groups are required to learn an association between the preexposed stimulus and some other event. The group that was preexposed to the stimulus is typically less successful than the non-preexposed group in learning the new association in the test phase. The interpretation of this finding is that in the preexposure phase, the random presentation of the target stimulus produces a subsequent inhibition of processing of that stimulus, as it has been encoded as meaningless. The LI of processing produces the learning deficits observed in the test phase for the preexposed group relative to the performance of the non-preexposed group. If inhibitory function is compromised in some population, the prediction for this paradigm would be for reduced LI; that is, preexposed and non-preexposed groups should show similar learning.

One of the unique aspects of the LI paradigm is that an inhibitory deficit results in better than normal performance in that an individual with decreased inhibitory function will learn the new association more quickly than will an individual with normal inhibitory function. This is an important advantage of this paradigm over the multitude of paradigms that reliably result in poorer performance on the part of the schizophrenia patients and older adults (Sutton 1973).

**Schizophrenia.** To observe LI in adult humans, it is necessary to include some task in the preexposure phase so that attention will be focused away from the preexposed stimulus. Lubow et al. (1987) developed a task for use with adults to test the hypothesis that because of inhibitory deficits, LI would be reduced in individuals with schizophrenia. This task involved the auditory presentation of two lists, each of which consisted of 40 pairs of nonsense syllables. Superimposed over one list was a white noise ranging in duration from 0.5 to 1.5 seconds, presented randomly 30 times across the 40-syllable-pair list. During the first phase of the study, all subjects were instructed to listen carefully to the recording and to count the number of syl-
The syllable counting task was the masking task, included to ensure that attention was directed to the syllables and not to the white noise.

The test phase immediately followed the preexposure phase just described. The subjects were informed that a new task was beginning. They were told that the recording of syllables would be presented again, but during the presentation, points on a scoreboard would be increased according to a rule involving the recording. The subjects’ task was to try to figure out the rule by which the points on the scoreboard increased and to indicate to the experimenter when they believed they knew the rule. All subjects heard the list containing both syllables and white noise, and the points were increased on the scoreboard after each presentation of the white noise. For the half of the subjects who had been preexposed to the white noise while counting syllable pairs, processing of white noise should have been inhibited in the first phase of the experiment, and those subjects were expected to be slower to learn the relationship between the white noise and the scoreboard in the second phase. The dependent measure of interest was the number of white noise presentations required for the subjects to learn the rule governing the increasing scoreboard points. The hypothesis regarding inhibitory deficits in schizophrenia put forth by Lubow et al.’s (1987) study had chronic schizophrenia and were on neuroleptic medications. Baruch et al. postulated that such medications may act to normalize any attentional deficits that are characteristic of unmedicated schizophrenia. Using the same task as Lubow et al., Baruch et al. tested normal adults, chronic (medicated) schizophrenia subjects, and acute (unmedicated) schizophrenia subjects. The prediction was that if neuroleptic medications did indeed ameliorate attentional deficits, only the acute (unmedicated) schizophrenia group would show a disruption of LI, whereas the chronic (medicated) group should more closely resemble the normal controls. Indeed that is just what Baruch et al. observed. The normal and chronic groups showed the typical pattern of LI, whereas the acute group showed an impairment in LI. In fact, the preexposed subset of the acute group actually outperformed the non-preexposed subset of that group. Baruch et al. interpreted this pattern of results as indicating a deficit in inhibitory function among acute schizophrenia patients, and they suggested that this deficit may be ameliorated by the neuroleptic drugs typically administered to patients with chronic schizophrenia.

Normal Aging. The only developmental studies of LI in humans have involved children of various ages (see Lubow 1989 for a review). However, there has been some work with rats in which LI has been used in the context of conditioned taste aversion. For example, Misanin et al. (1983, 1985) and Peterson et al. (1985) varied the duration of preexposure and the preexposure-test interval in five separate experiments involving conditioned task aversion. Together, the results of these studies show that in very old rats LI is present only weakly or is absent altogether. This pattern of results is consistent with the notion of an age-related weakening of inhibitory function. Clearly, LI is a paradigm with the potential to contribute to our understanding of inhibitory function in schizophrenia and human aging and merits further research.

Negative Priming

A fourth measure that is believed to index inhibitory function is termed “negative priming,” a measure of the efficiency with which an individual voluntarily inhibits attention to a distracting stimulus while focusing attention on a target. The logic of negative priming is as follows:

If the internal representation of an ignored stimulus is associated with inhibition during the selection of the attended stimulus, then the processing of a subsequent stimulus requiring the same internal representation as that of the previously ignored stimulus should be impaired. [Tipper and Cranston 1985, p. 592]

The negative priming paradigm typically involves the presentation of two competing stimuli; the subject is instructed to select one stimulus for processing and ignore the other. Reaction time for processing the target stimulus is the dependent measure. If a previously
ignored distractor stimulus is subsequently re-presented as a to-be-attended stimulus, processing of that stimulus is slower than if there had been no prior presentation. This slowing is attributed to the extra time required to access the just-inhibited stimulus and is taken as a measure of inhibitory strength. A strongly inhibited stimulus will take longer to access than a weakly inhibited stimulus. It is interesting to note that poorer inhibitory function actually produces faster responding in the negative priming condition. As in the case of LI, this aspect of the negative priming paradigm is important for distinguishing deficits in inhibitory function from any generalized cognitive dysfunction present in schizophrenia patients or older adults.

**Schizophrenia.** Interestingly, schizophrenia patients have been reported to show significantly less negative priming than normal adults (e.g., Beech et al. 1989). Beech et al. (1989) used a negative priming task based on the Stroop paradigm. The baseline measurement was the typical Stroop test (Stroop 1935): subjects were required to name the color of ink in which color names were printed. In the negative priming condition, however, the to-be-ignored color name on one trial was the to-be-named ink color on the subsequent trial. In this task, if the to-be-ignored color name on the first trial is successfully and efficiently inhibited, then the subject should take longer to output that same name on the next trial than he or she would take when successive trials involve different color names, as in the baseline condition. This lengthening of reaction time is known as negative priming. If, however, inhibitory function is compromised, the magnitude of the negative priming effect should be reduced or absent.

Beech et al. (1989) tested 18 young (mean age = 24.25) adults with schizophrenia in relative remission and 18 age-matched (mean age = 26.75) control psychiatric patients. The schizophrenia subjects met DSM-III-R (American Psychiatric Association 1987) criteria for schizophrenia; the control psychiatric patients were without major psychotic illness (12 had neurotic symptoms and 6 were diagnosed with personality disorder). In a comparison of reaction times in the baseline condition and the negative priming condition, Beech et al. reported that the control group showed significant slowing in the negative priming condition, whereas the schizophrenia group showed no significant slowing and thus no negative priming. This pattern of results is interpreted as reflecting an inhibitory deficit on the part of the schizophrenia group. It is important to note that in negative priming paradigms, as in the LI paradigm, the inhibitory deficit results in better performance by the schizophrenia subjects than by the controls (i.e., faster reaction times in the negative priming condition). Thus, this pattern of results cannot be attributed to any artifact created by poorer performance on the part of schizophrenia subjects across a variety of tasks. Instead, Beech et al.’s (1989) study provides additional support for the notion of a schizophrenia-related decrease in inhibitory function.

**Normal Aging.** Several studies of young and older adults used negative priming paradigms similar to those used with schizophrenia subjects, and the results indicate that older adults show less negative priming than do young adults. The inference from these studies is that inhibitory processes are weaker in old than in young adults. McDowd and Oseas-Kreger (1991) found this pattern of results in a study involving naming of selected letters of the alphabet that overlapped other distractor letters; Hasher et al. (1991) reported a similar pattern of results with non-overlapping alphabetic characters; and Tipper (1991) found an age-related decline in negative priming in a study using simple line drawings.

Filion et al. (1992) used a negative priming task in which selection of the target stimulus is made on the basis of spatial location. This speeded classification task, described by Tipper et al. (1991), involves the visual presentation of stimuli in one of four spatial locations on a computer screen. Stimuli are presented in two-trial sets. On each trial, one “X” and one “O” are presented; the subject’s task is to press a key corresponding to the location of the O as rapidly as possible and to simply ignore the X. Negative priming is measured on those trial sets in which the O appears in the second trial in the same location in which the to-be-ignored X appeared on the first trial of the set. Any slowing observed in this condition relative to a comparison condition in which the location of X’s and O’s within a set are unrelated to each other is interpreted as being due to the momentary inhibition of the location associated with the X, which has to be overcome before the subject can respond to the target O on the subsequent trial. Weakened inhibitory function would result in a reduc-
tion in the magnitude of the negative priming effect.

Using this paradigm, Filion et al. (1992) tested 24 young adults (mean age = 18.8) and 29 older adults (mean age = 72.6); they found that the older adults exhibited significantly less negative priming than the younger subjects. It is worth pointing out again that the finding of reduced negative priming in older adults (as well as in the schizophrenia group) means that they are actually performing faster in the negative priming condition (relative to their own baseline performance) than are the younger adult controls. This result, then, cannot be attributed to any generalized decrease in cognitive function. Together, these studies lend support to the notion that in situations requiring efficient selective attention, both schizophrenia subjects and older adults show weaker inhibitory function than normal young adults.

Preliminary Studies: PPI and Negative Priming in Late-Life Schizophrenia and Normal Aging

In an attempt to begin to address the questions regarding the possible interaction of schizophrenia and aging, we recently collected data on two of the measures just described from a small group of late-life schizophrenia patients and matched controls. We report the results of these preliminary studies, in which we examined PPI and negative priming. Across the two studies we compared three subject groups: young normal controls, older adult normals, and late-life schizophrenia subjects. Such a comparison allows us to begin to piece together the relative contributions of age and psychosis to the cognitive deficits observed in late-life schizophrenia.

PPI

Subjects. We examined both PPI and its attentional modulation in a group of 8 older early-onset schizophrenia subjects and a group of 10 age-matched nonschizophrenia control subjects. Table 1 lists demographics for the two subject groups.

Method and procedures. The experimental procedures for the startle testing were similar to those described earlier. The subjects were presented with a series of startle-eliciting noise bursts, which were occasionally preceded by a brief nonstartling prepulse presented at lead intervals of 60, 120, and 240 ms. During the first phase of the experiment, the subjects were instructed to simply sit quietly with their eyes open. During the second phase they were instructed to listen carefully for the prepulse and to press a button each time a prepulse was detected. Each phase consisted of two trial blocks composed of eight trials each. The eight trials consisted of two presentations of the startle-eliciting noise burst alone and six presentations of the startle stimulus preceded by the prepulse, two each at 30, 60, and 120 ms before startle-stimulus onset. The purpose of the first block of trials was to examine automatic sensorimotor gating in a no-task situation. The purpose of the second trial block was to examine the ability of the late-life schizophrenia patients and age-matched controls to increase their level of PPI by focusing their attention on the prepulse stimuli.

Results. Inspection of the blink data revealed that many subjects had habituated by the second trial block of each condition. Therefore, the results described here are for the first trial block of each condition only. The blink modification scores were submitted to a groups X condition X lead interval analysis of variance that yielded a marginal effect of lead interval (F = 2.99; df = 2.32; p = 0.06) as well as a significant group X condition interaction (F = 6.01; df = 1.16; p = 0.03). As can be seen in figure 1, both groups showed maximal PPI at the 120-ms lead

<p>| Table 1. Subject demographics and rating scale summaries |
|-------------|---------------|-------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>Mean (SEM)</td>
<td>Mean (SEM)</td>
</tr>
<tr>
<td>Duration of illness (yrs)</td>
<td>54.9 (2.5)</td>
<td>66.1 (1.1)</td>
</tr>
<tr>
<td>Age at onset (yrs)</td>
<td>33.6 (4.5)</td>
<td>0.0</td>
</tr>
<tr>
<td>Chlorpromazine equivalent (mg)</td>
<td>20.5 (0.8)</td>
<td>—</td>
</tr>
<tr>
<td>SAPS</td>
<td>1554.6 (1076.1)</td>
<td>0.0</td>
</tr>
<tr>
<td>SANS</td>
<td>5.1 (1.3)</td>
<td>0.0</td>
</tr>
<tr>
<td>BPRS</td>
<td>6.4 (1.3)</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>31.2 (4.0)</td>
<td>19.4 (0.2)</td>
</tr>
</tbody>
</table>

Note.—SEM = standard error of the mean; BPRS = Brief Psychiatric Rating Scale (Overall and Gorham 1962); SANS = The Scale for the Assessment of Negative Symptoms (Andreasen 1984a); SAPS = The Scale for the Assessment of Positive Symptoms (Andreasen 1984b).
interval. In addition, the schizophrenia subjects showed significantly less PPI than did the control group at each of the three lead intervals, particularly in the attention-to-prepulse conditions. In previous work with the attention-to-prepulse paradigm (Dawson et al., in press), attention effects and group differences were largest at the 120-ms lead interval. Therefore, we next performed a group × condition analysis of variance on the blink modification scores for the 120-ms lead interval separately. The results revealed a significant group × condition interaction (F = 5.54; df = 1.16; p = 0.04). T tests confirmed that the control subjects showed significantly greater PPI at the 120-ms lead interval during the attend condition than during the neutral condition (t = 2.24; df = 1.9; p < 0.05), whereas there was no significant difference between the conditions for the schizophrenia group.

Discussion. The pattern of results from the startle blink measures indicates that sensory gating is indeed disrupted in late-life schizophrenia. The failure of gating functions in older schizophrenia patients to be modulated by attentional constraints suggests further that this inhibitory dysfunction has implications for both conscious (voluntary) and preconscious (automatic) information processing.

Negative Priming.
Subjects. Following the PPI testing, we asked the same 8 older schizophrenia subjects and 10 age-matched control subjects to perform the spatial location version of the negative priming task described earlier. For purposes of comparison, we have included in our analyses here data from a randomly selected subset of 10 young adult subjects from our negative priming study described earlier (Filion et al. 1992).

Method and procedures. The method and procedures for all subject groups were identical to those described above for the Filion et al. (1992) study.

Results. The negative priming data are shown in figure 2. The left panel shows data for the 10 young adults selected from Filion et al. (1992). The middle and right-hand panels show the data from the normal older controls and the older schizophrenia subjects, respectively, from the present study. These reaction-time data were submitted to a groups (young control, older control, older schizophrenia subjects) × condition (baseline, negative priming) analysis of variance. The analysis revealed significant main effects of group (F = 15.17; df = 2.25; p < 0.001) and condition (F = 80.63; df = 1.25; p < 0.001) as well as a group × condition interaction (F = 104.58; df = 2.25; p < 0.001). Followup analyses indicated that in a comparison of baseline and negative prime conditions, both the young and older control groups showed significant negative priming (both p's < 0.001), whereas the older schizophrenia group showed significant facilitation in the negative priming condition (p < 0.001).

A subsequent analysis examining the magnitude of negative priming in the three groups indicated that the young adult controls showed more negative priming than the older adult controls and the older adult controls showed more nega-
Figure 2. Reaction time in baseline and negative priming conditions for young controls, older controls, and older schizophrenia subjects

From Filion et al., in press.

tive priming than the older schizophrenia subjects. As shown in figure 2, the reaction time of normal young adults was approximately 50 ms slower in the negative priming condition than in the baseline condition. The greater the slowing, the larger the negative priming effect. In comparison, normal older adults showed a negative priming effect of approximately 20 ms, less than half the size of the effect for young adults.

Discussion. The reduction in negative priming in older adults demonstrated by these data is again taken as evidence that declining inhibitory function characterizes the aging process. Of particular interest here, however, is the performance of the older schizophrenia subjects. They not only showed reduced negative priming, but actually produced facilitation of approximately 20 ms in the negative priming condition. Such a pattern of results would come about from a complete failure to inhibit the to-be-ignored X location; it provides strong evidence for inhibitory dysfunction in older schizophrenia patients.

The data shown in figure 2 also bear on the question of interacting effects of aging and schizophrenia. Older schizophrenia subjects show evidence of greater inhibitory dysfunction than normal older adults, suggesting that older schizophrenia patients suffer a deficit resulting from the combined effects of aging and schizophrenia. In addition, it is clear from these data that inhibitory dysfunction is not pathognomonic of schizophrenia. Inhibitory dysfunction appears to be common to the cognitive deficits of both schizophrenia and normal aging (Saccuzzo and Braff 1980), and further, it appears that there is a true interaction effect when both schizophrenia and aging occur in the same individual.

Conclusions and Directions for Future Research

Extending the work on sensory-gating and inhibitory function to the area of late-life schizophrenia results in many interesting questions. (1) Will older schizophrenia patients have greater inhibitory deficits than younger schizophrenia patients? (2) How will schizophrenia patients compare with age-matched nonschizophrenia patients? (3) Will older adults with early-onset schizophrenia have a greater or lesser deficit than older adults with late-onset schizophrenia? In the latter case, the effects of chronic schizophrenia interact with the effects of increasing age. These are fascinating questions that have yet to be answered.

The present review and new data document several experimental paradigms that have been used to study sensory gating and inhibitory impairments in aging and schizophrenia. These and a number of other paradigms have revealed similar deficits in the two subject groups, although few studies have included direct comparisons. In fact, to date no study has included the four subject groups (young controls, young schizophrenia subjects, older controls, and older schizophrenia subjects). Studies that did include such groups would allow researchers to disentangle the contributions of age, psychopathology, and perhaps...
There are still a number of crucial deficits that may well induce cognitive deficits associated with both schizophrenia and normal aging that may exceed the deficits seen in either state alone. What is clear now, however, is that older schizophrenia patients have profound inhibitory deficits in older schizophrenia patients. The data indicate that late-life schizophrenia produces cognitive deficits associated with schizophrenia and normal aging may exceed the deficits seen in either state alone. There are still a number of crucial studies that need to be accomplished. For example, it will be important to determine whether an earlier onset leads to accelerated deficits in older schizophrenia patients. What is clear now, however, is that older schizophrenia subjects have profound inhibitory deficits that may well induce cognitive disturbance and psychosocial deterioration in these individuals.

References


Lubow, R.E. Latent Inhibition and Conditioned Attention Theory.


Acknowledgments

This work was supported in part by USPHS grants MH-42228 to D.L. Braff and MH-45131 to D.V. Jeste from the National Institute of Mental Health. The authors thank Joyce Sprock for assistance in data collection and Gordon C. Baylis for providing the negative priming software.

The Authors

Joan M. McDowd, Ph.D., is Assistant Professor of Psychology, and Diane L. Filion, Ph.D., is Research Associate in Psychology and Gerontology at the University of Southern California. M. Jackuelyn Harris, M.D., is Assistant Professor of Psychiatry, School of Medicine, University of California at San Diego, and Medical Director of the Geropsychiatry Service, San Diego Veterans Affairs Medical Center. David L. Braff, M.D., is Professor of Psychiatry, University of California, San Diego Medical Center, San Diego, CA.

Minority Research Training in Psychiatry

Through its National Institute of Mental Health-funded Program for Minority Research Training in Psychiatry (PMRTP), the American Psychiatric Association (APA) is seeking to increase the number of minority psychiatrists going into psychiatric research.

The program provides medical students and psychiatric residents with funding for stipends, travel expenses, and tuition for an elective or summer experience in a research environment. Stipends are also available for 1- or 2-year post-residency fellowships for minority psychiatrists. Deadlines for applications are December 1, 1993 (for residents seeking a year or more of training and for post-residency fellows) or 3 months before training is to begin (for medical students and other residents).

Training takes place at research-oriented departments of psychiatry in major medical schools in the United States and other appropriate sites nationwide. An individual at the site (the research "mentor") oversees the research training experience.

The PMRTP is administered by the APA's Office of Research. The director of the program is Harold Alan Pincus, M.D.; the project manager is Jeanne Nevin, M.B.A. An advisory committee of senior researchers and minority psychiatrists developed guidelines for applicants and criteria for selection. The members of this committee evaluate and select trainees.

For more information about the PMRTP, call Ms. Nevin at the toll-free number for the PMRTP, 1-800-852-1390, or at 202-682-6225, or write to her at the American Psychiatric Association, 1400 K Street, NW, Washington, DC 20005.