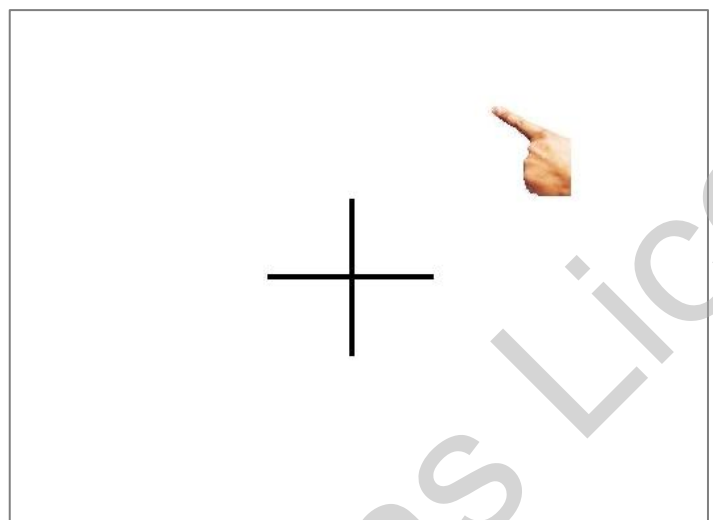


Introduction

- Parkinson disease (PD) produces hypometric movement, meaning an initial under-reaching of a body part toward an intended goal.
 - Typically a first movement undershoots the target, and subsequent catch-up movements span smaller and smaller distances until the target is reached.
 - This is evident in eye movements as well; PD patients have hypometric saccades [6].
- PD also affects nonmotor brain functions including cognitive, affective and perceptual domains
 - Spatial working memory (SWM) refers to short-term storage of information on the relations of objects in space.
 - The spatial delayed response (SDR) task is a measure of working memory in humans and other species in which the subject fixates a central point while a transient target appears peripherally, then after a set delay touches the remembered target position [7].
 - PD patients touch the target accurately when it remains visible, but show impaired SDR performance with increasing memory load [5].
 - This is not due to motor impairment, because when the memory load is reduced to zero, patients perform the task as accurately as healthy controls [3].
 - The impairment in SDR relates especially to the severity of PD on the left side of the body (right side of brain) [3].
- Prior studies have suggested that PD patients also underestimate *remembered* distances
 - Hypometric memory-guided saccades (see [7])
 - Underestimate distances even when no movement is required [8]
- **We hypothesized** that PD patients' increased error in the SDR task was not random in direction but was biased towards shorter remembered distances to the target location from the central fixation point.
- In other words, we hypothesized that PD patients would show hypometria for memory, as they do for movement.

Methods

- **Subjects**
 - Healthy control group, N=17
 - Tourette syndrome (TS), N=5
 - Idiopathic PD, N=9
- **Protocol**
 - Overnight withdrawal of antiparkinsonian medications
 - With and without a levodopa infusion [1] with carbidopa
 - Subjects 1-20: before and after infusion, unblinded; most subjects also had single blind placebo on a different day
 - Subjects 21-60: double blind crossover, two weeks apart; levodopa one day and placebo the other day
- **SDR task**
 - Performed as described [4,7]
 - Over 2,800 trials examined
 - Target and response locations converted to polar coordinates r and θ with respect to the fixation point
 - Dependent variable was $\Delta r = r_{\text{response}} - r_{\text{target}}$
 - Compared over all trials, collapsing across delays
 - t test
 - 2 tails except for primary hypothesis



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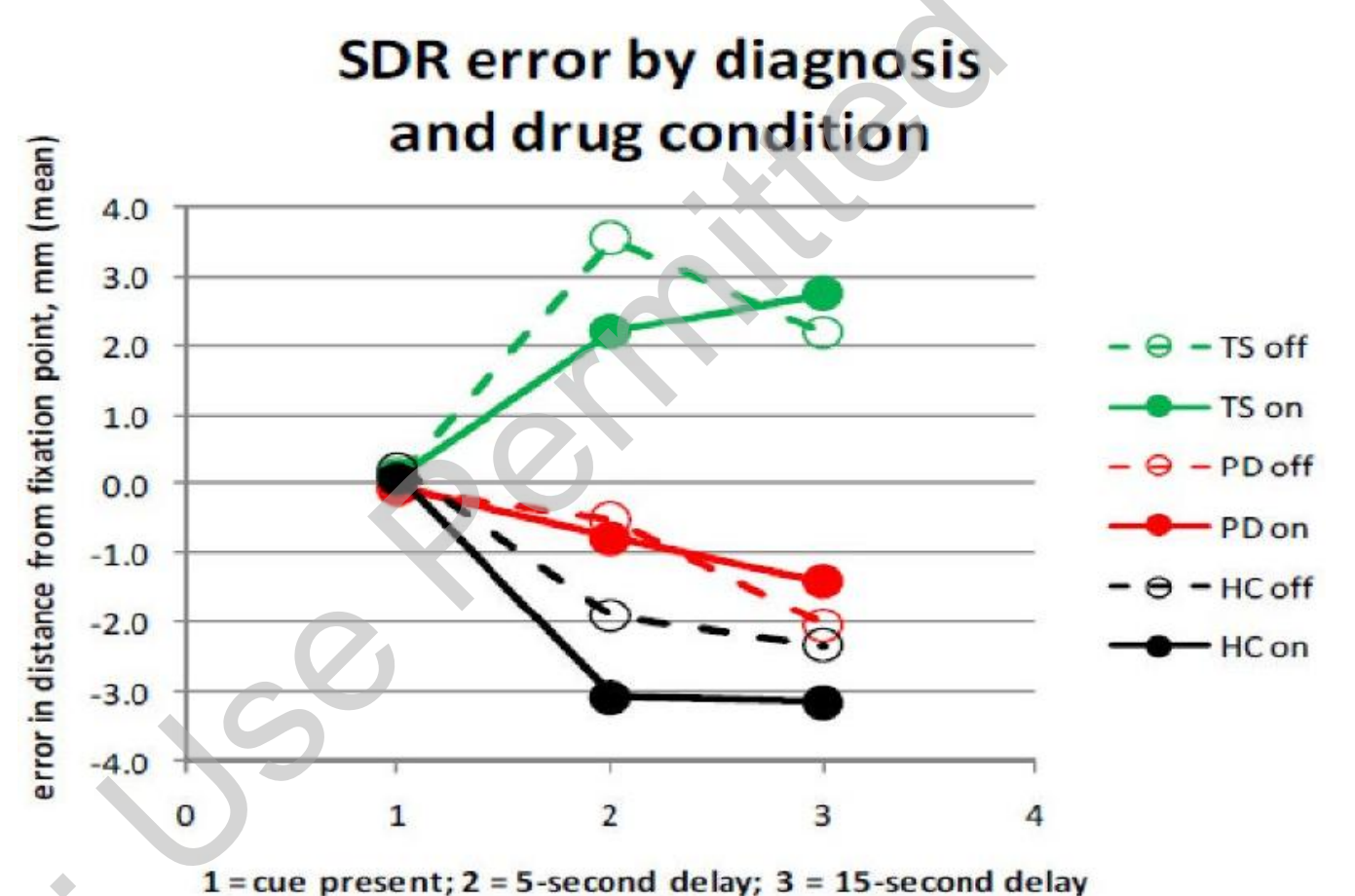
Results

1. **Was error biased towards lower r in PD patients?**

Yes, PD subjects did on average underestimate recalled distance when in the off state (mean $\Delta r = -0.86 \pm 9.79\text{mm}$, mean $\pm$ S.D., $p < 0.02$). (red lines in graph)
2. **If so, were they more biased than control subjects?**

No, so did HCs ($\Delta r = 1.31 \pm 10.34$ mm, $p < 0.00002$) (black lines in graph)
3. **Did levodopa correct the hypometric bias?**

There was some correction in the healthy control graph (dotted vs. solid black line in graph), but it was not statistically significant ($p > 0.10$ for all groups) (dotted vs. solid lines in graph)
4. **TS subjects overestimated distance** ($\Delta r = +1.97 \pm 7.09\text{mm}$, $p < 3 \times 10^{-7}$, green lines in graph), and this was significantly different that of HCs ($p < 2 \times 10^{-11}$, green vs black lines in graph).
5. **These results were attributable to memory**, as all groups were accurate with the cue present (leftmost points in graph).



Discussion

- In this sample of patients with mild PD and reasonably matched controls, we found that
 - PD subjects did not underestimate recalled distances more than healthy controls did
 - Levodopa did not correct the bias
- Similarly, Crucian and colleagues found that PD subjects and controls both underestimated distances in different paradigms. However, PD subjects did so to a significantly greater degree, including when asked to estimate distance to several American cities from St. Louis [2,8].
- The sample size may have been too small to detect an effect.
- Interestingly, TS subjects significantly overestimated recalled distances. This may reflect a cognitive parallel to the hyperkinetic nature of the movement disorder in TS, but this result requires confirmation in a larger sample; Hikosaka et al [6] describe opposite results, with TS showing a PD-like difficulty when making memory-guided saccades
- Future directions
 - Could hypometria apply to other cognitive tasks in PD? Do patients underestimate sums in addition problems? Does this affect economic predictions in PD, or relate to underestimating the magnitude of future rewards in PD-related apathy or major depression?
 - Follow up on TS result in a larger sample
 - We have not yet examined other trials with a higher memory load, in which PD subjects' SDR performance is poorest, and those trials may reveal the hypothesized effect.

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