Effect of Novel Plasticizers, Bisphenol S and F, on The Meiotic Maturation and Spindle Structure of Mouse Oocytes

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According to the WHO, infertility is a growing health problem across the world. One of the potential reasons for this situation is increasing exposure to endocrine-disrupting chemicals (EDCs), such as a widespread plasticizer bisphenol A (BPA). Due to its xenoestrogenic properties and harmful health effects, it has been often substituted with analogs, such as bisphenol S (BPS) and bisphenol F (BPF). BPS/BPF were detected in human body fluids, including (for BPS) follicular fluid. Their impact on organismal functions, including the reproductive system and fertility remains still largely unknown, although some studies suggest that they may influence the quality of mammalian oocytes. In our preliminary study, we checked whether BPS and BPF affect *in vitro* meiotic maturation of mouse oocytes and structure of their metaphase II spindles. Briefly, we cultured prophase I oocytes for 16 hrs in a medium supplemented with increasing concentrations of BPS or BPF, corresponding to their reported or expected concentration in human follicular fluid. Oocytes cultured in pure medium or medium with BPS/BPF solvent DMSO (in the respective concentration) served as controls. Afterwards, oocytes were fixed and stained for β-tubulin and DNA to visualize the spindle structure. Metaphase II spindles were classified as abnormal if did not display a typical bipolar shape and/or had misaligned chromosomes. Additionally, spindle volume and ratio of length to width were measured. Our data showed that meiotic maturation was not disturbed by any of BPS/BPF analyzed concentrations (2, 20, 200 ng/ml for BPS and 0.2 ng/ml for BPF). On the other hand, we found that 20ng/ml BPS (n=53; 32.08%) exposure significantly elevated the percentage of abnormal meiotic spindle formation compared with oocytes cultured in pure medium (n=117; 16.24%) and medium with DMSO (n=40; 12.50%) ($p<0.05$). Furthermore, we showed that 20ng/ml BPS during *in vitro* maturation modifies spindle morphology (classified previously as normal): significantly decreased spindle volume (n=10; 1385±161μm^3) compared to pure medium (n=8; 1732±222μm^3; $p<0.01$) or DMSO (n=10; 1624±251μm^3; $p<0.05$) groups. Additionally, 20ng/ml BPS significantly elevated the ratio of spindle length to width (n=10; 2.44±0.21) compared to pure medium (n=8; 2.12±0.21; $p<0.05$) or DMSO (n=10; 2.09±0.11; $p<0.01$) groups. To sum up, our preliminary data suggests that at least BPS may not be neutral for oocyte quality, which is why further research on their action is needed.

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