Neonatal stress may permanently alter hypothalamic-pituitary-gonadal function and accelerate the onset of puberty in female rats. Heterotrimeric G proteins, found coupled to membrane-bound receptors on the inside of cell membranes, form a central link in cell signaling. Inactive G proteins bind guanosine diphosphate (GDP). When a signaling molecule, such as gonadotropin releasing hormone (GnRH), binds to membrane receptors of cells in the anterior pituitary gland, GDP is displaced by guanosine triphosphate (GTP), and the alpha subunit separates from the beta and gamma subunits. The alpha-GTP subunit then triggers a cell signaling cascade. In pituitary gonadotrophs, this cascade results in the release of follicle stimulating hormone (FSH) and luteinizing hormone (LH). These hormones will cause female gonads (ovaries) to release estrogen and progesterone and, if hypothalamic-pituitary-gonadal function is altered, may trigger early onset of puberty in female rats. The Valders SMART Team modeled a G Protein using 3D printing technology to study structure-function relationships in cell signaling. Hydrophobic amino acids form the switch interface between the alpha subunit and the beta-gamma subunits stabilizing the heterotrimeric G protein. When the alpha subunit binds GTP, Gly199 interacts with the terminal (gamma) phosphate of GTP, and the activated alpha subunit separates from the beta-gamma subunits resulting in cell signal propagation. Understanding how the hypothalamic-pituitary-gonadal axis is influenced by neonatal stress in rats may help scientists to better understand puberty onset in humans.

Male rats: Male Wistar rat litters were divided into two groups. For the Maternal Separation (MS) subgroup mothers were separated from the pups three hours a day for two weeks starting on the first postnatal day (PND). For the control group, the mothers and pups were not disturbed except for three bedding changes. Onset of puberty in males was measured by the separation of the prepuce (foreskin) from the penis. To measure serum concentrations of testosterone, blood samples were taken via the sublingual (under the tongue) vein on PND 38, 40, and 42.

The average day of preputial separation (Fig. 9 B) during puberty in maternally separated rats increased in comparison to the control rats, demonstrating a significant delay in the onset of puberty.

VI. Conclusion
It has been shown that neonatal stress may permanently alter hypothalamic-pituitary-gonadal function; affecting the onset of puberty in rats. In female rats, puberty is accelerated by premature vaginal opening and elevated plasma levels of luteinizing hormone. Conversely, in male rats, puberty is delayed, as demonstrated by decreased postnatal levels of testosterone and delayed preputial separation. The hypothalamus, which is affected by neonatal stress, releases Gonadotropin releasing hormone (GnRH) that binds to the GnRH receptor on anterior pituitary cells. Activated G proteins then complete the cellular response by triggering protein phosphorylation. As a result, anterior pituitary cells secrete luteinizing hormone and follicle stimulating hormone that target the gonads, determining the onset of puberty.

Learning how neonatal stress effects hypothalamic-pituitary-gonadal function in rats may give insight into the understanding of puberty onset in humans.