

**TABLE FOUR: Acupuncture and polycystic ovarian syndrome (PCOS).**

Author, date	Study Design	Methods/Outcome Measured	Control Group (n)	Acupuncture Method and Timing (n)	Additional Information	Conclusion
Lai <i>et al</i> , 2010	Prospective, randomised, controlled.	Changes in BMI, menstrual frequency and ovarian volume, serum LH and FSH, free testosterone, fasting blood glucose and blood fats among other variables measured.	Patients given metformin (250 mg/time, t.i. d. in the 1st week, and 500 mg/time, t.i.d. thereafter) for 6 months (n = 43).	Patients given abdominal acupuncture once daily for 6 months (n = 43).	ONLY ABSTRACT AVAILABLE. All patients had obesity-type PCOS.	Both groups showed improvements in PCOS symptoms, but acupuncture group showed significant changes in BMI, menstrual frequency and free testosterone levels compared to medication (control) group. Therefore abdominal acupuncture can improve endocrine and metabolic symptoms.
Jedel <i>et al</i> , 2010	Prospective, randomised, controlled.	Changes in menstrual frequency, concentrations of androgens (inc precursors and metabolites), oestrogens, acne and hirsutism.	Group 1: 16 weeks physical exercise: 30 mins 3 times a week to increased HR to $\geq 120$ beats/min (n = 18). Group 2: no intervention (n = 11).	Patients receiving 16 weeks of electro-acupuncture: twice weekly for 2 wk, once weekly for 6 wk, and once every other week for 8 wk, for a total of 14 treatments (n = 21).	All patients aged 18-37 years. Outcomes assessed at baseline, after 16 wks of intervention and after a 16 wk follow up.	Low-frequency EA and physical exercise improved hyperandrogenism and menstrual frequency more effectively than no intervention. EA was superior to physical exercise and may be useful for treating hyperandrogenism and oligo/amenorrhea.
Xu <i>et al</i> , 2009	Prospective.	Changes in clinical symptoms of PCOS.	No controls.	Patients receiving electroacupuncture combined with auricular point tapping and pressing. (= 39).	ONLY ABSTRACT AVAILABLE. All patients had obesity-type PCOS. Timing and duration of acupuncture unknown	Acupuncture has good clinical effects: 10 cases were cured, 25 cases were effective, 4 cases were ineffective. NB: Definitions of 'cured' and 'effective' unknown.

Stener-Victorin <i>et al</i> , 2009	Prospective, randomised, controlled.	Changes in muscle sympathetic nerve activity, and changes in biometric, endocrine and metabolomic variables.	Group 1: 16 weeks physical exercise (n = 5) Group 2: No intervention (n = 6).	Patients receiving 16 weeks of low frequency electro-acupuncture (n = 9).	Exercise and acupuncture timings as in Jedel <i>et al</i> , 2010.	EA and physical exercise lowers high sympathetic nerve activity in women with PCOS. Thus, treatment with low-frequency EA or physical exercise with the aim to reduce MSNA may be of importance for women with PCOS. ONLY EXERCISE REDUCED BMI
Chen <i>et al</i> , 2007	Prospective, randomised, controlled.	Changes in hormone levels and clinical symptoms.	Patients orally given domiphen and intramuscular injection of chorionic gonadotropin (HCG) (n = 60).	Patients receiving needle-pricking therapy at sacral plexus stimulating points on both sides of the spine and lateral points of Dazhui (CV 14) (n = 61).	ONLY ABSTRACT AVAILABLE. Patients observed after 3 cycles of treatment and the 6th cycle after treatment.	Hormonal profile and ultrasound examination results were improved in both groups after 3 cycles of treatment. However, symptoms returned after 6 cycles in the control group, but normal menstruation and ovulation was maintained in the acupuncture group. Pregnancy rates were significantly higher in acupuncture group (raw data unknown). Acupuncture has long term effects on PCOS.
Stener-Victorin <i>et al</i> , 2000(b)	Prospective, longitudinal.	Changes in menstrual and ovulation frequency, BMI, androgens and insulin.	No controls.	Patients with PCOS and oligo-/amenorrhea (n = 24).	Patients aged 24-40 years. Blood samples collected within a week before the first EA, within a week after the last EA and 3 months after EA.	Nine women (38%) experienced a good effect and experienced more ovulations after acupuncture compared to before treatment. These women had a less androgenic hormonal profile and a less pronounced metabolic disturbance before treatment compared with the group with no effect. Acupuncture may help some women with PCOS.
Alieva <i>et al</i> , 1993	Unclear.	Reduction in BMI.	Patients undertaking exercise.	Patients receiving acupuncture.	ONLY ABSTRACT AVAILABLE. Protocol and sample numbers unclear.	Exercise reduced weight in 60 patients, acupuncture reduced weight in 20 patients. Authors concluded both techniques were recommended for PCOS patients.

## Animal Models

Author, date	Study Design	Methods/Outcome measured	Control Group (n)	Acupuncture Method and timing (n)	Additional Information	Conclusion
Johannson <i>et al.</i> , 2010	MURINE MODEL: prepubescent rats implanted with 90-day continuous-release pellets containing DHT to mimic PCOS.	Changes in lipid profile, insulin sensitivity and level of muscle glucose transporter expression.	Group 1: rats implanted with pellets lacking DHT (n = 12). Group 2: Model group, no treatment (n = 12).	Electro-acupuncture given for 20-25 mins five times/wk for 4-5 weeks (n = 12).	All interventions began at age 70 days.	Electro-acupuncture resulted in normalized insulin sensitivity, lower levels of total cholesterol, and increased expression of GLUT4 in skeletal muscle compared with model rats not receiving acupuncture. In rats with DHT-induced PCOS, low-frequency EA has systemic and local effects involving intracellular signaling pathways in muscle that may, at least in part, account for the marked improved insulin sensitivity.
Zhang <i>et al.</i> , 2009	MURINE MODEL: 24 day old immature rats continuously injected with an oil solution of DHEA for 20 days to mimic PCOS.	Uterus and ovaries inspected, blood hormonal levels measured.	Model group, no treatment	Acupuncture given for 15 mins once a day for 5 continuous days, starting from the 80th day after birth	ONLY ABSTRACT AVAILABLE	Acupuncture can downregulate the expression of serum levels of testosterone and oestrogen, improve the development of ovaries and uterus, promote ovulation, enhance endometrial receptivity, and advance blastocyte implantation.
Feng <i>et al.</i> , 2009	MURINE MODEL: prepubescent rats implanted with 90-day continuous-release pellets containing DHT to mimic PCOS.	Oestrous cyclicity and expression of androgen receptor (AR), gonadotropin-releasing hormone (GnRH), GnRH receptors, and corticotrophin-releasing hormone (CRH) in the hypothalamus.	Group 1: rats implanted with pellets lacking DHT (n = 12). Group 2: Model group, no treatment (n = 12).	Electro-acupuncture (2-Hz) five times/week for 4-5 weeks (n = 12).	DHT treated rats were initially acyclic, with increased androgen receptors and GnRH. All interventions began at age 70 days.	Electro-acupuncture restored normal oestrus cyclicity within 1 week and reduced the elevated hypothalamic GnRH and AR expression levels. GnRH-receptor and CRH levels were not affected by acupuncture.

Mannerås <i>et al</i> , 2009	MURINE MODEL: Rats receiving continuous DHT starting before puberty to induce PCOS.	Changes in mRNA expression of sympathetic nervous system activity markers in adipose tissue and ovarian morphology.	Group 1: rats implanted with pellets lacking DHT (n = 13). Group 2: Model group, no treatment (n = 12).	Group 1: Model rats receiving free access to exercise wheel (n = 13). Group 2: rats receiving acupuncture 3 times/week for 4-5 weeks (n = 11).	All interventions began at age 11 weeks. PCOS rats initially displayed pathologically altered beta(3)-adrenergic receptor (ADRB3), nerve growth factor (NGF), and neuropeptide Y (NPY) levels compared to group 1 controls.	EA and exercise improved ovarian morphology, as reflected in a higher proportion of healthy antral follicles and a thinner theca interna cell layer than in untreated PCOS rats. Exercise and EA modulated sympathetic nervous system activity in adipose tissues. These findings support the theory that increased sympathetic activity contributes to the development and maintenance of PCOS and that the effects of EA and exercise may be mediated by modulation of sympathetic outflow to the adipose tissue and ovaries.
Mannerås <i>et al</i> , 2008	MURINE MODEL: Rats receiving continuous DHT starting before puberty to induce PCOS.	Changes in adiposity, plasma leptin, insulin sensitivity and expression of selected genes in adipose tissues.	Group 1: rats implanted with pellets lacking DHT. Group 2: Model group, no treatment (n = 12).	Group 1: Model rats receiving free access to exercise wheel. Group 2: rats receiving acupuncture 3 times/week for 4-5 weeks.	PCOS rats initially displayed increased leptin and IL-6 expression and decreased 'uncoupling protein 2' expression in visceral adipose tissue compared to controls.	Exercise and EA improved insulin sensitivity. Exercise restored leptin and IL-6 levels. EA restored leptin and 'uncoupling protein 2' levels. Only exercise reduced adiposity. EA and exercise each <i>partially</i> restore abnormal adipose tissue gene expression associated with PCOS. In contrast to exercise, EA improves insulin sensitivity and modulates adipose tissue gene expression without influencing adipose tissue mass and cellularity.

Manni <i>et al</i> , 2005	MURINE MODEL: Rats receiving a single injection of oestradiol valerate (EV) to induce Polycystic ovaries (PCO) - results in an increase in ovarian sympathetic outflow	Changes in mRNA expression and the distribution of proteins of $\alpha 1a$ -, $\alpha 1b$ -, $\alpha 1d$ -, and $\beta 2$ -adrenoceptors (ARs), and low-affinity neurotrophin receptor (p75NTR).	Group 1: rats not receiving EV (vehicle only) and no acupuncture (n = 8). Group 2: no EV administered but given acupuncture (n = 8). Group 3: EV administered but no acupuncture (n = 8).	Model rats receiving electro-acupuncture for 25 mins every 2 days. 12 treatments in total (n = 8).	PCOS rats initially displayed alterations in all mRNA levels except p75NTR and $\beta 2$ -AR, and all protein levels.	Acupuncture normalised most of the EV induced changes seen in PCO rats. Suggested to occur by acupuncture's ability to normalise the sympathetic nervous system response to increased ovarian nerve growth factors seen in PCO ovaries.
Stener-Victorin <i>et al</i> , 2004(a)	MURINE MODEL: Rats receiving a single injection of oestradiol valerate (EV) to induce Polycystic ovaries (PCO).	Changes in ovarian blood flow and the involvement of the two ovarian sympathetic nerves; superior ovarian nerve (SON) and plexus ovarian nerve (OPN).	Rats not receiving EV (vehicle only), receiving acupuncture. Two frequencies--2 Hz (low) and 80 Hz (high)--with three different intensities--1.5, 3, and 6 mA--were applied for 35secs.(n = 7).	PCO rats receiving acupuncture in same protocol as controls (n = 7).	Sympathetic nerves (SON and OPN) were severed in both control and PCO rats in order to determine whether they are involved in ovarian blood flow responses. Experiment timing differed between individual rats to ensure data was obtained throughout the oestrus cycle.	Low-frequency EA stimulation with a strong intensity (6 mA) increased OBF in PCO rats but the same was seen with a less strong intensity (3 mA) in control rats. Severance of the ovarian sympathetic nerves abolished this OBF increase in both study groups, which suggests that the responses of OBF to EA are mediated via the ovarian sympathetic nerves.

Bai <i>et al.</i> , 2004	MURINE MODEL: Rats receiving a single injection of oestradiol valerate (EV) to induce Polycystic ovaries (PCO). Results in clear increase in NGF expression.	Changes in protein expression of nerve growth factor (NGF).	Group 1: rats not receiving EV (vehicle only) Group 2: Rats injected with EV not receiving acupuncture.	Model rats receiving electro-acupuncture fat Sp-6 and E-128, twice weekly for 8 weeks.	ONLY ABSTRACT AVAILABLE. Sample numbers unknown.	Acupuncture partially reversed the NGF abundance, particularly in the ovaries, but not in the brain.
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Stener-Victorin <i>et al.</i> , 2004(b)	MURINE MODEL: Rats receiving a single injection of oestradiol valerate (EV) to induce Polycystic ovaries (PCO).	Changes in beta-endorphin levels and immune T cells.	Group 1: Rats not receiving EV (vehicle only), no acupuncture (n = 21); Group 2: Rats not receiving EV (vehicle only) receiving acupuncture (n = 20) Group 3: Model rats not receiving acupuncture (n = 20).	Model rats receiving 2 Hz electro-acupuncture for 25 mins, 3 times a week for 4 weeks.	PCO rats initially displayed significantly reduced $\beta$ -endorphin concentrations (hypothalamus and plasma) and reduced frequencies of CD4+ T cells and CD8+ T cells compared to vehicle only control rats.	Repeated EA treatments in EV-injected rats significantly increased $\beta$ -endorphin concentrations in the hypothalamus. No effect on immune cells. In conclusion, these findings show that both the $\beta$ -endorphinergic and the immune system are significantly impaired in rats with steroid-induced PCO and that repeated EA treatments can restore some of these disturbances.
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Stener-Victorin <i>et al</i> , 2003(b)	MURINE MODEL: Rats receiving a single injection of oestradiol valerate (EV) to induce Polycystic ovaries (PCO).	Changes in sympathetic nerve activity by measuring endothelin-1 (ET-1), a potent vasoconstrictor involved in ovarian functions, as well as nerve growth factor (NGF) and NGF mRNA expression.	Group 1: rats not receiving EV (vehicle only (n = 8); Group 2: rats not receiving EV (vehicle only ) receiving acupuncture (n = 8); Group 3: model rats not receiving acupuncture (n = 8).	Model rats receiving electro-acupuncture for 25 mins every 2 days. 12 treatments in total (n = 8).	ET-1 levels were measured in ovaries, hypothalamus and adrenals.	Repeated acupuncture treatments significantly decreased ovarian concentrations of ET-1, increased hypothalamic ET-1 and decreased NGF protein in rats with steroid-induced PCO compared to group 1 controls. This is an indication of lower activity in the sympathetic nerve fibres of the ovaries.
Stener-Victorin <i>et al</i> , 2001	MURINE MODEL: Rats receiving a single injection of oestradiol valerate (EV) to induce Polycystic ovaries (PCO).	Changes in corticotropin-releasing factor (CRF) concentrations in the brain, the adrenal glands, and the ovaries.	Group 1: rats not receiving EV (vehicle only (n = 17); Group 2: model rats not receiving acupuncture (n = 8).	Model rats receiving electro-acupuncture for 25 mins every 2 days. 12 treatments in total (n = 9).	EV injection significantly increases CRF levels in the median eminence compared to Group 1 controls.	Acupuncture was able to significantly decrease CRF concentration in the ovaries, but had no significant effects on other locations. Electro-acupuncture may improve PCOS symptoms by peripherally acting on CRF levels in the ovaries, but not the brain.
Stener-Victorin <i>et al</i> , 2000(a)	MURINE MODEL: Rats receiving a single injection of oestradiol valerate (EV) to induce Polycystic ovaries (PCO).	Changes in nerve growth factor (NGF) in the CNS and the endocrine organs, including the ovaries.	Group 1: rats not receiving EV (vehicle only (n = 8); Group 2: rats injected with NaCl as a control (n = 8); Group 3: model rats not receiving acupuncture (n = 8).	Model rats receiving electro-acupuncture for 25 mins every 2 days. 12 treatments in total (n = 8).	PCO induced in rats by a single injection of EV resulted in significantly higher concentrations of NGF in the ovaries and the adrenal glands, but not in brain tissue when measured 30 days after EV injection.	Acupuncture significantly decreased the elevated NGF concentrations in the ovaries, to within a normal range, without affecting NGF concentrations in the adrenal glands or brain tissue when measured 30 days after EV injection. Concluded EA inhibits hyperactivity in the sympathetic nervous system.