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EARLY ABNORMAL GROWTH AND SYNAPTIC ARCHITECTURE IN HIPPOCAMPAL NEURONS FROM FRAGILE X PREMUTATION MOUSE

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Premutation CGG repeat expansions (55-200 CGG repeats; preCGG) within the fragile X mental retardation 1 (*FMR1*) gene give rise to the neurodegenerative disorder, fragile-X associated tremor/ataxia syndrome (FXTAS), primary ovarian insufficiency and neurodevelopmental problems. Morphometric analysis of Map2B immunofluorescence reveals that neurons cultured from heterozygous female mice with 150-200 CGG repeats in defined medium display shorter dendritic lengths and fewer branches between 7 and 21 days *in vitro* (DIV) compared to wild type littermates (WT). Although the numbers of synapsin and phalloidin puncta do not differ from WT, preCGG neurons possess larger puncta. PreCGG neurons display lower viability, and express elevated stress protein. PreCGG neurons have inherently different patterns of growth, dendritic complexity, and synaptic architecture discernable early in the neuronal trajectory to maturation, and may reflect a cellular basis for the developmental component of the spectrum of clinical involvement in carriers of premutation alleles. The reduced viability of preCGG neurons is consistent with the neurodegeneration associated with FXTAS.

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