Exposing rodents to environmental enrichment (EE) increases neural activity and structural plasticity in the brain. Given the similarities in transcriptional signaling between neuronal plasticity and axonal outgrowth, we hypothesised that EE could promote axonal plasticity and regeneration by shifting neurons towards a regenerative profile. We demonstrate that 10 days exposure to EE alone or in combination with a conditioning injury dramatically increases dorsal root ganglia (DRG) neurite outgrowth on both permissive and inhibitory substrates. Strikingly, exposure to EE for just 10 days primed DRG neurons to provide a lasting increase in their outgrowth potential in vitro, which was retained for at least 4 weeks after the mice were placed back into standard housing. Following nerve injury, 10 days pre-exposure to EE leads to enhanced axon regeneration and significant electrophysiological improvements, which were again further enhanced when combined with a conditioning injury. After observing no changes in the levels of neurotrophic factors or cytokines in the DRG following EE we hypothesised that EE causes a lasting increase in the intrinsic growth potential of DRG neurons via epigenetic modulation and/or changes to gene expression. Combinational analysis of RNAseq from laser captured large-diameter DRGs and proteomic analyses from axoplasm demonstrate that EE increases neuronal activity and axonal transport. Furthermore, we show that EE modulates the epigenome of DRG neurons via activation of CBP and increased levels of H4K8ac, a marker of transcriptional activation. Ongoing experiments aim to elucidate the link between enhanced neural activity and the observed changes to the epigenome and gene expression following EE. Ultimately, while EE has been shown to be a promising post-injury rehabilitative therapy, here we demonstrate that pre-exposure to EE enhances axon regeneration by increasing the intrinsic regenerative-potential of DRG neurons.