Concerta 54-108 mg

Extracellular NE and DA

An evidence-bounded dose-time model

MODEL OUTPUT, NOT DIRECT SYNAPTIC MEASUREMENT

The curves combine adult OROS methylphenidate pharmacokinetics, human PET transporter occupancy, and a deliberately simple extracellular-transmitter translation. They visualize plausible central tendencies and uncertainty; they cannot predict an individual's response.

Evidence tiers

Measured PK | measured PET occupancy | inferred extracellular time course

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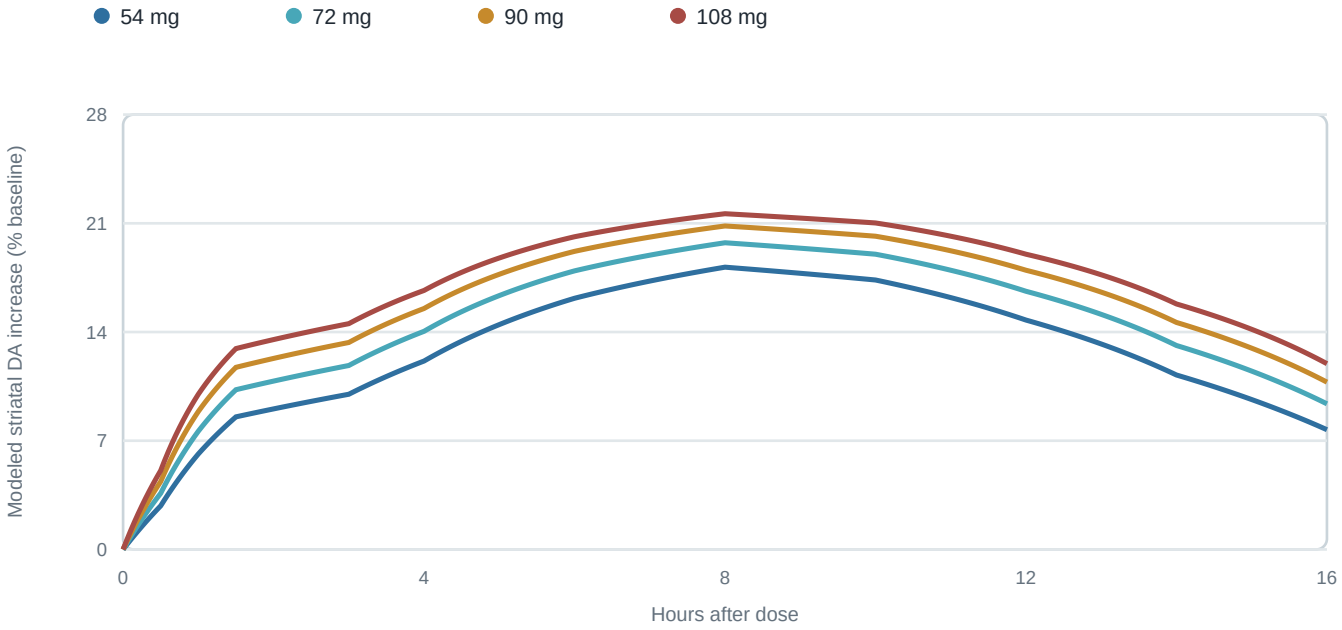
What the model says

Central estimates for a typical adult; variability is substantial

The shape is shared; the ceiling compresses

Concerta exposure rises quickly to an initial shoulder at 1-2 h, continues upward to a broad 6-8 h peak, then declines. Plasma exposure is approximately dose-proportional over this range, but transporter occupancy and transmitter effects saturate. The difference between 90 and 108 mg is therefore smaller in modeled extracellular effect than in plasma concentration.



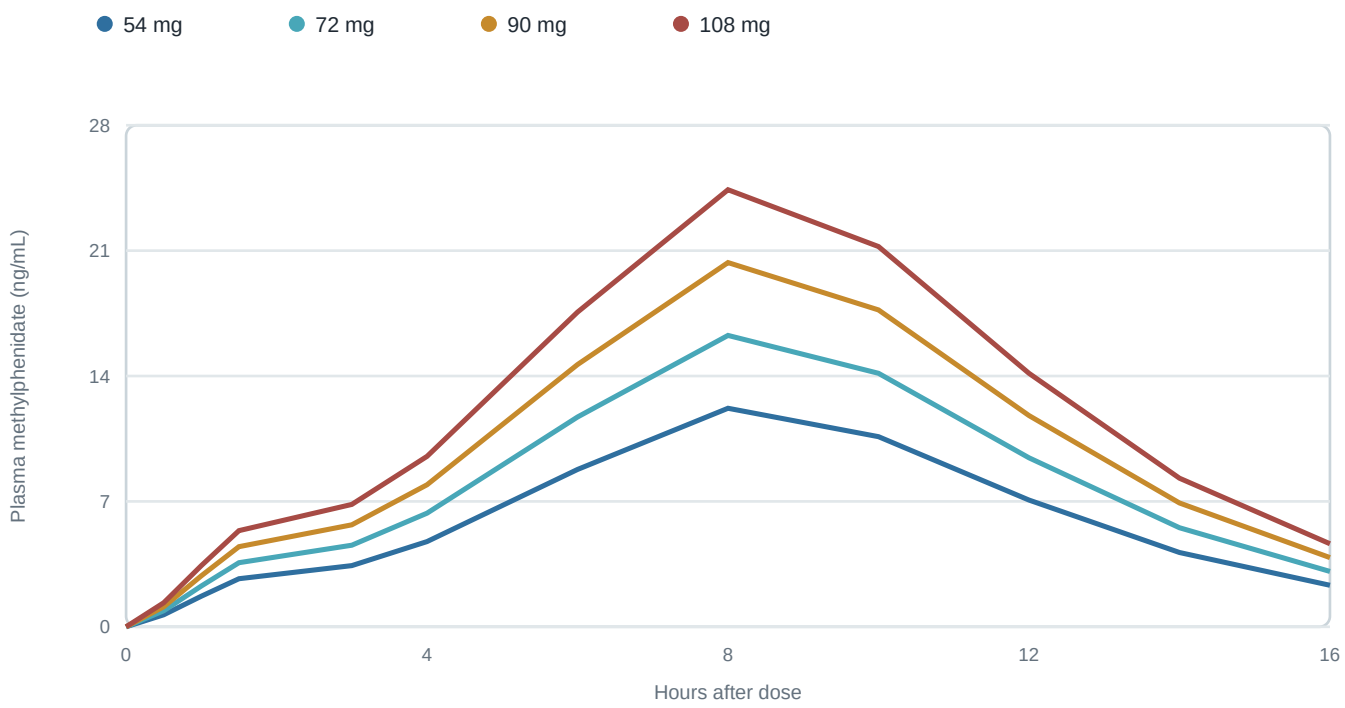
Interpretation boundary

DA is anchored to a small human PET study (60 mg immediate-release MPH: mean 60% DAT blockade and 16% raclopride displacement). NE has no equivalent time-resolved human extracellular measurement; its plotted magnitude is hypothesis-grade. Curves describe groups, not a safe or effective dose for any person.

1. Exposure model

OROS release architecture -> plasma methylphenidate

The central template is calibrated to a 54 mg peak of 12.2 ng/mL, bracketed by the current US label's 18 mg adult Cmax scaled dose-proportionally (11.1 ng/mL at 54 mg) and an independent 54 mg bioequivalence study (13.35 +/- 4.04 ng/mL). Timing follows product information: initial maximum at 1-2 h, main peak at 6-8 h, terminal half-life about 3.5 h.



Dose-proportional exposure is supported; individual exposure is not

Product information reports linear, dose-proportional Cmax and AUC from 54 to 144 mg in healthy adults. It also reports substantial between-person variation and lower exposure at the same dose in heavier people. A single dose number therefore cannot uniquely determine plasma concentration.

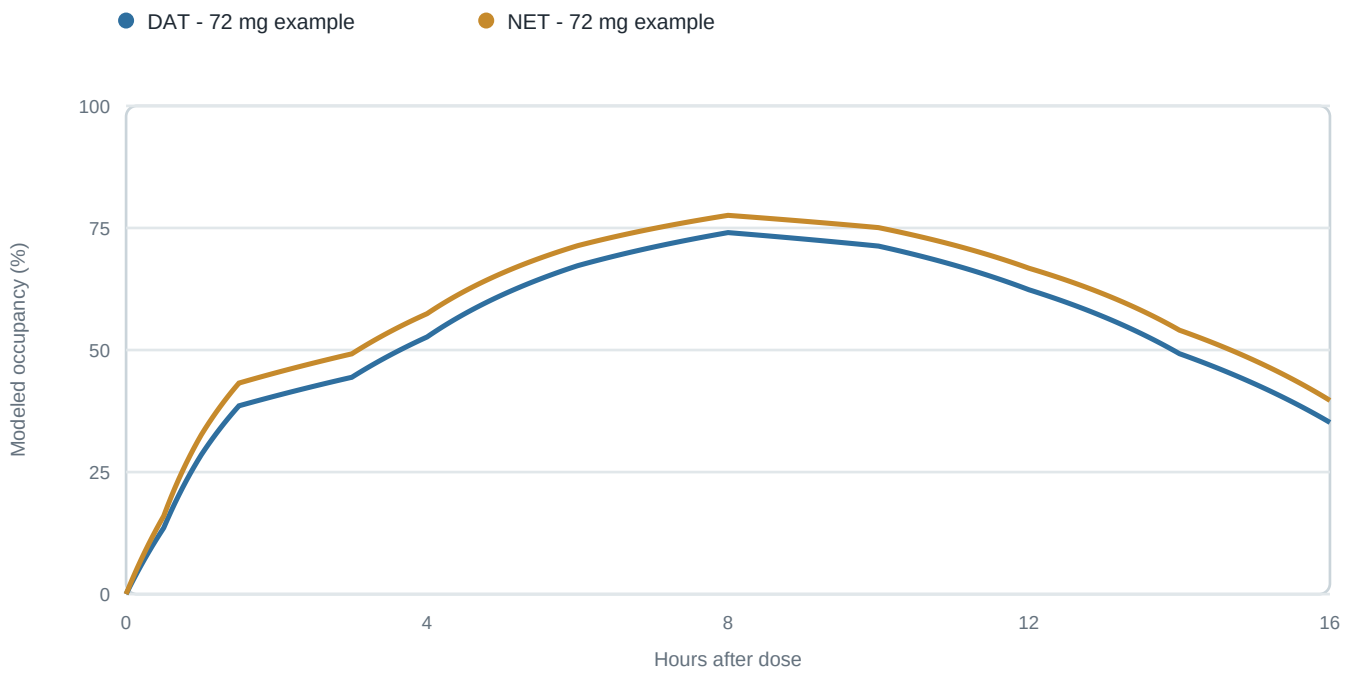
108 mg context

The 2026 US label recommends a maximum of 72 mg/day for adults. Australian product information describes an adult titration trial up to 108 mg/day, but its dosing section also caps adult dosing at 72 mg/day. Trial exposure is not a recommendation for routine use.

2. Transporter engagement

Plasma concentration -> DAT and NET occupancy

A saturable Emax model is used: occupancy = C / (C + EC50). Central EC50 values are 5.7 ng/mL for DAT and 4.7 ng/mL for NET, both from human PET work. These estimates differ by tracer, region, formulation, study design, and sample.



Why the curves flatten

Once most accessible transporters are occupied, additional plasma drug cannot create a proportional increase in blockade. This compresses modeled differences at the upper doses even while systemic exposure continues to rise.

Measured cross-check

At 10 h, a PET study found 36 mg OROS methylphenidate produced mean DAT occupancy of 44.3% (+/- 11.8), supporting persistent central engagement late in the active window. The model is directionally compatible but is not fitted to every PET time point.

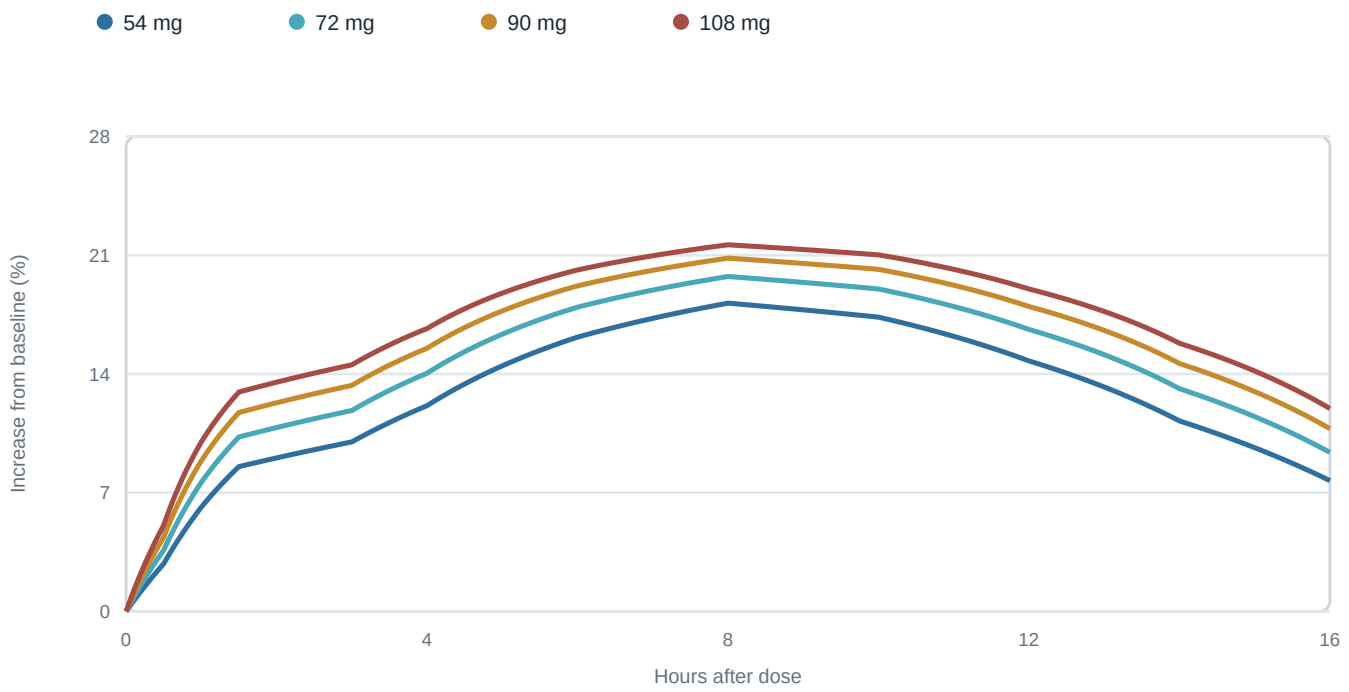
Regional caveat

Striatal DA is dominated by DAT. In prefrontal cortex, NET contributes importantly to clearance of both NE and DA, so one whole-brain DA curve would be biologically misleading.

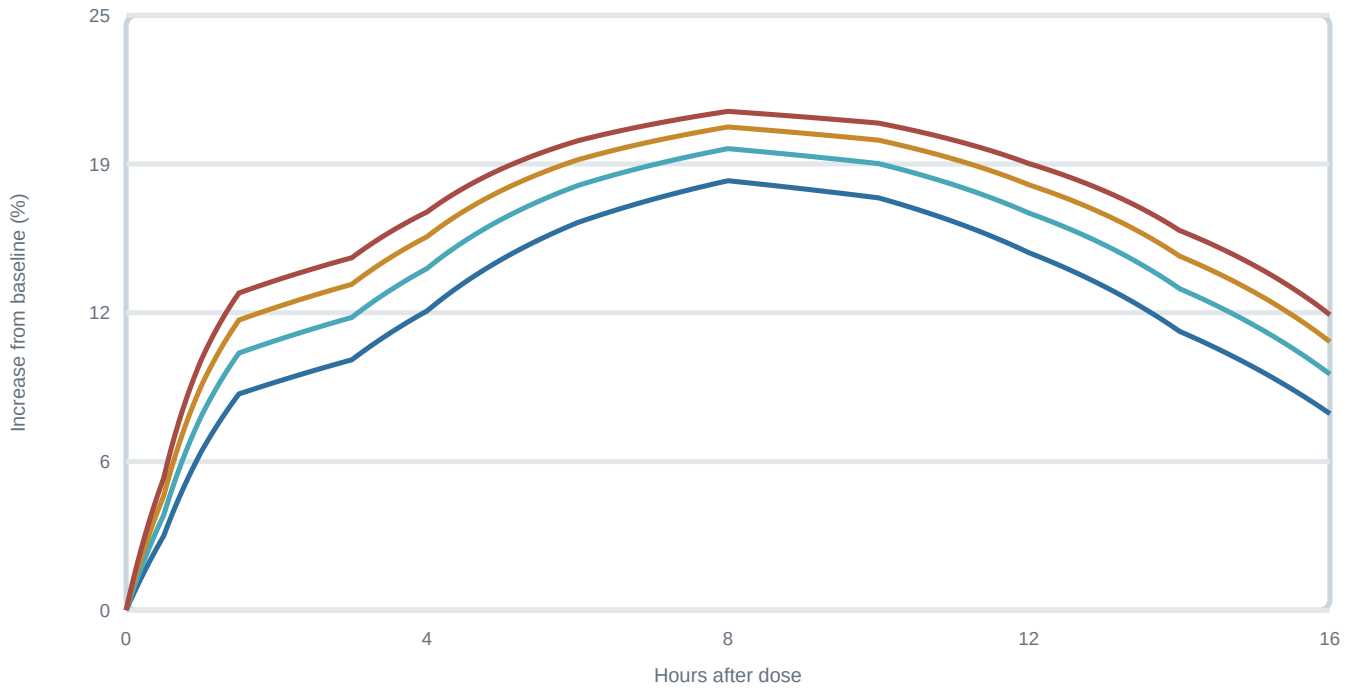
3. Extracellular transmitter outputs

Relative change from baseline; uncertainty is structural, not just statistical

A. Striatal extracellular DA



B. Extracellular NE proxy in NET-rich regions

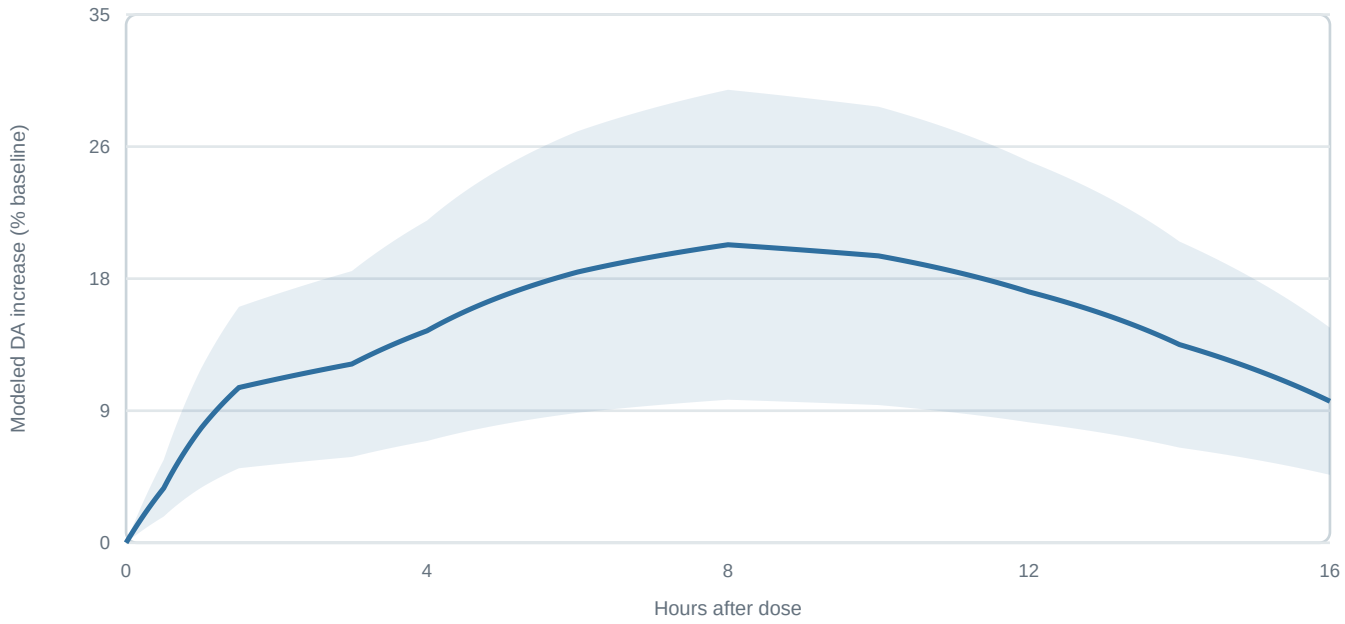


NE amplitude is a didactic proxy, not a directly validated human extracellular measurement.

4. Uncertainty and sensitivity

The honest answer is a band, not a single biological trace

For a 72 mg example, the shaded band combines +/-30% exposure variation with broad uncertainty in the occupancy-to-transmitter translation. It is illustrative, not a confidence interval. Real variability also reflects body size, metabolism, food timing, formulation behavior, prior exposure, age, neural firing, sleep, comorbidity, and interacting medicines.



Do not read the graph as...

- a prediction of how focused, motivated, calm, euphoric, or impaired someone will feel;
- evidence that a higher dose lasts proportionally longer or works better;
- a conversion between 54, 72, 90, and 108 mg for an individual;
- proof of extracellular concentration in nM, which human PET does not directly provide.

5. Methods, sources, and reproducibility

A compact audit trail for every transformation

Model chain

Dose -> piecewise OROS plasma template -> dose-proportional scaling -> saturable DAT/NET occupancy -> relative extracellular signal. Central equations: DAT = 100*C/(C+5.7); NET = 100*C/(C+4.7); DA increase = (16/60)*DAT; NE proxy = 0.25*NET.

Primary and official sources

1 FDA. Concerta Prescribing Information (2026).

2 Janssen-Cilag. Australian Product Information: Concerta (2026).

3 Volkow et al. DAT occupancy after therapeutic oral MPH. Am J Psychiatry (1998).

4 Volkow et al. DAT blockade and extracellular DA. Synapse (2002).

5 Hannestad et al. Human NET occupancy. Biological Psychiatry (2010).

6 Spencer et al. OROS MPH DAT occupancy at 10 h. J Clin Psychiatry (2010).

7 Adler et al. Adult OROS MPH titration to 108 mg trial. J Clin Psychopharmacol (2009).

8 Methylphenidate multiphasic-release bioequivalence, 54 mg PK. Pharmaceutics (2023).

Clinical safety boundary

Concerta is prescription-only and carries cardiovascular, psychiatric, misuse, and dependence warnings. Do not change dose, combine tablets, or use 90/108 mg because of this model. Discuss efficacy, adverse effects, blood pressure/heart rate, sleep, and duration with the prescribing clinician.