Modulation of White Adipose Tissue Lipolysis by Nitric Oxide*

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In isolated adipocytes, the nitrosothiols S-nitroso-N-acetyl-penicillamine (SNAP) and S-nitrosoglutathione stimulate basal lipolysis, whereas the nitric oxide (NO) donor 1-propamine, 3-(2-hydroxy-2-nitroso-1-propylhydrazine) (PAPA-NONOate) or NO gas have no effect. The increase in basal lipolysis due to nitrosothiols was prevented by dithiothreitol but not by a guanulate cyclase inhibitor. In addition the cyclic GMP-inhibited low Km, cyclic AMP phosphodiesterase activity was inhibited by SNAP suggesting that SNAP acting as NO donor increases basal lipolysis through a S-nitrosylation mediated inhibition of phosphodiesterase. Contrasting with these findings, SNAP reduced both isoproterenol-stimulated lipolysis and cyclic AMP production, whereas it failed to modify forskolin-, dibutyryl cyclic AMP-, or isobutylmethylxanthine-stimulated lipolysis, suggesting that SNAP interferes with the β-adrenergic signal transduction pathway upstream the adenylate cyclase. In contrast with SNAP, PAPA-NONOate or NO gas inhibited stimulated lipolysis whatever the stimulating agents used without altering cyclic AMP production. Moreover PAPA-NONOate slightly reduces (30%) the hormone-sensitive lipase (HSL) activity indicating that stimulated lipolysis inhibition by NO is linked to both inhibition of the HSL activity and the cyclic AMP-dependent activation of HSL. These data suggest that NO or related redox species like NO+/NO– are potential regulators of lipolysis through distinct mechanisms.

Nitric oxide (NO)† has emerged as a chemical messenger in several biological systems. This molecule, which is the smallest biological signal known in mammalian cells, can control vital functions such as neurotransmission and blood vessel tone as well as host defense and immunity (1, 2). Some of the effects due to NO are elicited through the activation of soluble guanylate cyclase, leading to an increase in intracellular cyclic GMP content (3). In addition NO and NO-related species interact with redox metal-containing proteins and/or with thiol groups of proteins (4). It has been suggested that S-nitrosylation of proteins could mediate signaling functions and that thiols may be involved in the stabilization and metabolism of NO (5, 6).

NO is synthesized via l-arginine oxidation by a family of nitric oxide synthase isofoms (NOS). NOS are either constitutively expressed and calcium/calmodulin-dependent (NOS I and NOS III were originally described in neuronal tissue and endothelial cells, respectively) or inducible and almost calcium/calmodulin-independent (NOS II was originally identified in macrophages) (7). We have recently shown that white adipose tissue expresses the NOS II and NOS III isofoms (8). The constitutive expression of NOS II in this tissue can be related to the fact that tumor necrosis factor α is expressed and secreted by adipose tissue, which is an important target of this cytokine (9). Indeed tumor necrosis factor α was reported to decrease lipoprotein lipase activity and expression (10, 11) and to stimulate lipolysis in white adipocytes (10, 12, 13). However, the role of NO in these cells is so far unknown. Because of the stimulatory effect of tumor necrosis factor α on both NOS II and lipolysis, a role for NO as a putative regulatory signal controlling lipolysis is questionable.

The purpose of this study was to test this hypothesis by investigating the influence of NO itself and different NO donors of various reactive nitrogen intermediates on lipolysis in rat fat cells. The donors tested were (i) two nitrosothiols, S-nitroso-N-acetyl-thiopenicillamine (SNAP) and S-nitrosoglutathione (GS-NO) that are described as performing protein S-nitrosylation through the NO+ properties of their NO group (14) and (ii) one compound belonging to the NONOate family, PAPA-NONOate, that generates NO (15). The rate-limiting step of adipocyte lipolysis is the hydrolysis of triacyl glycerol by the hormone-sensitive lipase (HSL). The main mechanism involves phosphorylation of the HSL by protein kinase A. Therefore, hormones that affect cyclic AMP levels modulate lipolysis. The stimulatory effect of catecholamines on lipolysis is connected to the β-adrenergic receptor-controlled increment of intracellular cyclic AMP concentrations. In the present study we report the effect of NO and related species on basal lipolysis as well as on stimulated lipolysis by isoproterenol or agents acting on cyclic AMP levels.

Here, we provide clear evidence that NO modulates lipolysis through different mechanisms that appear dependent on the redox forms of NO.

EXPERIMENTAL PROCEDURES

Materials—S-nitroso-N-acetyl-thiopenicillamine (SNAP), S-nitrosoglutathione (GS-NO), 2-(4-carboxyphenyl)-4,4,5,5-tetramethylimidazoline-1-oxyl-3-oxide (carboxy-PTIO), 1-propamine,3-(2-hydroxy-2-nitroso-1-propylhydrazine) (PAPA-NONOate) were purchased from Cayman (SPI-Bio, France); 1H(1,2,4)oxadiazolo-(4,3-a)quinoxalin-1-one (ODQ) was purchased from Alexis Corp. (Coger, France). Dibutyryl cyclic

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‡ The abbreviations used are: NO, nitric oxide; NOS, nitric oxide synthase; SNAP, S-nitroso-N-acetyl-thiopenicillamine; GS-NO, S-nitrosothiol; NO, S-nitrosoglutathione; DTTP, dithiothreitol; ODQ, 1H(1,2,4)oxadiazolo-(4,3-a)quinoxalin-1-one; PAPA-NONOate, 1-propamine, 3-(2-hydroxy-2-nitroso-1-propylhydrazine); ISO, (-)-isoproterenol; carboxy-PTIO, 2-(4-carboxyphenyl)-4,4,5,5-tetramethylimidazoline-1-oxyl-3-oxide; TES, N-tris(hydroxymethyl)methyl-2-aminoethanesulfonic acid; IBMX, 3-isobutyl-1-methylxanthine; PDE, phosphodiesterase; cG-PDE, cyclic GMP-inhibited low Km, cyclic AMP PDE; HSL, hormone-sensitive lipase; KRT, Krebs-Ringer-Tris buffer.
AMP, forskolin, 3-isobutyl-1-methylxanthine (IBMX), isoproterenol bitartrate salt, bovine serum albumin fraction V (free fatty acid), dithiothreitol (DTT), gum arabic, and snake venom were obtained from Sigma (France). Adenosine deaminase and glicerol kit assay were purchased from Boehringer Mannheim (France). Radiochemical binding assay kit for cyclic AMP (TRK-432), [³H]cyclic adenosine monophosphate NH₄ salt, glicerol tri[¹⁴C]oleate, [¹⁴C]oleic acid were purchased from Amersham International (France). Collagenase type I (267 units/mg) was obtained from Worthington and AG1-X2 resin from Bio-Rad.

**Preparation of Isolated Adipocytes**—Male Sprague-Dawley rats (240–250 g), fed ad libitum, were killed by decapitation and epididymal fat pads were removed for adipocyte isolation. According to a modification (16) of the method of Rodbell (17), 1 g of adipose tissue was digested in a plastic vial with 5 ml of Krebs-Ringer-Tris buffer (pH 7.4) (KRT) containing 1% (w/v) bovine serum albumin. After 15 min at 37 °C under constant shaking, cells were dispersed and filtered through a nylon mesh and washed four times with KRT containing 0.2 ml of enzyme preparation and 2 mg of collagenase/ml. After 15 min at 37 °C under constant shaking, cells were aspirated, and glycerol release was determined with an enzymatic method according to the procedure of Khoo and Steinberg (19). Fat pads of fasted rats were homogenized in buffer containing 0.25 mM sucrose, 1 mM EDTA, and 10 mM Tris/HC1 buffer, pH 7.4 (1 g/2.5 vol). The fat cake was discarded by slow centrifugation and the resulting infranatant was recentrifuged at 20,000 × g for 20 min. The supernatant was used for HSL activity determination. The assays were conducted as follows: each vial contained 0.2 ml of enzyme preparation and 0.4 ml of substrate emulsion consisting of glicerol tri[¹⁴C]oleate (specific activity 50 mCi/mmol) and unlabeled triolein (1.04 μmol), 20 mg of bovine serum albumin, 5 mg of arabic gum, all in 50 mM sodium phosphate buffer, pH 6.8. Incubations were performed for 30 min at 37 °C and released (1.14C)oleic acid was measured by the method of Belfrage and Vaughan (20). Recovery of the extraction procedure was tested with [14C]oleic acid alone and was about 80%. HSL activity was calculated as μmol of free fatty acid released per mg of protein per hour.

**Cyclic AMP Phosphodiesterase (PDE) Activity**—Isolated adipocytes were homogenized in buffer containing 20 mM Tris (pH 7.5), 1 mM EDTA, 0.25 mM sucrose, 2 mM benzanidine, and 0.1 mM phenylmethylsulfonyl fluoride. The fat cake was removed by centrifugation (3,000 × g). The infranatant was centrifuged at 48,000 × g for 30 min. The pellet was resuspended in 10 mM TES (pH 7.5), 5 mM MgCl₂, to yield a final protein concentration of 0.5 mg/ml. 20 μl of the resulting suspension was immediately used for cyclic AMP PDE assays as follows. The low Kₘ cyclic AMP PDE activity was determined at 30 °C during 10 min in the presence of 0.02 μM cyclic [³H]AMP, 0.5 μM cyclic AMP, 10 mM TES buffer (pH 7.5), 5 mM MgCl₂, 0.04% (w/v) bovine serum albumin and 0.5 units/ml adenosine deaminase, in a final volume of 100 μl (21). Incubations were stopped by a 1.5-min immersion in a boiling-water bath, followed by the addition of 50 μl of 2 mg/ml snake venom in 0.1 M Tris (pH 8) to each tube. After 10 min of incubation at 30 °C, reactions were achieved by a 1.5-min immersion in boiling water. 300 μl of 2.1 (v/v) H₂O/AG1-X2 resin were then added to each tube. The tubes were vigorously shaken for 5 min and centrifuged at 3,000 × g for 10 min. 100

**Figure 1.** Dose-dependent stimulatory effects of nitrosothiols on basal lipolysis. Isolated adipocytes were incubated in Krebs-Ringer-Tris buffer for 1 h with the indicated concentrations of SNAP with or without 200 μM carboxy-PTIO (A) or GS-NO (B). Lipolysis was measured as the amount of glycerol released to the incubation medium. Results are expressed as the percentage of basal lipolysis from nontreated adipocytes (control: A = 39 ± 7; B = 33 ± 9 nmol glycerol/10⁶ cells/h). Lipolysis was measured as the percentage of basal lipolysis from nontreated adipocytes (control: A = 39 ± 7; B = 33 ± 9 nmol glycerol/10⁶ cells/h) and are means ± S.E. of separate experiments performed in duplicate. Statistical comparisons were made by the paired Student’s t test. † p < 0.01 versus control; ‡ p < 0.01 versus SNAP. HSL Assay—HSL activity was performed according to a modification of the procedure of Kho and Steinberg (19). Fat pads of fasted rats were homogenized in buffer containing 0.25 mM sucrose, 1 mM EDTA, and 10 mM Tris/HCl buffer, pH 7.4 (1 g/2.5 vol). The fat cake was discarded by slow centrifugation and the resulting infranatant was recentrifuged at 20,000 × g for 20 min. The supernatant was used for HSL activity determination. The assays were conducted as follows: each vial contained 0.2 ml of enzyme preparation and 0.6 ml of substrate emulsion consisting of glicerol tri[¹⁴C]oleate (specific activity 50 mCi/mmol) and unlabeled triolein (1.04 μmol), 20 mg of bovine serum albumin, 5 mg of arabic gum, all in 50 mM sodium phosphate buffer, pH 6.8. Incubations were performed for 30 min at 37 °C and released (1.14C)oleic acid was measured by the method of Belfrage and Vaughan (20). Recovery of the extraction procedure was tested with [14C]oleic acid alone and was about 80%. HSL activity was calculated as μmol of free fatty acid released per mg of protein per hour.
mL of the supernatant were removed and counted. Blank values obtained from tubes incubated with boiled cells were subtracted.

Preparation of NO Solutions—NO solutions were prepared by bubbling N₂ through KRT buffer to remove O₂. NO gas was then bubbled in this buffer for 30 min to saturate the solution. NO concentration was determined by spectrophotometric assay using oxyhemoglobin (22). Aliquots of the NO solution were added to the incubation medium of adipocytes used for the determination of lipolysis.

Other Determinations—Protein concentrations were determined according to the method of Bradford (23) and cell numbers were calculated according to Hirsh and Gallian (24). All results were expressed as the mean ± S.E. Comparisons between groups were made using paired Student’s t test.

RESULTS

Effects of NO Donors on Basal Lipolysis—To evaluate the effect of NO or NO-related species on basal lipolysis, isolated adipocytes were incubated in the presence of different chemical NO donors. In a dose-dependent manner, the nitrosothiols, SNAP and GS-NO, produced an increase in glycerol release (Fig. 1). This effect was reversed when adipocytes were exposed to the NO scavenger carboxy-PTIO (200 μM) (25) (Fig. 1A), suggesting that the lipolytic effects due to this nitrosothiol are linked to NO generation. In contrast, adipocyte exposure to another NO donor (PAPA-NONOate) or to NO gas (10–500 μM) failed to elicit any significant effect on the basal lipolytic activity (Fig. 2, A and B). Thus NO only generated from nitrosothiols appears to be an activator of basal lipolysis.

To determine whether cyclic GMP plays any role in the lipolytic response of adipocytes to nitrosothiols, we tested the effect of ODQ, a potent and specific inhibitor of soluble guanylate cyclase (26). As shown in Fig. 3, a 15-min pretreatment of the fat cells by 100 μM ODQ did not prevent the increased lipolysis due to SNAP.
lipolysis induced by 0.5–2 mM SNAP, suggesting that the lipolytic effect of nitrosothiols is cyclic GMP-independent.

The nitrosothiol effect on basal lipolysis could be mediated through direct redox and/or S-nitrosylation reactions at a "redox switch(es)" containing critical thiol groups. To test this hypothesis, we examined the effect of DTT (0.5 mM), a thiol-reducing agent that is also able to modify the redox form of NO, on forskolin- and IBMX-stimulated lipolysis. Surprisingly, the antilipolytic effect elicited by 2 mM SNAP was not prevented by addition of 0.5 mM DTT or 100 μM ODQ (Fig. 5). Using GS-NO as another NO donor, the same results were observed (data not shown). Together, these results strongly suggest that the SNAP inhibitory effect toward catecholamine-stimulated lipolysis mainly results from the interaction of SNAP with the β-adrenergic receptors and/or the Gs protein.

Effects of PAPA-NONOate—The influence of PAPA-NONOate was also studied on lipolysis stimulated by agents acting at different steps of the lipolytic cascade. As shown in Fig. 7, an important inhibitory effect of this NO donor was observed not only on lipolysis stimulated by isoproterenol but, in contrast with SNAP, on forskolin-, dibutyryl cyclic AMP-, or IBMX-stimulated responses as well. The cyclic AMP response induced by isoproterenol was significantly modified by SNAP (Fig. 6) as was the cyclic AMP response to 10 μM forskolin (Table II). Taken altogether, these results strongly suggest that the SNAP inhibitory effect toward catecholamine-stimulated lipolysis mainly results from the interaction of SNAP with the β-adrenergic receptors and/or the Gs protein.

The cyclic AMP phosphodiesterase activity, measured as described under "Experimental Procedures," was investigated. Table I shows that SNAP when used at concentrations activating lipolysis inhibits cGMP-PDE activity, contrary to PAPA-NONOate, which was without any effect. These findings led us to study the effect of SNAP on cyclic AMP production in the presence of IBMX, an inhibitor of PDE, to mask the potential inhibitory effect of SNAP on PDE. Under these conditions, we failed to observe any modification of cyclic AMP production in response to 0.5–2 mM SNAP (data not shown). Altogether, these results indicate that the increased basal lipolytic activity observed with nitrosothiols is likely due to the inhibition of PDE.

**Effects of NO Donors and Authentic NO on Stimulated Lipolysis**—Lipolysis was stimulated using different agents acting: (i) at the β-adrenergic receptor level (isoproterenol); (ii) at the adenylate cyclase level (forskolin); (iii) at the PDE level (isobutylmethylxanthine); (iv) or at the protein kinase level (dibutyryl-cyclic AMP). The influence of PAPA-NONOate was also studied on lipolysis stimulated by agents acting at different steps of the lipolytic cascade. As shown in Fig. 7, an important inhibitory effect of this NO donor was observed not only on lipolysis stimulated by isoproterenol but, in contrast with SNAP, on forskolin-, dibutyryl cyclic AMP-, or IBMX-stimulated responses as well. The cyclic AMP response induced by isoproterenol was significantly modified by SNAP (Fig. 6) as was the cyclic AMP response to 10 μM forskolin (Table II). Taken altogether, these results strongly suggest that the SNAP inhibitory effect toward catecholamine-stimulated lipolysis mainly results from the interaction of SNAP with the β-adrenergic receptors and/or the Gs protein.

**Effects of Nitrosothiols**—As shown in Fig. 5 and contrasting with the above described data, SNAP decreased isoproterenol-stimulated lipolysis. Surprisingly, the antilipolytic effect elicited by 2 mM SNAP was not prevented by addition of 0.5 mM DTT or 100 μM ODQ (Fig. 5). Using GS-NO as another NO donor, the same results were observed (data not shown). SNAP also decreased the magnitude of the isoproterenol-stimulated cyclic AMP response (Table II). However, lipolysis stimulated by 1 mM dibutyryl-cyclic AMP, 0.1 mM IBMX or 10 μM forskolin were not significantly modified by SNAP (Fig. 6) as was the cyclic AMP response to 10 μM forskolin (Table II). Taken altogether, these results strongly suggest that the SNAP inhibitory effect toward catecholamine-stimulated lipolysis mainly results from the interaction of SNAP with the β-adrenergic receptors and/or the Gs protein.
plus PAPA-NONOate treated adipocytes, respectively). To further establish the mechanism of the antilipolytic effect of PAPA-NONOate, we studied the HSL activity in adipose tissue homogenates. As shown in Table IV, PAPA-NONOate decreased by about 30% HSL activity, whatever the dose of PAPA-NONOate used, an effect which was prevented by 200 μM carboxy-PTIO, a NO scavenger.

**DISCUSSION**

In this study we provide the first evidence for a modulation of the lipolytic process in isolated adipocytes by NO donors and NO gas. Our results also indicate that there are at least two opposite effects of NO-related species in the control of lipolysis. Among the NO donors tested, only nitrosothiols were found to
dependently inhibits stimulated lipolysis whatever the stimulating agent used.
increase the rate of basal lipolysis through a mechanism apparently unrelated to cyclic GMP. Since the NO group of RS-NO has properties that enable S-nitrosylation of proteins (6, 14) one likely mechanism explaining the stimulatory effect of RS-NO on basal lipolysis could be the S-nitrosylation of SH group(s) belonging to critical protein(s) for lipolysis. Such a critical role for thiol has been previously emphasized from the observation that exposure of adipose tissue to N-ethylmaleimide (an irreversible thiol alkylating agent) results in a stimulation of basal lipolysis as well (32). As nitrosothiols are cell impermeables (27), interaction of nitrosothiols with extracellular or membraneous redox switch is likely. The particulate cGMP-PDE, containing critical thiol (31), appears to be the target of SNAP as we have observed an inhibitory effect of this enzyme activity by this nitrosothiol. Our present experiment showing that the SNAP-induced stimulation of basal lipolysis was prevented by DTT (thiol-reducing agent) adds further weight to the hypothesis.

It has been shown that addition of DTT (a 1–4 dithiol) to solution of nitrosothiol accelerates the nitrosothiol decomposition into hydroxylamine (NH₂OH) (14). This production of NH₂OH was attributed to a nitrosation of DTT via transnitrosation followed by formation of nitroxy anion (NO⁻) and disulfide (14). Thus DTT is able to modify the redox form of NO generated from nitrosothiols. From this finding and the results of the present study it can be concluded that NO⁺ donors increase basal lipolysis, whereas NO⁻ generated from SNAP in the presence of DTT or NO⁻ formed from NONOates and authentic NO have no influence on basal lipolysis.

Whereas SNAP increases basal lipolysis, it markedly reduced isoproterenol-stimulated lipolysis. This effect seems to be linked to the decrease in cyclic AMP production observed in isoproterenol-treated adipocytes after exposure to SNAP. A direct effect of SNAP on adenylate cyclase appears unlikely since SNAP failed to decrease the forskolin-induced lipolysis. Moreover, the production of cyclic AMP was unchanged under these conditions. These results are consistent with an interaction of SNAP with the early steps of the signal transduction pathway of isoproterenol i.e. the lipolytic β-adrenergic receptor and/or the Gs coupling protein but not with the adenylate cyclase. It is expected that S-nitrosylation or disulfide forma-

![Fig. 7. PAPA-NONOate decreases isoproterenol-, forskolin-, dibutyryl cyclic AMP-, and IBMX-stimulated lipolysis. Isolated adipocytes were incubated with increasing concentrations of PAPA-NONOate in the presence of 1 μM isoproterenol or 10 μM forskolin. Numbers in parentheses refer to the values obtained in PAPA-NONOate-exposed adipocytes and expressed as percentages of the control values. Results are expressed as mean ± S.E. of three separate experiments performed in duplicate.](image)

**Table III**

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<tr>
<th>Effector</th>
<th>cyclic AMP (pmol/mg protein/15 min)</th>
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<tr>
<td></td>
<td>Control</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
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<tr>
<td>Isoproterenol</td>
<td>162 ± 16</td>
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<tr>
<td>Forskolin</td>
<td>388 ± 92</td>
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![Fig. 8. Authentic NO solutions decrease dramatically isoproterenol-, forskolin-, or dibutyryl cyclic AMP-stimulated lipolysis. Isolated adipocytes were incubated in Krebs-Ringer-Tris buffer for 1 h in the presence of the indicated lipolytic agents with increased concentrations of NO gas from a saturated buffer solution. Lipolysis is expressed as pmol of glycerol/10⁶ cells/h. Results are means ± S.E. of three separate experiments performed in duplicate. Statistical comparisons were made by the paired Student’s t test. *p < 0.01, **p < 0.001 versus the indicated lipolytic agent.](image)

**Table IV**

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<th>Hormone Sensitive Lipase Activity</th>
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<tr>
<td>PAPA-NONOate (mM)</td>
<td>Control</td>
</tr>
<tr>
<td>Adipose tissue homogenates</td>
<td>100 ± 17</td>
</tr>
</tbody>
</table>

![Table showing the effects of PAPA-NONOate on hormone-sensitive lipase activity in adipose tissue homogenates.](image)
tion occurred on the β-receptor since this receptor contains key cysteines implicated in the hormone signal transduction process (33). Additional effects of SNAP on G proteins could be also suggested as G proteins have been shown to be targets of NO in human lymphocytes (34). Moreover, DTT failed to prevent SNAP inhibition, a finding which indicates that both NO+ (in the absence of DTT) and NO− (in the presence of DTT) are able to inhibit isoproterenol-induced lipolysis. Inhibition of isoproterenol-stimulated lipolysis by SNAP could also be mediated by NO as the holomeric cleavage of the S-N bound of SNAP generates NO+ (14). This possibility seems to be ruled out, however, since NO donors like NONOates failed to alter isoproterenol-stimulated cyclic AMP production in adipocytes.

The mechanism(s) whereby NO (issue from authentic NO or NONOates) inhibits lipolysis clearly appears different from that underlying the antilipolytic effect of nitrosothiols, although both are cyclic GMP-independent. As the matter of fact, NO elicited a marked antilipolytic effect regardless of the stimulatory agent used and NO failed to reduce the cyclic AMP responses to isoproterenol or forskolin. Moreover, the marked inhibition induced by NO on dibutyryl cyclic AMP- or IBMX-stimulated lipolysis excludes the possibility that an activation of phosphodiesterases could be involved in the inhibitory mechanism of NO. A direct effect of NO on HSL activity can be suggested as PAPA-NONOate slightly decreased the HSL activity. It appears thus that NO probably interferes at the level of the HSL but also on the cyclic AMP-dependent activation of cyclic AMP-dependent protein kinase and/or on cyclic AMP-dependent protein kinase-dependent HSL phosphorylation by a mechanism that remains to be determined.

Under physiological conditions, NO can be interconverted among different redox forms with distinctive chemistries (4). The present results obtained with different NO donors suggest that the intracellular or extracellular redox states are important factors in determining the type of response of the lipolytic process to NO. An increase in basal lipolysis can be observed with nitrosothiols. Nitrosothiols do occur naturally in human plasma mainly as the nitrosothiol of human serum albumin (5). The formation of NO by the interaction of NO with nitrosothiols can provide a nonenzymatic source of NO in the body. A process to NO. An increase in basal lipolysis can be observed among different redox forms with distinctive chemistries (4).

In summary, we have identified a potentially important modulation of lipolysis by NO. Our findings indicate that NO activates or inhibits lipolysis through cyclic GMP-independent mechanisms that are tightly linked to the redox state of NO.

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