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Open angle glaucoma effects on preattentive visual search (PAVS) efficiency for flicker, motion displacement and orientation pop-out tasks

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ABSTRACT

Background/aim: Preattentive visual search (PAVS) describes rapid and efficient retinal and neural processing capable of immediate target detection in the visual field. Damage to the nerve fibre layer or visual pathway might be expected to reduce the efficiency with which the visual system performs such analysis. The purpose of the research reported here was to test the hypothesis that patients with glaucoma would be impaired on parallel search tasks, and that this would serve to distinguish glaucoma in early cases.

Methods: Three groups of observers (Glaucoma, Suspects and Normals) were examined, using computer generated flicker, orientation, and vertical motion displacement targets to assess PAVS efficiency. The task required rapid and accurate localisation of a singularity embedded in a field of 119 homogenous distractors on either left or right hand side of a computer monitor. All subjects also completed a choice (CRT) reaction time task.

Results: Independent samples T tests revealed PAVS efficiency to be significantly impaired in the glaucoma group compared to both normals and suspects. Performance was impaired in all types of glaucoma tested. Analysis between normals and suspects revealed a significant difference only for motion displacement response times. Similar analysis using a PAVS/CRT index confirmed the glaucoma findings but also showed statistically significant differences between suspects and normals across all target types.

Conclusions: A test of PAVS efficiency appears capable of differentiating early glaucoma from both normals and suspects. Analysis incorporating a PAVS/CRT index enhances the diagnostic capacity to differentiate normals from suspects.

Abbreviations: PAVS - preattentive visual search; CRT – choice reaction time; IOP – intraocular pressure; POAG – primary open angle glaucoma; LTG – low tension glaucoma; PXG – pseudoexfoliative glaucoma; PSI – perceptual search index

Introduction

Preattentive vision describes the ability of the visual system to extract basic features from a visual scene in parallel i.e. parallel processing will prioritize feature differences within the scene; these will pop-out instantaneously from the background and attract attention.[1][2][3] Several studies have shown that the search for a target pattern among homogenous distractor patterns is fast and parallel once this target differs significantly from its background in some basic stimulus dimension such as orientation, flicker, motion etc.[4][5][6][7] A pre-attentively detected stimulus appears to “pop-out” [7] and this allows very rapid detection of a target among a field of distractors before a saccadic eye movement can be made.

Pre-attentive vision is a global visual function that can perform a simple analysis of image content simultaneously across an entire image, compared to foveal processing that provides a spotlight on only a limited portion of the visual field at any moment in time. Consequently it is a reasonable assumption that preattentive vision is dependent on neural mechanisms being intact across the retina. If this is the case, a suitably configured preattentive visual search (PAVS) test might be able to detect any condition that produces damage across a significant area of the visual field or to the neural hardware subserving vision. If pop-out does not occur, for example because glaucoma is present, the search will become dependent on foveal mechanisms whose small spatial coverage require a serial search strategy with each part of an extended image being examined in turn, and response times will increase accordingly.

Glaucoma remains an enigmatic condition, frustratingly elusive in the earliest stages, often progressing despite apparently “successful” therapeutic intervention. Traditional diagnostic techniques are limited to the extent that the earliest losses of glaucoma remain difficult to detect.[8][9] By impacting on the peripheral visual field rather than central vision, glaucoma should have an early detrimental impact on PAVS and therefore represents a good basis for a potential diagnostic test.

Given the apparently non-selective nature [10] of retinal ganglion cell death in glaucoma (magnocellular [11][12] and parvocellular [13][14] deficits occur), it would seem desirable to evaluate the functional integrity of different cell types during the course of a single examination to optimise sensitivity to the earliest losses in glaucoma. Preattentive vision operates across a range of stimulus attributes including colour, movement and flicker so that selective tests can be devised for these pathways.

A test of preattentive vision is inherently different from conventional psychophysical techniques. Such techniques characteristically rely on the presentation of single targets in isolated areas of the visual field. Preattentive vision requires retinal and neural integration of the combined responses of neighbouring and overlapping receptive fields of retinal ganglion cells. Other studies have confirmed that other population-response tests such as motion coherence [15] and pattern-discrimination perimetry [13] [16][17][18] are possibly more sensitive than achromatic perimetry.

Recently, several studies have looked at potential applications of PAVS to detection and diagnosis of clinical conditions, including glaucoma [19], Parkinson's disease [20] and dementia. [21] In the former case, the authors reported that PAVS tests successfully discriminated between patients with and without glaucoma. The intention here is to determine if those results could be substantiated and to evaluate PAVS in suspects without established conventional field loss.

Materials & Methods

The software used to present and control the experiment was adapted from that devised by Flitcroft et al. [19] Figure 1 shows a diagrammatic representation of the target and 119 distractors as presented for the orientation test. A two-alternative forced choice paradigm was adopted, with subjects required to accurately locate the feature pop-out as quickly as possible on left or right side of the screen using two handheld buttons. Subjects were allowed twenty practice presentations on each of the three targets. More

detailed descriptions of the apparatus, stimuli and subjects tasks have previously been described elsewhere. [22]

Insert Figure 1 here

All subjects were required to have minimum visual acuity of 6/12, no significant media opacity, no other known ocular or systemic disease, an open anterior chamber angle and a Humphrey visual field assessment performed within the past six months. Full ethics approval was granted by DIT ethics committee and informed, written consent obtained from each subject. Subjects were classified into one of three groups using strict entry criteria (Table 1).

GLAUCOMA	**GLAUCOMA SUSPECT**	**NORMAL**
N = 41 Mean Age = 67 Range = 49 - 83	N = 41 Mean Age = 62 Range = 44 - 83	N = 41 Mean Age = 64 Range = 49 - 83
Characteristic ONH/RNFL damage	Suspicious ONH/RNFL structure	Normal ONH & RNFL structure
Characteristic, repeatable, early Glaucomatous VF loss (Abnormal GHT and/or cpsd < 5%, and/or cluster criteria defect	No repeatable characteristic VF loss	Normal VF sensitivity
Classified based on IOP and gonioscopy findings		Normal intraocular pressure (IOP)
		CD ratio < 0.7

Table 1: Subject classification criteria

A total of 123 subjects were examined, 41 in each category. Following the practice session, the subject began the test proper, firstly for flicker, followed by displacement and finally for orientation, through their near optical prescription if any. Each test consisted of 40 presentations of each target type. Subjects subsequently performed a choice reaction time (CRT) test (Figure 2) that required the subject to discriminate the target from a non-target and indicate its relative location on the right or left side of the screen to test for any non-glaucomatous motor/neural deficiencies that could complicate interpretation of the results.

Insert Figure 2 here

Results

(A) – GLAUCOMA Vs SUSPECTS Vs NORMALS

2-tailed independent samples T test was used to compare the mean response times for each target type across the three groups.

Figure 3 illustrates a number of significant findings. There is an apparent increase in search times among suspects and particularly in the glaucoma group compared to the normals group for each preattentive task. The elevation is most apparent for the orientation task.

Insert Figure 3 here

Table 2 outlines the independent samples T test analysis, revealing a statistically significant difference between glaucoma subjects and both normals and suspects across all PAVS targets and interestingly, also for CRT. Differences between suspects and normals are non-significant for the flicker and orientation task, but statistically significant for the displacement task. No differences were detected in CRT means between normals and suspects.

	Flicker	Displacement	Orientation	CRT
Glaucoma Vs Suspect	T = 7.432 P < 0.001 dF= 63.822	T = 6.251 P < 0.001 dF= 80	T = 9.336 P < 0.001 dF= 63.258	T = 3.783 P < 0.001 dF= 80
Glaucoma Vs Normal	T = 9.157 P < 0.001 dF= 51.011	T = 7.535 P < 0.001 dF= 46.251	T = 10.963 P < 0.001 dF= 50.395	T = 2.352 P = 0.021 dF= 80
Suspect Vs Normal	T = 1.758 P = 0.083 dF= 68.798	T = 2.183 P = 0.032 dF= 71.038	T = 1.393 P = 0.168 dF= 68.196	T = -0.953 P = 0.343 dF= 80

Table 2: 2-tailed Independent samples T test for equality of PAVS and CRT mean response times across *normals, suspects and glaucoma subjects*

Given the possibility of psycho-motor reaction time effects in an elderly subject group, and the observed statistically significant difference between the CRT for glaucoma and both suspects and normals, it was appropriate to examine the effects of any processing differences in the statistical analysis. As such a new index was formed comprising the result of the PAVS time divided by the CRT for each subject, which we have termed perceptual search index (PSI).

Simple inspection of the group means of the PSI in Figure 4 again highlights a similar performance effect between the groups, with the glaucoma group mean substantially increased compared to the other groups.

Insert Figure 4 here

Independent samples T test analysis confirms the statistically significant performance impairment in the glaucoma group compared to both normals and suspects. More interestingly however, this index appears to differentiate between the normal and suspect groups on the basis of a statistically significant difference ($p < 0.05$) between the respective PSI scores across all target types (Table 3).

	Flicker PSI	Displacement PSI	Orientation PSI
Glaucoma Vs Suspect	T = 7.566 P < 0.001 dF = 69.38	T = 7.155 P < 0.001 dF= 61.749	T = 10.785 P < 0.001 dF= 64.623
Glaucoma Vs Normal	T = 10.960 P < 0.001 dF= 45.816	T = 9.956 P < 0.001 dF= 46.523	T = 13.685 P < 0.001 dF= 45.967
Suspect Vs Normal	T = 3.193 P = 0.002 dF= 53.001	T = 3.599 P = 0.001 dF= 60.624	T = 2.600 P = 0.012 dF= 56.640

Table 3: 2-tailed Independent samples T test for equality of PSI means across *normals, suspects and glaucoma subjects*

B: PRIMARY OPEN ANGLE GLAUCOMA Vs LOW-TENSION GLAUCOMA Vs PSEUDOEXFOLIATIVE GLAUCOMA

The glaucoma group was divided into three subgroups on the basis of the IOP level at time of diagnosis, and on the status of the anterior chamber drainage angle into either primary open angle glaucoma (POAG) – 22 subjects, low tension glaucoma (LTG) – 11 subjects, or pseudoexfoliative glaucoma (PXG) – 8 subjects. The data within the glaucoma group was reanalysed to determine any possible effect of glaucoma type on PAVS efficiency.

Figure 5 shows the primary open angle group to have slightly increased mean PAVS times compared to pseudoexfoliation and low tension glaucomas for each task (whose search efficiency appears similar in all cases).

Insert Figure 5 here

Table 4 charts Independent samples T test results. This reveals no difference in PAVS efficiency between any of the glaucoma subtypes tested. Similarly, no differences were detected in CRT means between any of the glaucoma subtypes. Even so, given the results obtained in section A when the PSI data was computed, it seemed appropriate to assess for similar effects here.

	Flicker	**Displacement**	**Orientation**	**CRT**
POAG Vs LTG	T = 1.110 P = 0.276 dF= 31	T = 1.113 P = 0.274 dF= 31	T = 1.844 P = 0.075 dF= 28.791	T = 0.167 P = 0.868 dF= 31
POAG Vs PXF	T = 1.012 P = 0.320 dF= 28	T = 0.803 P = 0.429 dF= 28	T = 1.243 P = 0.085 dF= 27.631	T = 1.696 P = 0.101 dF= 28
LTG Vs PXF	T = 0.026 P = 0.980 dF= 17	T = -0.410 P = 0.687 dF= 17	T = -0.706 P = 0.490 dF= 17	T = 2.096 P = 0.051 dF= 17

Table 4: 2-tailed Independent samples T test for equality of PAVS, SRT and CRT mean response times across *glaucoma subtypes*

Figure 6 shows an interesting PSI variation from the basic PAVS data above. The low tension glaucoma PSI means are consistently lower than the pseudoexfoliation and primary open angle glaucoma groups, which are remarkably similar. The effect is largest for the orientation task.

Insert Figure 6 here

Independent samples T test confirms similar performance effects between the primary open angle and pseudoexfoliation groups across all tasks. Again there are no significant differences between low tension glaucoma and both other groups for the flicker and displacement tasks. The orientation task however shows a statistically

significant difference between low tension glaucoma and both other glaucoma subtypes (Table 5).

	Flicker PSI	Displacement PSI	Orientation PSI
POAG Vs LTG	T = 1.237 P = 0.225 dF= 31	T = 1.407 P = 0.170 dF= 31	T = 2.218 P = 0.034 dF= 29.987
POAG Vs PXF	T = 0.085 P = 0.933 dF= 28	T = 0.056 P = 0.956 dF= 28	T = 0.397 P = 0.694 dF= 28
LTG Vs PXF	T = -0.974 P = 0.344 dF= 17	T = -1.696 P = 0.108 dF= 17	T = -2.171 P = 0.044 dF= 17

Table 5: 2-tailed Independent samples T test for equality of PSI means, across *glaucoma subtypes*

Discussion

The nature of the various target/distractor design combinations here is such as to create a test with the potential to preferentially stimulate and assess the integrity of different ganglion cell populations within a single examination.

The temporal characteristics of the flicker and motion displacement targets used here was designed to stimulate the transient, faster conducting magnocellular pathway. The high spatial frequency, stationary orientation target/distractor combination was designed to be preferentially coded by the sustained parvocellular pathway. [23][24]

It is therefore unsurprising that the orientation task employed here has consistently increased PAVS response times compared to the flicker and motion targets. This may reflect a difference in the processing speed of the two pathways involved, a fundamental difference in the processing capacity of the two pathways, a difference in the capacity for attentional capture of a stationary versus a motion/flicker singularity

(moving targets may be visually more important from an evolutionary perspective), or possibly nothing more than a basic difference in the task complexity.

All three targets appear to have the capacity to differentiate glaucoma from non-glaucoma on the basis of preattentive search efficiency. Our results confirm those of a previous study [19] that patients with established early glaucoma have impaired parallel search capabilities when compared to either age-matched normal subjects or glaucoma suspects without established visual field loss. The degree of impairment was highly statistically significant for each target type.

The use of a reaction time paradigm instead of a thresholding strategy has significant benefits with regards to task simplicity and speed. It does however leave interpretation of data based solely on a subjects speed of response open to misdiagnosis were a subjects response time artificially increased due to non-visual functional deficits. Physical limitations, sensory degradations [25] or attentional/neural losses with normal aging or in neurodegenerative diseases [26][27] are known to impact cognitive performance and could conceivably cause impaired search times in the absence of any true loss of preattentive vision.

The CRT test requires a subject to indicate the location of a specific target with only one distractor. If preattentive search efficiency is compromised, a decision can still be made following a rapid saccade at stimulus onset to one of two possible locations. A decision on target location can thus be made almost instantaneously. By its very nature, preattentive search times should not increase significantly above the CRT regardless of the number of distractors. The CRT therefore gives an indication as to the approximate search time a subject should achieve given normal preattentive processing skills.

The CRT was thus used to determine an alternative, more robust performance index (perceptual search index – PSI), presumed to be free of any such potential artifactual defects.

The PSI analysis confirms the loss of search efficiency in the glaucoma group to be statistically significant. The finding that the suspect group PSI data is significantly different from the normal group data is of particular interest. The magnitude of the effect is obviously lower than that observed in the glaucoma group, reflecting perhaps the fact that neural loss is more advanced in the glaucoma group. The PSI mean is on average 15 – 17% higher for suspects compared to normals depending on target type, and between 76% (flicker) and 230% (orientation) increased for glaucoma above normal. While the current results are not sufficient to say that the test is capable of defining those patients classified as suspects most likely to develop glaucomatous field loss, they are however encouraging enough to suggest that a longitudinal analysis of such patients might be worthwhile to determine if those with the largest PSI values are those who will progress. A test that can determine those most at risk of developing glaucoma is of obvious merit.

While the end result is always ganglion cell death, the pattern of damage and timeframe for cell death in glaucoma may vary and may therefore have different effects on preattentive performance at different stages. Analysis of PAVS efficiency among glaucoma subtypes however does not reveal any significant differences in performance between the three glaucoma groups. The observed PSI difference for low tension glaucoma compared to both primary open angle and pseudoexfoliative glaucoma for the orientation target however poses some interesting questions. Search remains marginally less affected in LTG than the other two groups. Does this suggest a relative preservation of parallel mechanisms in the pathogenesis of LTG compared to high-tension cases? Is this preservation limited to or more significant in the parvocellular pathway? One might thus hypothesize that smaller diameter parvocellular fibres are less susceptible to vascular insufficiency, while the compressive effects of higher IOP are less selective for pathway at this stage of glaucoma. Such a hypothesis remains to be tested.

While the test does not appear to clarify issues relating to the pathophysiology of the subtypes of glaucoma, the results here indicate that the tests ability to detect

glaucomatous damage does not depend on the type of glaucoma. This may prove beneficial in the context of screening for glaucoma.

The importance of early detection to glaucoma management and visual prognosis is well known [28]. Evidence of selective damage to large ganglion cells in glaucoma, [29][30] psychophysical losses of M cell function [12] and observations of reduced axonal flow to the magnocellular layers of the lateral geniculate body[31] have led to attempts to develop tests that isolate the magnocellular pathway.

Retinal sampling has become central to the development of novel tests of retinal function in glaucoma. Cells that have sparse representation may yield the earliest detectable losses of visual function [10]. The insensitivity of conventional perimetric stimuli most likely reflects the non-selective nature of the achromatic stimuli used, and the significant degree of overlap of ganglion cell receptive fields in all retinal locations masks early functional losses.

The current test, which incorporates stimuli capable of testing both pathways to varying degrees, may provide a useful alternative screening technique for the rapid clinical evaluation of visual functional status in those at risk of glaucoma.

The use of a response time here, rather than a threshold experimental paradigm, also simplifies the nature of the PAVS test. This has potential advantages if the test is to be applied to patients with limited span of attention, including elderly patients amongst whom most types of glaucoma are most prevalent [32][33]. It is also a very rapid test taking as little as one minute per eye to perform a complete assessment using all three targets on a normal subject (under three minutes in glaucoma subjects). The current test remains resistant to the potentially confounding effects of optical blur, with the exception of the high spatial frequency orientation target that is resistant only to approximately 1D of optical defocus [22]. Such rapid means of assessment, simplicity of task [34] and resistance to optical blur have obvious merit for development of a clinically viable test for glaucoma.

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Competing Interests Statement

The authors declare that they have no competing financial interests.

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Legend

Figure 1: Orientation test target N surrounded by 119 distractors Z (representing a 90 degree orientation shift). The subject was instructed to fixate a central fixation cross that appeared centrally between each presentation.

Figure 2: Choice reaction time test required the subject to indicate the location of the empty box (using two handheld buttons) on left or right side of the screen as quickly as possible following stimulus onset after a variable time delay.

Figure 3: Mean PAVS response times for normals, suspects and glaucoma subjects for flicker, displacement and orientation targets.

Figure 4: PAVS efficiency as a function of choice reaction time (CRT) - Mean PSI among *normals, suspects and glaucoma subjects*

Figure 5: Relationship between *glaucoma subtype* and PAVS efficiency for flicker, displacement and orientation targets.

Figure 6: PAVS efficiency as a function of choice reaction time (CRT) – mean PSI across glaucoma subtypes

Table 1: Subject classification criteria

Table 2: 2-tailed Independent samples T test for equality of PAVS and CRT mean response times across *normals, suspects and glaucoma subjects*

Table 3: 2-tailed Independent samples T test for equality of PSI means across *normals, suspects and glaucoma subjects*

Table 4: 2-tailed Independent samples T test for equality of PAVS and CRT mean response times across *glaucoma subtypes*

Table 5: 2-tailed Independent samples T test for equality of PSI means across *glaucoma subtypes*

Figure 1

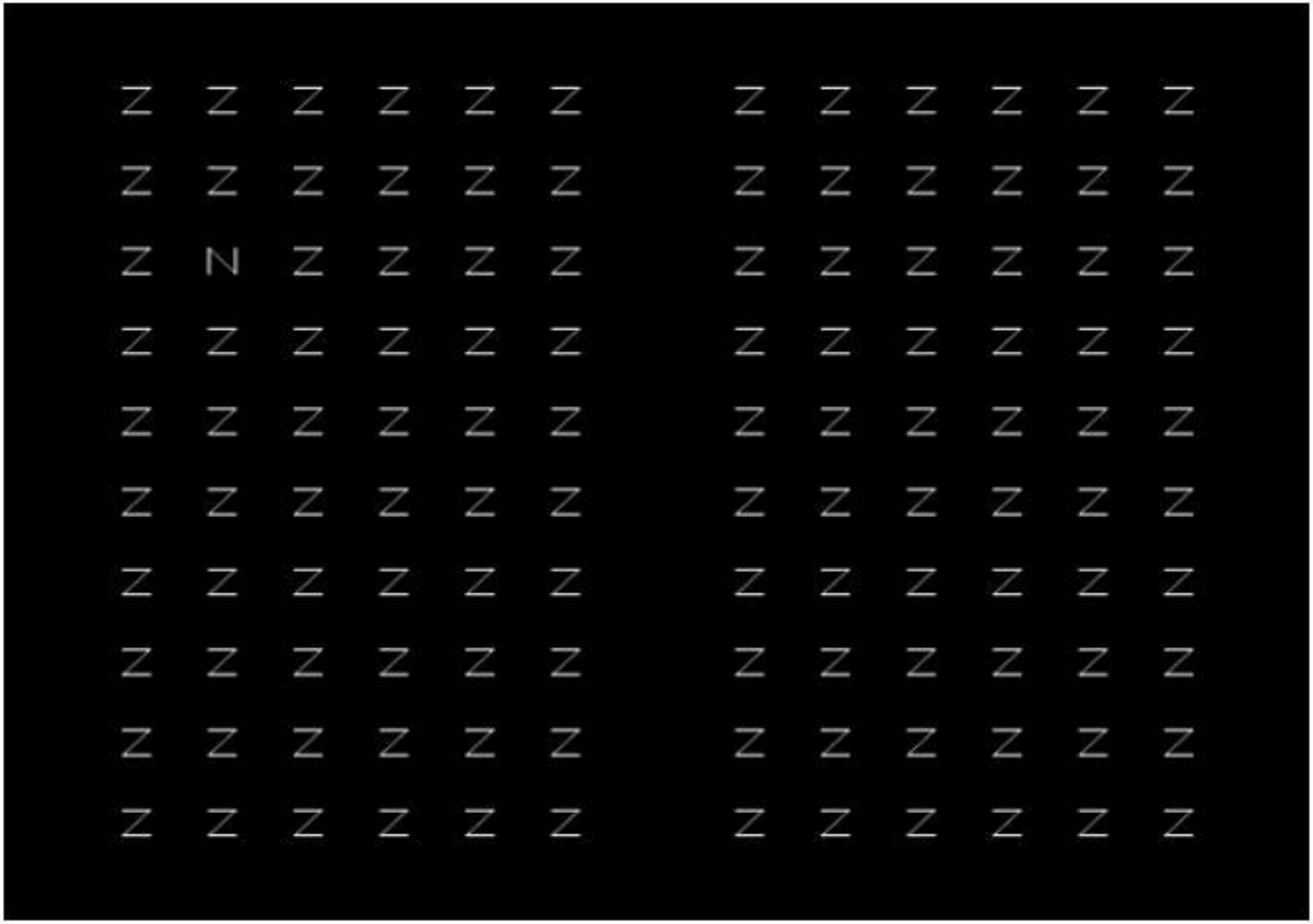
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Figure 2

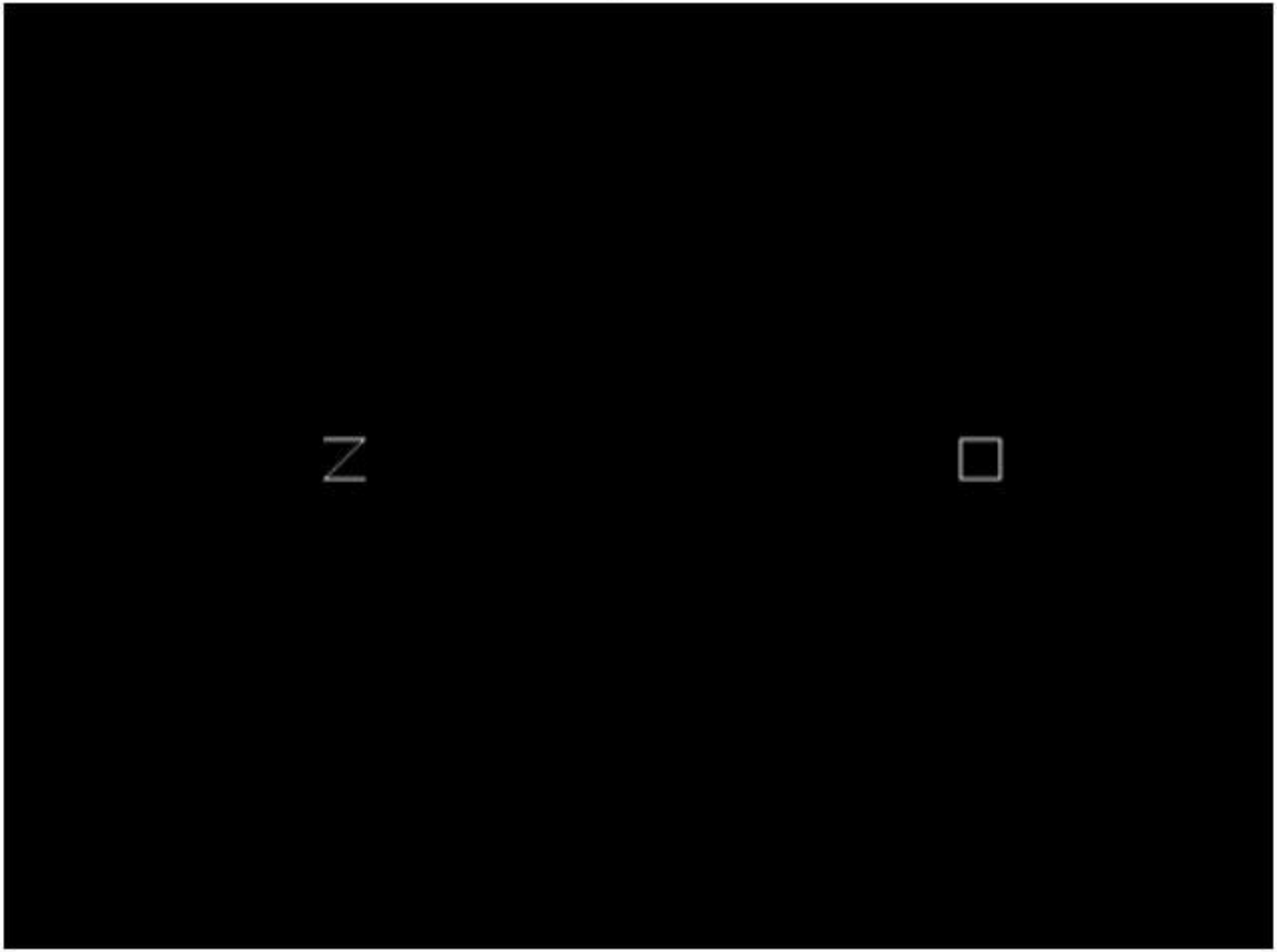
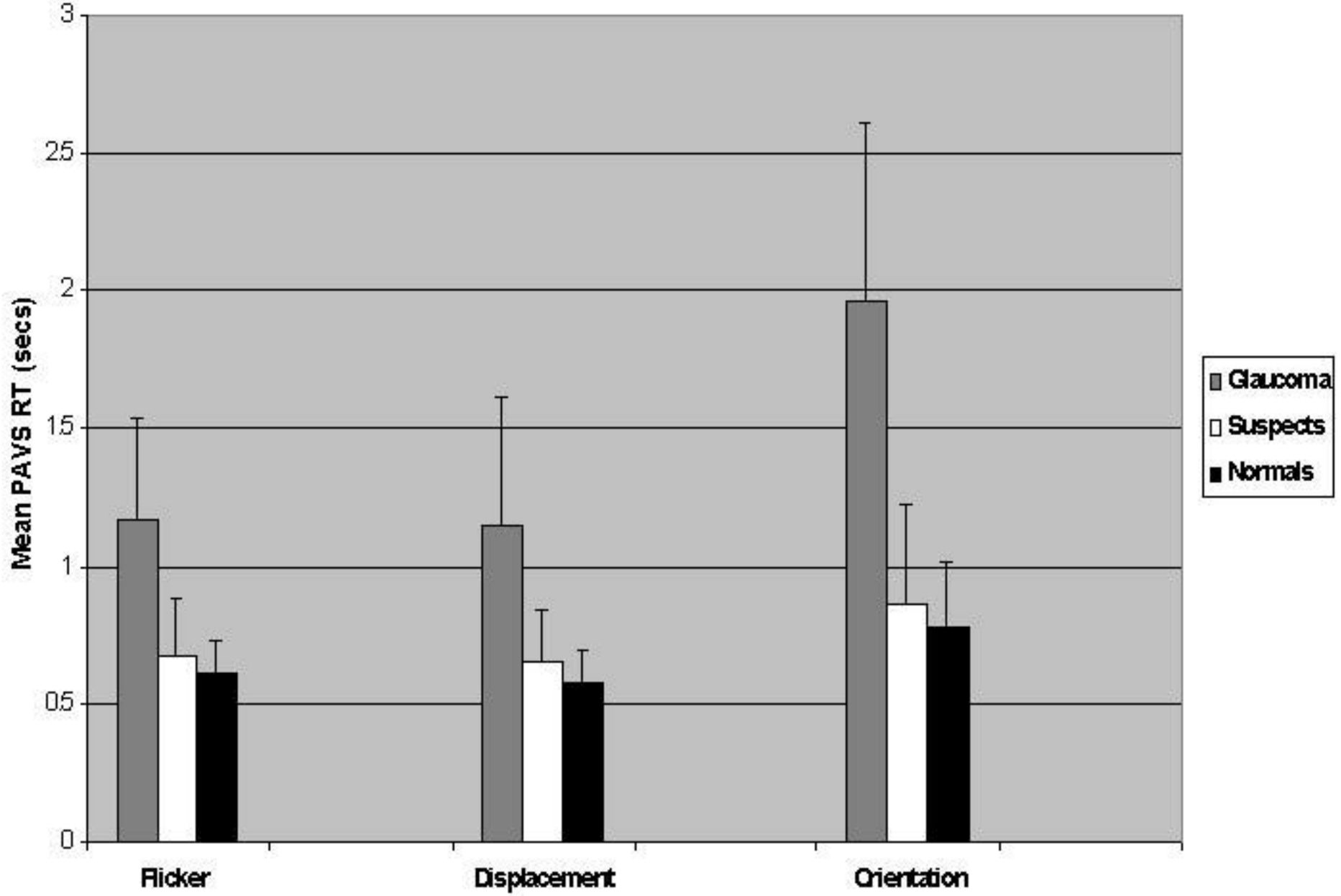


Figure 3


3
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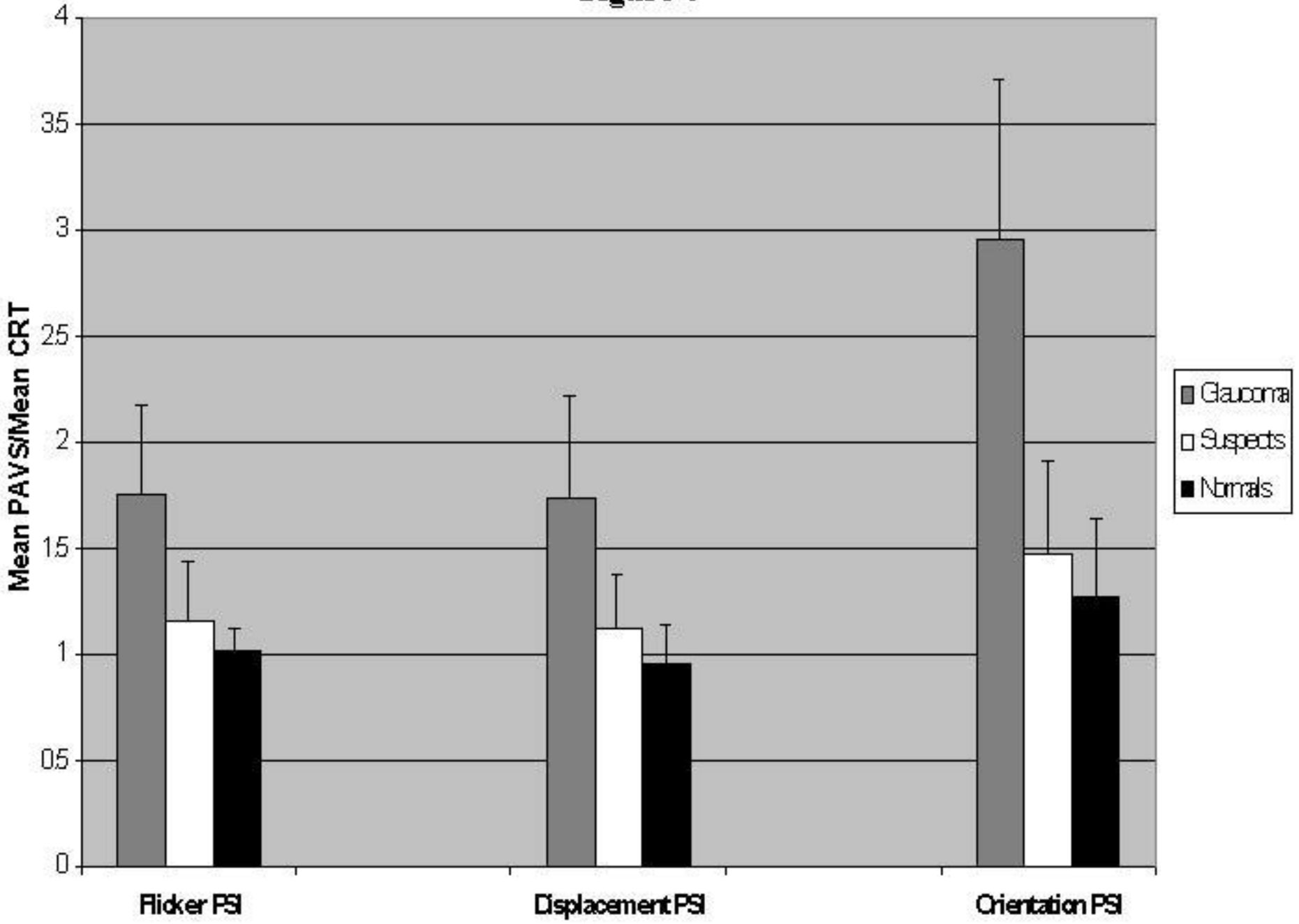
Mean PAVS RT (secs)
Flicker
Displacement
Orientation
Glaucoma
Suspects
Normals

Figure 4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Mean PAVS/Mean CRT
Glaucoma
Suspects
Normals
Flicker PSI
Displacement PSI
Orientation PSI

Figure 5

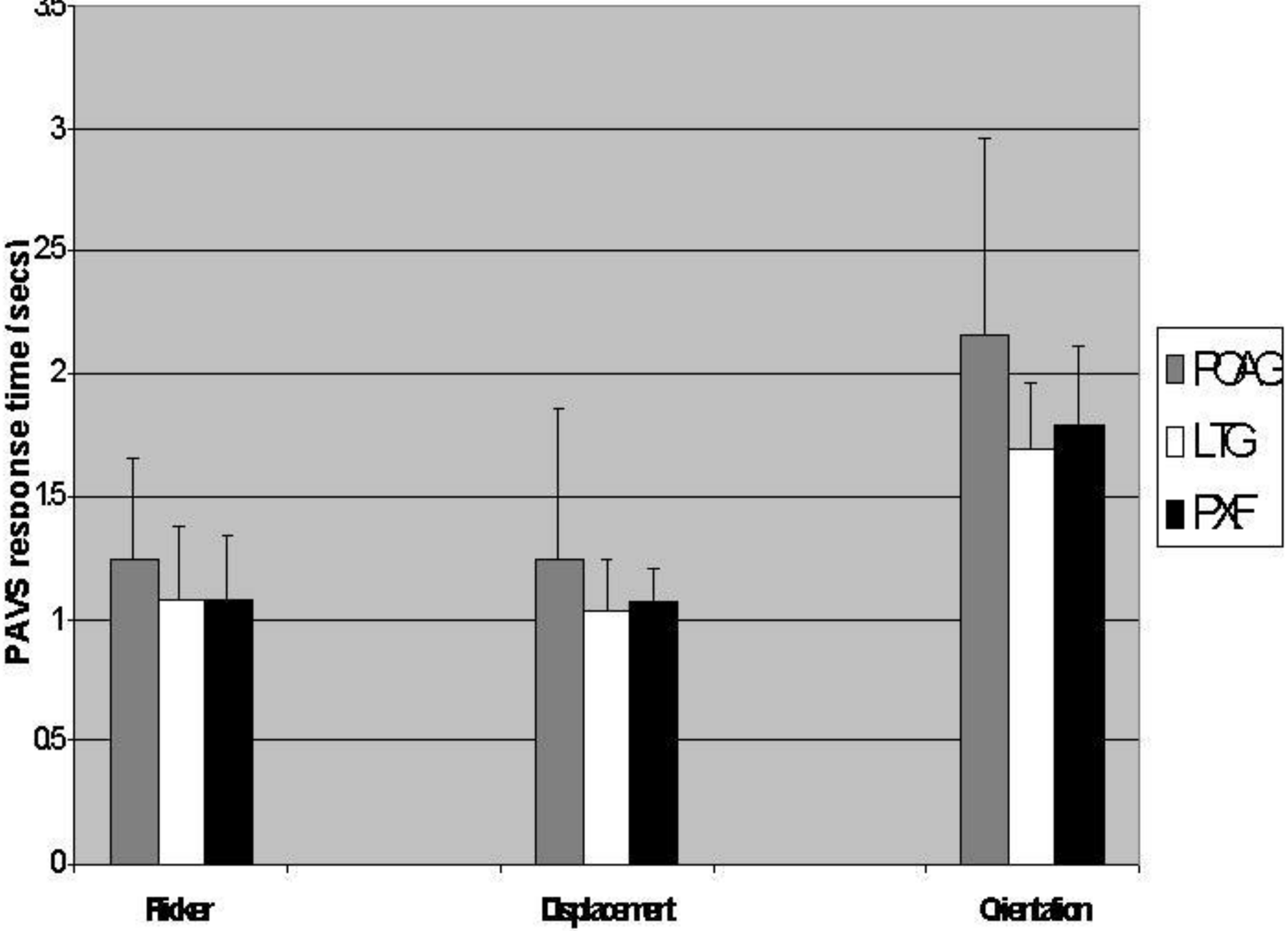
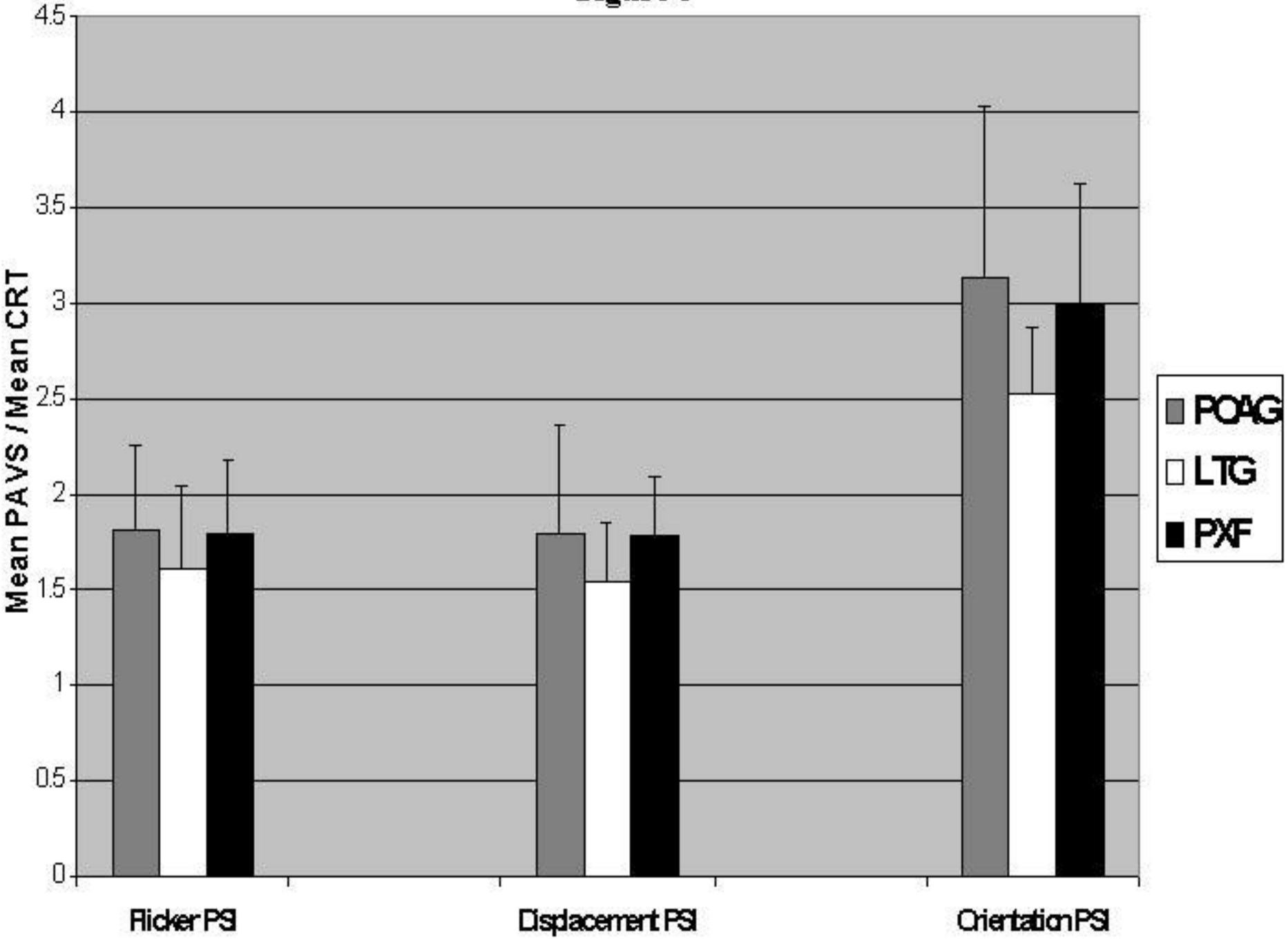

3.5
3
2.5
2
1.5
1
0.5
0
PAVS response time (secs)
POAG
LTG
PXF
Flicker
Displacement
Orientation

Figure 6


4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
Mean PAVS / Mean CRT
POAG
LTG
PXF
Flicker PSI
Displacement PSI
Orientation PSI