## Figure 1: Differential regeneration of $\mathbf{N v L W a m i d e}$-like neurons depends on the specific neuronal subtype.

 Mixed ANOVA analyses were performed for the data presented in Figure 1G\&I. The main effect of the repeated measure (observation time), between-subject factor (starting size category), and the interaction effect (time x size) are reported for longitudinal (G) and tripolar neurons (I). Main effects were interpreted within the context of any significant interaction effects. Bonferroni post-hoc testing was used to determine pairwise differences. Greenhouse-Geisser corrected $F$ statistics are reported for the repeated-measure variables for the longitudinal and tripolar neuron regeneration data sets (G, I), due to a lack of sphericity. Dpa, days post amputation; hpa, hours post amputation.| G) Regeneration of longitudinal neurons |  |  |  |
| :---: | :---: | :---: | :---: |
| Factors | Df $\quad F$ | $P$ | $\eta_{\mathrm{p}}{ }^{2}$ |
| - Observation time | 1.7,134.4 83.95 | < 0.001 | 0.52 |
| - Starting size | 3,79 79.11 | < 0.001 | 0.75 |
| - Time x Size | 5.1,134.4 13.46 | < 0.001 | 0.34 |
| Pairwise comparisons: |  | Mean difference | P |
| (Time by Size) |  |  |  |
| Small: | Time 0 cut vs. 24 hpa | 3.3 | < 0.001 |
|  | Time 0 cut vs. 7 dpa | -1.0 | 0.99 |
|  | 24 hpa vs. 7 dpa | -4.3 | < 0.001 |
| Medium: | Time 0 cut vs. 24 hpa | 6.1 | < 0.001 |
|  | Time 0 cut vs. 7 dpa | -0.6 | 1.00 |
|  | 24 hpa vs. 7 dpa | -6.6 | < 0.001 |
| Medium-large: | Time 0 cut vs. 24 hpa | 6.9 | < 0.001 |
|  | Time 0 cut vs. 7 dpa | 4.4 | 0.003 |
|  | 24 hpa vs. 7 dpa | -2.5 | 0.25 |
| Large: | Time 0 cut vs. 24 hpa | 12.8 | < 0.001 |
|  | Time 0 cut vs. 7 dpa | 10.6 | < 0.001 |
|  | 24 hpa vs. 7 dpa | -2.1 | 0.34 |
| (Size by Time) |  |  |  |
| Time 0 cut: | Small vs. Medium | -9.9 | < 0.001 |
|  | Small vs. Medium-large | - 17.5 | < 0.001 |
|  | Small vs. Large | -27.1 | < 0.001 |
|  | Medium vs. Medium-large | - 7.7 | < 0.001 |
|  | Medium vs. Large | - 17.2 | < 0.001 |
|  | Medium-large vs. Large | -9.5 | < 0.001 |
| 24 hpa | Small vs. Medium | -7.2 | < 0.001 |
|  | Small vs. Medium-large | -14.0 | < 0.001 |
|  | Small vs. Large | - 17.6 | < 0.001 |
|  | Medium vs. Medium-large | -6.8 | < 0.001 |
|  | Medium vs. Large | - 10.5 | < 0.001 |
|  | Medium-large vs. Large | - 3.7 | 0.19 |
| 7 dpa | Small vs. Medium | -9.5 | < 0.001 |
|  | Small vs. Medium-large | - 12.2 | < 0.001 |
|  | Small vs. Large | -15.5 | < 0.001 |
|  | Medium vs. Medium-large | -2.7 | 1.00 |
|  | Medium vs. Large | -6.0 | 0.05 |
|  | Medium-large vs. Large | -3.3 | 0.96 |


| I) Regeneration of tripolar neurons |  |  |  |
| :---: | :---: | :---: | :---: |
| Factors | Df $\quad$ F | $P$ | $\eta_{p}{ }^{2}$ |
| - Observation time | 1.5,116.2 22.75 | < 0.001 | 0.23 |
| - Starting size | 3,77 54.18 | < 0.001 | 0.68 |
| - Time x Size | 4.5,116.2 3.93 | 0.003 | 0.13 |
| Pairwise comparisons: |  | Mean difference | P |
| (Time by Size) |  |  |  |
| Small: | Time 0 cut vs. 24 hpa | 0.9 | 1.00 |
|  | Time 0 cut vs. 7 dpa | 1.2 | 1.00 |
|  | 24 hpa vs. 7 dpa | 0.4 | 1.00 |
| Medium: | Time 0 cut vs. 24 hpa | 4.4 | 0.001 |
|  | Time 0 cut vs. 7 dpa | 4.2 | 0.08 |
|  | 24 hpa vs. 7 dpa | -0.2 | 1.00 |
| Medium-large: | Time 0 cut vs. 24 hpa | 3.8 | 0.013 |
|  | Time 0 cut vs. 7 dpa | 3.0 | 0.46 |
|  | 24 hpa vs. 7 dpa | -0.8 | 1.00 |
| Large: | Time 0 cut vs. 24 hpa | 6.8 | < 0.001 |
|  | Time 0 cut vs. 7 dpa | 10.2 | < 0.001 |
|  | 24 hpa vs. 7 dpa | 3.4 | 0.055 |
| (Size by Time) |  |  |  |
| Time 0 cut: | Small vs. Medium | -13.6 | < 0.001 |
|  | Small vs. Medium-large | -23.9 | < 0.001 |
|  | Small vs. Large | - 38.3 | < 0.001 |
|  | Medium vs. Medium-large | - 10.3 | 0.03 |
|  | Medium vs. Large | -24.7 | < 0.001 |
|  | Medium-large vs. Large | - 14.4 | 0.001 |
| 24 hpa: | Small vs. Medium | - 10.1 | 0.003 |
|  | Small vs. Medium-large | -21.1 | < 0.001 |
|  | Small vs. Large | - 32.4 | < 0.001 |
|  | Medium vs. Medium-large | - 11.0 | 0.005 |
|  | Medium vs. Large | -22.3 | < 0.001 |
|  | Medium-large vs. Large | -11.3 | 0.004 |
| 7 dpa : | Small vs. Medium | - 10.6 | 0.003 |
|  | Small vs. Medium-large | -22.2 | < 0.001 |
|  | Small vs. Large | -29.3 | < 0.001 |
|  | Medium vs. Medium-large | -11.6 | 0.005 |
|  | Medium vs. Large | - 18.7 | < 0.001 |
|  | Medium-large vs. Large | -7.1 | 0.22 |

Figure 2: Regeneration of longitudinal neurons depends on the size of the regenerating fragment. Repeated measure ANOVA analyses were performed for the data presented in Figure 2C, E, G. Observation time served as the repeated measure for large animals with an aboral shift in cut site (C), medium animals with an oral shift in cut site (E), and small animals with an oral shift in cut site (G). Bonferroni post-hoc tests were used to evaluate pairwise differences when there was a significant main effect of observation time on the number of neurons observed. Dpa, days post amputation; hpa, hours post amputation.

| C) Regeneration of large animals with aboral shift in cut site |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: |
| Factors | Df | $F$ | P | $\eta_{p}{ }^{2}$ |
| - Observation time | 2,14 | 5.58 | 0.017 | 0.44 |
| Pairwise comparisons: |  |  | Mean difference | P |
| Time 0 cut vs. 24 hpa |  |  | 5.8 | 0.04 |
| Time 0 cut vs. 7 dpa |  |  | -1.0 | 1.00 |
| 24 hpa vs. 7 dpa |  |  | -6.9 | 0.046 |
| E) Regeneration of medium animals with oral shift in cut site |  |  |  |  |
| Factors | Df | $F$ | P | $\eta_{p}{ }^{2}$ |
| - Observation time | 2,24 | 21.67 | < 0.001 | 0.64 |
| Pairwise comparisons: |  |  | Mean difference | P |
| Time 0 cut vs. 24 hpa |  |  | 7.0 | < 0.001 |
| Time 0 cut vs. 7 dpa |  |  | 7.1 | 0.001 |
| 24 hpa vs. 7 dpa |  |  | 0.05 | 1.00 |
| G) Regeneration of small animals with oral shift in cut site |  |  |  |  |
| Factors | Df | $F$ | $P$ | $\eta_{p}{ }^{2}$ |
| - Observation time | 2,24 | 8.56 | 0.002 | 0.42 |
| Pairwise comparisons: |  |  | Mean difference | $P$ |
| Time 0 cut vs. 24 hpa |  |  | 5.1 | < 0.001 |
| Time 0 cut vs. 7 dpa |  |  | 2.9 | 0.12 |
| 24 hpa vs. 7 dpa |  |  | -2.2 | 0.47 |

## Figure 4: The Nematostella nerve net scales with changes in size.

Mixed ANOVA analyses were performed for the data presented in Figure 4C\&E. The main effect of the repeated measure (observation time), between-subject factor (feeding regime), and the interaction effect (time x feeding) are reported for the number of longitudinal (C) and tripolar neuron data (E). Main effects were interpreted within the context of any significant interaction effects. Bonferroni post-hoc testing was used to determine pairwise differences. S-F, starved then fed; F-S, fed then starved.

| C) Number of longitudinal neurons |  |  |  |
| :---: | :---: | :---: | :---: |
| Factors | Df | P | $\eta_{\mathrm{p}}{ }^{2}$ |
| - Observation time | 2,16 23.89 | < 0.001 | 0.75 |
| - Feeding regime | 1,8 2.47 | 0.16 | 0.27 |
| - Time x Feeding | 2,16 102.01 | < 0.001 | 0.93 |
| Pairwise comparisons: |  | Mean difference | P |
| (Feeding by Time). |  |  |  |
| Week 1: | S-F vs. F-S | 12.7 | 0.35 |
| Feeding switch: | S-F vs. F-S | -88.0 | < 0.001 |
| Week 14: | S-F vs. F-S | 138.6 | < 0.001 |
| (Time by Feeding). |  |  |  |
| Starved then fed: | Week 1 vs. Feed switch | 37.3 | 0.004 |
|  | Week 1 vs. Week 14 | - 115.7 | <0.001 |
|  | Feed switch vs. Week 14 | - 153.0 | < 0.001 |
| Fed then starved | Week 1 vs. Feed switch | - 63.4 | < 0.001 |
|  | Week 1 vs. Week 14 | 10.2 | 1.00 |
|  | Feed switch vs. Week 14 | 73.6 | 0.003 |
| E) Number of tripolar neurons |  |  |  |
| Factors | Df $\quad$ F | $P$ | $\eta_{p}{ }^{2}$ |
| - Observation time | 2,16 11.10 | 0.001 | 0.58 |
| - Feeding regime | 1,8 2.09 | 0.19 | 0.21 |
| - Time x Feeding | 2,16 48.60 | < 0.001 | 0.86 |
| Pairwise comparisons: |  | Mean difference | P |
| (Feeding by Time). |  |  |  |
| Week 1: | S-F vs. F-S | 13.4 | 0.61 |
| Feeding regime switch: | S-F vs. F-S | - 115.1 | < 0.001 |
| Week 14: | S-F vs. F-S | 184.6 | < 0.001 |
| (Time by Feeding). |  |  |  |
| S-F: | Week 1 vs. Feed switch | 64.9 | 0.03 |
|  | Week 1 vs. Week 14 | - 147.5 | < 0.001 |
|  | Feed switch vs. Week 14 | -212.4 | < 0.001 |
| F-S: | Week 1 vs. Feed switch | - 63.6 | 0.032 |
|  | Week 1 vs. Week 14 | 23.7 | 0.70 |
|  | Feed switch vs. Week 14 | 87.3 | 0.03 |


| G) Oral-aboral length |  |  |  |
| :---: | :---: | :---: | :---: |
| Factors | Df $\quad$ F | P | $\eta_{p}{ }^{2}$ |
| - Observation time | 2,34 6.63 | 0.004 | 0.28 |
| - Feeding regime | 1,17 1.02 | 0.326 | 0.06 |
| - Time x Feeding | 2,34 25.75 | < 0.001 | 0.602 |
| Pairwise comparisons: |  | Mean difference | P |
| (Feeding by Time) |  |  |  |
| Week 1: | S-F vs. F-S | 0.22 | 0.280 |
| Feeding regime switch: | S-F vs. F-S | - 0.62 | 0.003 |
| Week 14: | S-F vs. F-S | 0.91 | 0.002 |
| (Time by Feeding). |  |  |  |
| S-F: | Week 1 vs. Feed switch | 0.32 | 0.098 |
|  | Week 1 vs. Week 14 | - 0.72 | 0.002 |
|  | Feed switch vs. Week 14 | -1.04 | < 0.001 |
| F-S: | Week 1 vs. Feed switch | - 0.52 | 0.008 |
|  | Week 1 vs. Week 14 | - 0.03 | 1.00 |
|  | Feed switch vs. Week 14 | 0.49 | 0.008 |

Supplemental Figure 2: Length measurements and neural quantifications in Nematostella. One-way ANOVA analyses were performed for the data presented in Supplemental Figure 2B\&C. Supplemental Figure 2B analysis is not included here because the result of the one-way ANOVA was not significant. (C) Percent length regenerated by 7dpa was evaluated using shifted cut site location in small, medium and large animals as a factor. Bonferroni post-hoc testing was used to evaluate pairwise differences.

| C) Percent length regenerated at 7dpa based on cutsite in different sized animals |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Factors | Df | F | P |  |  |
| - Cut site | 2,28 | 10.92 | $<\mathbf{0 . 0 0 1}$ | $\eta_{\mathrm{p}}{ }^{2}$ |  |
| Pairwise comparisons: |  |  | Mean difference | $P$ |  |
| Small animal oral cut vs. Medium animal oral cut | -0.03 | 1.00 |  |  |  |
| Small animal oral cut vs. Large animal aboral cut | 0.25 | $\mathbf{0 . 0 0 1}$ |  |  |  |
| Medium animal oral cut vs. Large animal aboral cut | 0.28 | $<\mathbf{0 . 0 0 1}$ |  |  |  |

Supplemental Figure 5: Independent experiment demonstrating Nematostella nerve net scales with changes in size. Mixed ANOVA analyses were performed for the data presented in Supplemental Figure $1 \mathrm{~A} \& \mathrm{C}$. The main effect of the repeated measure (observation time), between-subject factor (feeding regime), and the interaction effect (time x feeding) are reported for the number of longitudinal (A) and tripolar neuron data (C). Main effects were interpreted within the context of any significant interaction effects. Bonferroni post-hoc testing was used to determine pairwise differences. S-F, starved then fed; F-S, fed then starved.

| A) Number of longitudinal neurons |  |  |  |
| :---: | :---: | :---: | :---: |
| Factors | Df $\quad F$ | P | $\eta_{p}{ }^{2}$ |
| - Observation time | 2,16 4.35 | 0.03 | 0.35 |
| - Feeding regime | 1,8 0.60 | 0.46 | 0.07 |
| - Time x Feeding | 2,16 38.88 | < 0.001 | 0.83 |
| Pairwise comparisons: |  | Mean difference | P |
| (Feeding by Time) |  |  |  |
| Week 1: | S-F vs. F-S | 23.9 | 0.17 |
| Feeding regime switch: | S-F vs. F-S | - 171.1 | < 0.001 |
| (Time by Feeding). |  |  |  |
| Starved then fed: | Week 1 vs. Feed switch | 51.8 | 0.03 |
|  | Week 1 vs. Week 14 | -84.8 | 0.05 |
|  | Feed switch vs. Week 14 | - 136.6 | < 0.001 |
| Fed then starved | Week 1 vs. Feed switch | - 143.2 | < 0.001 |
|  | Week 1 vs. Week 14 | 8.0 | 1.00 |
|  | Feed switch vs. Week 14 | 151.2 | 0.001 |
| C) Number of tripolar neurons |  |  |  |
| Factors | Df $\quad$ f | P | $\eta_{\mathrm{p}}{ }^{2}$ |
| - Observation time | 2,16 51.00 | < 0.001 | 0.86 |
| - Feeding regime | 1,8 4.60 | 0.06 | 0.37 |
| - Time x Feeding | 2,16 206.13 | < 0.001 | 0.96 |
| Pairwise comparisons: |  | Mean difference | P |
| (Feeding by Time) |  |  |  |
| Week 1: | S-F vs. F-S | 15.3 | 0.61 |
| Feeding regime switch: | S-F vs. F-S | -219.9 | < 0.001 |
| Week 14: | S-F vs. F-S | 324.0 | < 0.001 |
| (Time by Feeding). |  |  |  |
|  | Week 1 vs. Feed switch | 48.9 | 0.09 |
|  | Week 1 vs. Week 14 | -290.1 | < 0.001 |
|  | Feed switch vs. Week 14 | - 339.0 | < 0.001 |
|  | Week 1 vs. Feed switch | - 186.3 | < 0.001 |
|  | Week 1 vs. Week 14 | 18.7 | 1.000 |
|  | Feed switch vs. Week 14 | 205.0 | < 0.001 |

