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The Area under the Main Sequence as an Alternative Method to Measure Saccadic Dynamics

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Abstract

Significance: This study shows that the area under the main sequence (MSAREA) is a valid alternative to the standard peak velocity main sequence in measuring saccadic dynamics. A 1-parameter area model, $MSAREA = G_{PW=1.55} \times SACSIZESIZE^{1.55}$, with SACSIZESIZE the size of the saccade, 1.55 a power factor, and $G_{PW=1.55}$ a gain parameter, is presented.

Purpose: $SACPEAK = V_{max} \times (1 - e^{-SACSIZESIZE/SAT})$ is the traditional model used to describe the saccadic main sequence, the relationship between the size of the movement and its peak velocity (SACPEAK). In the previous paper, we have shown that there is a strong linear correlation between the two parameters V_{max} and SAT, which severely affects the model's clinical applicability. The purpose of this study is to see if, by using the area under the main sequence as an alternative approach, we can overcome the limitations of the traditional model.

Methods: Participants and main sequence data are the same of the previous study. A trapezoidal integration was used to estimate the area under the main sequences as a function of SACSIZESIZE.

Results: A 2-parameter area model was computed to determine the range of variability of its parameters and R^2 values. These were then used as reference values in the search for 1-parameter alternatives. The 1-parameter model $MSAREA = G_{PW=1.55} \times SACSIZESIZE^{1.55}$ performed well for all data sets. We tested its validity by performing a comparison with other 1-parameter area models.

Conclusions: Area models are superior to peak velocity models in terms of R^2 and stability and can be reduced to robust 1-parameter expressions with only limited degradation in R^2 . This greatly simplifies not only the determination if a set is inside or outside a reference population but also allows for direct comparisons between sets, with the saccadic dynamics expressed by a simple linear gain factor ($G_{PW=1.55}$).

Keywords

saccade; main sequence; area; dynamics; eye movements; concussion

The 2-parameter function $SACPEAK = V_{max} \times (1 - e^{-SACSIZE/SAT})$ is the traditional model used to describe the saccadic main sequence,¹ the direct relationship between the size of the saccade (SACSIZE) and its peak velocity (SACPEAK). For all the models in this paper, the parameters are reported in bold font. V_{max} is the asymptotic peak velocity, i.e., the peak velocity associated with very large saccades. SAT, the saturation coefficient, determines the speed with which this asymptotic value is approached. In the previous paper, we have shown that the two parameters V_{max} and SAT are correlated. The correlation is not strong enough to estimate reliably V_{max} from SAT and, therefore, to obtain a 1-parameter model in SAT only, but it negatively affects the clinical applicability of this model. The availability of a 1-parameter model of saccadic dynamics would have allowed direct comparisons between data sets, for example, sets acquired pre-concussion and post-concussion from the same athlete, or to follow the progression of a neurodegenerative disease in time. The stability of the model is also compromised by the correlation, with small variations in the main sequence profiles potentially causing large variations in the two parameters due to their reciprocal interactions. The 95% confidence intervals (C.I.) of the two parameters at the population level are severely inflated when compared with the actual variation in saccadic dynamics, particularly for small saccades. As partial solution, we introduced a 3-step process that takes into account this co-variability to better determine if a patient's main sequence is inside or outside a reference population. The main problems remain, including the impossibility of using the V_{max} and SAT values for direct comparisons between data sets. The V_{max} and SAT 95% C.I.s of the two sets will most likely overlap even if the dynamical variations are clinically significant. Could the area under the main sequence (MSAREA) be a more robust measure of saccadic dynamics and perhaps offer reliable 1-parameter models?

PURPOSE

The initial goal of this study will be to determine a 2-parameter area model that can fit all the 116 participants x 4 saccadic directions data sets. The model $MSAREA = G \times SACSIZE^{PW}$ perfectly matches our requirement with extremely high R^2 values. We will show that the parameters G, a linear gain factor, and PW, a power factor, also present a strong correlation. As for the traditional main sequence model, we will test if G can be predicted from PW and the model reduced to a 1-parameter model in PW. The 1-parameter area model $MSAREA = G_{PW=1.55} \times SACSIZE^{1.55}$, with $G_{PW=1.55}$ the model parameter - a simple linear gain - and PW set to 1.55, the population average of PW of the 2-parameter area model, will be tested against other four 1-parameter area models to evaluate its stability. Reproducibility between sessions will also be evaluated.

METHODS

Participants (or parent or legally authorized representative for minors) gave written informed consent and all protocols and procedures were conducted in accordance with the Declaration of Helsinki and were approved by the University of Alabama at Birmingham Institutional Review Board.

The main sequence data used to determine the area models, i.e., the peak velocity (SACPEAK) vs. size (SACSIZE) pair for each primary saccade (n = 12) of the 116

participants $\times$ 4 saccadic directions sets and the 35×4 repeated sets are the same of the previous paper. Thus, information about participants, experimental protocols, computation of the eye position and velocity traces and determination of the main sequence are not reported here for brevity. The additional step in the analysis for this study is a trapezoidal integration applied to the main sequence data points (see Fig. 1), in order to obtain the area under the main sequence (MSAREA) as a function of saccadic size. We preferred this direct approach to a numerical or analytical integration of the main sequence model in $V_{\max}$ and SAT because it does not require the intermediate step of computing the main sequence model. There is an analytical solution to the integral of the equation $SACPEAK = V_{\max} \times (1 - e^{-SACSIZE/SAT})$ with the area function expressed by the same parameters $V_{\max}$ and SAT. Preliminary tests comparing the three methods showed that there is very strong overlap in the resulting area functions, which supported our direct approach. The results obtained with the 1x (non-interpolated) and 10x (interpolated) data are very similar, and for brevity, only the results from the non-interpolated data will be described in this report.

To avoid inflating the quality of the parametric estimates of the area models, determined using the Gauss-Newton method with least-square optimization, the point (0; 0), i.e., $MSAREA = 0^{\circ^2}/s$ for $SACSIZE = 0^{\circ}$, was not included in the estimations. The reported R^2 is the mean-corrected R^2 , which is the most conservative of the R^2 . The amplitude of the 95% C.I.s is the difference between the upper $P = .975$ and the lower $P = .025$ limits, i.e., the full amplitude of the interval, not the $\pm$ value. The statistical tests for normality and the selection of the bin size in the histograms are identical to the first paper.

RESULTS

2-parameter Model of the Area under the Peak Velocity vs. Size Main Sequence

The 2-parameter area model $MSAREA = G \times SACSIZE^{PW}$, abbreviated “G-PW model”, was found to fit all data sets with extremely high R^2 . The parameter G is a linear gain element and PW a power factor. Figure 1 shows one of the data sets with the worst fit of the 2-parameter peak velocity vs. size main sequence (left panel) and its associated 2-parameter area fit in black (right panel). The right panel also illustrates the trapezoidal algorithm used to obtain the area function. Main sequence points and main sequence model fit (in red) are the same of the left panel. At each $SACSIZE$ value, the trapezoidal area between the previous ($SACPEAK$; $SACSIZE$) point and the current ($SACPEAK$; $SACSIZE$) point is added to the area sum up to that point. Even for this data set, with the value of the R^2 of the main sequence model of only 0.592, the G-PW area model has a R^2 of 0.9966. The estimate, asymptotic standard error (ASE) and range of the 95% Wald C.I. of each of the two parameter pairs ($V_{\max}$; SAT) and (G ; PW) are reported below the x-axis of the graphs.

As for the standard 2-parameter main sequence model, we determined the range of variability of the two parameters G and PW for the 116×4 data sets. The best average R^2 is 0.9991 [range 0.9965 to 0.99995] for the 116 rightward data sets. The worst average R^2 is 0.9986 [range 0.9951 to 0.9998] for the 116 downward data sets. The 2-parameter area model in G and PW fits all data sets with extreme accuracy. Figures 2 and 3 illustrate the histograms of the distribution of the area parameters G and PW for the 4 saccadic directions with the associated normal distribution models (solid curves). Table 1 shows the parameters

of these normal distribution models. By using the maximum likelihood method implemented in Systat and the χ^2 test of normality, we verified that these distributions could be modeled as normal distributions, with $P < .01$ selected as the criteria for rejection of the normal distribution hypothesis (χ^2 , df and P values in Table 1). All histograms have $P > .01$, indicating that a normal distribution is a reasonable assumption. As population ranges for G and PW, reported in Table 1, we determined the $P = .025$ and $P = .975$ values of G and PW. The 95% C.I.s are the difference between the $P = .975$ and the $P = .025$ values. In a cross-comparison, the G mean values are lower for the vertical saccadic directions with respect to the horizontal saccadic directions (* in the upper section of the table; $P < 10^{-4}$, paired and unpaired t-tests). The two horizontal pairs and the two vertical pairs are not statistically different ($P > .01$) with respect to each other. For the parameter PW, only the upward direction differs from the other three directions (* in the lower section of the table, $P < .01$, paired and unpaired t-tests), albeit both G and PW present wide overlaps in their 95% C.I.s. The population ranges for G and PW are large, comparable to the population ranges of $V_{\max}$ and SAT: a clear indication of correlation between the two parameters.

Correlation between G and PW

The strength of the correlation between G and PW, illustrated in Figure 4 for the 4 saccadic directions, is similar to the one found between $V_{\max}$ and SAT. The intercept A and slope B of the linear regressions and the R^2 values are almost identical between the two horizontal data sets and between the two vertical data sets, but the horizontal values are outside the 95% C.I.s of the vertical data sets or barely overlapping and vice versa. This is the only case in these two studies where horizontal and vertical data sets clearly differ in terms of parameters and not just in a higher scatter for the vertical sets. The strong correlation between G and PW is also reflected in the large 95% C.I.s of the parameter G at the single-set level, as it can be seen in the example in Figure 1 right panel. Even with a $R^2 = 0.9966$, the 95% C.I. of the parameter G is very large ($\pm 26\%$ of the G value), although it is narrower for the parameter PW ($\pm 6\%$ of the PW value).

Estimating G from PW and Search for 1-parameter Area Models

As for the traditional main sequence model in $V_{\max}$ and SAT, we attempted to use the correlation between G and PW of the 2-parameter area model to determine a G_{est} using the linear regression parameters in Figure 4 and the PW value given by the G-PW model of the set. The histograms of the deviations of the actual value of G of the set from $G_{\text{est}} = A_{\text{FIG4}} + B_{\text{FIG4}} \times \text{PW}$ for the 4 saccadic directions are reported in Figure 5. The curves are normal distribution models, the parameters of which are illustrated in Table 2 with layout identical to Table 1. Is the ability to predict G from PW better than the ability to predict $V_{\max}$ from SAT, due to the much higher R^2 of the area model? For each saccadic direction, we normalized the 95% C.I.s of the Gaussian distributions of $V_{\max} - V_{\max\text{est}}$ and $G - G_{\text{est}}$ (Tabs. 2 in the two papers) with respect to the corresponding mean value of $V_{\max}$ and G (Tabs. 1 in the two papers). Interestingly, the ability to predict G from PW is actually slightly worse. For the rightward direction, the 95% C.I. of $V_{\max} - V_{\max\text{est}}$ is 128.9°/s and the mean $V_{\max}$ is 514°/s, giving a ratio of 0.25. The 95% C.I. of $G - G_{\text{est}}$ is 16.8°(2-PW)/s and the mean G is 60.8°(2-PW)/s, giving a ratio of 0.28. For the downward direction is 0.40 vs. 0.48.

We therefore expect that the 1-parameter area model $MSAREA = (A_{FIG4} + B_{FIG4} \times PW_{1-par}) \times SACSIZES^{PW_{1-par}}$, abbreviated “ PW_{1-par} model”, which attempts to use the correlation between the two parameters G and PW to obtain a 1-parameter model in PW_{1-par} , will not perform any better than the 1-parameter main sequence model $SACPEAK = (A_{FIG5} + B_{FIG5} \times SAT_{1-par}) \times (1 - \exp^{-SACSIZES / SAT_{1-par}})$ described in the preceding paper. The italics subscripts indicate that the Figure 5 referred here is from the previous paper. As before, we will test the model in PW_{1-par} using data sets which (G ; PW) pairs are the furthest away from the regression lines to maximally challenge the model fit. Those are the open points A and B in the upward direction panel in Figure 4. We will also use points C and D, near the extreme 95% C.I.s of G and PW , for reasons that will be clear later. For point C, being very close to the regression line, the 1-parameter model in PW_{1-par} will necessarily perform as well as the 2-parameter model in G and PW .

Before testing the 1-parameter model in PW_{1-par} on the 4 sets A-D in Figure 4, we want to explore how changing the value of G by keeping PW constant and how changing the value of PW by keeping G constant affect the area profiles. As we discussed in the previous paper, V_{max} and SAT of the standard 2-parameter main sequence model influence the peak velocity main sequence profiles in a complex interacting way, as it can be seen in panels A and B in Figure 6. Mean values and ranges of V_{max} and SAT for panels A and B are from Table 1 of the preceding paper. Changing V_{max} also affects the profile for small saccades, while SAT also influences the profile for large saccades. For data sets far off the linear regression line between V_{max} and SAT (Figure 5 previous paper), the fitting algorithm applied to the 1-parameter model in SAT_{1-par} $SACPEAK = (A_{FIG5} + B_{FIG5} \times SAT_{1-par}) \times (1 - \exp^{-SACSIZES / SAT_{1-par}})$ unsuccessfully tries to modify SAT_{1-par} from the original SAT value to compensate for the difference between V_{max} and V_{maxest} (Figure 7 of the previous paper). The actions on the main sequence profiles by the two parameters V_{max} and SAT are too different, and at the same time too interdependent, for SAT_{1-par} to achieve this task without introducing unacceptable profile distortions. On the contrary (panels C and D of Figure 6), for the 2-parameter area model $MSAREA = G \times SACSIZES^{PW}$ the effects on the area profiles of G and PW are strikingly similar. Mean values and ranges for panels C and D are from Table 1. This suggests that the 1-parameter model $MSAREA = (A_{FIG4} + B_{FIG4} \times PW_{1-par}) \times SACSIZES^{PW_{1-par}}$ might have a much larger usable range of PW_{1-par} to compensate for the difference between G and G_{est} before the area profile is deformed by unacceptable amounts. This is actually not the case, but for a different reason than the one encountered with V_{max} and SAT . A_{FIG4} and B_{FIG4} have opposite sign. The higher is PW_{1-par} , the smaller is the term $A_{FIG4} + B_{FIG4} \times PW_{1-par}$, with the term B_{FIG4} being negative. The higher is PW_{1-par} , the higher is the term $SACSIZES^{PW_{1-par}}$, being PW_{1-par} an exponential term > 1 . Thus, there will be a point where increasing PW_{1-par} will actually drive the area profile to lower values. To quantify this interaction, we computed the value of $MSAREA @ SACSIZES = 30^\circ$ as a function of PW_{1-par} . The results, illustrated in Panel E (rightward and leftward directions) and panel F (upward and downward directions) of Figure 6, clearly show this effect. Note as the differences in the A_{FIG4} and B_{FIG4} values between the horizontal and vertical saccadic directions have a large impact on where the saturation point is reached. Data sets requiring large upward modifications of PW_{1-par} to compensate

for large positive deviations of G with respect to G_{est} , e.g. points B and D in Figure 4, will likely show a poor fit for the $\text{PW}_{1\text{-par}}$ model.

Panels C and D of Figure 6 suggest a different approach altogether. G and PW have very similar effects on the area profiles: it might be possible to set PW to a fixed value and leave G to be a free parameter or, in alternative, to set G to a fixed value and leave PW to be a free parameter. By ignoring the correlation between G and PW , with opposite sign for A_{FIG4} and B_{FIG4} , and setting one of the two parameters to a constant value, the area profile can freely increase with increasing G or PW . The amount of distortion in the area model profiles when setting one the two parameters to a fixed value and how it compares with the 2-parameter G - PW model or the 1-parameter $\text{PW}_{1\text{-par}}$ model are the key questions. The most logical choice for the fixed values are the population averages for all directions combined of G and PW of the G - PW model (Table 1). Thus, we selected $\text{PW} = 1.55$ for the 1-parameter model in G , obtaining the 1-parameter model $\text{MSAREA} = G_{\text{PW}=1.55} \times \text{SACSIZE}^{1.55}$, abbreviated “ $G_{\text{PW}=1.55}$ model”. Similarly, we selected $G = 57.0^{(2-\text{PW})/s}$ for the 1-parameter model in PW , obtaining the 1-parameter model $\text{MSAREA} = 57.0 \times \text{SACSIZE}^{\text{PW}_{G=57.0}}$, abbreviated “ $\text{PW}_{G=57.0}$ model”. We expect these two new $G_{\text{PW}=1.55}$ and $\text{PW}_{G=57.0}$ models to perform as well as the 2-parameter G - PW model for the data sets identified by the points A and B in Figure 4, which are near the mean values of G and PW . For these two points, the 1-parameter $\text{PW}_{1\text{-par}}$ model, based on the linear regression, is expected, on the contrary, to perform poorly, with their strong deviation from the linear regression line. The question is how the $G_{\text{PW}=1.55}$ and $\text{PW}_{G=57.0}$ models perform for data sets far from the mean values of G and PW , like the data sets identified by the points C and D in Figure 4. Figure 7 and Table 3 report the performance of the 4 area models G - PW , $\text{PW}_{1\text{-par}}$, $G_{\text{PW}=1.55}$, and $\text{PW}_{G=57.0}$ for those 4 upward data sets. The fits in black are associated to the 2-parameter G - PW model with free parameters G and PW ; the fits in violet to the 1-parameter $\text{PW}_{1\text{-par}}$ model, based on the linear regressions and free parameter $\text{PW}_{1\text{-par}}$; the fits in red to the 1-parameter $G_{\text{PW}=1.55}$ model, with $\text{PW} = 1.55$ and free parameter $G_{\text{PW}=1.55}$; and the fits in green to the 1-parameter $\text{PW}_{G=57.0}$ model with $G = 57.0^{(2-\text{PW})/s}$ and free parameter $\text{PW}_{G=57.0}$. The arrows indicate the model(s) with the worst fit. As expected, the $\text{PW}_{1\text{-par}}$ model performed worst (underlined R^2 in Table 3) for point B, with $\text{PW}_{1\text{-par}}$ forced to enter in the saturation zone illustrated in panel F of Figure 6 for the upward direction. It also gave the worst fit for points D and A, which are also off the linear regression. Nonetheless, when compared with the dramatic failures in panels C and D of Figure 7 in the previous paper for the peak velocity main sequence model in $\text{SAT}_{1\text{-par}}$, these fits still gave R^2 values above 0.981. For the $G_{\text{PW}=1.55}$ and $\text{PW}_{G=57.0}$ models the test points are C and D. As expected, both performed worse than the $\text{PW}_{1\text{-par}}$ model for point C, but were still slightly better than the $\text{PW}_{1\text{-par}}$ model for point D. Truly remarkable, the “worst” R^2 of all $G_{\text{PW}=1.55}$ and $\text{PW}_{G=57.0}$ models in Figure 7, associated with point C, was still a 0.9938 (underlined R^2 in Table 3).

On average, the two area models in $G_{\text{PW}=1.55}$ and $\text{PW}_{G=57.0}$ performed better than the area model in $\text{PW}_{1\text{-par}}$ for the 4 test sets. When using the $\text{PW}_{1\text{-par}}$ model with patients with abnormal area profiles and the model parameters G and PW possibly further off the regression line, there might be a higher probability to end inside the saturation zones in Figure 6 panels E and F. Moreover, the regression parameters used for the model in $\text{PW}_{1\text{-par}}$

need to be direction-specific, due to the significant differences in these parameters between the horizontal and the vertical directions (Figure 4). The selected $PW = 1.55$ and $G = 57.0^\circ$ ($2-PW$)/s values are the PW and G population averages for all directions combined and the same model could potentially be used for all sets. Thus, due its limitations, the PW_{1-par} model was not further considered.

Additional preliminary evidence that the reduction of the 2-parameter G - PW model to 1-parameter models has minor effects on the quality of the fits due to the fact that G and PW have similar effects on the area profiles and therefore the free parameter can compensate for the other parameter forced to a constant, is shown in Figure 8. The set in Figure 8 is the same set of Figure 1. The left panel compares the G - PW (in black), the $G_{PW=1.55}$ (in red), and the $PW_{G=57.0}$ (in green) models, with strikingly similar R^2 values. An important question is if the value of PW is a critical factor in the $G_{PW=CONSTANT}$ models in terms of R^2 values or if there is some flexibility in the selection of this constant. From Table 1, the average of the $P = .025$ confidence limits of PW of the 2-parameter area model is 1.40, while the average of the $P = .975$ limits is 1.69. To test our $G_{PW=CONSTANT}$ models, we selected the values $PW=1.50$ and $PW=1.60$, which are still well inside the average C.I. limits but different enough to evaluate the stability of these models. Thus, we evaluated two additional 1-parameter area models, $MSAREA = G_{PW=1.50} \times SACSIZEL^{1.50}$, abbreviated “ $G_{PW=1.50}$ ”, and $MSAREA = G_{PW=1.60} \times SACSIZEL^{1.60}$, abbreviated “ $G_{PW=1.60}$ ”. The right panel in Figure 8 illustrates the $G_{PW=1.50}$, $G_{PW=1.55}$ and $G_{PW=1.60}$ models applied to the same data of Figure 1. The superimposition of these three models is remarkable, suggesting that the selection of the value of the constant PW offers significant flexibility.

Most important, by observing the ASE and 95% C.I. limits in Figure 8, there is a dramatic reduction in the asymptotic standard error (ASE) and in the size of the 95% Wald C.I. for all the 1-parameter models in Figure 8 when compared with the 2-parameter G - PW model. This observation applies even to the $G_{PW=1.55}$ and $PW_{G=57.0}$ examples in Figure 7 and Table 3, where these 1-parameter models are maximally challenged. Interestingly, the 95% C.I.s for the PW_{1-par} model (Table 3) are often wider than the 95% C.I.s for the PW parameter of the 2-parameter G - PW model. This is due to the two terms $A_{FIG4} + B_{FIG4} \times PW_{1-par}$ and $SACSIZEL^{PW_{1-par}}$ having opposing effects and therefore the determination of PW_{1-par} becoming unstable, particularly around the saturation zones illustrated in panels E and F of Figure 6.

Application of 1-parameter Area Models to the Subject Population

As first step, we fitted all 116×4 directions data sets with the 1-parameter area model $MSAREA = G_{PW=1.55} \times SACSIZEL^{1.55}$. Figure 9 and Table 4 illustrate the range of variability of the parameter $G_{PW=1.55}$ for the 4 saccadic directions. The solid lines are normal distributions, the parameters of which are reported in Table 4 with the same layout of Table 1. The mean values are very similar for the 4 directions. The downward mean (asterisk) is statistically different from the mean of the other 3 directions ($P < .01$) but the 95% C.I.s widely overlap. The R^2 values remain very high for all sets, consistent with the examples in Figs. 7 and 8. The best average R^2 is 0.9982 [range 0.9912 to 0.9998] for the 116 rightward data sets. The worst average R^2 is 0.9974 [range 0.9887 to 0.9997] for the 116

downward data sets. The drastic reduction in ASE and C.I. observed in Figs. 7 and 8 was confirmed at the population level. For the 116 rightward data sets, the ratio between the parameter estimate $G_{PW=1.55}$ and its ASE, ratio that is often used as measure of the robustness of a parameter estimate, is on average 175 [range 65 to 498]. For the downward sets, the ratio is on average 157 [range 61 to 526]. A value of 157 means that the ASE is, on average, 157 times smaller than the parameter value, which is truly remarkable for the low number of data points ($n = 12$ to 15) in each set. Similarly, the ratio between the parameter estimate and the size of its 95% Wald C.I. has, for the rightward sets, an average of 41 [range 16 to 179] and for the downward sets an average of 36 [range 15 to 77]. A value of 36 means that the size of the 95% C.I. is, on average, 36 times smaller than the value of the parameter. This makes the estimate of the parameter $G_{PW=1.55}$ extremely robust. To give a better sense of these values, the average ratio between the parameter estimate V_{max} and its ASE for the 2-parameter standard main sequence model is, for the same sets, 29 [range 10 to 71] and 21 [range 5 to 70], respectively. The average ratio between the parameter estimate V_{max} and the size of its 95% C.I. for the rightward saccades is 7 [range 2 to 16] and for the downward saccades is 5 [range 1 to 16]. The estimates of $G_{PW=1.55}$ are, on average, 6 times more robust for the rightward sets and 7 times more robust for the downward sets than the V_{max} estimates of the 2-parameter standard main sequence model. The same observations apply to the leftward and upward directions.

Comparison of the $G_{PW=1.55}$ Area Model with other 1-parameter Area Models

In order to test the robustness of the $G_{PW=1.55}$ area model, we will compare this model with the other 1-parameter area models introduced in Figure 8 applied now over the entire subject population.

The upper panels of Figure 10 report the $PW_{G=57.0}$ values of the $PW_{G=57.0}$ model plotted against the $G_{PW=1.55}$ values of the $G_{PW=1.55}$ model for the rightward and downward saccadic directions. Linear fits are in black and quadratic fits are in red. The relationship, extremely robust, is slightly nonlinear, with the quadratic term small but strongly significant. The non-linear deviation mostly affects the pairs outside the 95% C.I.s of $G_{PW=1.55}$, indicated by the dashed vertical lines. With respect to R^2 values, the two models are equivalent, albeit with a slightly better R^2 of the $PW_{G=57.0}$ model for the data sets with the smallest $PW_{G=57.0}$ values. The improvement in the R^2 values, as population average, is negligible. The largest difference is for the upward direction, with the average $R^2 = 0.9980$ for the $PW_{G=57.0}$ model vs. $R^2 = 0.9977$ for the $G_{PW=1.55}$ model. More interesting, all distributions of the $PW_{G=57.0}$ estimates present a slight leftward skew, which causes the leftward and upward directions to fail the χ^2 test of normality ($P < .004$). This leftward skew corresponds to the non-linear deviation between $PW_{G=57.0}$ and $G_{PW=1.55}$ for their lowest values, indicated with an arrow in the upper right panel “Down” of Figure 10. The highest values present a similar non-linearity but in our population the number of data points in the upper non-linear range is lower and does not significantly impact the shape of the distribution of the $PW_{G=57.0}$ values. The normal distribution of the parameter $G_{PW=1.55}$ in our population makes the $G_{PW=1.55}$ model more manageable from a clinical standpoint than the $PW_{G=57.0}$ model, $G_{PW=1.55}$ being also a simple linear scaling factor.

With the focus now restricted to the $G_{PW=CONSTANT}$ models, the question is how sensitive these models are to the selection of the value of PW. The average R^2 obtained using $PW=1.50$ is practically identical to the average R^2 using $PW=1.55$, and slightly worse using $PW=1.60$. For example, for the rightward sets the average R^2 values are 0.9982 for $PW=1.50$, 0.9982 for $PW=1.55$ and 0.9973 for $PW=1.60$. Thus, from the point of view of average fit quality, the selection of any PW value inside the 1.50 to 1.60 interval would have been appropriate. Does the power factor PW act, inside its restricted C.I.s, as a close-to-linear gain factor? If this hypothesis is correct, we expect that the effect of varying PW on the values of G is equivalent to a linear scaling. Figure 10 lower panels show that this is the case. For the rightward direction (left panel) and for the downward direction (right panel), the G values for $PW=1.50$ (black dots and black linear regression) and the G values for $PW=1.60$ (red dots and red linear regression) are plotted with respect to the G values for $PW=1.55$. For all 4 saccadic directions, the relationships between $G_{PW=1.50}$ and $G_{PW=1.55}$ and between $G_{PW=1.60}$ and $G_{PW=1.55}$ are extremely linear and the intercepts are never greater than $0.87^{(2-PW)}/s$, indicating an almost pure linear scaling of $G_{PW=1.55}$. The model $MSAREA = G_{PW=1.55} \times SACSIZEL^{1.55}$ not only quantifies the area under the main sequence with great accuracy and stability, but the selection of the value of PW is not restricted to an excessively narrow range around 1.55, which is the population mean of the PW value of the 2-parameter G-PW model. For our population, any PW value between 1.50 and 1.60 would have given a robust 1-parameter area model applicable to all the data sets with comparable average R^2 values. The similarity in R^2 for the three models tested suggests that this range is actually larger. It remains to be seen if different saccadic protocols, different reference populations, or patients with brain damage/disease affecting the saccadic system require further tuning of the value of PW. It is important to note that the selected PW value has, as evident in the lower panels of Figure 10, a determinant effect on the range of G values. An initial analysis using the 2-parameter G-PW area model is a key tool in determining which is the best value of PW to be used inside a specific study. The identical PW value must be used for all data sets and subject populations of the study.

Application of the Area Models to a Clinical Case

The 3-step process in V_{max} and SAT used to determine if a data set is inside or outside a reference population, proposed in the previous paper, can be applied, with identical steps, to the 2-parameter G-PW area model, of which the parameters G and PW are also linearly correlated. Although the availability of 1-parameter models greatly simplifies the comparison between a reference population and a data set and between sets, as described below, the 3-step process may still be clinically relevant. Wide fluctuations in saccadic dynamics inside a subject population or between populations may cause excessive variability in PW values with the $G_{PW=CONSTANT}$ models performing poorly for sets at the edges of the PW range or a common PW value cannot be found for all the subject populations of a study. For each saccadic direction, the reference population is defined by 8 parameters: the upper and lower limits of the 95% C.I.s of G and PW (Table 1), the intercept and slope of the linear regression between G and PW (Figure 4), and the upper and lower limits of the 95% C.I. of $G-G_{est}$ (Table 2). The first step is to see if the G and PW values of the data set under evaluation are inside the G and PW 95% C.I.s of the reference population in Table 1. If the answer is no, the set is flagged as “outside” the reference population and the process

concludes. If both the G and PW values are inside the reference ranges, the second step is to determine the G_{est} value from the PW of the data set, using the direction-specific regression parameters reported in Figure 4. The third step is to determine the $G-G_{\text{est}}$ value and if this value is inside or outside the 95% C.I. of the reference population, given in Table 2. Figure 11 describes this 3-step process in G and PW on the same rightward data set that was used to illustrate the 3-step process in V_{max} and SAT (Figure 10 of the previous paper). Is our patient's rightward set inside or outside the reference population? The 2-parameter area model of this patient, illustrated in the upper panel of Figure 11 as the black curve, has a remarkable $R^2 = 0.9986$, with $G = 60.3^{\circ(2-\text{PW})}/\text{s}$ and $\text{PW} = 1.47$ (red dot in Figure 11 middle panel). Both G and PW values are inside their respective 95% C.I.s in Table 1 for rightward saccades, i.e., they are inside the grey area in the middle panel of Figure 11. The dashed lines are parallel to the regression line and shifted by the upward and downward values of the 95% C.I. of the $G-G_{\text{est}}$ distribution. This panel clearly illustrates how the actual 95% range of variability of G and PW in our population, i.e., the area simultaneously contained inside the grey area and the dashed lines, is only a fraction of the grey area. The G_{est} value is $70.0^{\circ(2-\text{PW})}/\text{s}$ (green dot in Figure 11 middle panel), estimated using the regression parameters in Figure 4 for the rightward saccadic direction and $\text{PW} = 1.47$, and therefore $G-G_{\text{est}} = -9.7^{\circ(2-\text{PW})}/\text{s}$. For rightward saccades, the $P = .025$ value for $G-G_{\text{est}}$ in Table 2 is $-8.8^{\circ(2-\text{PW})}/\text{s}$. Following our 3-step criteria, the area under the main sequence for the rightward saccades of this patient is slightly outside the 95% adjusted range of the reference population.

Using a 1-parameter model, the process is much more direct, as illustrated in the lower panel of Figure 11. The $G_{\text{PW}=1.55}$ model of the patient (red curve in the upper panel) has a $R^2 = 0.9975$, with $G_{\text{PW}=1.55} = 47.7^{\circ(2-1.55)}/\text{s}$. The ASE and 95% Wald C.I. of $G_{\text{PW}=1.55}$ are again much smaller than the ones of G of the 2-parameter G-PW area model. The determination if the area of the main sequence of the model is inside or outside our reference population is a simple step: is the 95% Wald C.I. of the parameter $G_{\text{PW}=1.55}$ of the patient inside or outside the 95% C.I. of the parameter $G_{\text{PW}=1.55}$ of the reference population, with ending points 46.7 and $64.7^{\circ(2-1.55)}/\text{s}$? Our set is slightly inside the 95% C.I. of the population. The same conclusion is achieved using the $\text{PW}_{G=57.0}$ model. The Wald 95% C.I. endpoints of the parameter $\text{PW}_{G=57.0}$ for this data set are 1.488 and 1.496. The endpoints for the population are 1.488 and 1.594. The comparison between data sets is also a simple step: are the 95% Wald C.I.s of $G_{\text{PW}=1.55}$ (or $\text{PW}_{G=57.0}$) of the two sets overlapping or not overlapping?

Parametric Values and Area Profiles

One of the main issues regarding the clinical applicability of the 2-parameter peak velocity main sequence model is that, due to the correlation between V_{max} and SAT, the variability of V_{max} and SAT greatly overestimate the actual variability in the saccadic profiles. (Figure 12 and Table 3 previous paper), particularly for small saccades. The 3-step process, by including the linear regression, better defines the actual 95% C.I.s of the population by treating V_{max} and SAT as a pair. Does this overestimate apply also to the 2-parameter area model in G and PW? As in the previous paper, in order to understand the consequences of the correlation between G and PW from a biological point of view, we analyzed the changes in the area profiles while moving inside the adjusted 95% C.I.s of the two parameters G and

PW (area simultaneously inside the grey area and the dashed lines in Figure 11). As area profiles to compare, for each direction we selected three (G; PW) pairs, based on the 95% C.I.s in Table 1: the ($P = .025$; $P = .975$) pair, the mean pair, and the ($P = .975$; $P = .025$) pair. For the rightward set, these are the three light-blue dots in the middle panel of Figure 11. Note that the ($P = .025$; $P = .975$) and the ($P = .975$; $P = .025$) pairs, which define the upper left and lower right corners of the grey area, as well as the mean pair, are very close to the regression line. This observation applies to all directions. Thus, these pairs also well represent the changes in the area under the main sequence profile while moving along the regression line. The upper panels in Figure 12 show their area profiles for the rightward and downward saccadic directions. The results are quite striking. The ($P = .975$; $P = .025$) pair, which has the highest value of G inside its 95% C.I., has actually the lowest area profile, squashed by the lowest value of PW inside its 95% C.I. The mean pair and the ($P = .025$; $P = .975$) pair are practically superimposed for the rightward direction. For data sets outside the linear regressions, the profiles will differ from the ones described here (e.g. points A and B in Figure 4) and with the squashing effect of the correlation affecting small and large saccades with different modalities. Similar results were obtained for the other two directions. This is somewhat not a surprise when considering the profiles in panels C and D of Figure 6, showing that the two parameters have very similar effects on the area profiles. The much larger 95% C.I.s of G and PW of the 2-parameter G-PW area model, when compared with $G_{PW=1.55}$ and $PW_{G=57.0}$, are the result of crosstalk between G and PW, with large fluctuations, in opposite directions, of the values of G and PW even for minimal actual changes in the area under the main sequence. This conclusion is also supported by the fact that the very different intercepts and slopes of the G vs. PW linear regressions between the horizontal and vertical saccadic directions (Figure 4) do not translate into distinct horizontal and vertical distributions of $G_{PW=1.55}$ (Table 4). Even more than for the 2-parameter peak velocity main sequence model in V_{max} and SAT, the values of G and PW, per se, have little meaning if not considered together as a pair.

The two upper panels of Figure 12 open the possibility that the much better ratio between asymptotic standard error and parameter estimate for $G_{PW=1.55}$ when compared with the same ratio for V_{max} is the consequence of a much smaller range of variability of the area profiles with respect to the peak velocity main sequences profiles in our population. A clinical test with all the subjects, including patients, giving the same result would be of no use. Strong evidence that this is not the case is seen in the lower panel of Figure 11 when we compare the 95% C.I. of the population with the 95% C.I. of the data set from the patient. The range of variability of $G_{PW=1.55}$ of our subject population is much larger than the C.I. of the $G_{PW=1.55}$ of the patient. More quantitatively, we compared the relative ranges of variability for the population, i.e., the ratio between the 95% C.I. and the parameter main value, of V_{max} from Table 1 of the preceding paper and of $G_{PW=1.55}$ from Table 4. For the rightward direction, these ratios are $\pm 30\%$ for V_{max} and $\pm 16\%$ for $G_{PW=1.55}$. The relative range of variability of $G_{PW=1.55}$, is approximately half of the relative range of variability of V_{max} , but we know that the latter is an overestimate of the actual dynamical variation. Furthermore, the improvement in the ratio between asymptotic standard error and parameter value of $G_{PW=1.55}$ and V_{max} is, for the rightward direction, 7 times, which fully compensates

the halving of the relative range of variability of $G_{PW=1.55}$ with respect to V_{max} . For the downward data, the values are $\pm 40\%$, $\pm 26\%$ and 6.

The changes in area profiles associated with the $G_{PW=1.55}$ model for the rightward and downward saccadic directions, with the $G_{PW=1.55}$ values the $P = .025$, mean, and $P = .975$ values from Table 4, are illustrated in the lower panels of Figure 12. Note as, for this model, the relative area changes are the same for all SACSIZ values, with $G_{PW=1.55}$ acting as a simple linear gain element. The difference regarding the variability in area profiles between the upper and lower panels of Figure 12 is due to the fact that the variability illustrated in the lower panels covers the entire population range of $G_{PW=1.55}$, while the variability in the upper panels is limited to sets along the G-PW regression line. The very high R^2 values obtained with the $G_{PW=1.55}$ model, combined with the very narrow C.I.s of $G_{PW=1.55}$ at the set level, indicate that this model is a reliable measure of the range of area profiles of a population as well as a powerful method to establish if a subject is inside or outside this population. The question if two data sets are statistically different or not can be answered by a simple comparison of the C.I.s of their $G_{PW=1.55}$ values.

Repeatability between Sessions

We used the data from the 35 repeated sessions to determine the variability between sessions of the area measures. The results are illustrated in Figure 13. Black dots and black regressions are from the first sessions. Red dots and red regressions are from the second sessions. The session variability of the correlation between G and PW in the G-PW area model is comparable to the session variability of the correlation between V_{max} and SAT. The 35 data sets from the first session were used to define the reference area (polygon in black), following the protocol illustrated in Figure 11. Note as some of the first session sets are outside the reference area. The confines of the reference area are defined by 95% confidence intervals, not absolute ranges. Three sets from the second session are outside the reference area for the rightward saccades, 4 for the leftward saccades, and 2 for the upward saccades. All sets from the second session are inside the reference area defined by the first session for the downward saccades. Due to the opposite sign of the offset and slope of these regressions and the complex profile variability when moving along the regression line (upper panel of Figure 12), it is not possible to interpret the difference in slopes as a possible sign of fatigue of the subjects during the second session.

Figure 14 reports the comparison of the $G_{PW=1.55}$ values of the 1-parameter $G_{PW=1.55}$ model from the two sessions for the 4 saccadic directions. Each subject has its own saccadic dynamics, which is remarkably reproducible between sessions, as indicated by the high R^2 values of the linear regressions. This also implies that the large range of variability of $G_{PW=1.55}$ is an actual variability in saccadic dynamics among the subjects and not random scatter. A random scatter would have destroyed the intra-subject reproducibility. The reduction in dynamics in the second session with respect to the first session is also evident, with the effect stronger for the subjects with higher $G_{PW=1.55}$.

The superiority of the $G_{PW=1.55}$ model with respect to the traditional main sequence model in terms of repeatability between sessions is also evident in Figure 15 and Table 5, where the distribution of the relative change in V_{max} of the second session with respect to the first

session, i.e., $(V_{\max 2} - V_{\max 1})/V_{\max 1}$ is compared with the distribution of the relative change in $G_{PW=1.55}$, i.e., $(G_2 - G_1)/G_1$ for each saccadic direction. The histograms and the normal density functions in black illustrate the relative change in $G_{PW=1.55}$, while the red normal density functions illustrate the relative change in $V_{\max}$. The vertical dotted bars identifying the ceiling-adjusted and distribution-adjusted ranges selected for the histograms of $(V_{\max 2} - V_{\max 1})/V_{\max 1}$ are often outside the range of the horizontal axis and are reported near the lower corners of the panels with their actual position on the x-axis indicated below them. Table 5 reports the parameters of these normal distributions. With the exclusion of the leftward distribution of the relative change of $V_{\max}$ ($P < .0005$ of the Shapiro-Wilk test of normality), all distributions have $P > .01$, suggesting that a normal distribution is a reasonable model for these data sets. The reduction in the value of σ and of the 95% C.I. for the relative changes in $G_{PW=1.55}$ between sessions with respect to the relative change of $V_{\max}$ is remarkable. All 4 mean relative changes in $G_{PW=1.55}$ are negative, suggesting an overall reduction in saccadic dynamics during the second session, but only the means for the rightward and leftward directions are significantly different from 0 ($P < .01$ 1-sample t-test).

DISCUSSION

In the previous paper, we have described how the two parameters $V_{\max}$ and SAT of the standard 2-parameter peak-velocity main sequence model $SACPEAK = V_{\max} \times (1 - e^{-SACSIZE/SAT})$ cannot be used as standalone measures of saccadic dynamics. The correlation between the two parameters overestimates the actual variability in the main sequence profiles, particularly for small saccades. We proposed a 3-step process to determine if a data set is inside or outside a reference population that, by taking into account this correlation, much better defines the actual dynamical variability of a population and utilizes the two parameters $V_{\max}$ and SAT as a pair. A second negative consequence of the correlation is that the 95% Wald C.I.s of $V_{\max}$ and SAT of a data set are very large. Thus, when comparing two sets, for example a pre- and a post-concussion set from the same athlete, it is likely that the 95% Wald C.I.s of the two sets present large overlapping sections even if the dynamical changes are clinically significant. Attempts to obtain 1-parameter models of the peak-velocity main sequence were not successful.

Changes in the peak-velocity main sequence profile are obviously matched by changes in the area covered by it. Integrated area measures are much less sensitive to local variations and can be easily obtained by trapezoidal integration. We are aware of only one attempt, very preliminary, to use area measures to estimate changes in saccadic dynamics.² The first goal of our study was to search for a 2-parameter area model that could fit all our data sets and then use it as reference in the search for 1-parameter area models. The model $MSAREA = G \times SACSIZE^{PW}$ met our requirement with extreme precision, but, as for $V_{\max}$ and SAT, the parameters G and PW are strongly correlated. For the way G and PW affect the area profiles, we found that it is possible to reduce this 2-parameter model to 1-parameter models while maintaining very high R^2 values. As described in the results, the 1-parameter model $MSAREA = G_{PW=1.55} \times SACSIZE^{1.55}$ has many positive features, making not only the determination if a data set is inside or outside a reference population a 1-step process, but also direct comparisons between sets possible. The value 1.55 is the overall population average of the PW values of the 2-parameter G - PW model.

Population Variability and Session Reproducibility

Figure 14 shows that each subject has their own saccadic dynamics, which is fairly reproducible between sessions, but the variability among subjects is very large. This dichotomy was already observed in earlier works.^{3–6} A powerful neural mechanism, the local feedback, allows reaching of the saccadic goal with a wide range of initial dynamics of the motor command, by keeping track, in real-time, of the progress towards the saccadic goal.⁷ Rapid corrective saccades can bring the eyes close to the desired target even if the main (primary) saccade is strongly hypermetric or hypometric. The possibility of corrective saccades being driven by a forward predictor of motor outcome – in other words, that they may have been included in the initial programming of the movement and not determined by the post-saccadic visual estimate of the landing error – is discussed in J Tian, HS Ying, DS Zee.⁸ Corrective saccades, both as metrics and frequency, also may be affected by brain damage and disease. From a clinical standpoint, the presence of a neural local feedback and of corrective saccades, which subjects are mostly unaware of, means that severely altered saccadic eye movements may still achieve their goal of transferring the two foveae on the new target, and therefore those gain and/or dynamical alterations remain undetected by the subject. The experimental protocol significantly alters saccadic dynamics even in normal subjects. Memory saccades and antisaccades have longer latencies and are significantly slower than visually-driven prosaccades.⁹ Saccades associated with blinks or even partial blinks present major alterations in their dynamics, but are often accurate.¹⁰ Unless the dynamical variations are severe and directly interfere with vision, subjects are not aware of this variability. An interesting consequence of this is that there is no strong functional pressure to engage in dynamic recalibration, as long as the saccadic goal is reached, by adding corrective saccades if necessary. Thus, it is not too surprising that even normal populations present a large scatter in saccadic dynamics, making it difficult to discern the difference between “normal” and “abnormal” dynamics when the analysis is made by comparing a patient against a reference population, even when using our 3-step processes or one of our 1-parameter models. The patient we used as an illustrative example shows borderline dynamics as $G_{PW=1.55}$ value, but still inside the range of the reference population (Figure 11 lower panel). Without knowing his baseline values, it is impossible to determine if the observed borderline dynamics was always present and therefore the saccadic test is “normal” for this subject or if he had a much faster dynamics prior to injury, considering the wide natural variability of saccadic dynamics even in our matching reference population. For example, if the (unknown) baseline value of $G_{PW=1.55}$ for this subject was, hypothetically, 63.0, still inside the reference C.I. for rightward saccades (Figure 11 lower panel), a change to the observed 47.7 value would have meant a 24.3% decrease in $G_{PW=1.55}$. When comparing this value with the sub-population ($n=35$) relative variability between repeated sessions (Table 5), giving a 10.7% decrease in $G_{PW=1.55}$ from the first session as the lower limit of the 95% C.I., the 24.3% change would have been flagged as highly abnormal. Actually, if we consider the overall shift of the mean probably due to tiredness and use instead, conservatively, half of the C.I. range of the sub-population for rightward saccades, i.e., 6.5%, a 24.3% change would have been even more significant. The availability of baseline values can have a major impact in the determination if the dynamics of the subject presents an abnormal alteration, due to the much narrower natural intra-subject variability between sessions. The acquisition of baseline data is often impractical, but direct

comparisons between sets, for example acquired during an ongoing rehabilitation therapy or to study the effects of a pharmacological intervention^{11,12} are now directly implementable with our 1-parameter area models. Even when limited to comparisons against a reference population, the 3-step processes and the 1-parameter area models are able to minimize the devastating effects of the non-linear crosstalk and of the linear correlation between $V_{\max}$ and SAT that practically undermine the use of the traditional main sequence model in saccadic studies.

Clinical Applications

Saccadic eye movements are very rapid transfers of gaze between objects of interest¹³ and involve a large number of cortical, subcortical and cerebellar brain areas.^{13, 14} Interest in saccadic dynamics in association with concussion has a strong neurological and historical background. More than 50% of the primate brain is directly or indirectly involved in visual processing.¹⁵ Not surprisingly, 76% of patients affected by traumatic brain injury (TBI) observed at a Veterans Affairs polytrauma network site reported visual dysfunctions.¹⁶ Due to the tight functional linkage between vision and eye movements, KJ Ciuffreda, N Kapoor, D Rutner, et al.¹⁷ found, in 160 individuals with visual dysfunctions due to TBI, that 90% of these patients also presented with oculomotor dysfunctions, including saccadic abnormalities. Thus, there is strong interest in these eye movements as potential TBI and mild-TBI (mTBI) biomarkers, supported by a long clinical history of correlating saccades with several neurological^{18–21} and psychiatric disorders.²² Several studies reported abnormalities in visually-driven prosaccadic eye movements in association with TBI and even mTBI.^{23–29} Volitional saccadic protocols, known to have higher cortical and cognitive involvement,^{30, 31} and different dynamics,⁹ like memory-guided saccades and sequences of saccades,^{27,28,32} predictive saccades,²⁹ self-paced saccades^{25,27,28} and antisaccades^{25,27,28,33} seem to be more affected by TBI/mTBI than visually-driven prosaccades towards stationary targets. A review by Ventura, Balcer, Galetta and Rucker³⁴ clearly indicates that the use of saccades as TBI/mTBI biomarkers is still a work in progress, with variable and sometime conflicting results, but again suggesting that volitional saccades might have higher specificity and sensitivity than reflexive prosaccades. A recent study,³⁵ using identical stimuli protocols and hardware, found that the acute cumulative effects (4 to 166 hours from the concussive accident) of clinically confirmed mTBI brain insults on predictive saccades, antisaccades and a vestibular high-dynamics transient rotation test (crHIT) reached 89% sensitivity and 95% specificity in supporting the mTBI diagnosis. The same authors, in a follow-up preliminary study using the area under the main sequence, demonstrated also dynamical alteration in prosaccades.² Although the focus regarding volitional saccades is usually on latencies and number of errors, a direct comparison of the patient's saccadic dynamics between reflexive and volitional protocols⁹ is of particular clinical interest if the dynamics of the volitional saccades in the reference population is found to be a % of the dynamics of the reflexive saccades of each subject. In this case, the use of the dynamics of the subject's reflexive saccades as reference may enhance the ability of detecting abnormal dynamics of volitional saccades, with the focus shifted from absolute values, with their natural wide range of variability, to relative changes in dynamics with respect to the subject's reflexive values.

The need for a methodology able to directly compare saccadic data sets goes well beyond concussion. Of particular interest is the monitoring of the progression of a neurological disease in time. Our focus will be on the potential issues that could be encountered while using the area models in the evaluation of parkinsonian syndromes and similar progressive neurodegenerative diseases. These patients present worsening saccadic dynamics, gain and latency in time, as well as error-rate increases for volitional saccades, which well correlate with the associated physical, behavioral and cognitive deterioration, and therefore are considered a valuable objective measure of the overall progression of the disease. In some cases, saccadic alterations are detectable well in advance of other symptoms in carriers of the disease gene.³⁶ Cerebral palsy, a non-progressive brain disorder, presents similar saccadic alterations and will be include in this brief review.

The most obvious limitation in the usage of the area under the main sequence is the ability to obtain a reliable main sequence from the subject. Several factors may interfere with this goal. The first is the velocity profile of the saccades. When the velocity profile of a saccade resembles the typical Gaussian-like profile, albeit this profile can be highly skewed and there may be severe dynamical undershooting or overshooting around the end of the saccade, the peak velocity remains well defined. As pointed out in the Methods section of the preceding paper, the use of a cubic spline and of a 2-point backward differentiation on the position traces to obtain the velocity profiles, together with the optimization process used in determining the spline weight, is a very conservative process aimed at preserving the integrity of even very abnormal saccadic profiles. With profiles with multiple peaks or where the peak velocity is not well defineable, a potential solution may be the use of the average velocity, defined as the ratio between size of the saccade and its duration, which also presents a well-defined main sequence.³⁷ The algorithm that we used in the determination of saccadic onset and offset is able to determine the offset of the saccade even in the presence of strong post-saccadic drifts. The second aspect is the range of saccadic sizes that can be obtained from the subject, with the need of comparing data sets that have similar ranges and distributions of SACSIZ values along the main sequence. The ability, in progressive supranuclear palsy, of generating vertical saccades gradually degrades up to complete vertical palsy in most subjects, while the ability to generate horizontal saccades, albeit with degraded gain and dynamics, is usually preserved.³⁸ Deep alterations in saccadic range as the disease progresses, like in Niemann-Pick Type C disease,³⁹ clearly interferes with the ability to compare data sets in time. It might be possible to estimate the future reduction in saccadic gain and acquire additional data in these reduced ranges for future use. Alterations in the saccadic trajectory, due to the differential rate of degeneration between the horizontal and vertical systems, can also complicate the saccadic analysis. An abnormal curvature in the trajectory of vertical saccades, developing much earlier than the vertical palsy and called the “round the houses” sign, is often found in subjects with progressive nuclear palsy⁴⁰ and Niemann-Pick disease type C.⁴¹ Oblique saccades are neurally generated as oblique commands and only later are parsed into horizontal and vertical motor components. Behavioral evidence for this is the so-called “component stretching” phenomenon, where, during oblique saccades, the smallest of the two vector components appears slowed and stretched in time to match the duration of the largest vector component with, as a result, a straight trajectory towards the oblique target.⁴² Thus, the horizontal and

vertical components of oblique saccades do not follow the main sequence of the pure horizontal and vertical saccades for similar SACSIZ values and dynamical comparisons between sets with significant differences in saccadic trajectories may be of limited value.

In patients with oculomotor abnormalities, proper calibration of the eye tracking system can also be an issue. Both static (strabismus) and dynamical disconjugacy may be present,⁴³ requiring monocular calibrations of the eye tracker, in order to force the viewing eye to follow the targets during the calibration. Sometimes, monocular saccadic tasks may be needed, for example in cases of patients with strabismus, amblyopia or when alternate fixators. It is important to consider, particularly in children with severe cerebral palsy, the possibility of the subject presenting uncompensated refractive errors or visual loss, peripheral or cortical in origin.⁴³ An optometric evaluation may be necessary in these patients prior to oculomotor testing. Finally, it is not uncommon, for example in spinocerebellar ataxia SCA 6,⁴⁴ to observe nystagmus, with no periods of static fixation of the calibrating targets. In these cases, the endpoints of the resetting saccades of the nystagmus might be used as an approximate estimate of when the subject's fovea is on the target. When a reliable calibration is not achievable, video eye trackers and search coil systems can be calibrated offline using an eye model with adjustable orientation placed in the same location of the subject's eyes.

SUMMARY

The guiding hypothesis of this study was that models based on the area under the peak velocity main sequence might be a valid alternative to the traditional 2-parameter peak velocity main sequence model $SACPEAK = V_{max} \times (1 - e^{-SACSIZ/SAT})$ in quantifying saccadic dynamics. The 2-parameter area model $MSAREA = G \times SACSIZ^{PW}$ presented the same limitations of the 2-parameter traditional peak velocity main sequence model described in the previous paper, but it helped identify extremely promising 1-parameter area models. The 1-parameter area model $MSAREA = G_{PW=1.55} \times SACSIZ^{1.55}$, with 1.55 the population average of the PW value of the 2-parameter G-PW model, is equally applicable to all 4 saccadic directions. It also eliminates the crosstalk problem of using 2-parameter models with non-orthogonal parameters and gives remarkably high R^2 and robust estimates of the parameter $G_{PW=1.55}$ for all 116×4 data sets. In terms of R^2 and normality of the distribution of the parameter value, it performs as well or better than the other four 1-parameter models that we tested. Based on the R^2 values and the very narrow 95% Wald C.I.s at the single set level, the range of variability of the parameter $G_{PW=1.55}$, a simple gain factor, is a veridical estimate of the range of dynamical variability of our population. One-parameter models greatly simplify the determination if a set is inside a reference population and the comparisons between data sets.

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Figure 1.

Example of standard main sequence model in $V_{\max}$ and SAT and corresponding 2-parameter area model in G and PW. Left panel: main sequence measures and standard 2-parameter main sequence model of a data set with one of the poorest R^2 (#4160 downward). The R^2 is only 0.592. Right panel: area measures (black dots) and area model (black curve). The 2-parameter area model in G and PW has a R^2 of 0.9966. The estimate, asymptotic standard error (ASE) and range of the 95% Wald C.I. of each of the two parameter pairs ($V_{\max}$; SAT) and (G; PW) are reported below the x-axis of the graphs. The right panel also illustrates, in red, the integration process (see text).

Distribution of G Values of the 2-parameter Area Model $MSAREA = G \times SACSIZEPW$

Figure 2.

Histograms for the 4 saccadic directions of the distribution of the values of the parameter G of the 2-parameter area model $MSAREA = G \times SACSIZEPW$. The solid curves are normal distribution models, the parameters of which are reported in Table 1. The two dotted vertical bars identify the ceiling-adjusted and distribution-adjusted range selected for each histogram. This range was then parsed into 12 equal-size bars. To ease the comparison between directions, each x-axis was then resized to be identical for all saccadic directions while maintaining the original bin size. This applies to all the histograms illustrated in the report.

Figure 3. Histograms for the 4 saccadic directions of the distribution of the values of the parameter PW of the 2-parameter area model $MSAREA = G \times SACSIZ^{PW}$. The solid curves are normal distribution models, the parameters of which are reported in Table 1. Identical layout of Figure 2.

Correlation between G and PW of the 2-parameter Area Model $MSAREA = G \times SACSIZEPW$

Figure 4.

Correlation between G and PW for the 4 saccadic directions of the 2-parameter area model $MSAREA = G \times SACSIZEPW$. The lines are linear regressions and the R^2 values are indicated near the regressions lines. The values of the intercept A and slope B of the linear regressions, together with their asymptotic standard error (ASE) and Wald 95% C.I. limits are reported near the x-axis. For the rightward and leftward sets, a quadratic term was slightly significantly different from zero, but the improvement in R^2 was very small. Thus, we used a linear regression for all 4 directions. The four open dots (A-D) in the Up graphs indicate the data sets utilized in Figure 7 to evaluate the performance of 1-parameter models.

Figure 5.

Histograms of the distributions of the $G - G_{est}$ values for the 116×4 saccadic directions. G is the actual value of the set from the G-PW model. G_{est} is estimated from the PW value of the set using the regression reported in Figure 4 for its saccadic direction. The solid curves are normal distribution models, the parameters of which are reported in Table 2. Same layout of Figure 2.

Figure 6.

Effects of changing parameters in the 2-parameter peak velocity main sequence and area models and failure of the 1-parameter area model PW_{1-par} based on the linear regression between G and PW . Panel A: Main sequence profiles obtained by keeping $SAT = 9.9^{\circ}$ constant and varying V_{max} . Panel B: Main sequence profiles obtained by keeping $V_{max} = 517^{\circ}/s$ and varying SAT . Panel C: Area profiles obtained by keeping $PW = 1.55$ constant and varying G . Panel D: Area profiles obtained by keeping $G = 57.0^{\circ(2-PW)}/s$ and varying PW . Panel E: Value of the model $(A_{FIG4} + B_{FIG4} \times PW_{1-par}) \times SACSIZEx^{PW_{1-par}}$ @ $SACSIZEx = 30^{\circ}$ as a function of PW_{1-par} for the rightward and leftward saccadic directions. Panel F: for the upward and downward directions.

Figure 7.

Testing of the 2-parameter area model in G and PW and of the three 1-parameter area models in PW_{1-par} , $G_{PW=1.55}$ and $PW_{G=57.0}$ for the 4 upward data sets indicated as open dots in Figure 4. Black: 2-parameter G-PW area model (free parameters: G and PW); Violet: 1-parameter PW_{1-par} area model based on the regression (free parameter: PW_{1-par}); Red: 1-parameter $G_{PW=1.55}$ area model with $PW = 1.55$ (free parameter: $G_{PW=1.55}$); Green: 1-parameter $PW_{G=57.0}$ area model with $G = 57.0^{\circ(2-PW)}/s$ (free parameter: $PW_{G=57.0}$). The values of G and PW of the 2-parameter area model are reported on the top left in each panel. The arrows indicate the model(s) with the worst fit.

Figure 8.

Comparison of area models. The set is the same of Figure 1. The color-coded models are identified on the lower right of the two panels, with the associated R^2 at the end of the model fit. The parameter estimates, with associated asymptotic standard error (ASE) and range of the 95% Wald C.I. are reported below the x-axis of each panel.

Distribution of the $G_{PW=1.55}$ Values of the 1-parameter Area Model $MSAREA = G_{PW=1.55} \times SACSIZEL^{1.55}$

Figure 9.

Histograms of the distributions of the $G_{PW=1.55}$ estimates of the 1-parameter area model $MSAREA = G_{PW=1.55} \times SACSIZEL^{1.55}$ for the 4 saccadic directions ($n=116$). The solid curves are normal distributions, the parameters of which are reported in Table 4. Same layout of Figure 2.

Figure 10.

Comparisons between the $G_{PW=1.55}$ area model and other 1-parameter area models for the rightward (left panels) and the downward (right panels) directions. Upper panels: comparison between the parameter $PW_{G=57.0}$ and the parameter $G_{PW=1.55}$. Black lines are linear fits and red lines are quadratic fits. The non-linear deviation for the lowest values (arrow) invalidated the normality of the distribution of the $PW_{G=57.0}$ values for the leftward and upward directions. The dashed vertical lines identify the 95% C.I.s of $G_{PW=1.55}$ from Table 4. Lower panels: linear scaling of the parameter G when PW is changed from 1.55 to 1.50 (black dots and black linear regression line) and from 1.55 to 1.60 (red dots and red regression line) for the same directions. Not shown, for the leftward direction $G_{PW=1.50} = -0.45 + 1.18 \times G_{PW=1.55}$ ($R^2=0.9969$) and $G_{PW=1.60} = 0.29 + 0.85 \times G_{PW=1.55}$ ($R^2=0.9966$). For the upward direction $G_{PW=1.50} = 0.15 + 1.16 \times G_{PW=1.55}$ ($R^2=0.9982$) and $G_{PW=1.60} = -0.18 + 0.86 \times G_{PW=1.55}$ ($R^2=0.9983$).

Figure 11.

Graphical illustration of the 2-parameter and 1-parameter processes used to determine if the area under the main sequence of the rightward set of a sample patient (#21073) is inside the area range of the reference population. Upper panel: MSAREA measures as a function of SACSIZ (black dots) of this set, 2-parameter area model in G and PW (black curve) and 1-parameter area model in $G_{PW=1.55}$ (red curve). The R^2 of the models are reported near the fits and the model parameters are reported near the x-axis with the same color code. Middle panel: 2-parameter process. The panel replicates the rightward data from Figure 4. The grey area is delimited by the 95% C.I.s of G and PW from Table 1. The dashed lines are parallel to the regression line and shifted by the upward and downward limits of the 95% C.I. of the rightward $G-G_{est}$ distribution from Table 4. Only data sets with G and PW simultaneously inside the grey area and the dashed lines are considered inside the reference population. The three light-blue dots identify the ($P = .025$; $P = .975$) pair, the mean pair, and the ($P = .975$; $P = .025$) pair of the G and PW estimates of the 2-parameter G - PW area model from Table 1 (rightward) used in Figure 12 upper left panel. Lower panel: 1-parameter process: The curve

replicates the population normal distribution model of $G_{PW=1.55}$ for the rightward direction in Figure 9, the 95% C.I.s of which are from Table 4. A data set is considered inside the reference population if the $G_{PW=1.55}$ 95% Wald C.I. of the data set is entirely inside the 95% C.I. of the population.

Effects of the Correlation between G and PW on the Area Profiles in Model $MSAREA = G \times SACSIZ^{PW}$

Range of Variability of Area Profiles in Model $MSAREA = G_{PW=1.55} \times SACSIZ^{1.55}$

Figure 12.

Sample area profiles from the G-PW and $G_{PW=1.55}$ models for the rightward and downward directions. Upper panels: area profiles associated with the ($P = .025$; $P = .975$) pair, the mean pair, and the ($P = .975$; $P = .025$) pair of the G and PW estimates of the 2-parameter G-PW area model from Table 1. Lower panels: area profiles associated with the $P = .025$, mean, and $P = .975$ $G_{PW=1.55}$ values of the 1-parameter $G_{PW=1.55}$ model from Table 4.

Figure 13.

Comparison of the results from the first and the second session (n=35) utilizing the 3-step process on the G and PW estimates from the 2-parameter G-PW model. The reference areas, computed from the 35 (G; PW) pairs from the first session, are determined as in Figure 11 middle panel. Superimposed to these reference areas are the (G; PW) pairs from the first session (in black) and from the second session (in red). The linear regressions, R^2 and regression parameters are reported with the same color code.

Figure 14.

Comparison of the $G_{PW=1.55}$ values of the 1-parameter $G_{PW=1.55}$ model from the two sessions for the 4 saccadic directions. The solid lines are linear regressions, with the R^2 values at the end of the respective regression lines and the regression parameters near the x-axis.

Figure 15.

In black, histograms and normal distribution models of the relative change in $G_{PW=1.55}$ of the second session with respect to the first session, i.e., $(G_2 - G_1)/G_1$, for each saccadic direction ($n=35$). In red, normal distribution models of the relative change in $V_{\max}$ of the second session with respect to the first session, i.e., $(V_{\max 2} - V_{\max 1})/V_{\max 1}$. Same layout of Figure 2. The vertical dotted bars identifying the ceiling-adjusted and distribution-adjusted ranges selected for the histograms of $(V_{\max 2} - V_{\max 1})/V_{\max 1}$ (not shown) are often outside the range of the horizontal axis and are reported near the lower corners of the panels with their actual position on the x-axis indicated below them.

Table 1.

Parameters of the normal distributions of the G and PW values of the model $MSAREA = G \times SACSIZEPW$ applied to the 116×4 directions data sets (Figs. 2 and 3). Each row reports: saccadic direction, mean value, standard deviation σ , value of the χ^2 test statistic of normality with in parenthesis the degrees of freedom of the estimation (df), probability of the χ^2 test statistic of normality, value of the parameter @ $P = .025$ and @ $P = .975$, and size of the 95% Wald C.I., defined as the difference between the values @ $P = .975$ and @ $P = .025$. A $P < .01$ in the probability of the χ^2 test statistic was selected as rejection threshold of the normal distribution model and all sets had $P > .01$. The overall population averages of G and PW, obtained by merging all directions together, are $G = 57.0^{(2-PW)}/s$ and $PW = 1.55$. For the meaning of the asterisks, see text.

Area Model Parameter G [$\alpha^{(2-PW)}$] MSAREA = G $\times$ SACSIZEPW (n=116)							
Direction	Mean	σ	χ^2 (df)	P	G @ P = .025	G @ P = .975	95% C.I.
Right	60.8	11.3	5.9 (5)	0.32	38.7	82.9	44.2
Left	59.6	10.6	3.2 (6)	0.79	38.8	80.4	41.6
Up	53.0*	11.2	5.6 (5)	0.35	30.9	75.0	44.1
Down	54.5*	12.3	11.2 (4)	0.02	30.3	78.7	48.4
Area Model Parameter PW [-] MSAREA = G $\times$ SACSIZEPW (n=116)							
Direction	Mean	σ	χ^2 (df)	P	PW @ P = .025	PW @ P = .975	95% C.I.
Right	1.53	0.07	4.1 (5)	0.54	1.39	1.67	0.27
Left	1.53	0.06	12.0 (6)	0.06	1.41	1.65	0.25
Up	1.58*	0.08	1.8 (4)	0.77	1.42	1.74	0.32
Down	1.55	0.08	4.3 (4)	0.37	1.39	1.71	0.32

Variables: G and PW normal distribution parameters of model $MSAREA = G \times SACSIZEPW$

Direction: Saccadic direction

Mean: mean value (normal distribution)

σ : standard deviation (normal distribution)

χ^2 (df): χ^2 value and degrees of freedom of the χ^2 test of normality (Systat) used to verify if the distribution can be modeled with a normal distribution

P: probability of the of the χ^2 test of normality ($P < .01$ selected as threshold to reject the normal distribution hypothesis)

@ P = .025: Parameter estimate at $P = .025$ of the normal distribution model

@ P = .975: Parameter estimate at $P = .975$ of the normal distribution model

95% C.I.: 95% confidence interval of the normal distribution model, defined as the value of the parameter @ $P = .975$ minus the value @ $P = .025$

Table 2.

Parameters of the normal distribution models of the $G - G_{\text{est}}$ values for the 116×4 data sets (Figure 5). Same layout of Table 1.

$G - G_{\text{est}} [^{a(2-PW)}/s] (n=116)$							
Direction	Mean	σ	χ^2 (df)	P	@ $P = .025$	@ $P = .975$	95% C.I.
Right	-0.4	4.3	7.2 (5)	0.21	-8.8	8.0	16.8
Left	0.4	4.8	3.9 (5)	0.57	-9.0	9.8	18.8
Up	0.1	6.3	6.5 (4)	0.17	-12.2	12.4	24.6
Down	-0.6	6.8	2.6 (4)	0.63	-13.9	12.7	26.6

Layout and abbreviations/acronyms identical to Table 1, applied to the variable $G - G_{\text{est}}$.

Table 3.

Fitting parameters of the 2-parameter area model in G and PW and of the three 1-parameter models in PW_{1-par}, GPW=1.55 and PW_{G=57.0} for the 4 upward data sets indicated as open dots in Figure 4 and fits illustrated in Figure 7. Each row reports: parameter and [unit], estimate, asymptotic standard error (ASE), $P = .025$ and $P = .975$ values of the 95% Wald C.I., size of the 95% Wald C.I. (defined as the difference between the $P = .975$ and the $P = .025$ values), and R^2 of the fit. The underlined R^2 entries identify the model with the worst R^2 for each of the 4 points.

Model Comparisons – From Figure 7														
Point in Figure 4	2-parameter model MSAREA=G×SACSIZE ^{PW} (black trace)						1-parameter model (234–115×PW _{1-par})×SACSIZE ^{PW1-par} (violet trace)							
	Parameter [unit]	Est	ASE	@ P=0.025	@ P=0.975	95% Wald	R ²	Parameter [unit]	Est	ASE	@ P=0.025	@ P=0.975	95% Wald	R ²
A	G [^α (2-PW)/s]	36.9	1.0	34.8	39.0	4.2	0.9998		1.271	0.013	1.244	1.298	0.054	<u>0.9816</u>
	PW [-]	1.549	0.008	1.531	1.567	0.036								
	G [^α (2-PW)/s]	66.0	3.4	58.6	73.4	14.8	0.9993		1.694	0.076	1.532	1.856	0.324	<u>0.9843</u>
	PW [-]	1.544	0.017	1.507	1.581	0.074								
B														
C	G [^α (2-PW)/s]	36.2	1.9	32.0	40.5	8.5	0.9994	PW _{1-par} [-]	1.710	0.018	1.671	1.749	0.078	0.9991
	PW [-]	1.723	0.018	1.684	1.761	0.077								
D	G [^α (2-PW)/s]	83.0	5.9	70.3	95.6	25.3	0.9980		1.606	0.024	1.556	1.657	0.101	<u>0.9890</u>
	PW [-]	1.436	0.024	1.383	1.488	0.105								
Point in Figure 4	1-parameter model MSAREA=G _{PW=1.55} ×SACSIZE ^{1.55} (red trace)						1-parameter model MSAREA=57.0×SACSIZE ^{PWG=57.0} (green trace)							
	Parameter [unit]	Est	ASE	@ P=0.025	@ P=0.975	95% Wald	R ²	Parameter [unit]	Est	ASE	@ P=0.025	@ P=0.975	95% Wald	R ²
A		36.8	0.08	36.6	37.0	0.4	0.9998		1.409	0.004	1.402	1.417	0.015	0.9956
B	G _{PW=1.55}	64.8	0.26	64.2	65.3	1.1	0.9993		1.592	0.002	1.588	1.595	0.007	0.9989
C	[^α (2-1.55)/s]	60.5	0.75	58.9	62.1	3.2	<u>0.9938</u>	PW _{G=57.0} [-]	1.571	0.004	1.563	1.579	0.016	0.9951
D		59.4	0.63	58.0	60.7	2.7	0.9946		1.563	0.004	1.555	1.571	0.016	0.9938

G and PW of model MSAREA = G × SACSIZE^{PW}

PW_{1-par} of model MSAREA = (AFIG4 + BFIG4 × PW_{1-par}) × SACSIZE^{PW1-par}

GPW=1.55 of model MSAREA = GPW=1.55 × SACSIZE^{1.55}

PWG=57.0 of model MSAREA = 57.0 $\times$ SACSIZEPWG=57.0

Est: estimated value of the parameter **ASE:** asymptotic standard error

@ **P** = .025 and @ **P** = .975; Estimate of the parameter at **P** = .025 and **P** = .975 (Wald)

95% Wald: 95% Wald confidence interval, defined as value @ **P** = .975 - value @ **P** = .025

R²: mean-corrected R² of the fit

Table 4.

Parameters of the normal distributions of the $G_{PW=1.55}$ values (Figure 9) obtained applying the 1-parameter area model $MSAREA = G_{PW=1.55} \times SACSIZEL^{1.55}$ to the 116×4 data sets. Same layout of Table 1. For the meaning of the asterisk, see text.

Area Model Parameter $G_{PW=1.55} [^{(2-1.55)}]$ $MSAREA = G_{PW=1.55} \times SACSIZEL^{1.55}$ $n=116$							
Direction	Mean	σ	χ^2 (df)	P	A @ $P = .025$	A @ $P = .975$	95% C.I.
Right	55.7	4.6	5.3 (4)	0.26	46.7	64.7	18.0
Left	55.5	4.7	8.2 (6)	0.22	46.3	64.7	18.4
Up	56.6	7.8	8.4 (5)	0.14	41.3	71.9	30.6
Down	53.2*	7.1	4.4 (5)	0.49	39.3	67.1	27.8

Layout and abbreviations/acronyms identical to Table 1, applied to the variable $G_{PW=1.55}$.

Table 5.

Parameters of the normal distributions of the relative change in $V_{\max}$ of the second session with respect to the first session, i.e., $(V_{\max 2} - V_{\max 1})/V_{\max 1}$ compared with the distribution of the relative change in $G_{PW=1.55}$, i.e., $(G_2 - G_1)/G_1$ from the 35 subjects for which we have repeated data (Figure 15). Each row reports: saccadic direction, mean value, standard deviation σ , Shapiro-Wilk test statistic, probability of the Shapiro-Wilk test statistic, value of the parameter @ $P = .025$ and @ $P = .975$, and size of the 95% C.I., defined as the difference between the values @ $P = .975$ and @ $P = .025$. For $n=35$, the χ^2 test of normality was substituted with the Shapiro-Wilk test. A $P < .01$ in the probability of the Shapiro-Wilk test statistic was selected as rejection threshold of the normal distribution model and all sets had $P > .01$ with the exclusion of the relative change of $V_{\max}$ for the leftward direction, indicated with an asterisk. For this set, the normal C.I. values are approximate estimates. The ampersand symbol indicates that the mean is significantly different from 0 ($P < .01$ 1-sample t-test).

Relative Variation of $V_{\max}$ between Sessions (n=35)							
Direction	Mean	σ	Sh-Wi	P	@ $P = .025$	@ $P = .975$	95% C.I.
Right	-0.016	0.111	0.945	0.085	-0.234	0.202	0.435
Left*	-0.023	0.114	0.818	0.0005	-0.246	0.200	0.446
Up	0.002	0.221	0.970	0.447	-0.431	0.435	0.866
Down	-0.045	0.146	0.978	0.702	-0.331	0.241	0.572

Relative Variation of $G_{PW=1.55}$ between Sessions (n=35)							
Direction	Mean	σ	Sh-Wi	P	@ $P = .025$	@ $P = .975$	95% C.I.
Right	-0.042&	0.033	0.983	0.846	-0.107	0.023	0.130
Left	-0.023&	0.038	0.988	0.956	-0.097	0.051	0.148
Up	-0.024	0.082	0.982	0.809	-0.185	0.137	0.322
Down	-0.024	0.077	0.979	0.718	-0.175	0.127	0.302

Parameters of the normal distributions of the relative change in $V_{\max}$ of the second session with respect to the first session, i.e., $(V_{\max 2} - V_{\max 1})/V_{\max 1}$ and of the relative change in $G_{PW=1.55}$, i.e., $(G_2 - G_1)/G_1$ of the second session with respect to the first session

Direction: Saccadic direction

Mean: mean value and **σ :** standard deviation (normal distribution)

Sh-Wi: Shapiro-Wilk normal distribution test (n=35)

P : probability of the Shapiro-Wilk test ($P < .01$ selected as threshold to reject the normal distribution hypothesis)

@ $P = .025$: Estimate of $(V_{\max 2} - V_{\max 1})/V_{\max 1}$ or $(G_2 - G_1)/G_1$ at $P = .025$ of the normal distribution model

@ $P = .975$: Estimate of $(V_{\max 2} - V_{\max 1})/V_{\max 1}$ or $(G_2 - G_1)/G_1$ at $P = .975$ of the normal distribution model

95% C.I.: 95% confidence interval of the normal distribution model, defined as the difference between the value @ $P = .975$ and the value @ $P = .025$