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Bisphenol A Disrupts the Thyroid Hormone Actions as an Antagonist.

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Bisphenol A (BPA) is reported to be a weak agonist for the estrogen receptors. Although an epidemic-based investigation is suggesting that some chemicals could disrupt thyroid hormone action, the effect on the thyroid hormone receptors (TRs) is unkown. We show here that BPA coula disrupt TR-mediated transcription as an environmental antagonist. In the transient experiments, BPA significantly suppressed transcriptional activity stimulated by thyroid hormone (T3) in a dose- dependent manner. The suppressive effects were constantly observed in the presence of physiological concentrations of T3, which range between 0.03 and 6 nM. To examine possible mechanisms of this inhibitory effect of BPA, mammalian two-hybrid assay and T3-binding assay were performed. BPA recruited the corepressor to the receptor, resulting in transcriptional repression. The Ki value for BPA was 200 μM on ^{125}I-T3 binding to the rat hepatic nuclear extract. This is the first report that BPA disrupted transcriptional activities of TRs as an antagonist. BPA may have varying effects at transcriptional level on different nuclear hormone receptors and their cofactors.