Dopamine D₂ Receptors Mediate Glomerular Hyperfiltration Due To Amino Acids

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ABSTRACT
Renal dopamine has been proposed to be involved in the regulation of glomerular filtration rate (GFR). Because inhibition of dopamine D₂ receptors abolishes the renal hyperfiltration due to amino acid load, we tested the hypothesis that pharmacological activation of D₂-like receptors mimicked this renal response. In anesthetized rats, quinpirole (0.3 μg · 100 g⁻¹ · min⁻¹), an agonist for receptors of the D₂-like family, caused an increase in GFR by 20 ± 2%, which corresponded to that provoked by infusion of an 10% amino acid solution. The D₂ receptor antagonist S(−)-sulpiride that acts both centrally and peripherally completely abolished the renal hemodynamic response to quinpirole and to amino acids whereas domperidone, a peripherally acting D₂ receptor antagonist, inhibited this hyperfiltration only in part. Urinary dopamine excretion increased in response to amino acid infusion whether GFR increased or not. We conclude that, in anesthetized rats, dopamine D₂ receptors contribute to the amino acid-induced hyperfiltration and that both central and peripheral receptors might be involved, whereas dopamine excreted into the urine does not appear to play a functional role in this renal hemodynamic response.

Although the increase in GFR and renal blood flow after an AA load are well-known phenomena, the underlying mechanisms are unsatisfactorily understood (see for review Woods, 1993; Lang et al., 1995). Because 1) i.v. infusion of dopamine induces similar changes of renal hemodynamics as a solution of amino acids (ter Wee et al., 1986) and 2) specific inhibition of D₂ receptors abolished the AA-induced increase in GFR (Mendez et al., 1991; Mühlbauer et al., 1994), renal dopamine might be involved in this GFR response. Dopamine receptors have been classified into the D₁-like and the D₂-like family (Seeman and van Tol, 1994) and could be demonstrated in the central nervous system (Seeman, 1980) as well as various peripheral tissues (Clark, 1981; Jose et al., 1992). Earlier, D₁ receptors were suggested to mediate the renal hemodynamic effects of dopamine (Bhat et al., 1986), but D₂ receptors might be involved as well (Seri and Aperia, 1988). To test the hypothesis that pharmacological activation of D₂-like receptors mimicked the AA-induced hyperfiltration, the renal effects of QP, an agonist of the D₂ receptor family (Brodlo, 1989), were compared with those of an AA infusion in anesthetized rats. In an attempt to differentiate the involvement of central and peripheral D₂ receptors, the experiments were performed also during administration of SUL, a centrally and peripherally acting D₂ receptor antagonist, or DOM that, due to its inability to cross the blood-brain barrier (Laduron and Leysen, 1979), affects only peripheral D₂ receptors.

Methods

Animals and microsurgical preparation. Experiments were performed in male Sprague-Dawley rats (Charles River, Sulzfeld, Germany), 220 to 290 g in weight, with free access to standard rat food (Altromin 1320, Altromin, Lage, Germany) and tap water. On the day of the clearance studies, rats were anesthetized with thiopental sodium (80 mg · kg⁻¹ · i.p.; TRAPANAL, Byk Gulden, Konstanz, Germany) and placed on a heated table (RT, Effenerberger, Munich, Germany), which was thermo-controlled to maintain the rectal temperature at 37.2°C. After tracheostomy, two PE catheters were inserted into the right jugular vein for infusion. Another PE-catheter in the left carotid artery was used for drawing of blood samples and continuous monitoring of blood pressure by means of a recorder (WK 280 WKK, Kaltbrunn, Switzerland) connected to an electronic transducer (TBM4, WPI, Heidelberg, Germany). A PE-catheter, inserted deeply in the bladder, served for urine collection.

Design of clearance experiments. The time course of the experiments is shown in figure 1. After surgical preparation the animals were allowed to reach steady-state conditions, defined by stable perfusion and the absence of signs of stress. On the day of the clearance experiments, the animals were allowed to reach near-steady-state conditions, defined by stable perfusion and the absence of signs of stress.

ABBREVIATIONS: AA, amino acid; CON, time controls; CP, clearance period; DOM, domperidone; FEₜₘₑₜ, fractional urinary sodium excretion; HR, heart rate; Hct, hematocrit; L-DOPA, L-3,4-dihydroxyphenylalanine; MAP, mean arterial blood pressure; NaPlasma, sodium plasma concentration; QP, quinpirole; SUL, S(−)-sulpiride; Uₜₘₑₜ, total urinary sodium excretion; UV, urinary flow rate; UₜₘₑₜDₐV, urinary dopamine excretion; VHC, vehicle controls; PE, polyethylene.
infusion (in 0.85% NaCl) for assessment of GFR contained no additional drug for vehicle animals; other groups were pretreated with S(-) sulphuride (SUL) or domperidone (DOM), respectively. NaCl was infused throughout the entire experiment in time control animals. In all other groups, after two baseline clearance periods (CP 1 and CP 2) either quinpirole (QP) or amino acid (AA) solution was administered with 10 min break until performance of experimental clearance periods (CP 3 and CP 4).

Fig. 1. Time course of the clearance experiments in anesthetized rats. Animals were allowed to recover from surgery for 60 to 80 min. 3H-inulin infusion (0.85% NaCl) for assessment of GFR contained no additional drug for vehicle animals; other groups were pretreated with S(-)- sulphuride (SUL) or domperidone (DOM), respectively. NaCl was infused throughout the entire experiment in time control animals. In all other groups, after two baseline clearance periods (CP 1 and CP 2) either quinpirole (QP) or amino acid (AA) solution was administered with 10 min break until performance of experimental clearance periods (CP 3 and CP 4).

systemic hemodynamics and constant urinary flow rate. Via the first i.v. catheter 3H-inulin (1.5 μCi ml⁻¹; NEN, Dreieich, Germany) dissolved in isotonic saline (0.85% NaCl) was infused at a rate of 0.6 ml hr⁻¹ throughout the entire experiment for assessment of GFR. In experiments in which animals were pretreated with D₂ receptor antagonists, this infusion also contained SUL (15 μg 100 g⁻¹·min⁻¹; Sigma Chemicals, Deisenhofen, Germany) or DOM (0.8 μg 100 g⁻¹·min⁻¹; Boitrend, Cologne, Germany). Via the second catheter, isotonic NaCl was infused at a rate of 2.4 ml hr⁻¹. After reaching steady-state, urine was collected in 20-min periods. Blood samples were drawn at the midpoint of each clearance period. After two baseline periods, NaCl infusion was continued in the CON group (n = 6), whereas all other groups (n = 6–7) received either a standard AA solution (10%; Delta-Pharma, Pfüllingen, Germany) or QP (Boitrend, Cologne, Germany) at a dose of 0.3 μg 100 g⁻¹·min⁻¹. Both solutions (AA and QP) were prepared with isotonic saline. Ten minutes after onset of the AA or QP infusion both CP were performed. The composition of the AA solution (in g liter⁻¹) was: L-isoleucine 3.8, L-leucine 6.6, L-lysine 9.3, L-methionine 2.8, L-phenylalanine 4.1, L-threonine 4.6, L-tryptophan 1.2, L-valine 4.1, L-arginine 9.3, L-histidine 4.4, L-aspartic acid 7.7, L-alanine 14.3, L-proline 9.2, L-cysteine 0.7, L-glutamic acid 9.9, L-ornithine-L-aspartate 4.6, L-serine 5.9, L-tyrosine 0.5.

Analyses. Urine volume was measured gravimetrically. Blood samples were centrifuged and the hematocrit was assessed. Both plasma and urine samples were stored at −80°C until analysis. Sodium was determined by flame photometry (ELEX 6361, Eppendorf, Hamburg, Germany), 3H-inulin radioactivity by a liquid scintillation counter (2550 TR, Canberra Packard, Frankfurt, Germany). Dopamine was measured by HPLC with electrochemical detection (Sykam, Gilching, Germany) as described previously (Mühlbauer et al., 1997b). In brief, dihydroxybenzylamine was added to the urine sample as internal standard. After pH was adjusted to 8.6, neutral alumina oxide was added. After this absorption step, the samples were washed twice with distilled water and finally eluted with phosphoric acid. The eluate was applied onto the reversed phase HPLC system. The mobile phase consisted of a citrate buffer, octane sulfonic acid (sodium salt), methanol and acetonitrile in bi-distilled water. Internal standard-corrected recovery of dopamine added to the urine averaged 96 to 104%.

Calculations and statistics. GFR as renal clearance of inulin and fractional sodium excretion were calculated according to the standard formulas. Means of the two base-line and experimental periods were calculated individually. Statistical significance of the differences between baseline (NaCl) and experimental periods (AA or QP infusion) within groups was assessed by the paired two-sided t test. Statistical analysis of the differences among groups was performed by the analysis of variance. P < .05 was considered to be statistically significant. All values are expressed as means of groups ± S.E.M.

Results

Time controls and baseline values of all groups. In the CON group no significant changes in GFR, UV, U NaV as well as FE Na were observed during the entire experiments. U DAV, MAP and HR remained unchanged as well (tables 1 and 2). When comparing the baseline values observed in CON animals with those of the other groups, no significant variations among the different pretreatment protocols could be detected.

Renal response to AA or QP infusion in vehicle-treated rats. AA infusion in the AA-VHC group increased GFR significantly by 20 ± 4% (fig. 2). UV, U NaV and FE Na were elevated during infusion of AA by 1.5- to 2.5-fold compared to baseline; also mean U DAV was significantly increased by 2.0-fold (table 1). QP infusion in the QP-VHC group caused a significant increase of GFR by 20 ± 2% (fig. 3). QP increased UV, U NaV and FE Na by factors 1.6 to 2.0, whereas U DAV was slightly reduced compared to baseline (table 1). Neither AA nor QP administration significantly

TABLE 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Infusion</th>
<th>GFR (ml·min⁻¹)</th>
<th>UV (μl·min⁻¹)</th>
<th>U NaV (μmol·min⁻¹)</th>
<th>FE Na (%)</th>
<th>U DAV (μmol·min⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CON</td>
<td>NaCl</td>
<td>0.59 ± 0.08</td>
<td>10.9 ± 1.3</td>
<td>1.26 ± 0.19</td>
<td>1.00 ± 0.14</td>
<td>5.40 ± 0.41</td>
</tr>
<tr>
<td>(n = 6)</td>
<td>NaCl</td>
<td>0.87 ± 0.05</td>
<td>10.5 ± 1.5</td>
<td>1.42 ± 0.28</td>
<td>1.05 ± 0.16</td>
<td>5.17 ± 0.26</td>
</tr>
<tr>
<td>AA-VHC</td>
<td>AA</td>
<td>0.90 ± 0.04</td>
<td>9.9 ± 2.4</td>
<td>0.98 ± 0.63</td>
<td>0.87 ± 0.60</td>
<td>5.73 ± 0.25</td>
</tr>
<tr>
<td>(n = 7)</td>
<td>AA</td>
<td>1.09 ± 0.07⁷</td>
<td>15.4 ± 3.0</td>
<td>2.36 ± 0.34</td>
<td>1.41 ± 0.19</td>
<td>12.7 ± 2.55⁸</td>
</tr>
<tr>
<td>AA-SUL</td>
<td>NaCl</td>
<td>0.91 ± 0.03</td>
<td>10.0 ± 2.6</td>
<td>1.50 ± 0.22</td>
<td>1.02 ± 0.16</td>
<td>6.44 ± 0.23</td>
</tr>
<tr>
<td>(n = 7)</td>
<td>AA</td>
<td>0.93 ± 0.03</td>
<td>17.7 ± 1.7</td>
<td>3.49 ± 0.38⁷</td>
<td>2.53 ± 0.34</td>
<td>13.0 ± 0.68⁹</td>
</tr>
<tr>
<td>AA-DOM</td>
<td>NaCl</td>
<td>0.95 ± 0.04</td>
<td>13.4 ± 3.5</td>
<td>1.29 ± 0.36</td>
<td>1.38 ± 0.40</td>
<td>5.95 ± 0.57</td>
</tr>
<tr>
<td>(n = 6)</td>
<td>AA</td>
<td>1.05 ± 0.02⁶</td>
<td>28.7 ± 6.5⁸</td>
<td>4.36 ± 0.61⁶</td>
<td>2.51 ± 0.32</td>
<td>11.5 ± 0.85⁹</td>
</tr>
<tr>
<td>QP-VHC</td>
<td>NaCl</td>
<td>0.93 ± 0.06</td>
<td>7.2 ± 1.9</td>
<td>0.87 ± 0.17</td>
<td>0.78 ± 0.17</td>
<td>6.14 ± 0.60</td>
</tr>
<tr>
<td>(n = 7)</td>
<td>QP</td>
<td>1.11 ± 0.06⁸</td>
<td>13.2 ± 2.0⁸</td>
<td>1.84 ± 0.18⁸</td>
<td>1.37 ± 0.14</td>
<td>5.58 ± 0.32</td>
</tr>
<tr>
<td>QP-SUL</td>
<td>NaCl</td>
<td>1.00 ± 0.02</td>
<td>6.6 ± 1.3</td>
<td>1.36 ± 0.32</td>
<td>0.93 ± 0.30</td>
<td>6.10 ± 0.51</td>
</tr>
<tr>
<td>(n = 7)</td>
<td>QP</td>
<td>1.03 ± 0.02²</td>
<td>18.5 ± 3.4⁴</td>
<td>2.21 ± 0.20</td>
<td>1.34 ± 0.11</td>
<td>5.66 ± 0.65</td>
</tr>
<tr>
<td>QP-DOM</td>
<td>NaCl</td>
<td>0.93 ± 0.03</td>
<td>12.1 ± 3.2</td>
<td>1.48 ± 0.27</td>
<td>1.09 ± 0.18</td>
<td>5.95 ± 0.21</td>
</tr>
<tr>
<td>(n = 6)</td>
<td>QP</td>
<td>1.03 ± 0.04⁴</td>
<td>34.3 ± 5.0⁴</td>
<td>2.76 ± 0.35⁴</td>
<td>1.91 ± 0.23⁵</td>
<td>5.45 ± 0.27</td>
</tr>
</tbody>
</table>

GFR, glomerular filtration rate; UV, urinary flow rate; U NaV, total urinary sodium excretion; FE Na, fractional sodium excretion; U DAV, urinary dopamine excretion; CON, control group; AA or QP, amino acid or quinpirole infusion during experimental period, respectively; VHC, SOL or DOM, pretreatment with isotonic saline (NaCl), S(-)-sulpiride or domperidone; see Methods for doses of drugs. Means ± S.E.M.

⁷ P < .05; comparison of baseline (NaCl) with experimental period (AA or QP), paired two-sided t test.
affected MAP, Hct or Na\textsubscript{plasma}. There was a slight but significant decrease in HR due to QP whereas no change was observed during amino AA infusion (table 2).

**Effect of S\textsuperscript{(-)}-sulpiride on the renal response to AA or QP infusion.** As shown in figure 2 and table 1, pretreatment with SUL completely abolished the AA-induced hyperfiltration (AA-SUL group), in contrast, UV, U\textsubscript{Na}V and F\textsubscript{ENa} were still elevated 1.5- to 2.5-fold in response to AA administration. The increase of mean U\textsubscript{DAV} during infusion of AA in AA-SUL animals was similar to that observed in the AA-VHC animals (table 1). SUL also blocked the QP-induce GFR-rise (QP-SUL group; fig. 3), with baseline levels of GFR slightly higher compared to CON animals. The QP-induced increase in UV, U\textsubscript{Na}V and F\textsubscript{ENa} (factors 1.5 to 3.0) in SUL-treated rats was similar compared to the VHC group, although the difference was not statistically significant; U\textsubscript{DAV} did not change during infusion of QP and was similar to those observed in the CON group (table 1). In SUL-treated animals neither MAP, HR, Hct nor Na\textsubscript{plasma} showed significant changes due to administration of AA or QP (table 2).

**Effect of domperidone on the renal response to AA or QP infusion.** After DOM pretreatment the AA-induced increase in GFR was attenuated to 12 ± 4% (AA-DOM; fig. 2). In contrast, UV and F\textsubscript{ENa} increased 2-fold, U\textsubscript{Na}V by a factor of 3.5 during AA infusion; U\textsubscript{DAV} was also significantly enhanced (table 1). Compared to VHC, infusion of DOM also

### TABLE 2
Summary of systemic parameters during clearance experiments

<table>
<thead>
<tr>
<th>Group Infusion</th>
<th>MAP (mmHg)</th>
<th>HR (min\textsuperscript{-1})</th>
<th>Hct (%)</th>
<th>Na\textsubscript{plasma} (mmol\textcdot l\textsuperscript{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>CON NaCl (n = 6)</td>
<td>102 ± 2.3</td>
<td>367 ± 14.7</td>
<td>46 ± 0.6</td>
<td>142 ± 1.3</td>
</tr>
<tr>
<td>AA-VHC NaCl (n = 6)</td>
<td>100 ± 2.3</td>
<td>359 ± 16.3</td>
<td>45 ± 0.6</td>
<td>141 ± 1.3</td>
</tr>
<tr>
<td>AA-SUL NaCl (n = 6)</td>
<td>100 ± 2.4</td>
<td>382 ± 10.6</td>
<td>43 ± 0.6</td>
<td>145 ± 2.6</td>
</tr>
<tr>
<td>AA-DOM NaCl (n = 6)</td>
<td>99 ± 2.3</td>
<td>378 ± 12.8</td>
<td>42 ± 0.6</td>
<td>144 ± 2.7</td>
</tr>
<tr>
<td>AA-DOM NaCl (n = 6)</td>
<td>103 ± 3.7</td>
<td>383 ± 10.7</td>
<td>44 ± 0.3</td>
<td>143 ± 1.1</td>
</tr>
<tr>
<td>AA-DOM NaCl (n = 6)</td>
<td>106 ± 3.1</td>
<td>371 ± 13.8</td>
<td>44 ± 0.3</td>
<td>142 ± 0.6</td>
</tr>
<tr>
<td>AA-DOM NaCl (n = 6)</td>
<td>108 ± 2.7</td>
<td>371 ± 13.6</td>
<td>43 ± 0.5</td>
<td>142 ± 0.2</td>
</tr>
<tr>
<td>QP-VHC NaCl (n = 6)</td>
<td>106 ± 2.2</td>
<td>366 ± 10.4</td>
<td>45 ± 0.6</td>
<td>143 ± 1.2</td>
</tr>
<tr>
<td>QP-DOM NaCl (n = 6)</td>
<td>102 ± 2.4</td>
<td>347 ± 9.2\textsuperscript{a}</td>
<td>44 ± 0.4</td>
<td>143 ± 1.0</td>
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<td>QP-DOM NaCl (n = 6)</td>
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</tr>
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<td>101 ± 2.9</td>
<td>374 ± 11.0</td>
<td>45 ± 0.3</td>
<td>142 ± 1.1</td>
</tr>
<tr>
<td>QP-DOM NaCl (n = 6)</td>
<td>100 ± 2.5</td>
<td>357 ± 8.9\textsuperscript{a}</td>
<td>45 ± 0.2</td>
<td>142 ± 0.9</td>
</tr>
</tbody>
</table>

MAP, mean arterial blood pressure; HR, heart rate; Hct, hematocrit; Na\textsubscript{plasma}, sodium plasma concentration. See Table 1 for groups and experimental periods. Means ± S.E.M.

\*

Comparison of baseline (NaCl) with experimental period (AA or QP infusion), paired two-sided \( t \) test.
attenuated the QP-induced increase in GFR which was 10 ±
2% (QP-DOM; fig. 3). In contrast, DOM did not influence the
effects of QP on UV, UNaV and FEKNa which were 2- to 3-fold
increased, whereas UNaV remained unchanged. As observed in the
VHC group, QP also reduced HR slightly but significantly
in DOM-treated animals. Neither MAP, Hct, nor
NARperox were affected by QP or AA administration during
pretreatment with DOM (table 2).

**Discussion**

Our study showed that the increase in GFR during infu-
sion of AA was mimicked in a quantitatively similar manner
by QP which has been described as an agonist for receptors of the
d2-like family (Brodde, 1989). This result is in accordance
with the increase in single nephron GFR in anesthetized rats
during systemic QP administration reported by Seri and
Aperia (1988). In contrast to these studies, Siragy et al.
(1992) found a significant decrease in GFR due to QP in
conscious dogs. Possible reasons for this discrepancy might be
that the dose of QP used by Siragy et al. (1992) was,
although given directly into the renal artery, lower by orders of
magnitude compared to the other studies. Whether species
differences and, more important, the possible influence of
anesthesia might additionally contribute to the contrasting
observations has to be clarified in further studies.

To substantiate the involvement of d2-like receptors in the
AA-induced GFR increase, rats were pretreated with the d2
receptor antagonist SUL. In fact, both AA- and QP-induced
hyperfiltration were completely abolished by continuous ad-
ministration of SUL. These observations are in accordance
with the studies by Mendez et al. (1991) and by our group
(Mühlbauer et al., 1994, 1997b), in which the changes in
renal hemodynamics during AA infusion were inhibited by
d2 receptor blockade. Concerning the action of the d2-like
agonist, Seri and Aperia (1988) found that the QP-induced
single nephron-hyperfiltration was abolished in the presence
of SUL indicating a specific d2 receptor action. Taken to-
gether, the data strongly support the involvement of d2 rece-
ptors in the AA-induced hyperfiltration. Because QP might
also possess affinity to the d3 subtype of the d2-like receptor
family (Seeman et al., 1991), a possible contribution of this
receptor to the hyperfiltration needs further investigation.
Due to the lack of selective agonists, the role of d3 receptors
in the regulation of renal function has not been determined
so far.

In an attempt to compare the role of central and peripheral
d2 receptors in the modulation of glomerular filtration, we
administered DOM, a peripherally acting d2 receptor antag-
onist. DOM attenuated both the AA- and the QP-induced
hyperfiltration; however, the increase in GFR was not com-
pletely abolished as it was in SUL-treated animals. It might
be objected that the dose of SUL was markedly higher com-
pared to DOM. However, the dose of SUL used in our study
was orientated on data of recent experiments showing a
complete inhibitory effect of SUL on the renal hemodynamic
response to AA infusion; in that study the SUL effect was
dose-dependent suggesting a specific action (Mühlbauer et al.,
1997b). In preliminary experiments, the 5-fold higher
dose of DOM as used in our study produced no additional
inhibitory effect on AA-induced hyperfiltration but affected
the systemic hemodynamics (data not shown). Although sim-
ilar Ks values of SUL and DOM in the rabbit ear artery and
rectococcygeus muscle, respectively, have been reported
(Brodde, 1989) higher doses of SUL compared to DOM were
used in vivo (Brooks and Weinstock, 1991) or in vitro (Starke
et al., 1983; Rump et al., 1991) by other investigators. Taken
together, dose differences are unlikely to be the reason for the
varying modulation of the AA- or QP-induced hyperfiltration
by SUL and DOM. Concerning the higher lipid solubility of
SUL compared to DOM, it may be argued that the disparity
between both d2 receptor antagonists might be due to greater
penetration of SUL into peripheral neural or epithelial com-
partments. However, continuous administration of both an-
tagons was initiated approximately 2 hr in advance of the
functional experiments which should be a sufficient time
span for achieving constant tissue levels of the drugs. There-
fore, such an explanation appears unlikely. Taken together,
the data suggest that the increase in GFR is mediated by
central as well as peripheral D2-like receptors. Recently we
could demonstrate that the increase in GFR due to systemic
AA load was completely blocked by chronic renal denerva-
tion (Mühlbauer et al., 1997b). Thus, activation of a dopami-
nergic mechanism by AA infusion might modulate GFR via
the neuronal route. Because renal nerves contain both affer-
ent and efferent nerve fibers the exact site of action of the
proposed neuronal D2 mechanism needs further investiga-
tion.

Urinary dopamine excretion has been described to rise
after protein intake (Williams et al., 1986; Kaufman et al.,
1989) and AA load (Mühlbauer et al., 1997a). Renal dopa-
mine is mainly formed in the cells of the proximal tubules
from filtered L-DOPA by L-amino acid decarboxylase (Hay-
ashi et al., 1990). Only the catecholamine precursors,
L-tyrosine and L-phenylalanine, are responsible for the AA-
induced increase in urinary dopamine excretion (Mühlbauer
et al., 1997a). In our experiments, urinary dopamine was
elevated during infusion of AA which contained the catechol-
amine precursors but was unaffected by the d2 receptor
antagonists. However, because the latter affected the AA-
induced hyperfiltration the response of urinary dopamine
excretion and of GFR to AA appears to be dissociated. This
observation is in correspondence with a previous study (Mühl-
bauer et al., 1997b), in which systemic AA elevated GFR and
renal dopamine excretion simultaneously; however, if
L-tyrosine was omitted from the AA solution, urinary dopa-
mine remained at baseline despite the increase in filtration
rate. The enhancement of GFR by QP without affecting urin-
ary dopamine as observed in our study further argues
against the idea that dopamine released into the tubular lumen
might influence renal hemodynamics. However, urin-
ary excretion of dopamine does not reflect its potential
release at other intrarenal sites than the tubular lumen.
Thus, an additional paracrine action of dopamine cannot be
excluded. As for the gross release of dopamine into the prox-
imal tubule, a role in the regulation of renal hemodynamics
appears unlikely.

We conclude that, in the anesthetized rat, dopamine D2
receptors are involved in the AA-induced glomerular hyper-
filtration. Both central and peripheral dopamine receptors
appear to contribute to this renal response whereas dopa-
mine excreted into the urine does not seem to play a func-
tional role.
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References


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