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Short Communication

The level of prepulse inhibition in healthy individuals may index cortical modulation of early information processing

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ABSTRACT

This study examined whether baseline PPI levels reflect individual efficiency in tasks associated with routine versus supervisory attentional systems (SAS). PPI and neuropsychological data were collected from 30 healthy male subjects. High PPI was associated with shorter movement times on the 5-choice Reaction Time and shorter Subsequent Thinking Times in the Stockings of Cambridge test. These data suggest that high-PPI status reflects greater efficiency in tasks that engage SAS.

Prepulse inhibition (PPI) of the acoustic startle response measures the inhibition of the startle response to a sudden intense stimulus (pulse) by a weak sensory stimulus (the prepulse) preceding the pulse by 30–500 ms. PPI is considered a measure of "sensorimotor gating", which involves the ability to filter out irrelevant information in the early stages of processing so that attention can be directed to more salient environmental features (Braff and Geyer, 1990; Braff et al., 1978). However, as elegantly shown in previous studies, inhibition at this early stage of information processing is modulated by the cortex in a "top–down" fashion (Hazlett et al., 1998; Neumann, 2002). An additional and important characteristic of PPI is that it shows significant inter-individual variability (Hamm et al., 2001). The significance of such variability has been examined in connection to personality dimensions such as social anxiety and extraversion (Blumenthal et al., 1995), psychosis proneness (Cadenhead et al., 1996), novelty seeking (Hutchison et al., 1999), smoking habits (Kumari et al., 1998) and schizotypy (Abel et al., 2004). Perhaps a more pertinent question is whether PPI differences reflect individual variability in efficiency of attentional processing. In the present study, we explored this possibility within the theoretical framework of the control-to-action model developed by Norman and Shallice (1980). This model distinguishes 2 control mechanisms; one involved in routine situations where actions are triggered automatically while the second, the Supervisory Attentional System (SAS), is engaged in situations that require planning and willed actions (Shallice, 1994).

The study was approved by the Ethics Committee of the University of Crete, and all participants gave their written informed consent. Participants were selected using the following criteria: male gender, right-handed, general intellectual ability above 90 as estimated using Raven's Standard Progressive Matrices, no history of any major medical or neurological disorders, no personal or family history of major DSM-IV axis I disorders, no history of head trauma, no use of prescribed or recreational drugs, hearing threshold of 1 kHz > 20 dB and a "responder criterion" of 50 units (122 μV)

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startle reactivity. All participants underwent physical and psychiatric assessment using the Mini-International Neuropsychiatric Interview (M.I.N.I.) (Sheehan et al., 1998), urine toxicology screening and a hearing test.

A commercially available electromyographic startle system (EMG SR-LAB, San Diego Instruments, San Diego, CA, USA) was used to examine the eyeblink component of the acoustic startle response. Acoustic stimuli were administered binaurally through headphones (model TDH-39-P, Maico Minneapolis, MN). Electromyographic recordings were taken, while subjects were seated comfortably in an armchair, instructed to relax and stay awake. The eyeblink component of the startle reflex was indexed by recording EMG activity of the orbicularis oculi muscle directly beneath the right eye by positioning 2 miniature silver/silver chloride electrodes filled with Signa Gel electrolyte paste (Parker Laboratories, Inc, New Jersey, USA). The ground electrode was attached behind the right ear on the mastoid. Six acoustic startle-eliciting stimuli were administered, and after exclusion of the startle response to the first stimulus, the average of the remaining five was used to determine initial startle reactivity. Subsequently, subjects received a block of four pulse-alone and four prepulse-pulse stimulus trials in a pseudorandom order to calculate baseline startle and percent PPI of the startle reflex. Pulses consisted of 40 ms 115 dB white noise bursts and prepulses consisted of 20 ms 75 dB white noise bursts presented at an 80 ms lead interval (onset to onset), over a 70 dB background noise. We chose a weak prepulse (75 dB–5 dB above background) on the basis of its putative ability to discriminate better than an intense prepulse between subjects with different levels of startle inhibition by a prepulse. Percentage PPI (%PPI) was calculated using the formula $[(\text{Amplitude}_{\text{Pulse-alone}} - \text{Amplitude}_{\text{prepulse-pulse}}) / \text{Amplitude}_{\text{Pulse-alone}}] \times 100$. After a median split on their PPI, subjects were assigned to a “high-PPI” and a “low-PPI” group.

Reaction time and spatial planning were assessed by the Reaction Time (RTI) and the Stockings of Cambridge (SoC) subtests of the Cambridge Neuropsychological Test Automated Battery (CANTAB) (Sahakian and Owen, 1992). In the RTI, subjects are required to release a home button and touch either a single target stimulus or one out of five target stimuli appearing on a screen. Outcome measures used were simple and five choice reaction times (i.e. the time taken to release the home button) and simple and five choice movement latencies (i.e. the time taken from button release to screen touch). The SoC is a spatial planning test; subjects are shown two displays of stacked colored balls and are asked to move those in the lower display to match the pattern on the upper display. The level of difficulty increases in each trial, with the first one requiring 2 moves to match the target pattern while the last one requires 5. Outcome measures used were Initial and Subsequent Thinking Time (ITT and STT) (trials 3, 4 and 5) (i.e. the time taken to plan the first and subsequent moves to achieve the target pattern of colored balls) and accuracy (i.e. the number of problems solved correctly with minimum moves).

Subjects in the high- and low-PPI groups were compared on the RT and SOC outcome variables using separate one-way analyses of variance (ANOVA; two levels) or the equivalent Mann–Whitney ANOVA in case the overall distribution of the score within the group differed from normality (Kolmogorov–Smirnov test of normality). In order to decrease skew and stabilize variances, latency data were transformed using logarithmic transformations ($x = \log_{10}y$) in preparation for parametric analyses. Correlations between %PPI and cognitive outcome variables were examined using Spearman’s or Pearson’s correlation coefficients as appropriate.

Thirty participants aged 20–29 years (mean ± SD 23.57 ± 2.67) were recruited. Comparison between the “high-” and “low-PPI” groups did not reveal any differences in initial reactivity, baseline startle, onset and peak startle latencies with pulse-alone or prepulse-pulse trials, age, years of education, IQ, body weight and smoking status. The mean and standard deviation of the (untransformed) performance scores in the RTI and SoC in the high- and low-PPI groups are shown in Table 1. In the entire group, %PPI correlated negatively with 5-choice movement time (rho = −0.61, $P < 0.001$) and STT ($r = -0.43$, $P = 0.018$) and positively with accuracy ($r = 0.37$, $P = 0.044$). The two groups differed in 5-choice movement time of the RTI (Mann–Whitney Exact significance $P = 0.002$) but not in simple movement time ($F = 3.02$, $df = 1{,}29$, $P = 0.093$) and the mean STT (trials 3, 4 and 5) in the SoC ($F = 4.38$, $df = 1{,}29$, $P = 0.042$), but not in accuracy ($F = 1.69$, $df = 1{,}29$, $P > 0.1$).

Previous attempts to correlate behavioral measures such as negative priming, backward masking and the Wisconsin Card Sorting Test with startle inhibition in healthy subjects have yielded inconsistent results (Filion et al., 1998, 1999). Here, we report that healthy males with “low” PPI showed an overall increase in the 5-choice RTI movement latency and SoC mean STT when compared to “high” PPI subjects. There were no group differences in simple movement latency, accuracy or mean ITT.

The lack of group effect in simple movement latency suggests that PPI is unlikely to index individual differences at the level of contention scheduling, where actions are routine and require minimal attentional engagement. In contrast, group differences were apparent during the 5-choice RTI.

Table 1 – Mean ± SD%PPI and neuropsychological test performance in the “high” and “low” PPI groups

	High-PPI group ($n = 15$)	Low-PPI group ($n = 15$)
%PPI	37.97 ± 15.90	−5.42 ± 28.50
RTI		
Simple reaction time (ms)[a]	322.59 ± 28.17	332.52 ± 70.99
Simple movement time (ms)	320.51 ± 76.63	366.31 ± 67.42
5-choice reaction time (ms)	349.90 ± 45.86	345.33 ± 62.33
5-choice movement time (ms)[a]	308.44 ± 58.41	364.73 ± 50.48
SoC		
Mean initial thinking time (ms)	9002.84 ± 4097.74	9975.13 ± 6034.60
Mean subsequent thinking time (ms)	409.93 ± 296.01	1221.12 ± 1774.67

[a] For this measure, the overall distribution of the score differed from normality and the equivalent non-parametric Mann–Whitney procedure was applied; RTI = Reaction Time; SOC = Stockings of Cambridge.

Performance on this task makes greater demands on visual attention and requires a complex motor response as subjects must release a home button and then touch whichever of five target stimuli has been indicated on the touch screen.

The SoC is a test of planning which is considered a core function of the Supervisory Attentional System. Performance in the SoC depends on the participant's ability to analyze the problem and plan the sequence of moves before starting (Shallice, 1982). Relative prolongation of STT but not ITT in the "low" compared to the "high" PPI individuals may reflect a tendency in the latter to produce solutions before they are fully planned. Consequently, "low" PPI subjects may need to pause during the task to reconsider and refine their solutions (Owen et al., 1990). This interpretation is consistent with the lack of difference in accuracy between the two groups. As shown by Owen et al. (1990) as well as Newman et al. (2003), complex problem solving depends on the integrity of the frontal lobes. Executive time in the 5-choice RTI may be similarly dependent on the integrity of frontal projections to the striatum (Christakou et al., 2001). Therefore, our findings suggest that a higher level of PPI is associated with more effective cortical modulation of information processing.

PPI at short (less than 60ms) lead intervals is considered purely pre-attentive (Böhmelt et al., 1999). However, PPI at longer lead intervals, such as the one employed here, may index the early stages of attentional processing. This is in line with reports of frontal and parietal cortical activation in human functional imaging studies using attention-to-prepulse (Hazlett et al., 1998, 2001) and passive PPI paradigms (Kumari et al., 2003) at longer lead intervals.

Our results, although preliminary, indicate that the level of PPI at longer intervals is more closely associated with strategic rather than purely perceptual information processing since differences between "low" and "high" PPI groups were more notable in conditions requiring the engagement of the supervisory attentional system. Further studies are required to confirm and extend these findings.

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