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Age-Related Decline in Auditory Plasticity: Experience Dependent Changes in Gap Detection as Measured by Prepulse Inhibition in Young and Aged Rats

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Young adult and aged F344 rats were compared on a silent gap variant of the prepulse inhibition paradigm. Animals were tested using a 50-ms single tone cue, followed by 8 days of silent gap testing. The first 3 days of gap testing were long gaps (range 2 to 100 ms) followed by 5 days of short gaps (range 2 to 10 ms). The effects of gap length, prior experience, and age, on the magnitude and direction (facilitation vs. attenuation) of the acoustic startle response, were examined. The young rats showed stronger and more reliable acoustic startle responses (uncued trials) during all acoustic startle tasks as compared to the old. The younger animals also exhibited a more consistent attenuated response across cues and days. Depending on silent gap length, both reduction (inhibition) and enhancement (facilitation) of startle were observed. Finally, only the young adult animals showed an experience-related shift from facilitation to attenuation in response to very short silent gap cues, and this initial early facilitation predicted later attenuation following additional experience.

Keywords: startle, perception, startle attenuation, startle facilitation, aging

Prepulse inhibition (PPI) is used to study several clinical disorders, such as schizophrenia (de Bruin, van Luijtelaar, Cools, & Ellenbroek, 2003), Huntington's disease (Swerdlow et al., 1995), seizure disorders (Pouretemad, Thompson, & Fenwick, 1998), Parkinson's disease (Morton et al., 1995), Tourette syndrome, and obsessive–compulsive disorder (Castellanos et al., 1996; Swerdlow, Benbow, Zisook, Geyer, & Braff, 1993; Swerdlow et al., 2001). The PPI paradigms are based on the auditory startle response (ASR), which is part of a constellation of defensive responses to sudden, intense stimuli (Larrauri & Schmajuk, 2006; Swerdlow, Braff, & Geyer, 2000). This characteristic motor response is typically reduced or attenuated when the startling stimulus is preceded by a salient cue (Ison & Hoffman, 1983; Leitner et al., 1993), and this attenuation reflects PPI. Although the ASR is thought to be based on a relatively simple subcortical circuit, PPI is thought to involve several subcortical and cortical structures (Koch, 1999; Schmajuk & Larrauri, 2005; Threlkeld, Penley, Rosen, & Fitch, 2008). For a comprehensive review of PPI neurobiology, see Larrauri and Schmajuk (2006) or Koch (1999).

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The PPI paradigm also has been used as a model for sensorimotor gating (Koch, Fendt, & Kretschmer, 2000; Varty, Hauger, & Geyer, 1998) and is useful for assessing perceptual abilities in nonverbal organisms (Graham, 1975). PPI has further been used in rodents to examine visual (Buckland, Buckland, Jamieson, & Ison, 1969; Ison, Hammond, & Krauer, 1973), tactile (Lockey, Kavaliers, & Ossenkopp, 2009; Pinckeney, 1976), and auditory processing (Ison, McAdam, & Hammond, 1973; Threlkeld et al., 2008; Threlkeld, Rosen, & Fitch, 2007).

Aging causes a wide variety of changes, including impairments of specific sensory functions and reductions in experience related plasticity. During aging there is a decline in the function of some PPI circuit (Barsz, Ison, Snell, & Walton, 2002; Caspary, Ling, Turner, & Hughes, 2008; Popelar, Groh, & Syka, 2005; Walton, Frisina & O'Neill, 1998). However the specific mechanisms underlying the effects seen in aging on the attenuation of PPI are unclear. Studies examining acoustic PPI during aging have been inconsistent. During aging there are reports of greater PPI in humans (Ellwanger, Geyer, & Braff, 2003), no change in humans (Ludewig et al., 2003), and mice (Ison, Bowen, Pak, & Gutierrez, 1997); and of reductions (i.e., less PPI) in rats (Varty et al., 1998), and mice (Ouagazzal, Reiss, & Romand, 2006; Young, Wallace, Geyer, & Risbrough, 2010). These inconsistent results may be due to differences in procedure and the type of cue used. Experience-induced plasticity in PPI performance also has been reported (Chang et al., 2005; Habib, 2000; Hage et al., 2006; Plappert, Pilz, & Schnitzler, 2004) and modifying effects of aging on response to PPI experience (plasticity) may partly explain the inconsistent findings.

The basic PPI paradigm uses a single tone cue followed by a startle eliciting stimulus (SES). The cue can vary in temporal and acoustic characteristics. The silent gap task is a variant of this PPI

paradigm, in which the cue is a brief cessation of continuous background white noise (Ison, 1982).

Silent gap detection seems to involve a more complex circuitry than single tone detection and shows a developmental time course (Dean, Sheets, Crofton, & Reiter, 1990; Friedman, Peiffer, Clark, Benasich, & Fitch, 2004). Further, deficits in silent gap processing have been related to disruptions of cortical development in rodents, including focal microgyria (Peiffer, Friedman, Rosen, & Fitch, 2004), neonatal hypoxia-ischemia damage (McClure, Peiffer, Rosen, & Fitch, 2005), ectopias, and heterotopias (Clark, Sherman, Bimonte, & Fitch, 2000; Threlkeld, Hill, Rosen, & Fitch, 2009) as well as developmental interference with dyslexia-risk genes (Threlkeld, McClure, et al., 2007).

Using a silent gap task, reductions in PPI have been shown during aging in both rodents (Wang et al., 2009) and humans (Lister, & Tarver, 2004; Snell & Frisina, 2000). This paradigm also has been used to model tinnitus in rats (Turner et al., 2006; Turner & Parrish, 2008).

Manipulations of the acoustic and temporal properties of the cue can alter levels of PPI. For example, presentation of a salient cue preceding a startle-eliciting stimulus (generally 20 to 500 ms before the cue: Swerdlow et al., 2000) typically leads to reduction (or inhibition) of the startle response in an acoustic PPI paradigm. However, an increase (facilitation) in startle response has been observed using extremely short (<10 ms) cue burst intervals (Ison, McAdam, & Hammond, 1973; Reijmers, & Peeters, 1994; Reijmers, Vanderheyden, & Peeters, 1995), extremely complex acoustic stimuli (e.g., mismatch of a repeating complex background stimulus), and cross-modal processing (e.g., visual cues and acoustic startle (Pinckeney, 1976), for a review, see Fitch, Threlkeld, McClure, and Peiffer (2008)). Prepulse facilitation (PPF) can also be seen with initial testing of young inexperienced subjects, particularly on difficult tasks (Chang et al., 2005; Habib, 2000; Hage et al., 2006). Reijmers and Peeters (1994) found that in rats louder cues caused an increase in PPI but not in PPF, suggesting that facilitation and inhibition may be mediated by different neural systems. Mice studies also indicate independence between PPI and PPF (Plappert et al., 2004), and this relationship between facilitation and inhibition was examined further in the present study.

Specifically, acoustic PPI was administered to young adult and aged rats using both a single auditory cue, and also more complex silent gap cues of varying duration. We examined how gap length, prior experience, and age influenced the magnitude and direction (facilitation vs. attenuation) of the resulting acoustic startle response. Notably, although data in young animals show that the prepulse effects can change with experience (Chang et al., 2005; Habib, 2000; Hage et al., 2006; Plappert et al., 2004), the effects of aging on this type of plasticity have not to our knowledge been investigated.

We hypothesized that: (1) During aging there would be a reduction in the ability to process the silent gap resulting in reduced PPI; (2) Young rats would show more experience dependent plasticity in their responses than old; and also (3) PPI and PPF (as measured within subjects) would not be completely independent, with cross-day comparisons indicating correlations across these processes.

Method

Subjects

Subjects were male Fisher F344 rats, including 23 old (20 months) and 16 young adult (7 months) animals (NIH colony, Harlan, Indianapolis, IN). Animals were pair-housed until a month before testing. Subjects were then individually housed on a 12-hr light–dark cycle with food and water available ad libitum. All subjects received a 2-week visual acuity task prior to this study, and were retained after assessments described here for further behavioral testing. Data for nine animals (four young, five old) for the first day of the long silent gap task was lost due to technical problems, and these data were not included in the repeated-measures analysis for that task. All procedures were conducted in compliance with the National Institutes of Health *Guide for the Care and Use of Laboratory Animals* (National Research Council, 1996) and were approved by the Institutional Animal Care and Use Committee at the University of Connecticut.

Behavioral Procedure

Animals received 1 day of single tone testing, 3 days of long (2 to 100 ms) silent gap testing, and 5 days of short (2 to 10 ms) silent gap testing in sequential order (see Figure 1), with testing conducted Monday thru Friday. Animals were tested in four groups of nine to 10 rats. Each group contained four young and five to six old animals, to balance for time-of-day effects. Further details on individual procedures are provided below.

Single tone task. For single tone testing, 104 trials (cued or uncued) were presented in a pseudorandom order. Uncued trials consisted of a quiet (ambient 50 dB) background into which was periodically introduced a 50 ms duration, 105-dB sound pressure level (SPL) SES. Cued trials included a 75-dB SPL, 7 ms, 2300-Hz tone ending 50 ms prior to SES. Intertrial intervals were varied (16 to 24 s) to prevent anticipation of the SES.

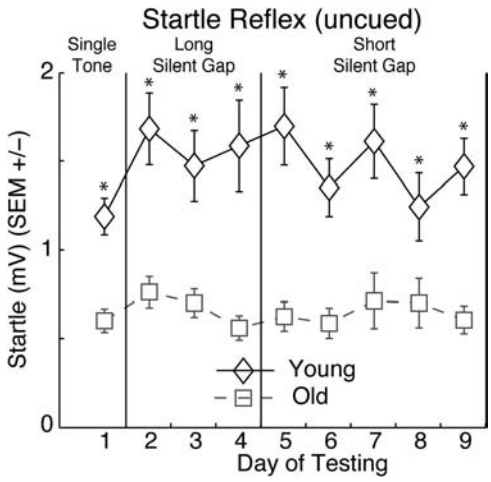

Figure 1. Mean uncued startle response for the young adult ($n = 12$) and old ($n = 18$) rats on each day of testing. Baseline startle response was relatively stable cross day and the three different tasks, aged animals showed less of an acoustic startle response than the young. * Independent samples t test for age group, $p < .05$.

Long silent gap task. The long silent gap sessions were presented once a day for 3 consecutive days. Each session (0 to 100 ms gaps) included 300 trials, each consisting of the presentation of a variable duration silent gap (0 [uncued], 2, 5,10, 20, 30, 40, 50, 75, or 100 ms) embedded in continuous 75-dB SPL broadband white noise. The gap ended 50 ms prior to the start of a 105-dB SPL burst of white noise (the SES). Intertrial intervals were again varied (16 to 24 s) to prevent anticipation of the SES. Cue and noncued SES were presented in a pseudorandom order.

Short silent gap task. Short silent gap sessions were presented once a day for 5 consecutive days, at the completion of long silent gap testing. The procedure was the same as the long silent gap task. The only difference was that the length of the silent gaps varied from 0 to 10 ms (0 [uncued], 2, 3, 4, 5, 6, 7, 8, 9, and 10 ms). Intertrial intervals were again varied (16 to 24 s) to prevent anticipation of the SES. Cue and noncued trials were presented in a pseudorandom order.

Apparatus

For testing, subjects were placed in a square (25 cm × 25 cm) opaque 40-cm high walled, polypropylene chamber, on a load cell platform (Med Associates, GA), which measured the subject's ballistic motor response to the SES as expressed in pressure applied to the platform in mV. These signals were acquired and passed through a linear load cell amplifier (PHM–250–60) into a Biopac MP100WS acquisition system (Biopac Systems, Santa Barbara, CA) connected to two Macintosh computers. These recorded the signals indexing subject's movement and ASR as an mV signal. Specifically, the maximum peak value defining the ASR for each trial was extracted from the 200 ms following the onset of the SES. Auditory stimuli were generated using a Pentium 4 Dell PC with custom programmed signal generation software (SigGen) and a Tucker Davis Technologies (Alachua, FL; RP2) real time processor. Stimulus files were played through a Marantz (Markham, Ontario, Canada) integrated amplifier connected to nine Cambridge Sound Works' Newton Series MC105 speakers with a frequency range of 100 Hz to 22 kHz (North Andover, MA). Sound levels were calibrated by sound-level meter (Peiffer, Rosen, & Fitch, 2002). All auditory stimuli were played through individual speakers centered and mounted 30 cm above each pair of load platforms. The polypropylene chambers provided visual but not auditory isolation. Presumably the background white noise played during the silent gap task masked vocalization across chambers.

Analysis

To assess baseline ASR, the average raw startle response (in millivolts) was examined for all uncued trials. Comparing the startle response on cued and uncued trials further provided a measure of cue detectability (Leitner et al., 1993; Wecker, Ison, & Foss, 1985). Specifically, PPI was calculated for the peak ASR, using the formula (mean cued response/mean uncued response) × 100 (Peiffer et al., 2002; Threlkeld, McClure, et al., 2007; Threlkeld et al., 2008; Threlkeld, Rosen, & Fitch, 2007). In this formula, absolute response scores (as measured by load-cell displacement for each subject's startle response) for cued and uncued trials are expressed as a ratio, multiplied by 100 (thus attenuation scores [ATT] represent a percentage of baseline startle). ATT scores were analyzed as a second dependent variable for all tasks. All analyses were performed using SPSS 17, and partial eta-squared (η_p^2) was used for effect size (SPSS Inc, Chicago, IL). For the silent gap tasks the single tone ATT score was used as a covariate to eliminated variance due to possible age related differences in the baseline response to a simple cue. Results were similar with and without using single tone ATT as a covariate. The figures display the raw data, while the statistical analyses are based on the covariate analysis.

Results

Baseline ASR (Uncued Trials)

A repeated-measures analysis of variance (ANOVA) examining differences in baseline ASR (uncued trials) as a function of age was performed (see Figure 1). There was an effect of age, $F(1, 28) = 19.10$, $p < .01$, $\eta_p^2 = .406$, but not for day, $F(8, 224) = 1.06$, $p > .10$, $\eta_p^2 = .036$. There was a trend for a Day × Age interaction, $F(8, 224) = 1.76$, $p = .087$, $\eta_p^2 = .059$. This indicates that animals' startle did not decrease across days and tasks.

To examine the effect of repetitive exposures to the SES on a single day, the individual responses on the first day of exposure to the SES (i.e., the single tone task) were analyzed (see Figure 2). There was a main effect of trial, $F(1, 49) = 4.45$, $p < .01$, $\eta_p^2 = .105$, indicating habituation within this initial session. There was also a main effect of age, with older rats showing less uncued startle than the young adult group throughout the session, $F(1, 38) = 14.18$, $p < .01$, $\eta_p^2 = .272$. However, there was no Age × Trial interaction ($p > .10$) indicating a similar habituation function for both age groups. There was no within day effect of trial on the subsequent testing days (i.e., the long or short gap tasks: $p > .10$).

ATT

Single tone task. A paired-samples *t* test comparing uncued ASR with cued ASR showed attenuation in both young adult, $t(15) = 5.83$, $p < .01$, and old, $t(22) = 6.36$, $p < .01$, subjects. An ANOVA showed a main effect of age, with young adult animals exhibiting more attenuation (lower ATT scores) as compared to aged animals, $F(1, 37) = 12.27$, $p < .01$, $\eta_p^2 = .249$ (see Figure 3).

Long silent gap task. A repeated-measures ANOVA using mean ATT score on the single tone as a covariate was conducted. This covariate eliminated variance due to aging differences in baseline response to a simple cue, with any remaining variance attributable to gap-mediated PPI. ATT differences for gap duration (nine levels), day (three levels), and age (young and old) during the 3 days of long silent gap task indicated a main effect of gap, $F(8, 216) = 32.19$, $p < .01$, $\eta_p^2 = .544$, but no effect for day, $F(2, 54) = 2.08$, $p > .10$ $\eta_p^2 = .071$, or age $F(1, 27) = 0.27$, $p > .10$, $\eta_p^2 = .010$ (see Figure 4). These results indicate that longer gaps produced more attenuation. There was a Gap × Age interaction, $F(8, 216) = 9.98$, $p < .01$, $\eta_p^2 = .270$, indicating a difference between the age groups in response to gap length. There was also a Day × Age interaction, $F(2, 54) = 6.09$, $p < .01$, $\eta_p^2 = .184$, indicating a differential effect of experience with age. Finally, there was a three-way interaction, $F(16, 432) = 2.31$, $p < .01$, $\eta_p^2 = .079$. Overall, young adult, but not old, animals showed facilitation for

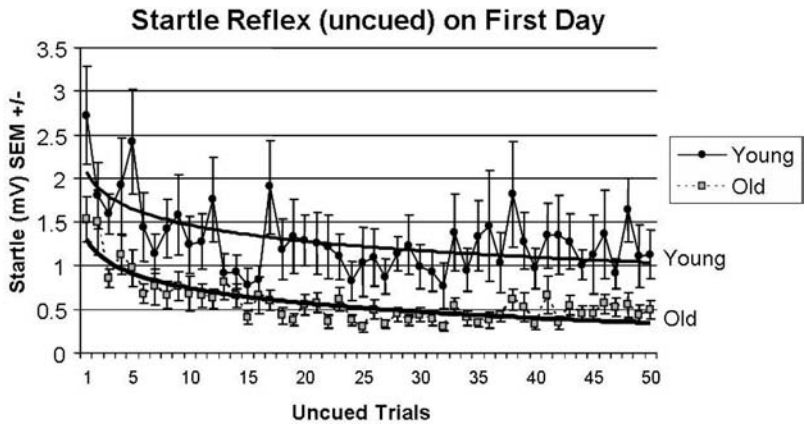

Figure 2. Acoustic startle response for the 50 uncued trials on first day of acoustic testing (single tone task) with logarithmic trend lines. There was an effect of trial ($p < .001$) and age ($p = .001$) but no interaction (young adult, $n = 16$ and old, $n = 23$).

the shorter gaps on the first day, and this pattern shifted toward less facilitation and/or nonsignificant attenuation over the following days (see Figure 4).

Short silent gap task. A repeated-measures ANOVA, again using mean of ATT score on the single tone as a covariate, was conducted. ATT differences for gap (nine levels), day (five levels), and age (two levels) during the 5 days of short silent gap indicated a main effect of gap, $F(8, 288) = 4.00$, $p < .01$, $\eta_p^2 = .100$, a trend for day, $F(4, 144) = 2.06$, $p = .089$, $\eta_p^2 = .054$, but no effects of age $F(1, 36) = 1.25$, $p > .10$, $\eta_p^2 = .033$. Again, there was more attenuation for longer gaps, but scores tended to remain stable throughout days of testing. There were no interactions (Figure 5: all $p > .10$).

Correlation of Performance Within Tasks

ATT scores for each subject, for each day of long silent gap and short silent gap, were cross-correlated (Pearson's *r*). Based on sample size, correlations of $r > .60$ for the young adult, or $r > .45$ for old, were significant at the .05 level.

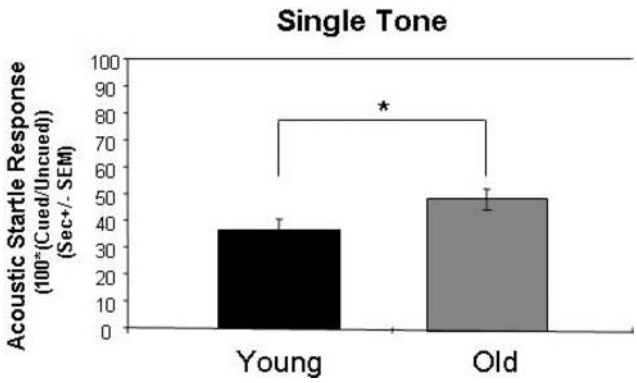

Figure 3. Attenuation scores for the single tone task for the young adult ($n = 16$) and old ($n = 23$) rats. Both groups showed an attenuated startle compared to the uncued baseline of 100% ($p < .05$). Young adult showed more attenuation (ATT) than old. $^{*}p < .05$ (ATT score: [mean cued response/mean uncued response] $\times$ 100).

Long silent gap task. Figure 6 shows the within-task correlations of responses to the different length gaps for the long silent gap task for young adult and old separately.

Young adult (figure 6a). Correlations in young rats showed a general pattern of positive intraday correlations. Day 1 had high positive correlation groupings for gaps of 2, 5, and 10 ms, and then again for gaps from 30 to 75 ms. For Day 2, performance on Gaps 10 thru 100 were correlated. All gap lengths on Day 3 were positively correlated with each other.

These results indicate that not all gap lengths showed a pattern of correlation across days. For Gaps 2 and 5 ms, on Day 1, performance did not correlate highly with other gaps on other task days. However, longer gap results were correlated with performance on the following days. This likely reflects initial facilitation for short gaps (2 and 5 ms) on Day 1, a pattern not seen for longer gaps. Performance was, however, correlated across Days 2 and 3 for all gaps, aside from the 2-ms gap.

Old (figure 6b). Old rats showed positive patterns of within-day performance for all cues on all 3 days. However, they showed little correlation between Day 1 performance, and Day 2 or 3. Performance across Days 2 and 3 was more strongly correlated, especially for gaps 10 ms and longer.

Short silent gap. Figure 7 shows the within-task correlations of responses to the different length gaps for the short silent gap task for young adult and old separately.

Young adult (figure 7a). Within Day 1, there were correlations of performance across Gaps 4 thru 10 ms. This pattern of within day correlations across gaps tended to strengthen and extend to include shorter gaps on Days 2 through 5.

Old adults (figure 7b). The older group showed within day patterns of positive correlations on all days of the short gap task. As the days progressed, increased patterns of between day positive correlations were seen. The patterns of between-day correlation for the old were, however, weaker than those seen in the young rats.

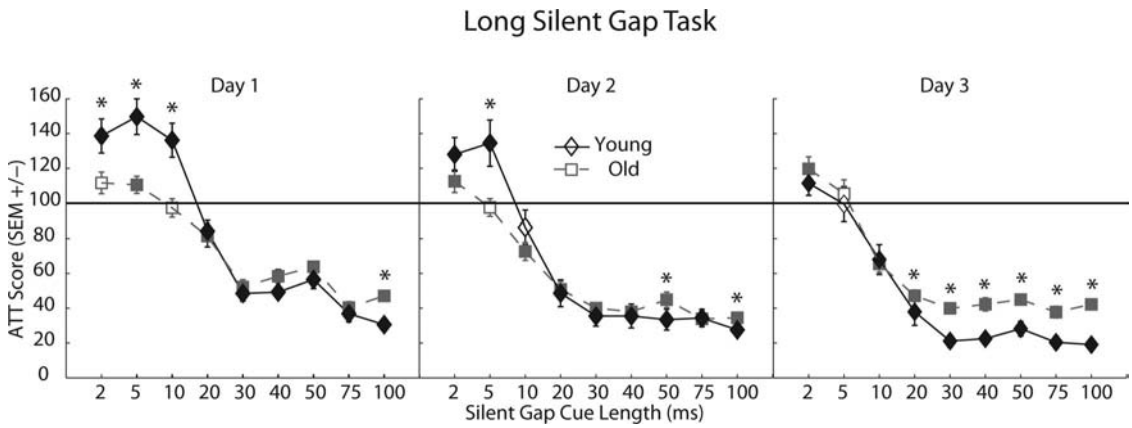

Figure 4. Attenuation (ATT) scores for the long silent gap task by silent gap size across the three days of testing. There was more attenuation in response to the easier (wider) gaps, while the response to harder gaps changed across days, especially in the young rats (young adult; $n = 12$ and old; $n = 18$). *Difference between age groups (independent-samples t test, $p < .05$.). Filled symbols (diamond = young, square = old) indicates a difference from the 100%, uncued baseline response (paired-samples t test, $p < .05$).

Correlation of Performance Across Tasks

Between single tone and long and short silent gap tasks. There was little correlation between performances on the single tone and long or short silent gap tasks. This was true for both age groups (see Figure 8).

Between long and short silent gap tasks. Figure 8 shows correlations of responses to the different length gaps between the long and short gap task, separated by age.

Young adult (figure 8a). Examination of correlations in the young adults between gap (duration), day, and task showed a consistent pattern of negative correlations between Long Gap Day 1 (Gaps 2 and 5 ms) and performance on nearly all gap cues for each day of short gap task. This pattern for Gaps 2 and 5 ms disappears by Day 2, and appears to change into a pattern of positive correlation by Day 3 of long gap task. This reflects a pattern of conversion from facilitation for short gaps on Day 1, shifting to attenuation on later days. That is, early facilitation on shorter gaps is predictive of later attenuation (with increasing experience). Other cues for Long Gap Task Day 1 did not show a pattern of correlation with short gap task, but Cues 10 thru 100 on Day 2 and 3 of long gap task were positively correlated.

Old adults (figure 8b). Older subjects did not show strong patterns of correlations between days across long and short gap tasks.

Discussion

The current study examined PPI in young adult and aged rats using a tone and silent gap paradigm. Young adult rats showed a larger ASR, and stronger cue-modulation of the startle response, as compared to the aged rats. There was no age difference in gap detection, but only the young animals showed an experience-related shift from facilitation to attenuation with regard to very short (2, 5, and 10 ms) silent gap cues during the long silent gap task.

Baseline ASR

Old rats showed less uncued ASR as compared to young adults. This was seen in both initial trials, and also after repeated exposures to the SES. These findings of an age-related decline in ASR in rodents have been reported by others (Ison et al., 1997; Krauter, Wallace, & Campbell, 1981; Varty et al., 1998) and also have been reported in humans (Ford et al., 1995; Kofler, Muller, Reggiani, & Valls-Sole, 2001).

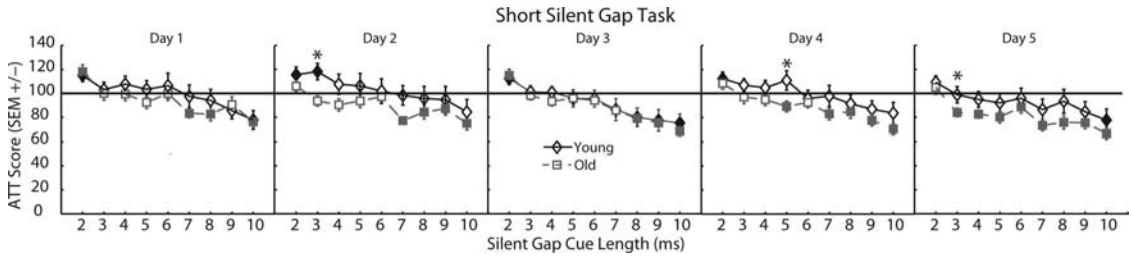

Figure 5. Attenuation (ATT) scores for the short silent gap task by silent gap size across the five days of testing. This task focused on only the harder gaps (<10ms). There was more attenuation to the easier (wider) gaps, and the responses tended to remain stable across days (young adult; $n = 16$ and old; $n = 23$). * Difference between age groups (independent-samples t test, $p < .05$.); filled symbols (diamond = young, square = old) indicates a difference from the 100%, uncued baseline response (paired-samples t test, $p < .05$).

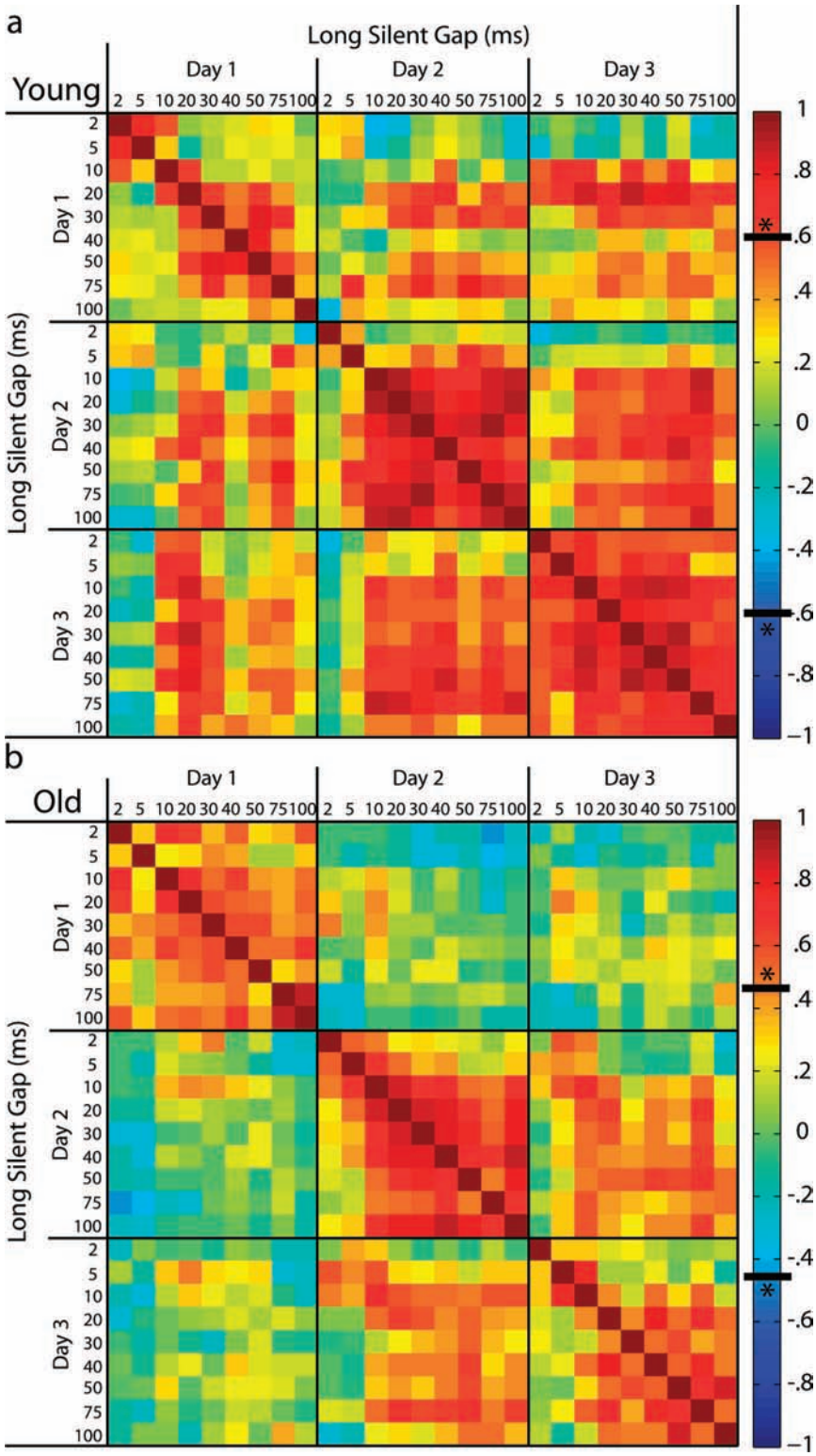

Figure 6. Correlations of the attenuated response to the different silent gaps across the three days of Long Silent Gap task, for young adult (A) and old (B) rats. As expected, correlation within days tended to be stronger than across days. For the young, on Day 1, responses appeared to split into two groups of high correlation (Gaps 2 thru 10 ms and Gaps 20 thru 75 ms), with almost no relationship observed between these two groupings. This was not seen in the aged. Young rats also showed a stronger pattern of correlations between days, as compared to the aged rats (young adult, $n = 12$ and old, $n = 18$). *Correlations more extreme than $r \pm .6$ for the young, or $r \pm .45$ for old, $p < .05$.

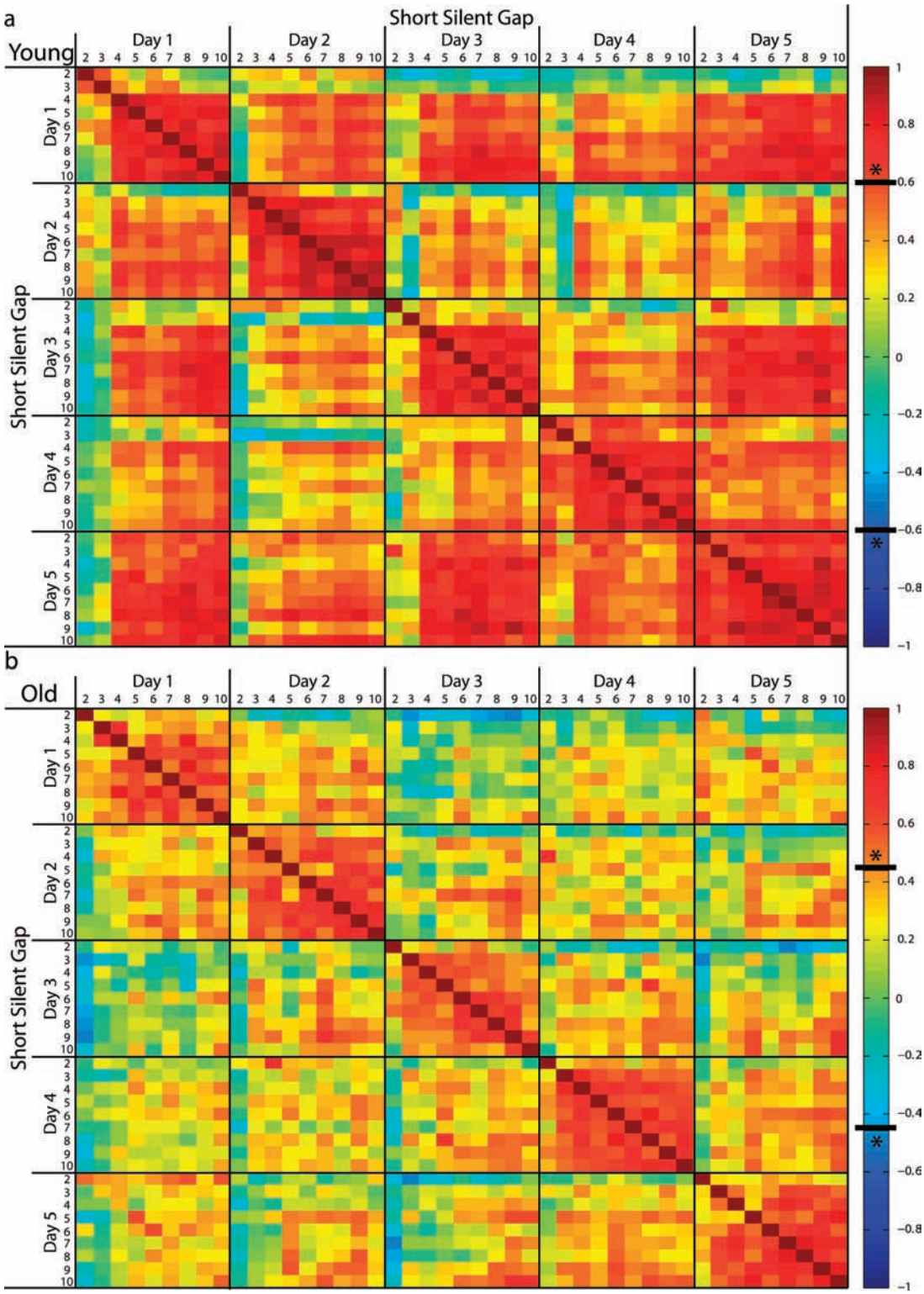

Figure 7. Within task correlations for the short silent gap task for young adult (A) and old (B) rats by gap length across the 5 days of the task. As expected, correlation within days tended to be stronger than across days. Young rats showed a stronger pattern of correlations between days as compared to the aged rats (adult, $n = 16$ and old, $n = 23$). * Correlations more extreme than $r \pm .6$ for the young, or $r \pm .45$ for old, $p < .05$.

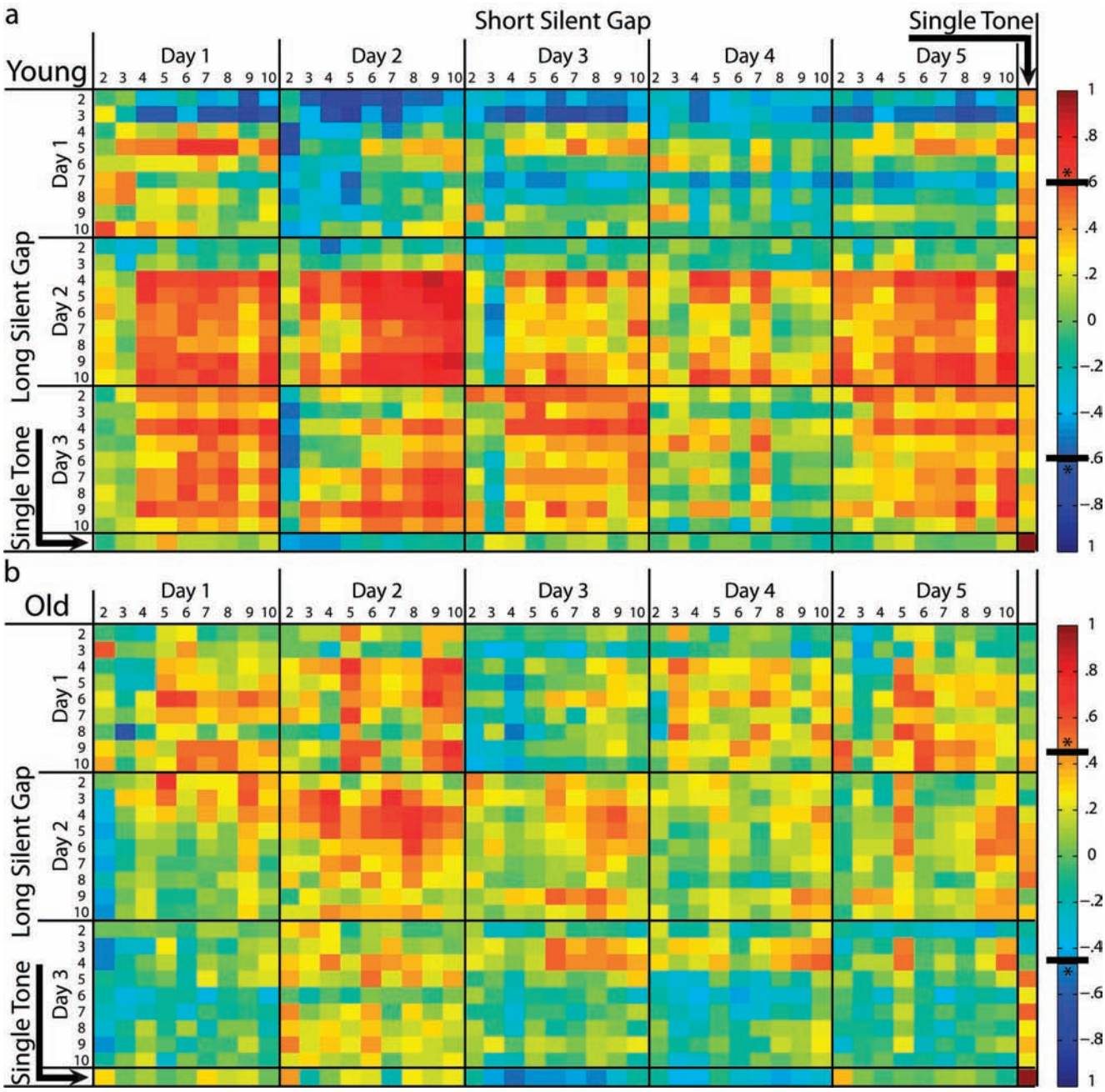

Figure 8. Across task correlations for the single tone, short gap, and long gap tasks for young adult (A) and old (B) rats by cue across days of tasks. Single tone responses were not correlated with the silent gap responses. Young rats showed a negative correlation between the initial (Day 1) attenuation (ATT) on the shortest gaps (2 and 5 ms) and later performance on the short gap task. The responses were positively correlated on subsequent days. The aged rats showed a weaker pattern of correlation across tasks and days (young adult, $n = 12$ and old, $n = 18$). * Correlations more extreme than $r \pm .6$ for the young, or $r \pm .45$ for old, $p < .05$.

Relative Startle, the Effect of Cue Duration and Experience

Auditory cues preceding the SES generally elicited a greater effect (more attenuation or facilitation) for young animals. Specifically, greater attenuation was found both for the single tone, and also for silent gaps greater than 20 ms. Although changes in ASR have been suggested to be directly related to detectability of the pre-SES cue (Ison & Hoffman, 1983; Leitner et al., 1993), the current results indicate that in the context of aging, interpretations of results are more complex. For example, first exposure (Day 1 long gap task) to short gaps (<10 ms) increased (facilitated) the

startle response in young adult but not old animals. The gap length (<10 ms) that elicited facilitation is consistent with previous observations (Ison, McAdam, & Hammond, 1973; Peiffer et al., 2004; Reijmers, & Peeters, 1994; Reijmers, Vanderheyden, & Peeters, 1995). In the current study, this facilitation diminished by Day 2 and disappeared by Day 3 of the long gap task for young animals. Thus the PPI response did not merely reflect pre-SES cue detection, but rather, PPI indexes interacted with both experience and also an apparent capacity for plasticity that is age dependent. Models of PPI focused on changes of length and strength of cue, inter-cue-stimulus length, and background noise (Schmajuk & Larrauri, 2005) might thus benefit from expanding their parameters to include change due to experience.

ATT Correlations Within and Across Sessions

ATT correlations within task. There were intraday correlations for ATT scores for both young adult and old, within long and short gap tasks. For the young adults, on Long Gap Task Day 1, responses appeared to split into two groups of high correlation (Gaps 2 thru 10 ms and Gaps 20 thru 75 ms), with almost no relationship observed between these two groupings. This suggests a difference in how these cues were processed. The increase in reliability on subsequent days of the task is consistent with the finding that pretesting diminishes variability in ASR (Davis & Wagner, 1969). Young adult rats showed a stronger pattern of correlations between days on both the long and short gaps, as compared to aged rats. The decrease in reliability during aging is also consistent with previous research. Increased PPI with training also has been previously seen in gap detection tasks (Crofton, Dean, Sheets, & Peele, 1990; Threlkeld, Rosen, & Fitch, 2007; Wu, Ison, Wecker, & Lapham, 1985).

ATT correlations across tasks. Performance on the single tone task was not predictive of silent gap performance. In fact, even comparing the first (and only) day of single tone to the first day of silent gap revealed only moderate correlations that were unaffected by the gap length. These findings support the view that the silent gap variant of PPI is qualitatively different than single tone and involves the recruitment of additional neural circuitry (Dean et al., 1990; Friedman et al., 2004). Across silent gap tasks, the situation was different. Specifically, the young adult rats showed a highly negative correlation between initial ATT scores on the shortest gaps (2 and 5 ms) and later performance on short gap task, versus positive correlations on subsequent days between shortest gaps and later performance on short gap task.

Early Facilitation as a Predictor of Later Performance

The young animals, which on Day 1 showed facilitation on the short (hard) gaps, later showed attenuation to these same cues. This transition was not seen for long gaps. This change of response with experience to gaps of 2 and 5 ms was also not found in the aged animals. The lack of early facilitation in aged animals is consistent with findings that show several deficits in components of the PPI circuit in aged subjects (Barsz et al., 2002; Caspary et al., 2008; Popelar et al., 2005; Walton et al., 1998), and has been postulated to result from a deficit in inhibitory function (e.g., Hasher & Zacks, 1988; Layton, 1975; Rabbit, 1965).

Facilitation and Attenuation

On Day 1 of the long gap task, facilitation was observed for the short gaps, while attenuation was seen for the long gaps. We find it interesting that there was no relationship between the degree of facilitation and attenuation within this day. Thus our data suggest that PPF may be mediated, at least in part, by neural mechanisms orthogonal to those modulating PPI. The fact that cortical inactivation results in facilitation for short gaps (<50 ms; Threlkeld et al., 2008) indicates that the PPI system is at least partly dependent on cortical processing (see Li, Du, Li, Wu, & Wu, 2009). The finding that those animals initially showing facilitation went on, with experience, to show the strongest inhibition (see Figure 8) is intriguing. Taken together, the data indicate that although facilitation and attenuation may be somewhat orthogonal to each other (see Plappert et al., 2004), the experience dependant plasticity affects both systems.

Changes in Auditory Processing During Aging

Our current data indicates reduced PPI and PPF, and decreased plasticity, in the old animals. Aged rats show a hearing loss for both extreme high and low frequency tones (Bielefeld et al., 2008; Popelar et al., 2005). It is likely that our aged animals were similarly affected. Furthermore, it is possible that the aged animals had motor deficits. Taken together, these factors could account for the reduced startle response in the aged (see Figure 1). However, the experiment was designed to assess age related changes in processing beyond the degree of startle response. Notably, threshold shifts at lower frequencies for 24-months-old F344 rats are only $\sim$ 25 dB (Bielefeld et al., 2008). The startle stimulus chosen (105 dB) included a wide spectrum (white noise), and was above that used by others (100 dB) to elicit a robust startle response (Bubser, & Koch, 1994; Koch et al., 2000; Li et al., 2008). Also, the fact that the aged animals showed similar discrimination to young on the short silent gap task indicates that the startle stimulus was loud enough to compensate for age-related hearing loss. Moreover, PPI was calculated individually for each animal (i.e., within-subject) as a ratio of raw ASR to cued response. Perhaps the strongest evidence of this being an age related change in processing rather than an epiphenomena of a reduced ASR is the fact that for many of the cues (especially the easier ones), there was no difference in the PPI of young and old animals. The striking changes were instead seen within an age group across days, suggesting a change in plasticity.

In addition to this reduced plasticity the old rats' responses were also less consistent both within and across sessions. That is, while both groups showed a wide range of responses, correlations of responses were much higher for young animals. Thus for the single tone task the range of attenuated (ATT) scores for aged was: (low) 26% to (high) 77% ($M = 52 \pm SD = 15$); and for young was (low) 16% to (high) 70% ($M = 38 \pm SD = 16$). For the long silent gap task over 3 days of 100-ms testing, the range for aged was (low) 20% to (high) 73% ($M = 44 \pm SD = 13$) and young was (low) 8% to (high) 73% ($M = 32 \pm SD = 15$). The increase in variability within an aged population is well documented (e.g., Collier & Colman, 1991; Gallagher & Rapp, 1997; Lindenberger & von Oertzen, 2006). The current data underlines the increased variability found in the response of an aged individual.

Implications of the Data

The findings of a dynamic shift from facilitation to attenuation make it difficult to interpret data taken from the first few days of exposure to short gap cues. Initially, individual animals differ in the degree and dynamics of their attenuation and facilitation, thus averaging across these days could mask cue detection. Furthermore, any conclusions regarding thresholds for detection could be erroneous, because the fulcrum point would be where the data from facilitating and attenuating animals cancel each other out. However, the strong patterns of correlation from Day 1 to later performance might be a useful tool for estimating auditory processing function. A detailed analysis of the initial response to short gap cues could eliminate the need for 2 to 3 weeks of data collection.

Finally, it would be interesting to see how the initial response to short auditory gaps would be related to startle responses using other cue modalities, such as vision. Similarly, decreases in experience related plasticity and in test–retest reliability in aged individuals in one domain may be predictive of impairments in others types of processing (Lövdén, Li, Shing, & Lindenberger, 2007).

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