**Introduction**

- Exogenous cortisol administration has been used to test the hormone’s influence on a variety of outcomes, including memory and affect.
- Careful control of factors known to influence cortisol and other endogenous hormone levels is central to the success of this research.
- While hormonal contraceptives are known to exert many physiological effects, including decreasing the salivary cortisol response to stress (Kirschbaum, Kudielka, Gaab, Schommer, & Hellhammer, 1999), it is unknown how hormonal birth control (HBC) influences cortisol after exogenous cortisol administration.

**Goal:** Examine the role of HBC on women’s cortisol levels after receiving synthetic cortisol (hydrocortisone, identical to the endogenous hormone).

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**Method**

**Study 1:** Participants were 22 men (Mean age: 21.8) and 24 women (Mean age: 22.4), in good health. All women were using HBC.
- In a double-blind design, participants received a dose of hydrocortisone tailored to body mass (0.1 mg/kg) and placebo in randomized order, in separate sessions 48 hours apart. Blood samples were collected to assess plasma cortisol: 3 samples pre-dose and 7 post-dose. Further details can be found in Wirth et al., 2011.

**Study 2:** Participants were 18 men (Mean age: 28.3), 10 women not taking HBC (Mean age: 28.2), and 13 women taking HBC (Mean age: 23.4), in good health.
- In a double-blind design, participants received an oral dose of 15 mg of hydrocortisone and placebo in randomized order, in separate sessions 48 hours apart. Six salivary cortisol samples were collected to assess free cortisol: 1 sample pre-dose and 5 post-dose. Further details can be found in Abercrombie et al., 2011.

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**Results**

**Study 1. Plasma cortisol after hydrocortisone (IV, 0.1 mg/kg) or placebo administration.**
- Area under the curve increase (AUCi) in plasma cortisol was significantly greater in women (all taking HBC) vs. men following hydrocortisone admin. ($t(42) = 10.13, p < 0.001$). This difference was not found following placebo infusion. Note: Dotted depict plasma cortisol change after hydrocortisone. Solid lines depict change after placebo.

**Study 2. Salivary cortisol after hydrocortisone (oral, 15 mg) or placebo administration.**
- Salivary cortisol AUCi was greater in women taking HBC following cortisol administration, compared to men ($t(29) = -2.75, p = 0.010$), and compared to a combined group of women not on HBC and men ($t(39) = -2.74, p = 0.009$); the latter two groups did not differ. There were no group differences following placebo administration. Note: Dotted lines depict salivary cortisol change after hydrocortisone. Solid lines depict change after placebo.

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**Discussion**

- In Study 1 women taking HBC had greater cortisol increases than men after IV cortisol, which we believe was at least partly driven by HBC use.
- Study 2 confirmed this pattern: Women on HBC had the greatest cortisol increase after an oral dose.
- Together findings suggest that elevations in both total and free cortisol after exogenous cortisol are greater in women using HBC.
- Differences in cortisol levels after exogenous cortisol manipulation in women on vs. off HBC may help explain any variations in behavioral or physiological effects of exogenous cortisol observed in women on HBC.
- These results could also be due to the effects of HBC on cortisol’s binding mechanisms (van der Vange, Blankenstein, Kloosterboer, Haspel, & Thijsen, 1990). HBC-induced increases in levels of blood proteins that bind cortisol/GCs could delay their breakdown and prolong cortisol elevations in the blood.

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**Future Directions**

- Investigate the role of binding globulins in relations among cortisol, HBC use, and/or endogenous reproductive hormones.
- Menstrual cycle variation in endogenous or exogenous estrogen and/or progesterone may have important effects on cortisol’s bioavailability, binding mechanisms, metabolism. Future research exploring those associations may have clinical implications, such as understanding depression and other clinical conditions that disproportionately affect women.

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**References:**