This study explored the effects of early-life (between 0 to 36 months) environmental unpredictability and environmental harshness on preschoolers’ cognitive, behavioral, and emotional self-regulation directly and indirectly through positive parenting at 36 months. Environmental unpredictability included number of maternal employment and marital transitions and residential mobility. Environmental harshness included average income-to-needs ratios, poverty status, and receipt of public assistance. Positive parenting practices included maternal warmth, supportiveness, and cognitive stimulation. Analyses revealed that early-life environmental unpredictability and environmental harshness make independent and unique contributions to preschoolers’ self-regulation. Findings also suggest that the effects of environmental unpredictability, environmental harshness, and parenting practices on children’s self-regulation are domain specific and do not operate equally across all children. Environmental unpredictability was directly and negatively associated with preschoolers’ emotion regulation, while environmental harshness was indirectly and negatively associated with preschoolers’ attention regulation through positive parenting. These associations were only significant for boys, suggesting that boys may be more susceptible to the influence of harsh and unpredictable environments early in life.