Arousal-Modulated Startle Reflex Hyporeactivity in Parkinson's Disease

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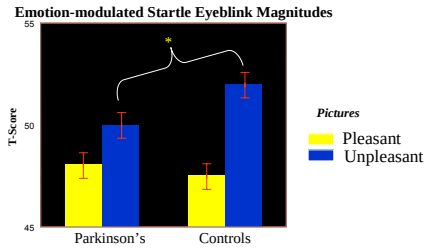
BACKGROUND

Prior work in our laboratory found that patients with Parkinson's disease (PD) demonstrate reduced psychophysiologic reactivity to unpleasant pictures as indexed by diminished startle eyeblink magnitude (Bowers et al., 2006):



HYPOTHESIS: In the present study, we tested the hypothesis that this physiological hyporeactivity was driven by diminished reactivity to *fear-eliciting pictures* as opposed to other types of aversive pictures.

This hypothesis was based on:

1. Evidence of neuropathological changes in the amygdala of PD patients, including volume loss and Lewy bodies (Braak & Braak, 2000; Harding, Stimson, Henderson, & Halliday, 2002)
2. Loss of dopaminergic terminals in the amygdala of PD patients (Ouchi et al., 1999)
3. In a neuroimaging study (Tessitore, 2002), levels of dopamine have been found to modulate the amygdala's response in PD patients, suggesting that low levels of dopamine characterizing PD may affect the amygdala's functional integrity
4. The known role of the amygdala in threat detection/ fear response (Amaral, 2003; Davis, 1992; Klüver & Bucy, 1939)

PARTICIPANTS

• Idiopathic PD patients were free of dementia and recruited from the University of Florida Movement Disorders Center. Age-, sex-, and education-matched controls were recruited from the community.

•All participants were given brief neuropsych screening (DRS-2, BNT, CVLT-II) and had to score within 1.5 SDs of normative mean.

•Participants with BDI-2 scores > 19 were excluded. In controls, no current psychatric dx or psychotropic medications were permitted. In the PD group, 7 patients were on antidepressants.

PARTICIPANTS (cont).

Participant Characteristics

Characteristic	Parkinson (*N*= 24)	Control (*N*= 24)	Statistical test
Age (years)	68.00 (6.92)	68.38 (7.73)	$t(46) = .18$
Sex ratio (men: women)	14:10	14:10	$\chi^2(1) = 0$
Education (yrs)	16.21 (3.16)	16.33 (2.88)	$t(46) = .14$
Disease duration (yrs)	5.54 (3.63)	—	
Hoehn and Yahr stage[a]	2.27 (0.42)	—	
UPDRS Motor[a]	23.46 (8.49)	—	
Levodopa equivalent dose (mg)	682.43 (323.26)	—	

PD patients completed the procedures below in the OFF medication state

PROCEDURES

1. Electrodes were placed under each eye, over the obicularis oculi muscle, to measure amplitude of startle reflex.
2. Participants viewed 48 pictures from the IAPS (Lang et al., 2001) set for 6 sec. each. From this stimulus set, pictures were categorized as *positive*, *negative*, or *neutral*.
2. Negative pictures were further categorized into FEAR, DISGUST: CONTAMINATIONS, and DISGUST: MUTILATIONS. Disgust pictures were chosen for comparison to fear pictures because they are similar with respect to unpleasantness and arousal levels. Disgust pictures were subdivided into contaminations and mutilations because fMRI work suggests they are associated with distinct neural substrates (Wright et al., 2004).

FEAR DISGUST MUTILATION CONTAMINATION

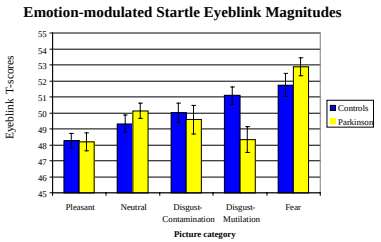
3. While viewing the pictures, white noise bursts were binaurally presented through headphones to elicit startle eyeblinks.
4. Immediately after each picture was shown, participants rated it with respect to
   - Valence (1-9 scale, 9 most positive rating)
   - Arousal (1-9 scale, 9 most arousing rating)
5. After completion of psychophysiology experiment, participants viewed each picture again and rated how much Happiness, Sadness, Disgust, and Fear they felt. These post-hoc ratings were to ensure pictures evoked the intended emotion.

RESULTS

•Hypothesis of fear-specific reactivity deficit was not supported

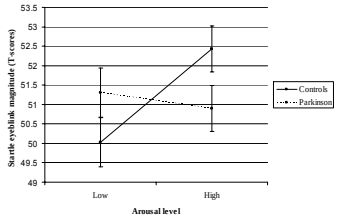
•PD patients did not show reduced emotion-modulated startle eyeblink magnitudes to fear pictures as predicted. Instead, they showed reduced eyeblink magnitudes for mutilation pictures relative to other types of negative pictures

• PD patients and controls did not differ with respect to subjective valence and arousal ratings, or happiness, sadness, fear, and disgust ratings



Could it be that the mutilation pictures are actually more physiologically arousing than the other negative pictures?

Secondary analysis: Examining emotion-modulated startle eyeblink magnitudes to negative pictures by Arousal Level, collapsing across picture contents



•Controls displayed a pattern of eyeblink magnitude modulation by arousal level (more arousing, greater magnitude)

•Eyeblink magnitudes were not modulated by arousal level in the PD group

CONCLUSIONS

•Results of the current study did not support our prediction that PD patients would showed diminished startle eyeblink magnitude to fear pictures. Instead, PD patients showed reduced startle eyeblink magnitudes specifically to mutilation pictures.

•One possibility is that mutilation pictures are actually more physiologically arousing than other negative picture contents. When we re-analyzed eyeblink magnitude data for negative pictures based on arousal level, controls showed a pattern whereby arousal level modulated startle eyeblink magnitude (with greater magnitudes for the higher arousal pictures). PD patients did not show any modulation by arousal level.

•One possible explanation may be that PD patients have a deficit in "translating" an aversive motivational state into a physiological response. This is supported by other work in our laboratory (Bowers et al., 2008) showing that PD patients do not display modulation of skin conductance response while viewing arousing pictures.

•Future work should examine whether this hyporeactivity is due to peripheral ANS dysfunction (e.g. Lewy bodies in sympathetic ganglion) or CNS dysfunction.