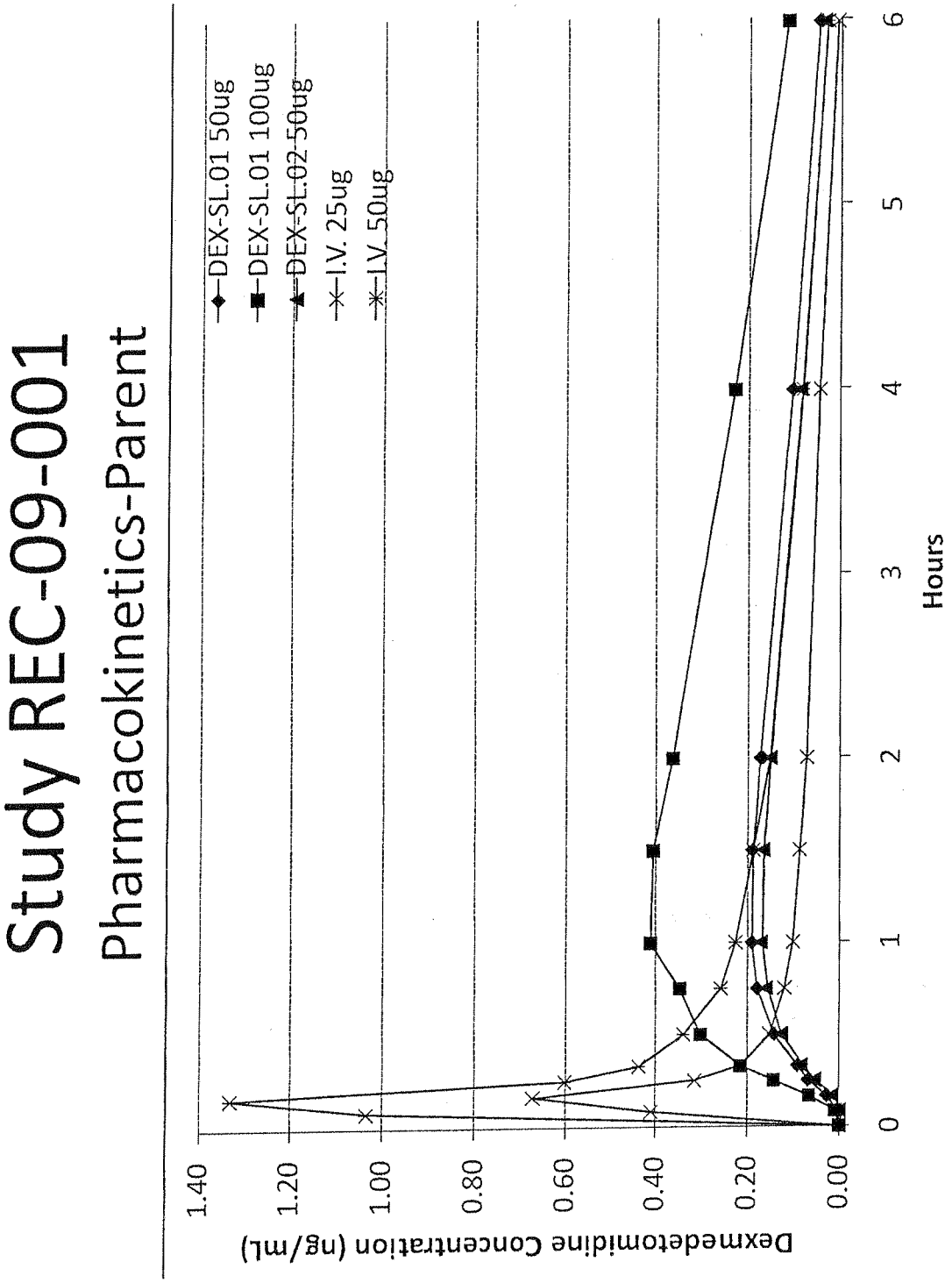

Study REC-09-001
Pharmacokinetics-Parent
DEX-SL.01 50ug
DEX-SL.01 100ug
DEX-SL.02 50ug
I.V. 25ug
I.V. 50ug
Dexmedetomidine Concentration (ng/mL)
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
0
1
2
3
4
5
6
Hours

Fig. 1

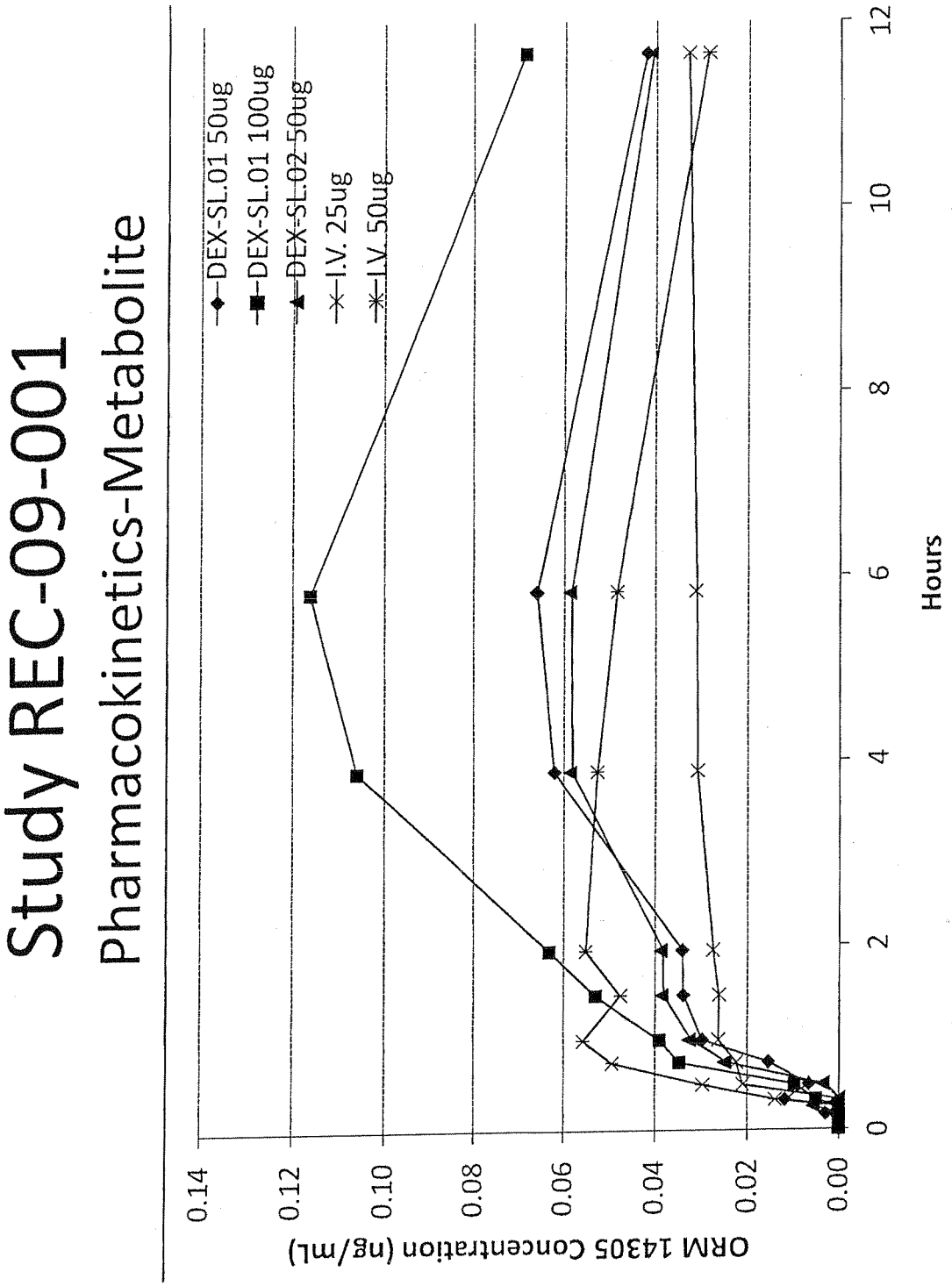

Study REC-09-001
Pharmacokinetics-Metabolite
DEX-SL.01 50ug
DEX-SL.01 100ug
DEX-SL.02 50ug
I.V. 25ug
I.V. 50ug
ORM 14305 Concentration (ng/mL)
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
0
2
4
6
8
10
12
Hours

Fig. 2

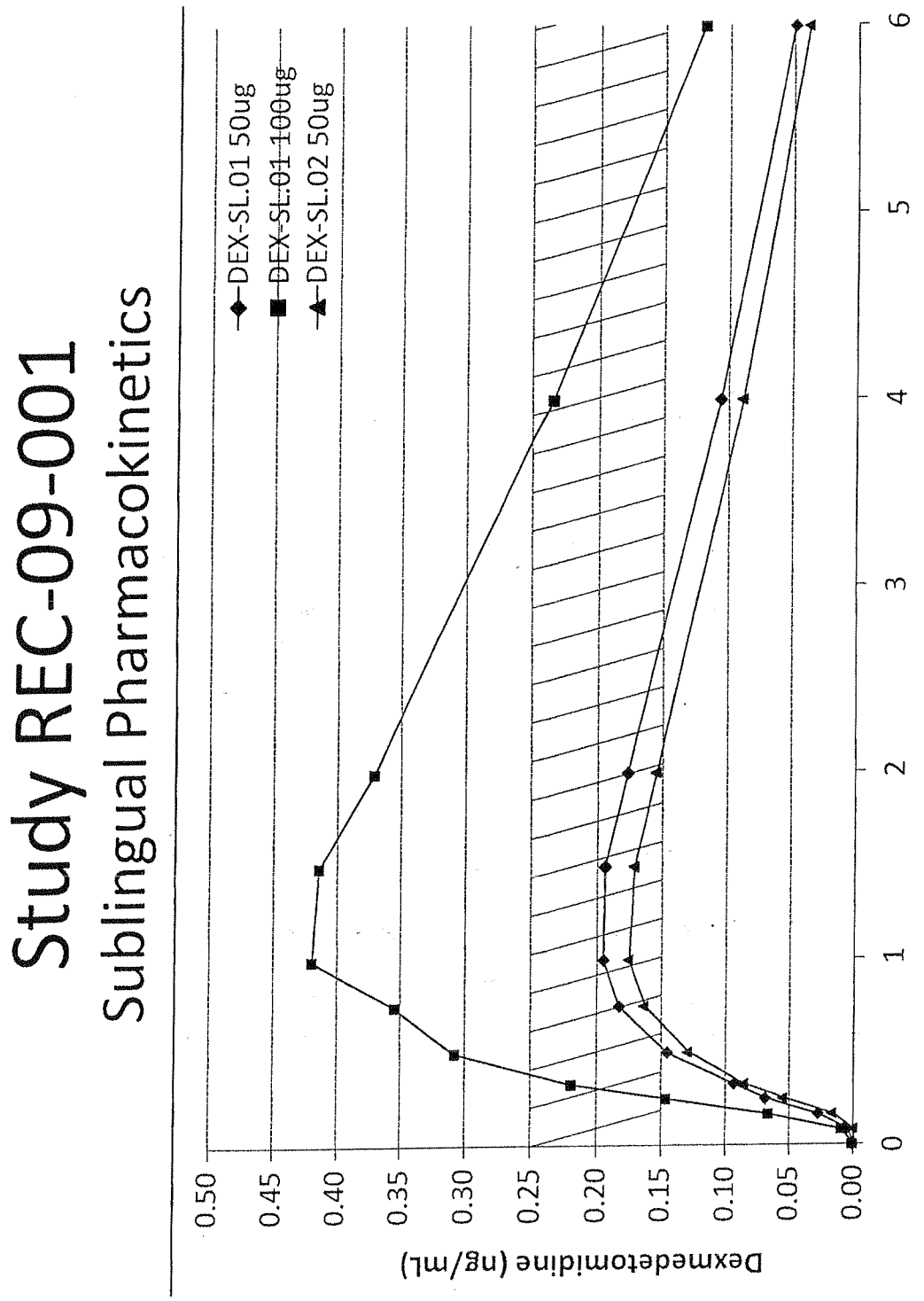

Study REC-09-001
Sublingual Pharmacokinetics
DEX-SL.01 50ug
DEX-SL.01 100ug
DEX-SL.02 50ug
Dexmedetomidine (ng/mL)
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
0
1
2
3
4
5
6
Hours

Fig. 3

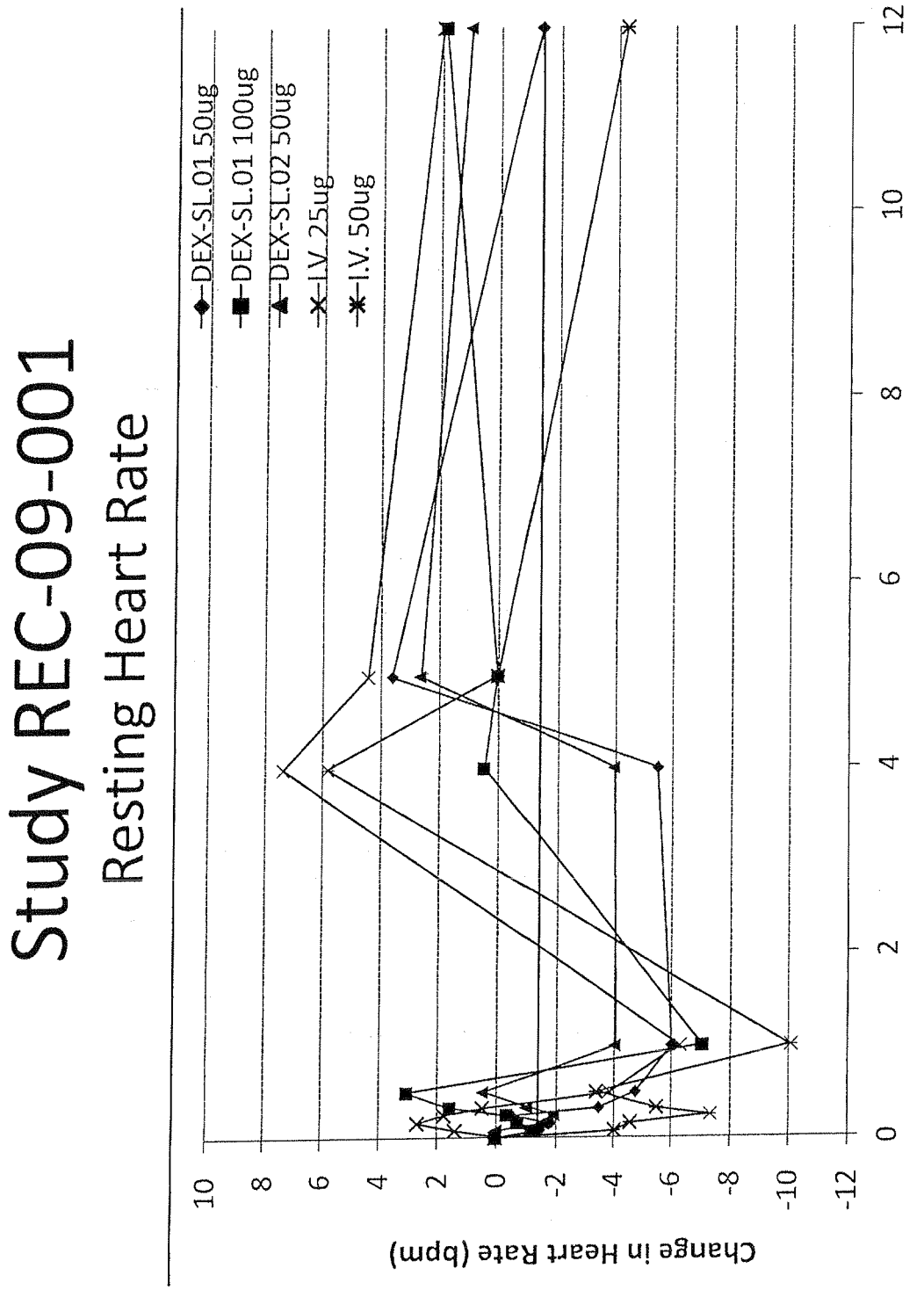

Study REC-09-001
Resting Heart Rate
DEX-SL.01 50ug
DEX-SL.01 100ug
DEX-SL.02 50ug
I.V. 25ug
I.V. 50ug
Change in Heart Rate (bpm)
10
8
6
4
2
0
-2
-4
-6
-8
-10
-12
0
2
4
6
8
10
12
Hours

Fig. 4

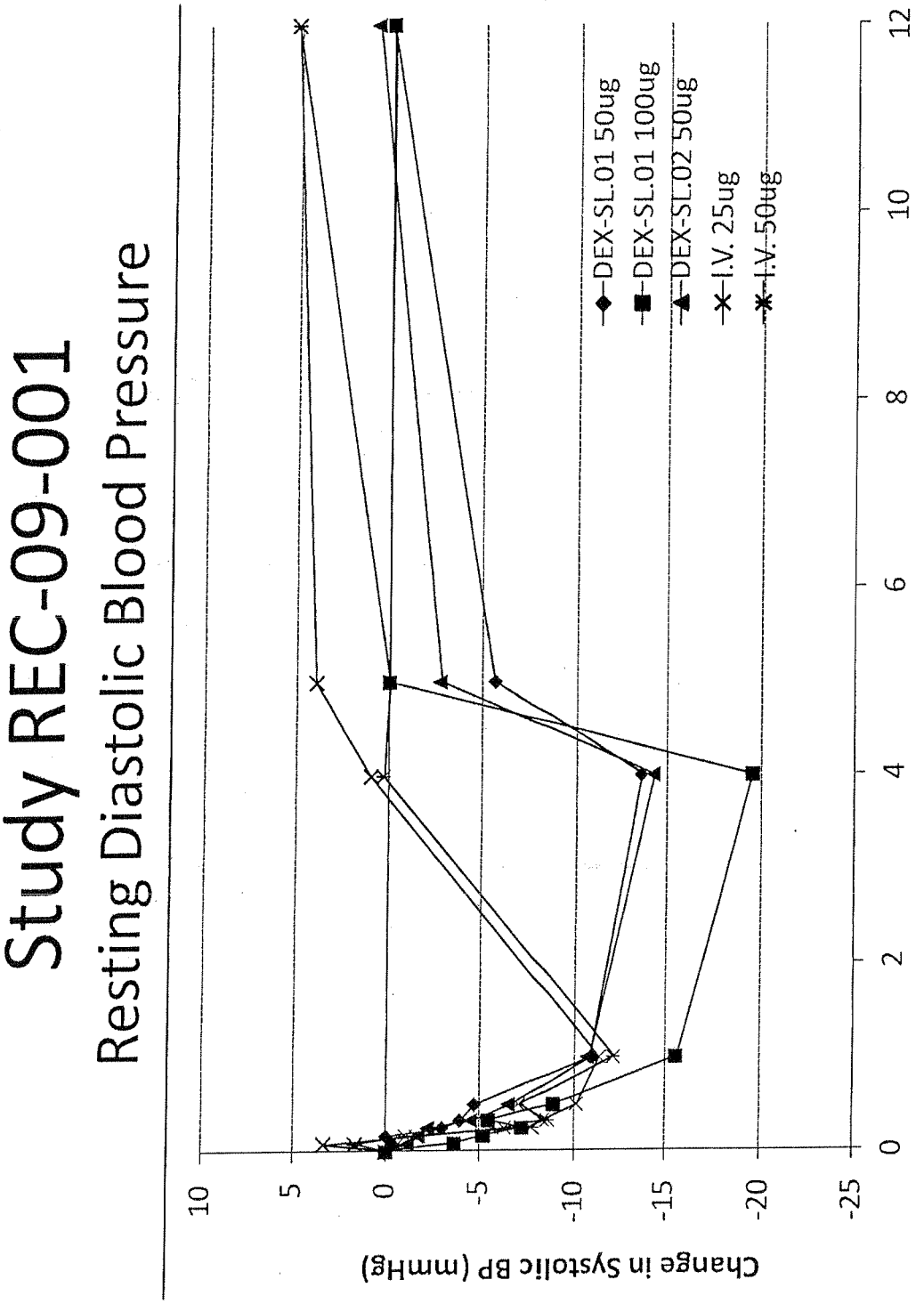

Study REC-09-001
Resting Diastolic Blood Pressure
Change in Systolic BP (mmHg)
10
5
0
-5
-10
-15
-20
-25
0
2
4
6
8
10
12
Hours
DEX-SL.01 50ug
DEX-SL.01 100ug
DEX-SL.02 50ug
I.V. 25ug
I.V. 50ug

Fig. 5

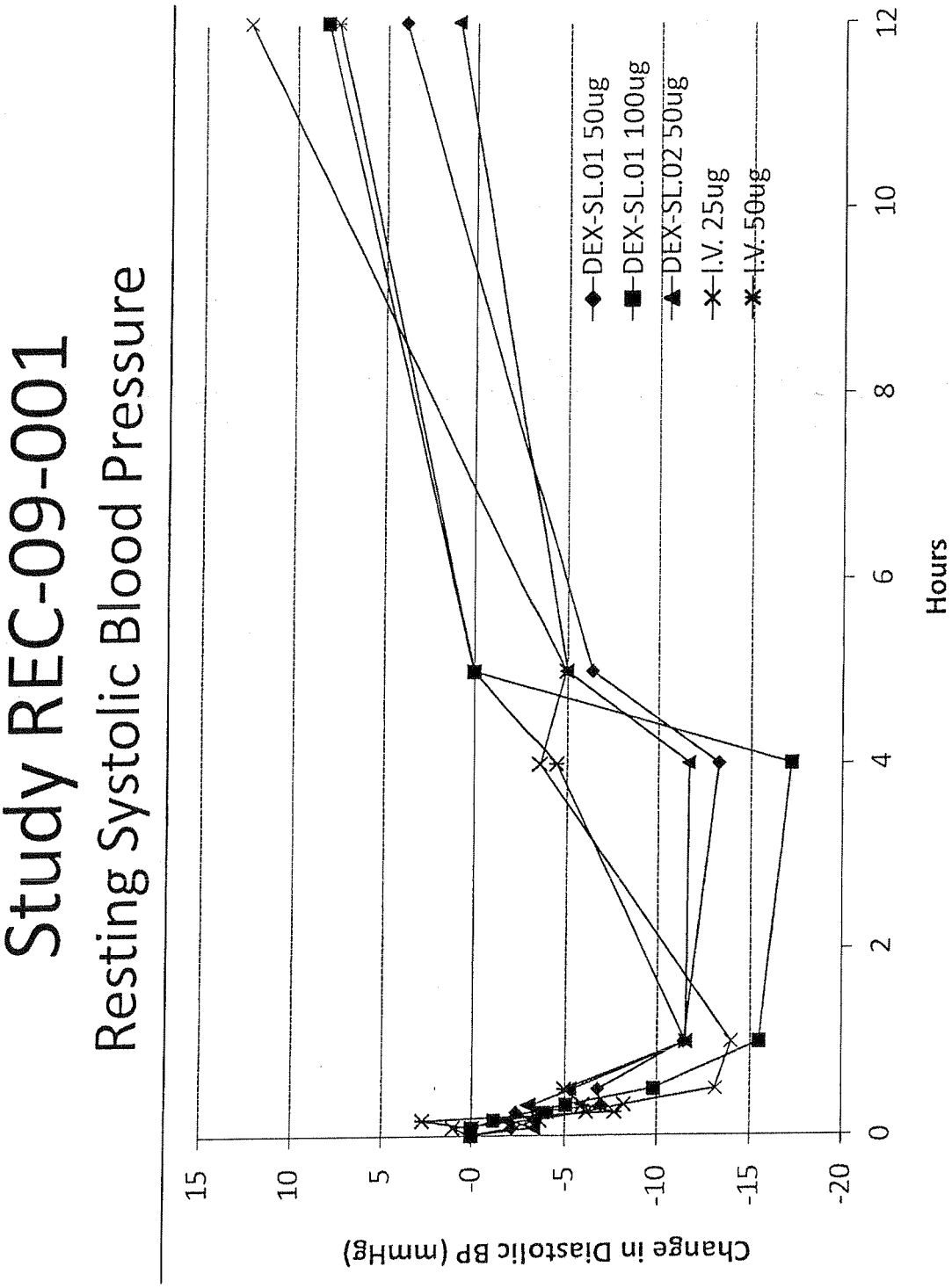

Study REC-09-001
Resting Systolic Blood Pressure
Change in Diastolic BP (mmHg)
15
10
5
-0
-5
-10
-15
-20
0
2
4
6
8
10
12
Hours
DEX-SL.01 50ug
DEX-SL.01 100ug
DEX-SL.02 50ug
I.V. 25ug
I.V. 50ug

Fig. 6

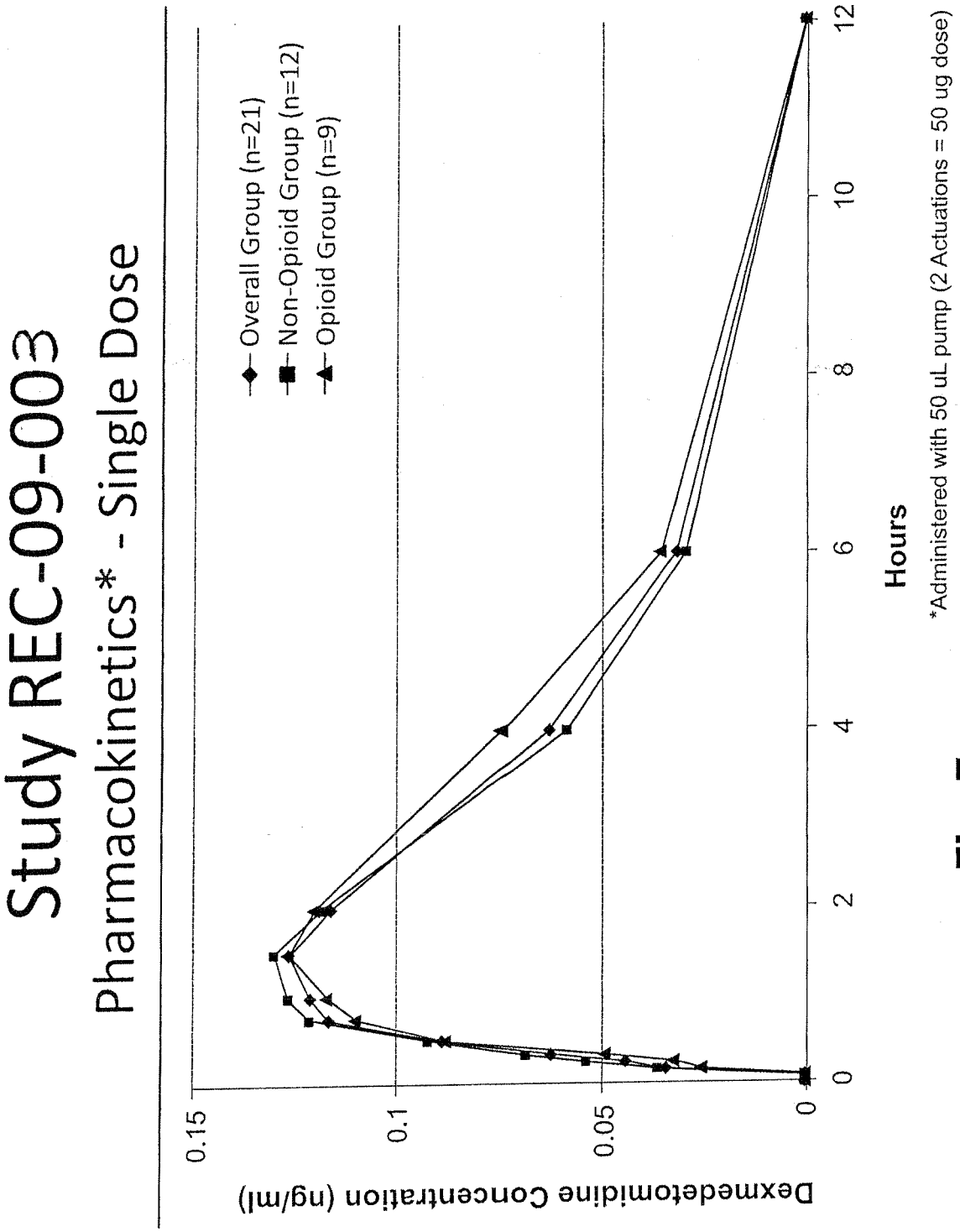

Study REC-09-003
Pharmacokinetics* - Single Dose
Overall Group (n=21)
Non-Opioid Group (n=12)
Opioid Group (n=9)
Dexmedetomidine Concentration (ng/ml)
0.15
0.1
0.05
0
0
2
4
6
8
10
12
Hours
*Administered with 50 uL pump (2 Actuations = 50 ug dose)

Fig. 7

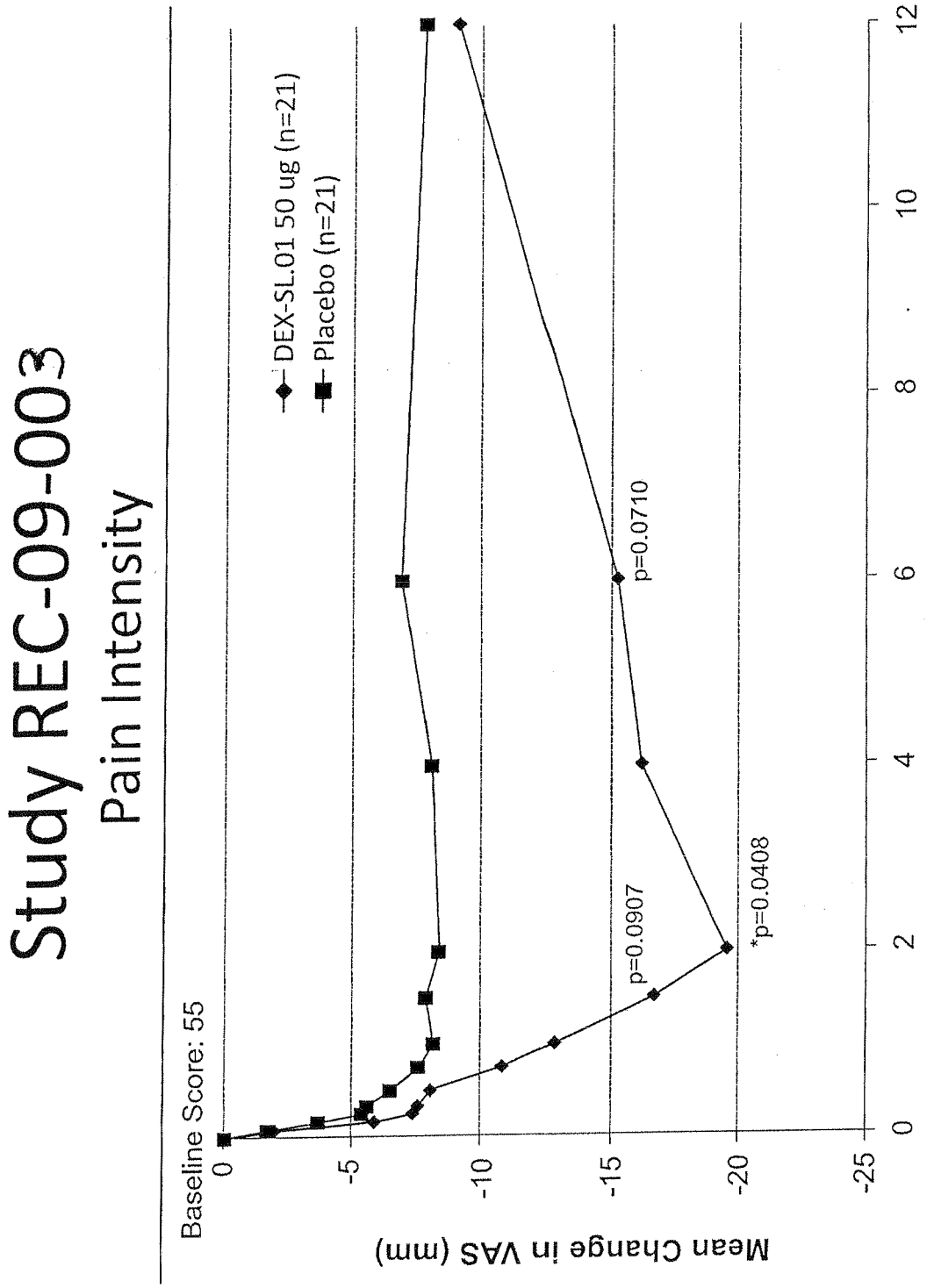
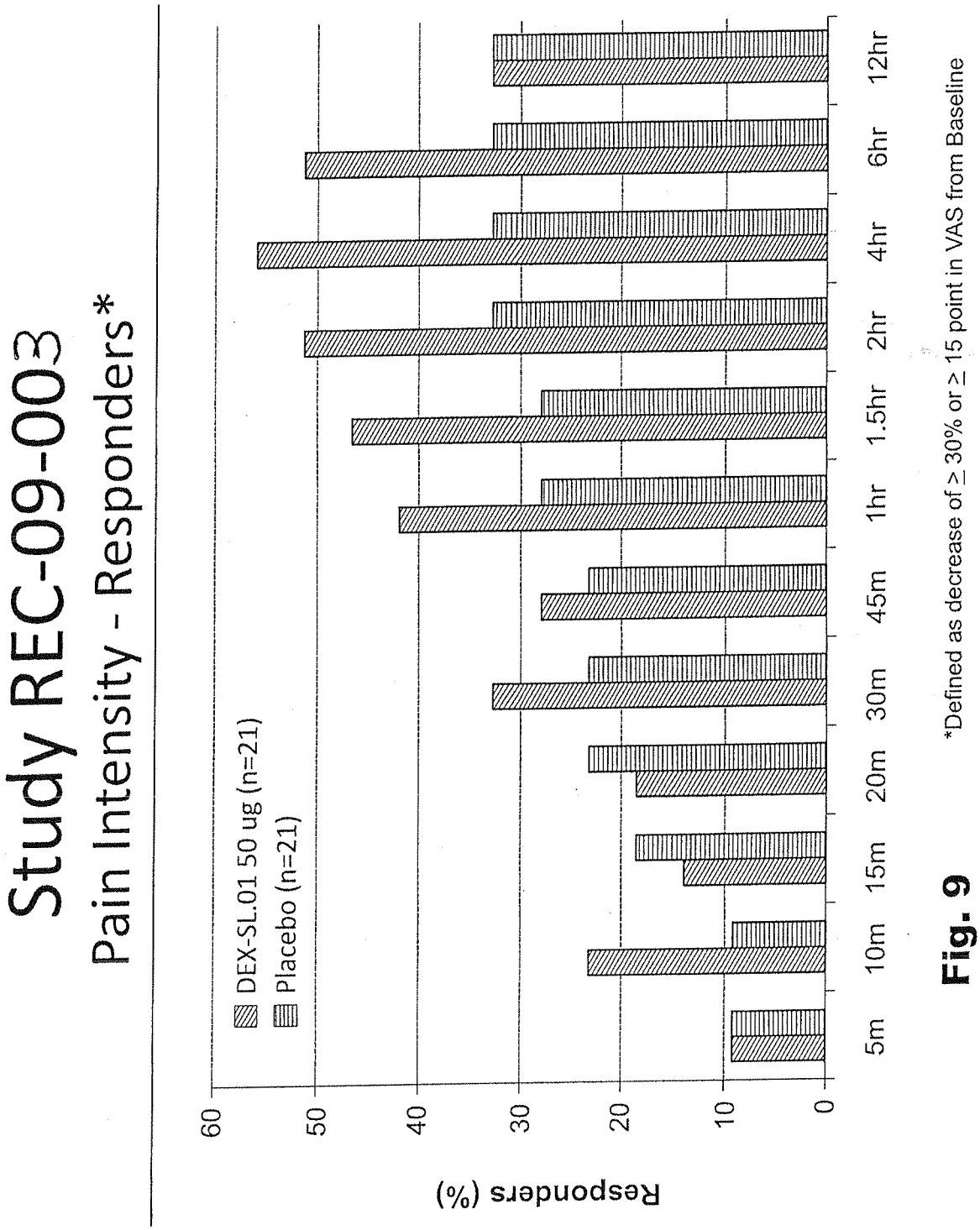

Study REC-09-003
Pain Intensity
Baseline Score: 55
DEX-SL.01 50 ug (n=21)
Placebo (n=21)
Mean Change in VAS (mm)
0
-5
-10
-15
-20
-25
0
2
4
6
8
10
12
Hours
p=0.0907
*p=0.0408
p=0.0710
Note: No difference in response between opioid and non-opioid groups

Fig. 8



*Defined as decrease of ≥ 30% or ≥ 15 point in VAS from Baseline

Fig. 9

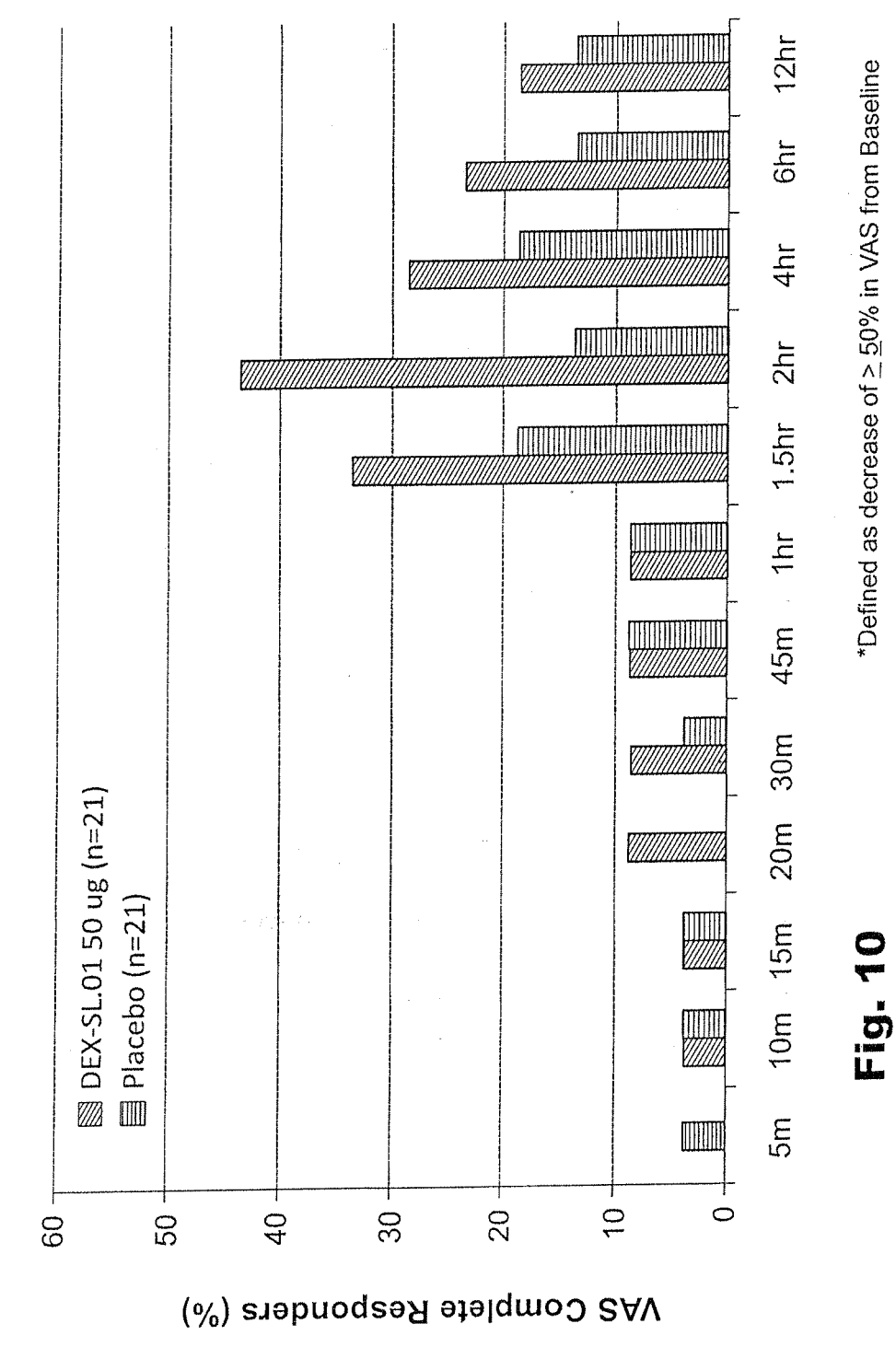
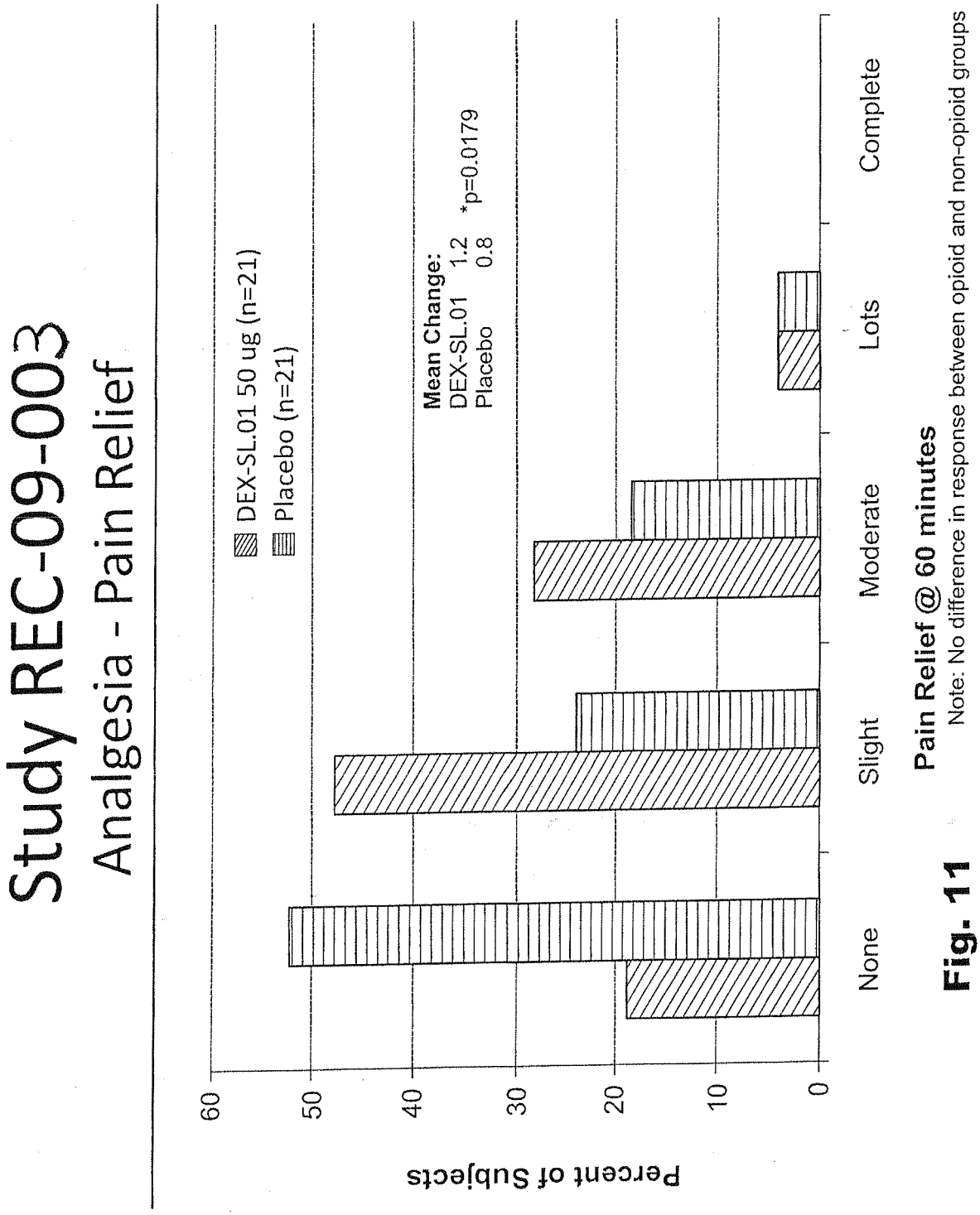

Study REC-09-003
Pain Intensity - Complete Responders*
DEX-SL.01 50 ug (n=21)
Placebo (n=21)
VAS Complete Responders (%)
0
10
20
30
40
50
60
5m
10m
15m
20m
30m
45m
1hr
1.5hr
2hr
4hr
6hr
12hr
*Defined as decrease of ≥ 50% in VAS from Baseline

Fig. 10



Note: No difference in response between opioid and non-opioid groups

Fig. 11

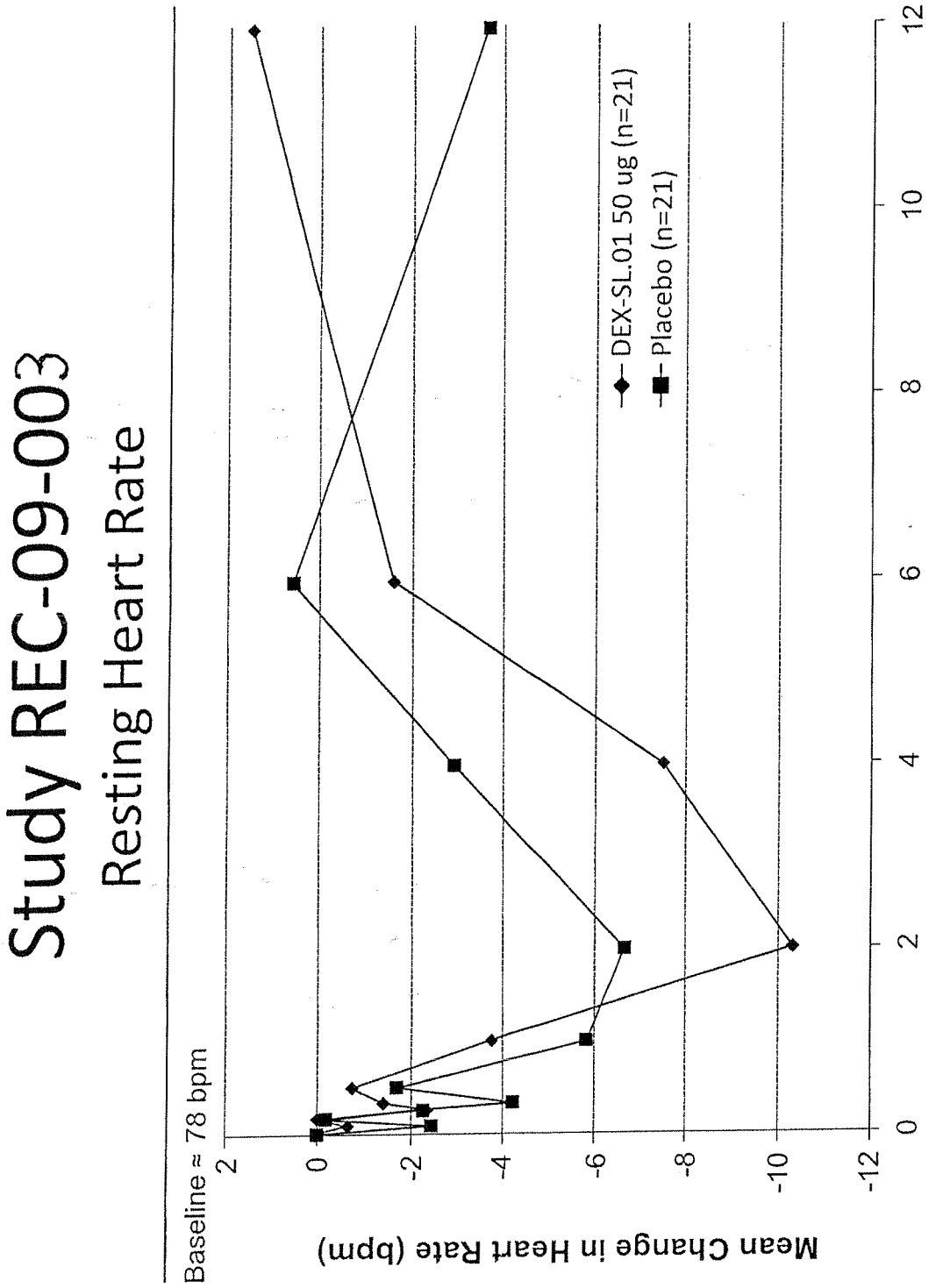

Study REC-09-003
Resting Heart Rate
Baseline ≈ 78 bpm
Mean Change in Heart Rate (bpm)
2
0
-2
-4
-6
-8
-10
-12
0
2
4
6
8
10
12
Hours
DEX-SL.01 50 ug (n=21)
Placebo (n=21)

Fig. 12

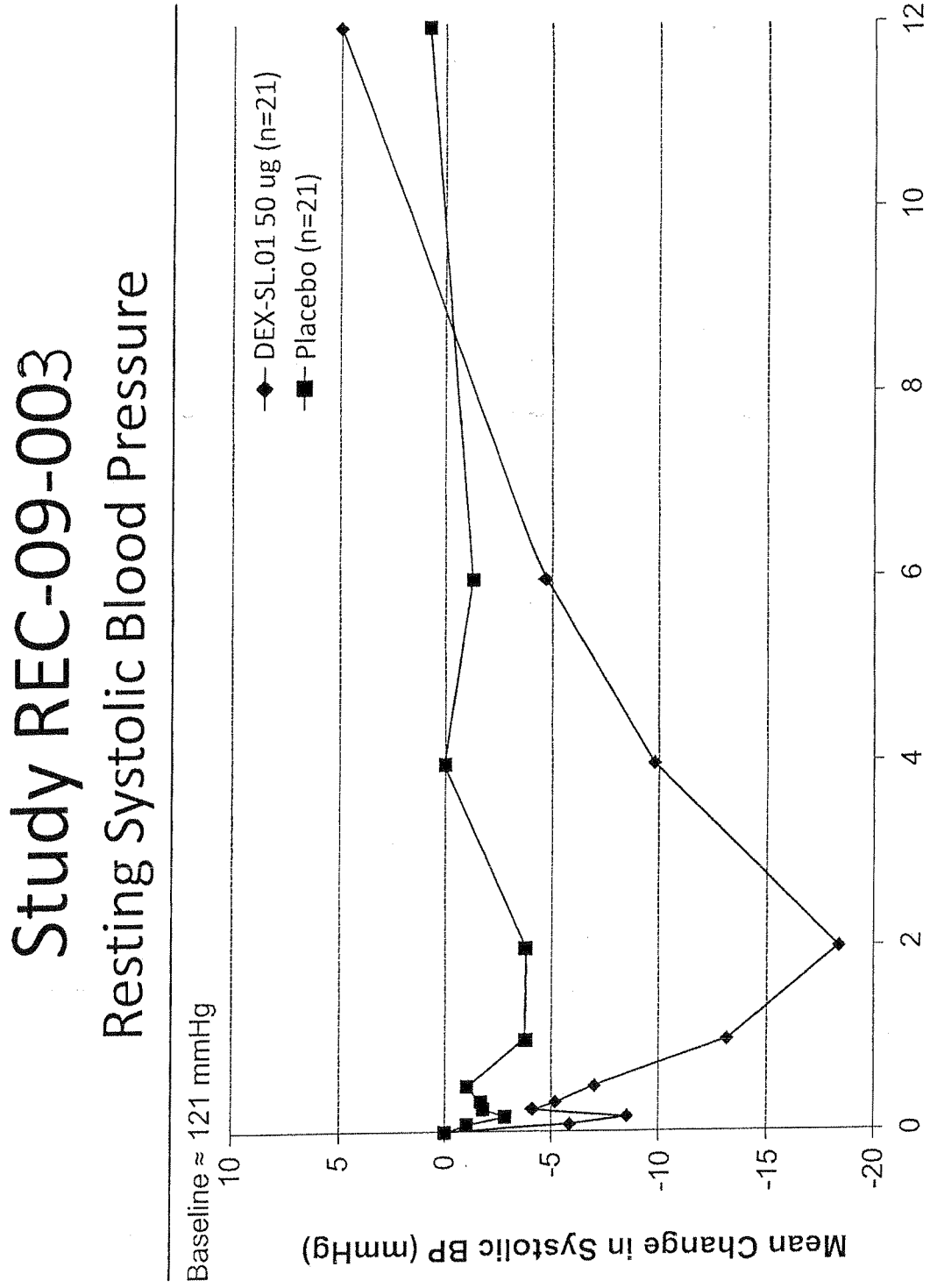

Study REC-09-003
Resting Systolic Blood Pressure
Baseline ≈ 121 mmHg
DEX-SL.01 50 ug (n=21)
Placebo (n=21)
Mean Change in Systolic BP (mmHg)
10
5
0
-5
-10
-15
-20
0
2
4
6
8
10
12
Hours

Fig. 13

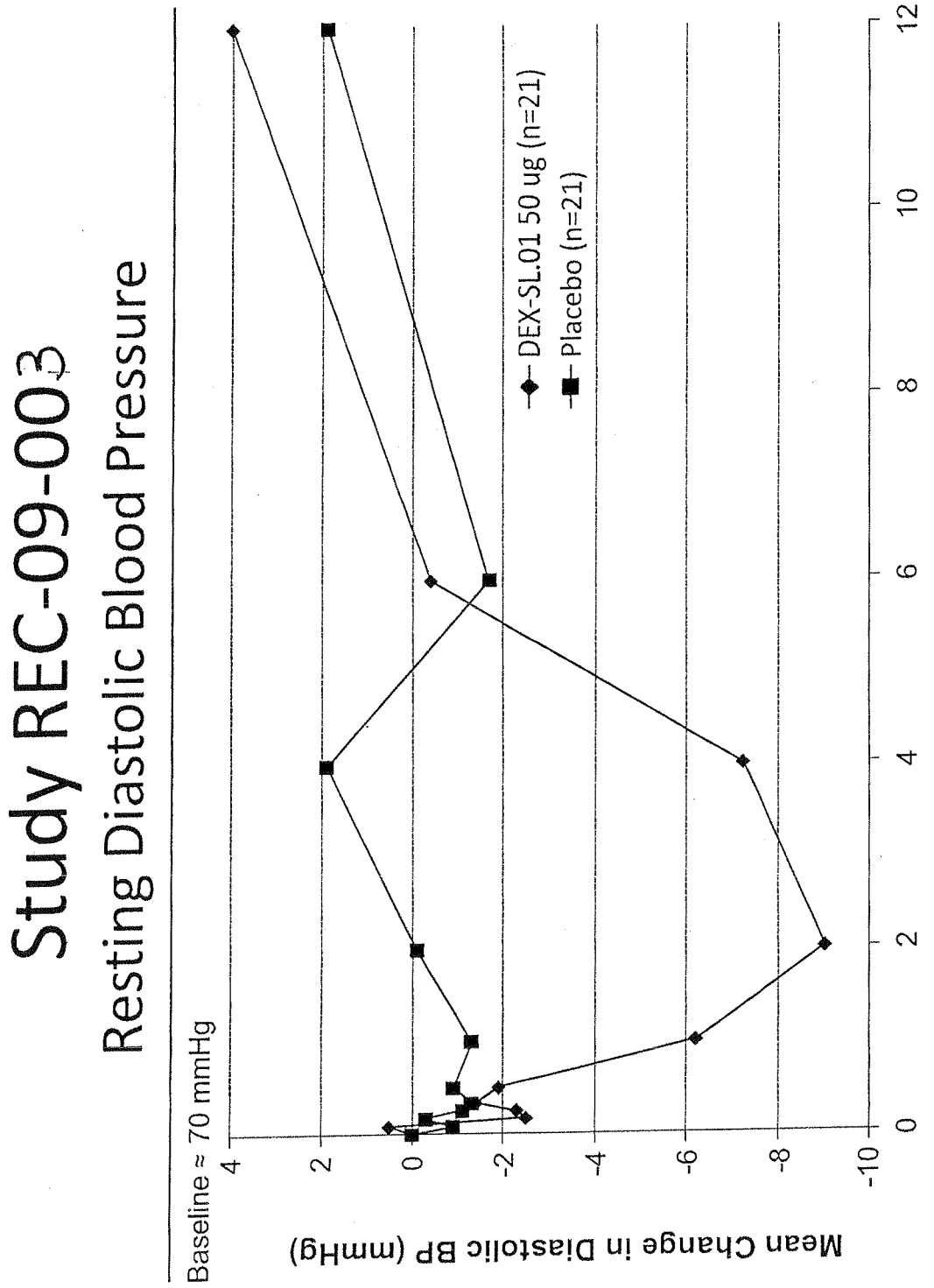

Study REC-09-003
Resting Diastolic Blood Pressure
Baseline ≈ 70 mmHg
Mean Change in Diastolic BP (mmHg)
4
2
0
-2
-4
-6
-8
-10
0
2
4
6
8
10
12
Hours
DEX-SL.01 50 ug (n=21)
Placebo (n=21)

Fig. 14

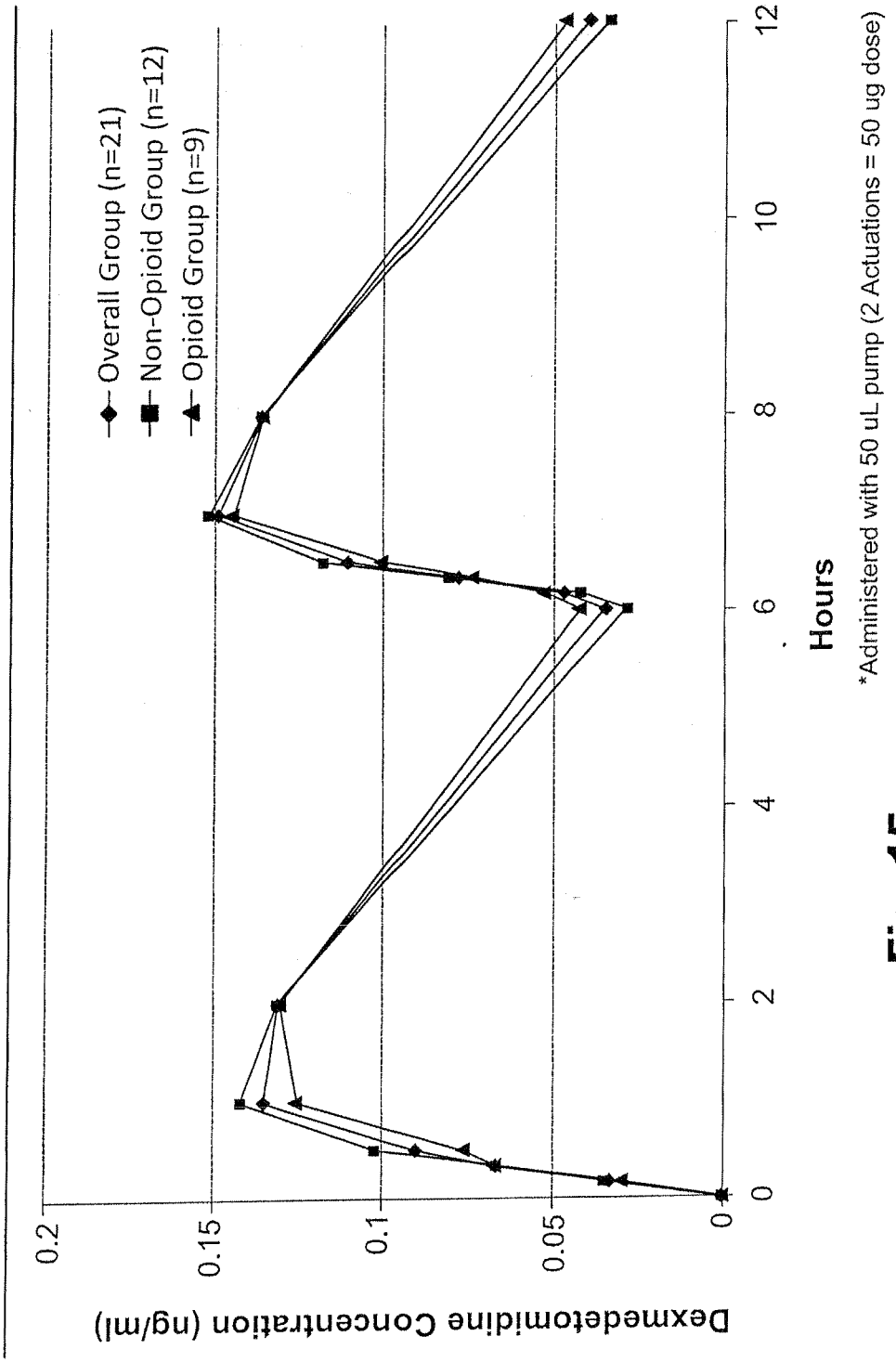

Study REC-09-003
Pharmacokinetics* - Multi-Dose
Overall Group (n=21)
Non-Opioid Group (n=12)
Opioid Group (n=9)
Dexmedetomidine Concentration (ng/ml)
0.2
0.15
0.1
0.05
0
0
2
4
6
8
10
12
Hours
*Administered with 50 uL pump (2 Actuations = 50 ug dose)

Fig. 15

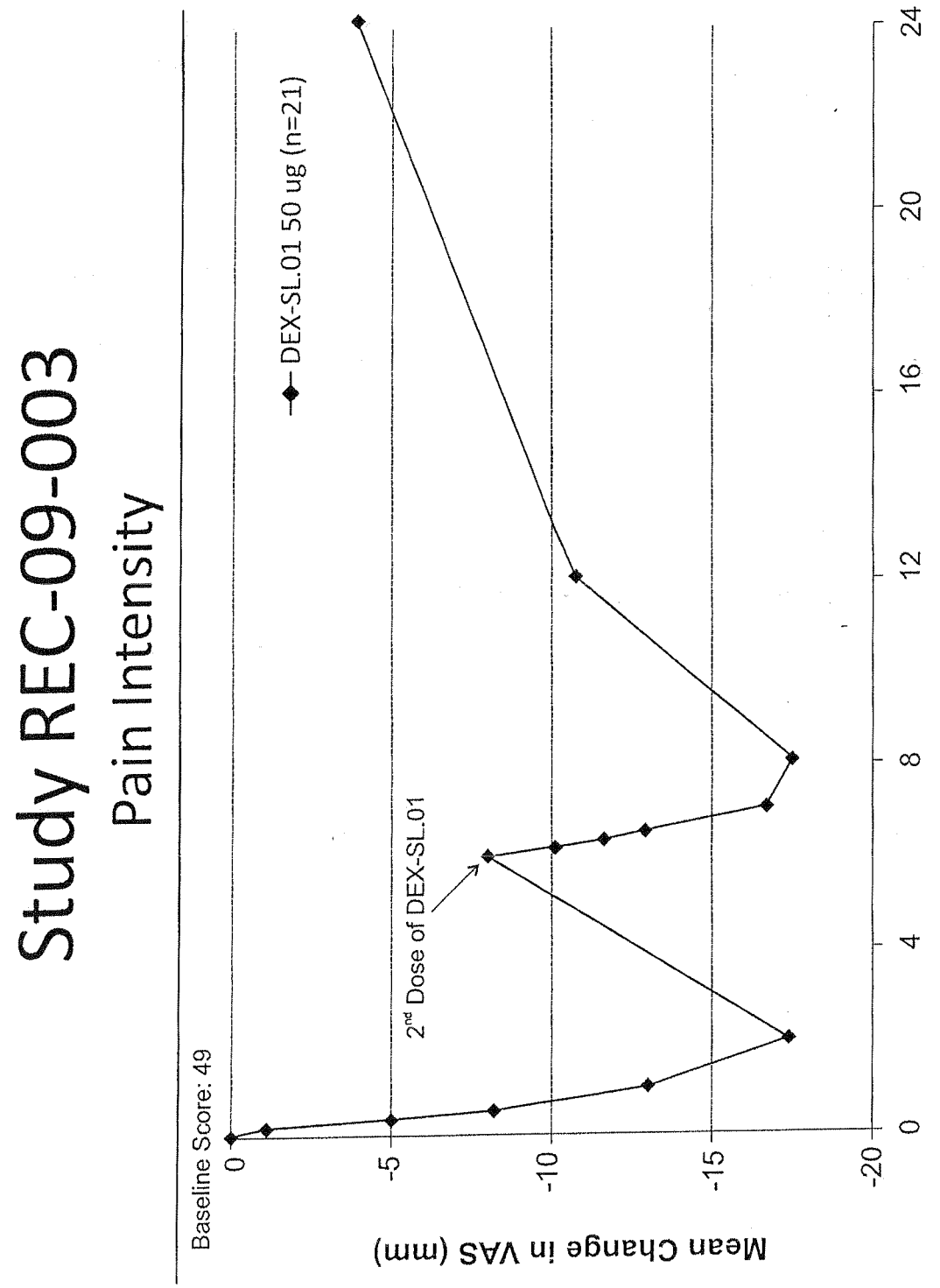

Study REC-09-003
Pain Intensity
Baseline Score: 49
DEX-SL.01 50 ug (n=21)
2nd Dose of DEX-SL.01
Mean Change in VAS (mm)
0
-5
-10
-15
-20
0
4
8
12
16
20
24
Hours

Fig. 16

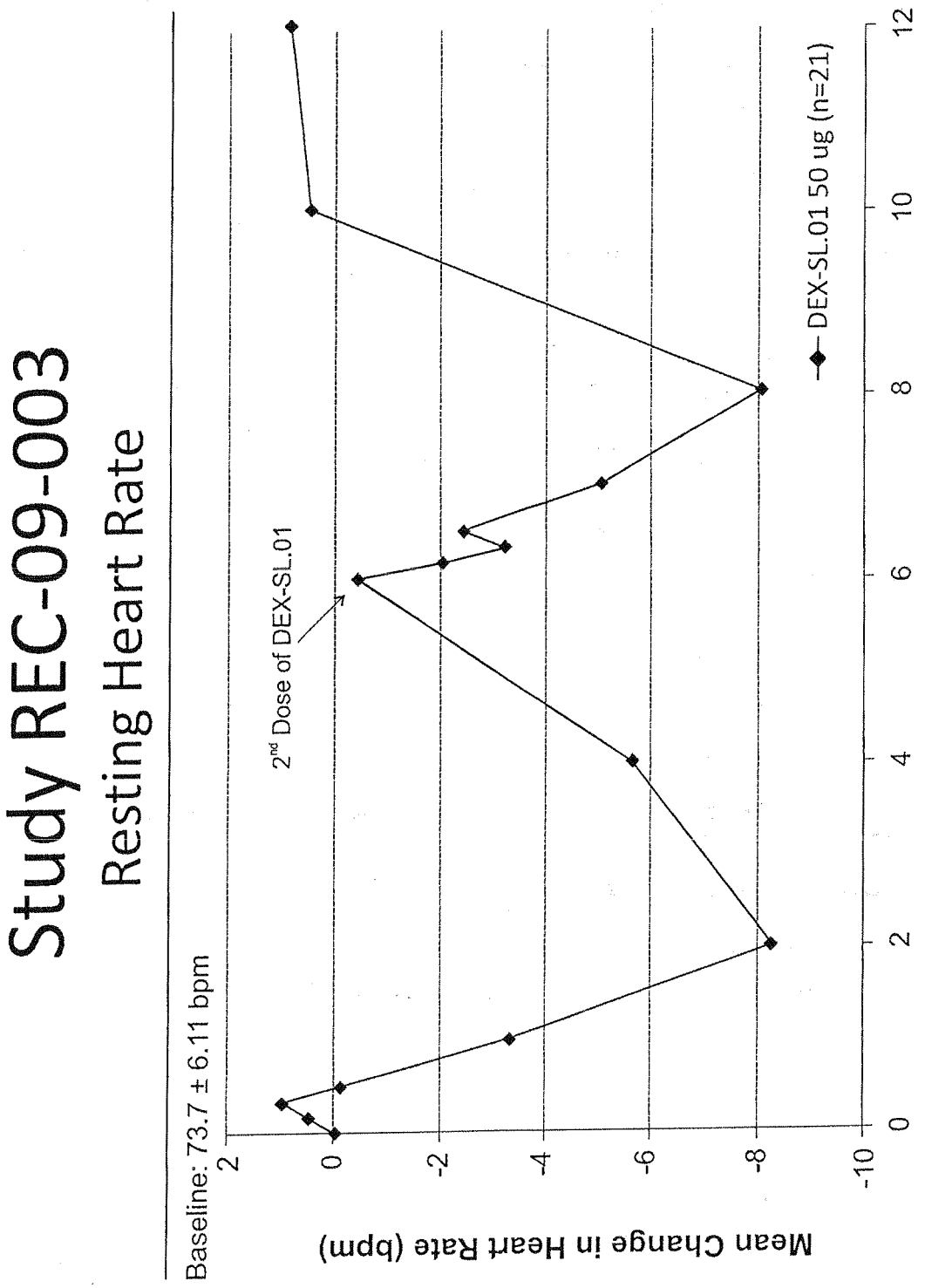

Study REC-09-003
Resting Heart Rate
Baseline: 73.7 ± 6.11 bpm
2nd Dose of DEX-SL.01
DEX-SL.01 50 ug (n=21)
Mean Change in Heart Rate (bpm)
Hours
2
0
-2
-4
-6
-8
-10
0
2
4
6
8
10
12

Fig. 17

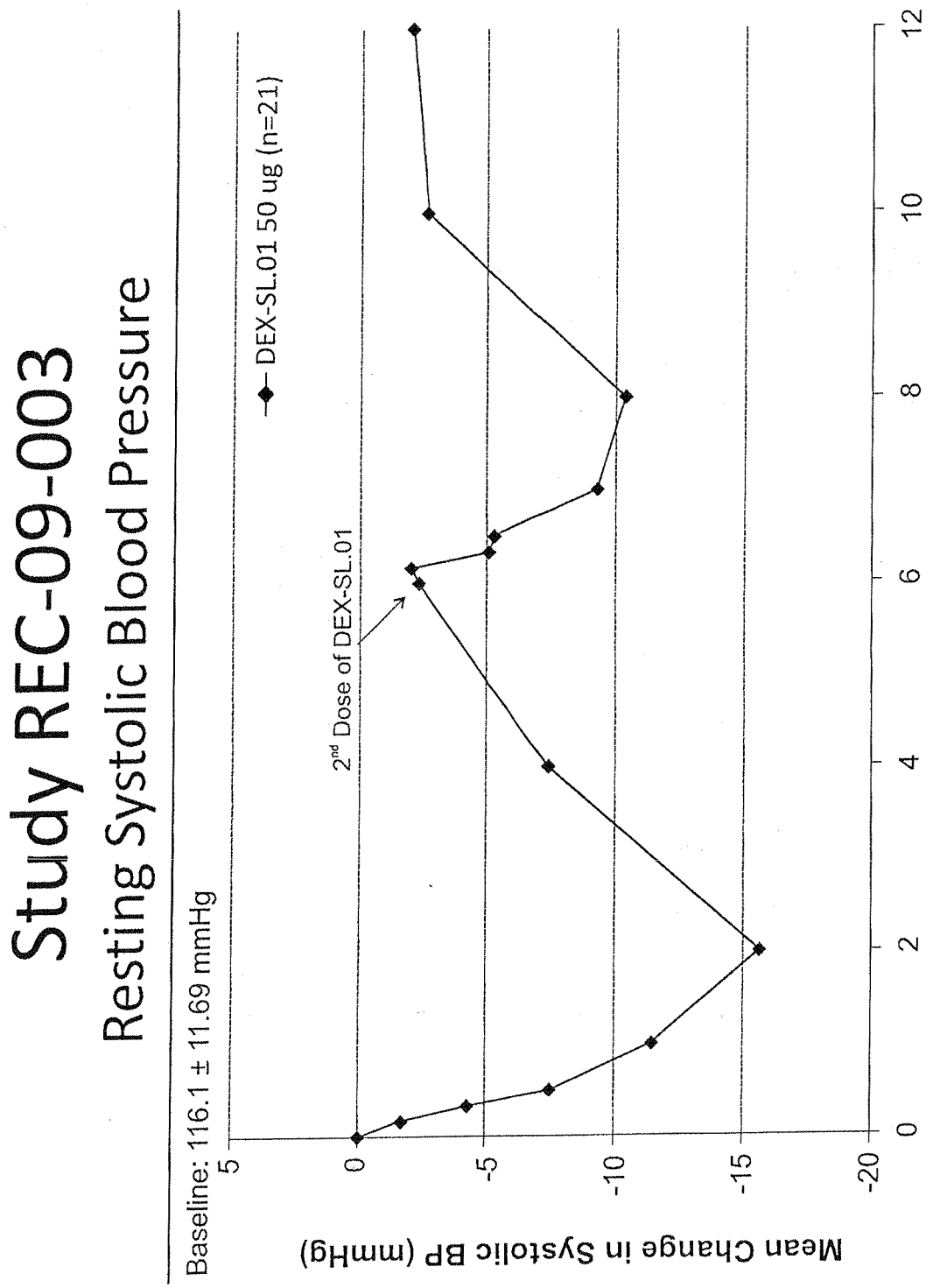

Study REC-09-003
Resting Systolic Blood Pressure
Baseline: 116.1 ± 11.69 mmHg
DEX-SL.01 50 ug (n=21)
2nd Dose of DEX-SL.01
Mean Change in Systolic BP (mmHg)
5
0
-5
-10
-15
-20
0
2
4
6
8
10
12
Hours

Fig. 18

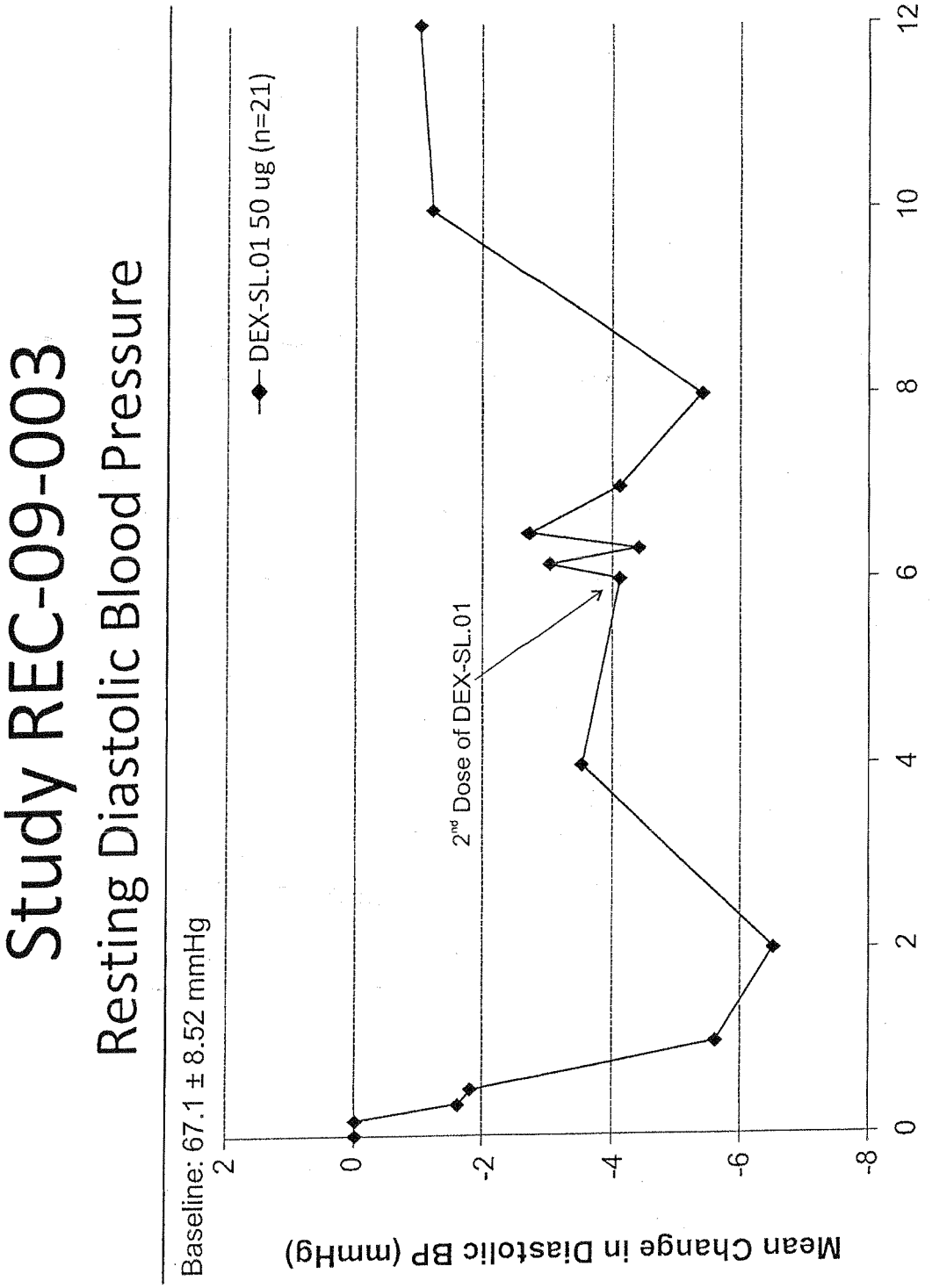

Study REC-09-003
Resting Diastolic Blood Pressure
Baseline: 67.1 ± 8.52 mmHg
DEX-SL.01 50 ug (n=21)
2nd Dose of DEX-SL.01
Mean Change in Diastolic BP (mmHg)
2
0
-2
-4
-6
-8
0
2
4
6
8
10
12
Hours

Fig. 19

Study REC-09-003

Adverse Events† (Number of Subjects)

	Periods 1 & 2 Cross-Over		Period 3 DEX-SL.01 50 ug		
	DEX-SL.01 50 ug (n=21)	Placebo (n=21)	Non-Opioid (n=12)	Opioid (n=9)	Total (n=21)
Dizziness	2	-	2	2	6
Headache	1	1	1	1	4
Hypotension	2	-	-	1	3
Orthostatic Hypotension	-	-	2	1	3
Dry Mouth	1	-	1	-	2
Migraine	1	1	1	-	2
Nasal Congestion	-	2	-	-	2

†Reported by more than one subject

Fig. 20