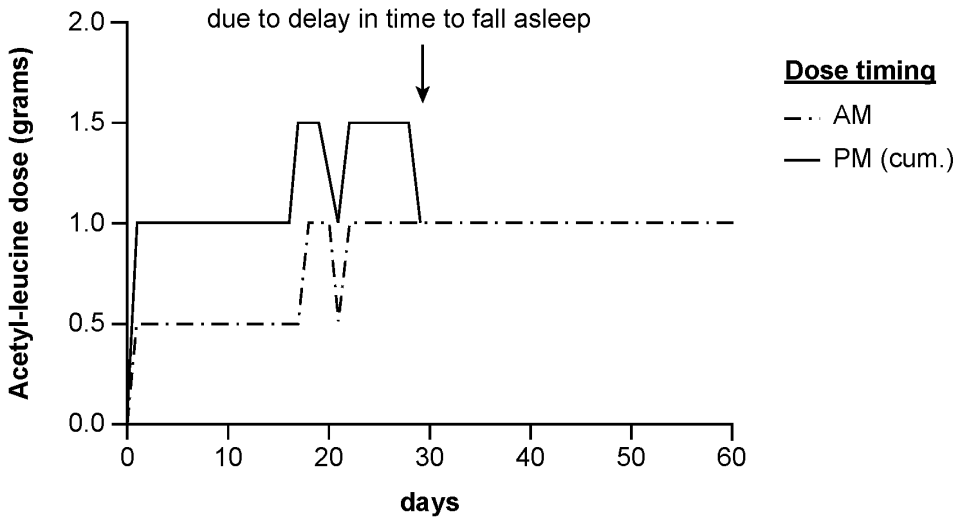

due to delay in time to fall asleep
Acetyl-leucine dose (grams)
2.0
1.5
1.0
0.5
0.0
0
10
20
30
40
50
60
days
Dose timing
AM
PM (cum.)

FIG. 1A

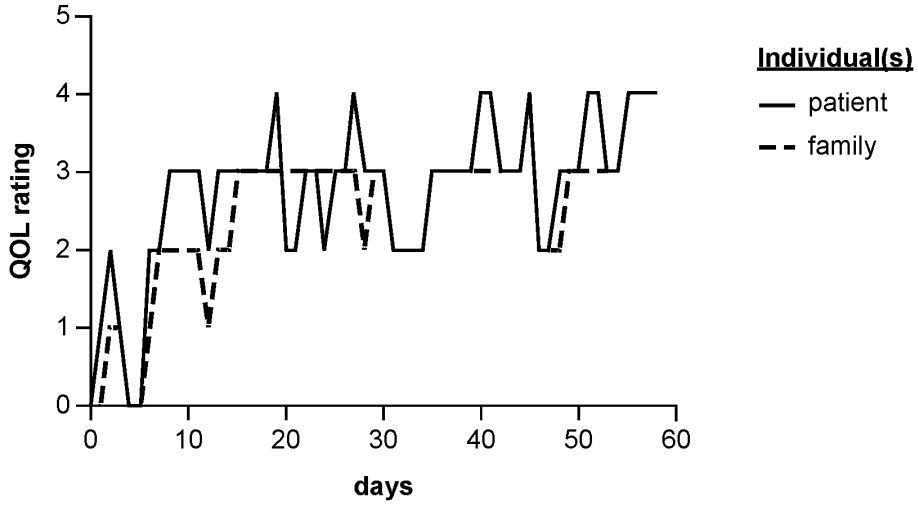

QOL rating
5
4
3
2
1
0
0
10
20
30
40
50
60
days
Individual(s)
patient
family

FIG. 1B

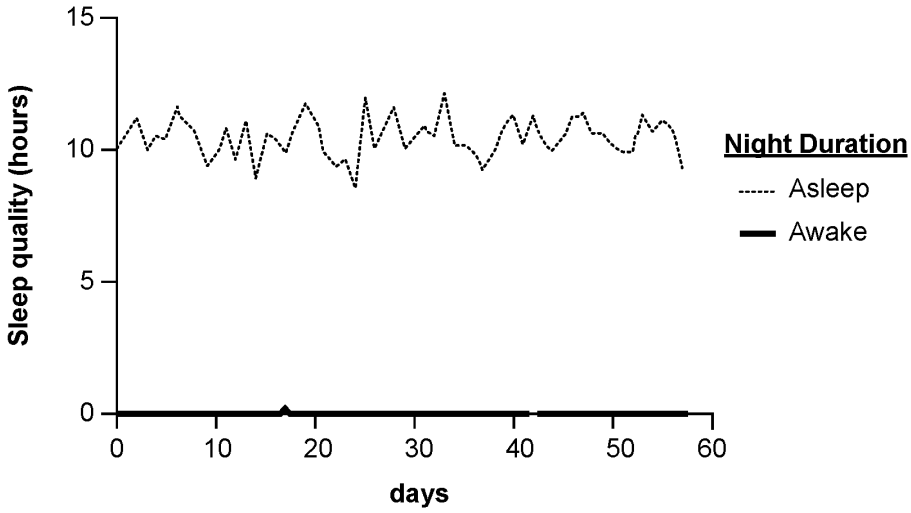

15
10
5
0
Sleep quality (hours)
0
10
20
30
40
50
60
days
Night Duration
Asleep
Awake

FIG. 1C

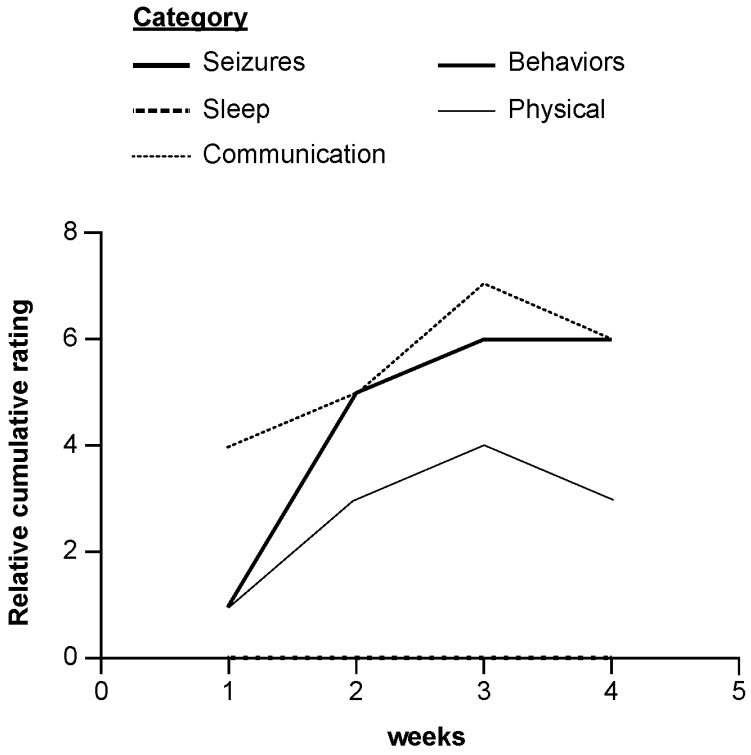

Category
Seizures
Behaviors
Sleep
Physical
Communication
8
6
4
2
0
Relative cumulative rating
0
1
2
3
4
5
weeks

FIG. 2A

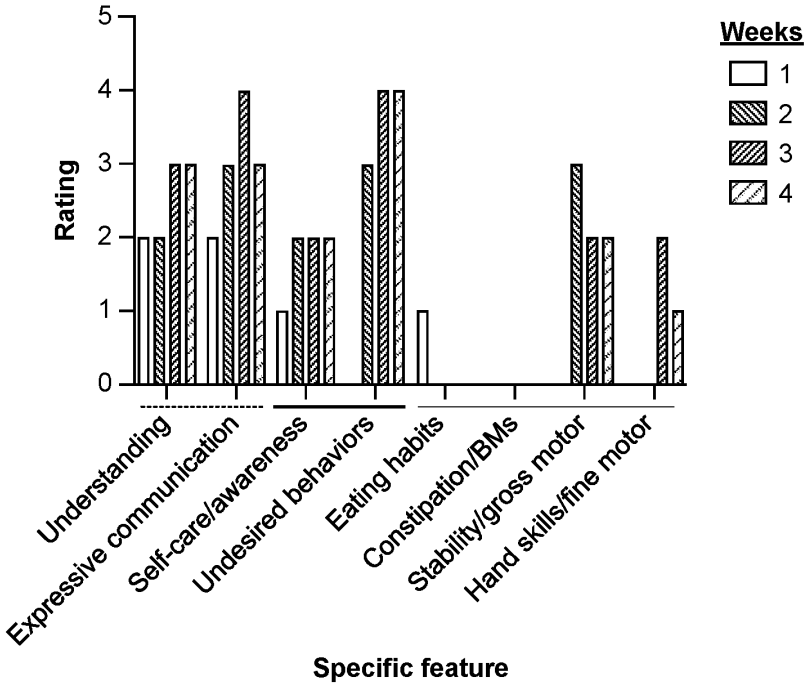

Rating
5
4
3
2
1
0
Weeks
1
2
3
4
Understanding
Expressive communication
Self-care/awareness
Undesired behaviors
Eating habits
Constipation/BMs
Stability/gross motor
Hand skills/fine motor
Specific feature

FIG. 2B

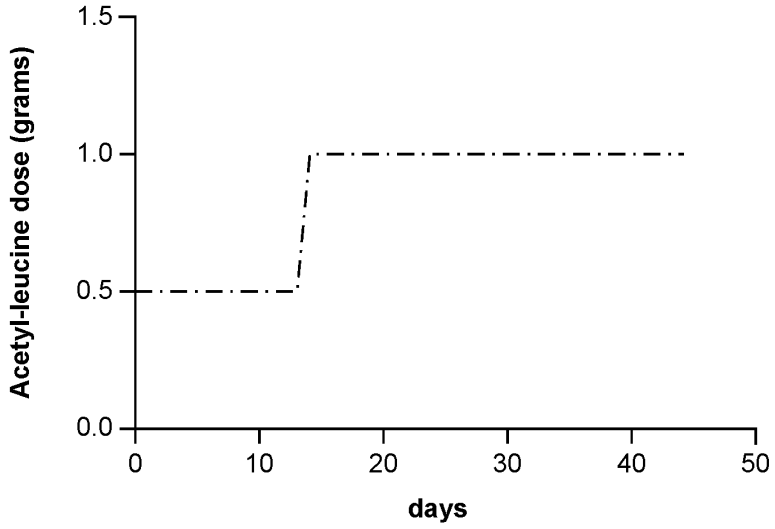

Acetyl-leucine dose (grams)
1.5
1.0
0.5
0.0
0
10
20
30
40
50
days

FIG. 3A

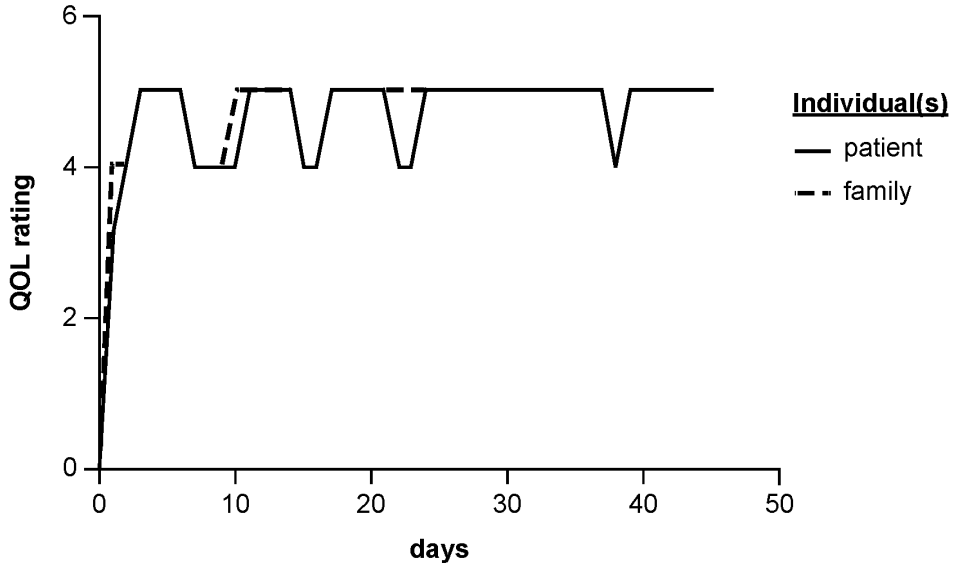

6
4
2
0
QOL rating
0
10
20
30
40
50
days
Individual(s)
patient
family

FIG. 3B

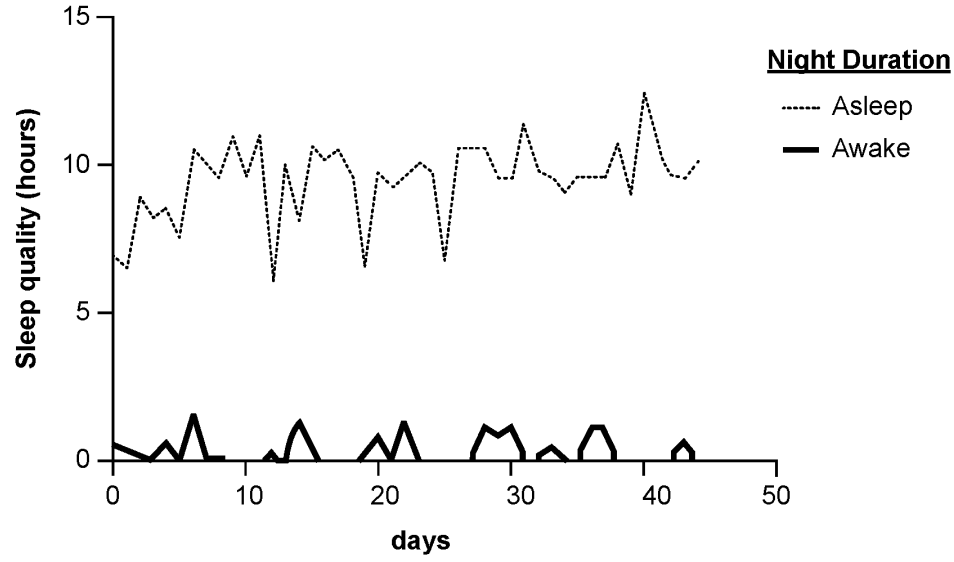

15
10
5
0
Sleep quality (hours)
0
10
20
30
40
50
days
Night Duration
Asleep
Awake

FIG. 3C

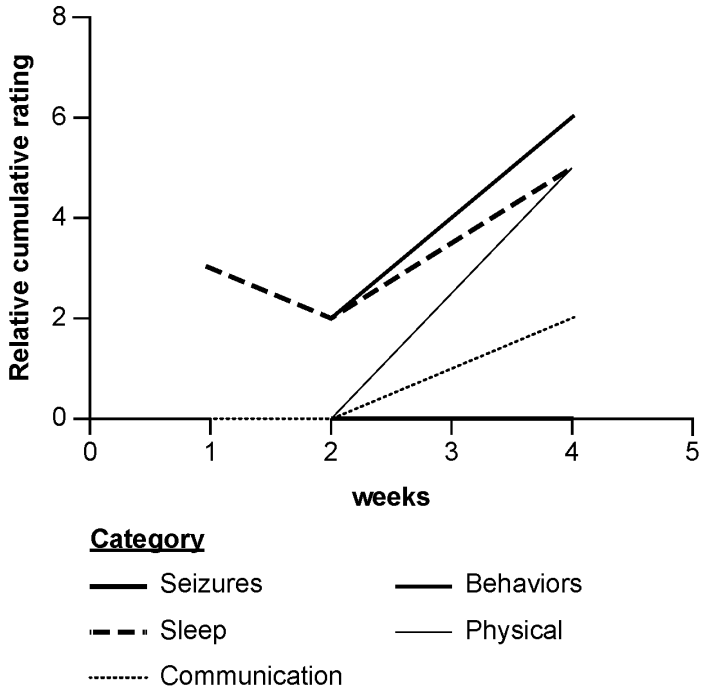

Relative cumulative rating
8
6
4
2
0
0
1
2
3
4
5
weeks
Category
Seizures
Behaviors
Sleep
Physical
Communication

FIG. 4A

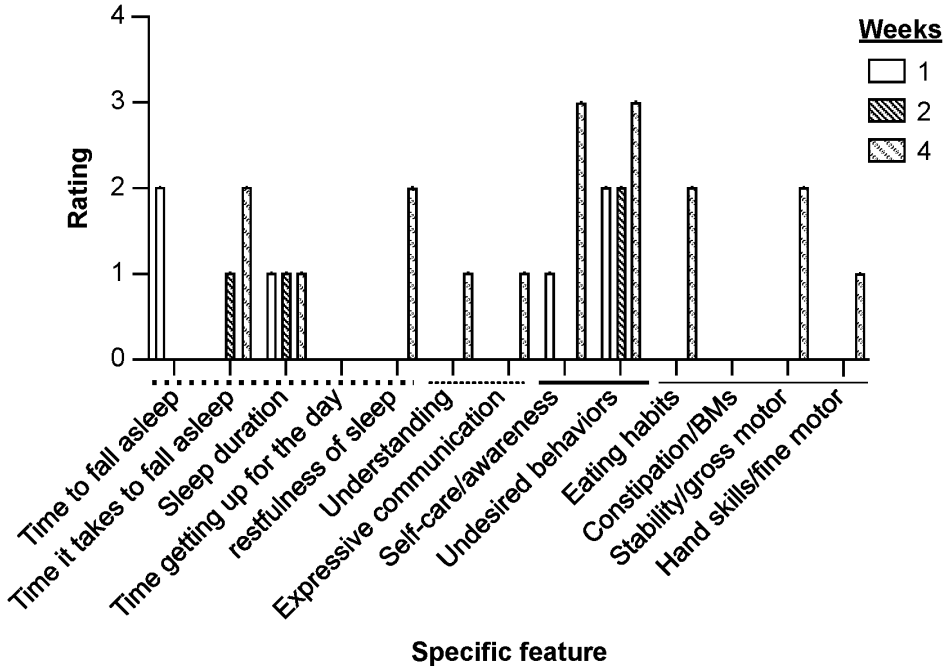

Rating
4
3
2
1
0
Weeks
1
2
4
Time to fall asleep
Time it takes to fall asleep
Sleep duration
Time getting up for the day
restfulness of sleep
Understanding
Expressive communication
Self-care/awareness
Undesired behaviors
Eating habits
Constipation/BMs
Stability/gross motor
Hand skills/fine motor
Specific feature

FIG. 4B

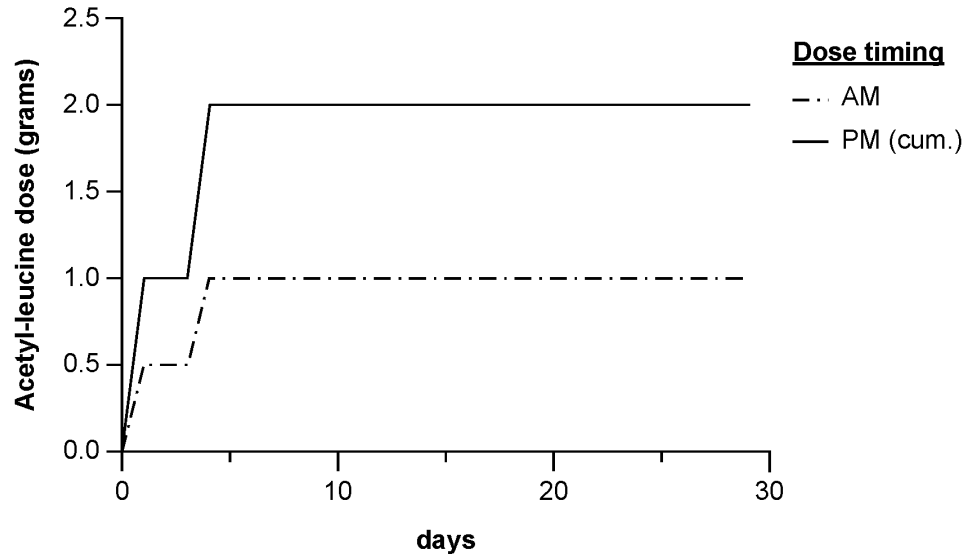

Acetyl-leucine dose (grams)
2.5
2.0
1.5
1.0
0.5
0.0
0
10
20
30
days
Dose timing
AM
PM (cum.)

FIG. 5A

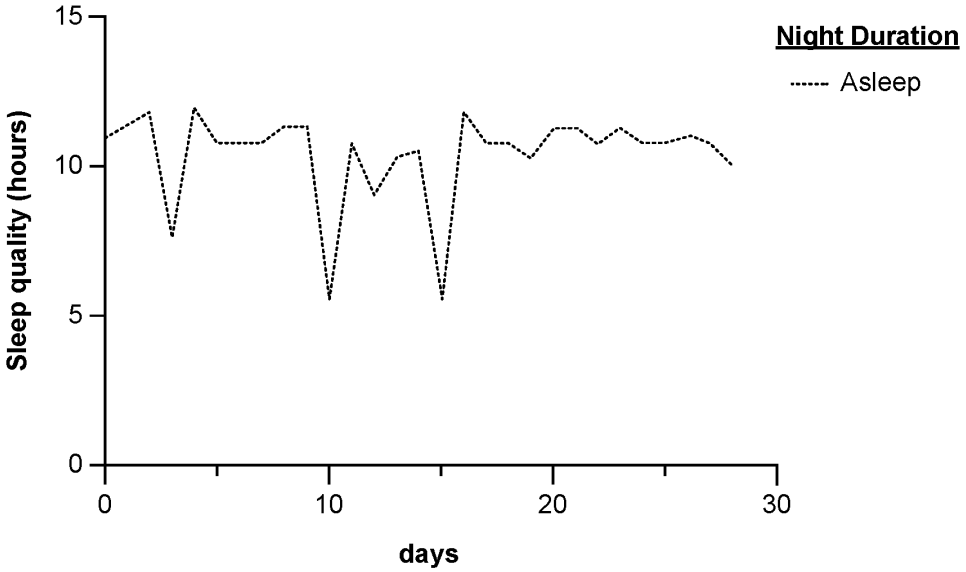

Sleep quality (hours)
15
10
5
0
0
10
20
30
days
Night Duration
Asleep

FIG. 5B

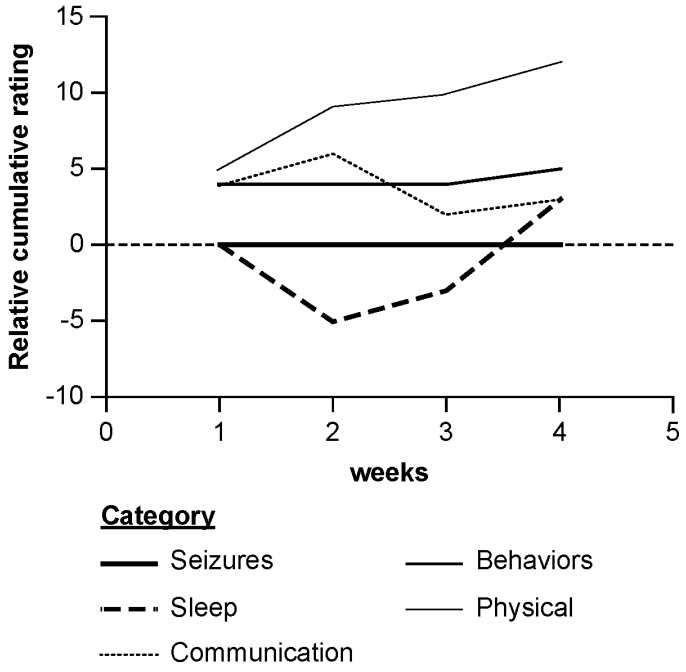

Relative cumulative rating
15
10
5
0
-5
-10
0
1
2
3
4
5
weeks
Category
Seizures
Behaviors
Sleep
Physical
Communication

FIG. 6A

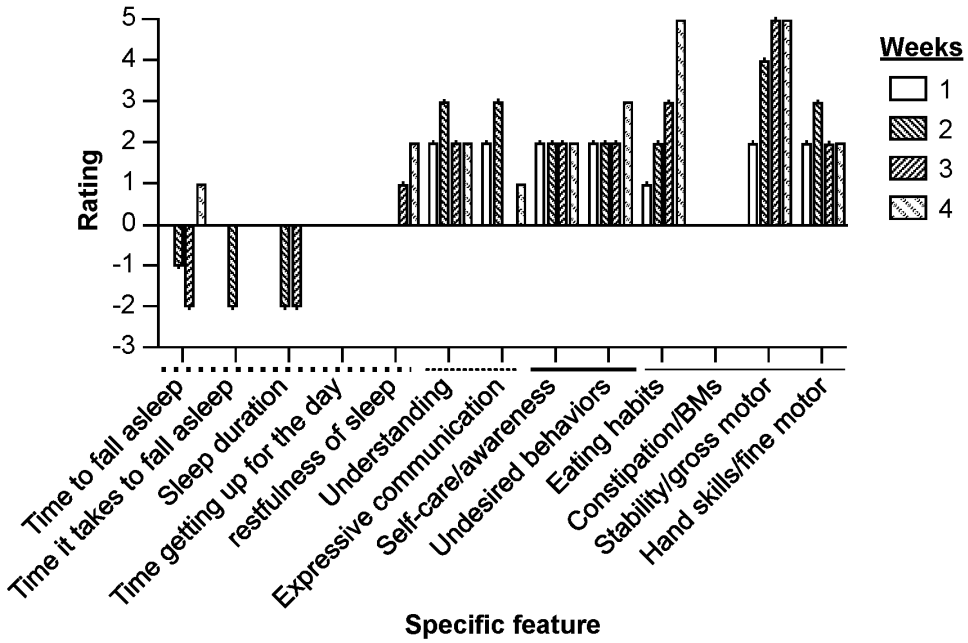

Rating
5
4
3
2
1
0
-1
-2
-3
Weeks
1
2
3
4
Time to fall asleep
Time it takes to fall asleep
Sleep duration
Time getting up for the day
restfulness of sleep
Understanding
Expressive communication
Self-care/awareness
Undesired behaviors
Eating habits
Constipation/BMs
Stability/gross motor
Hand skills/fine motor
Specific feature

FIG. 6B

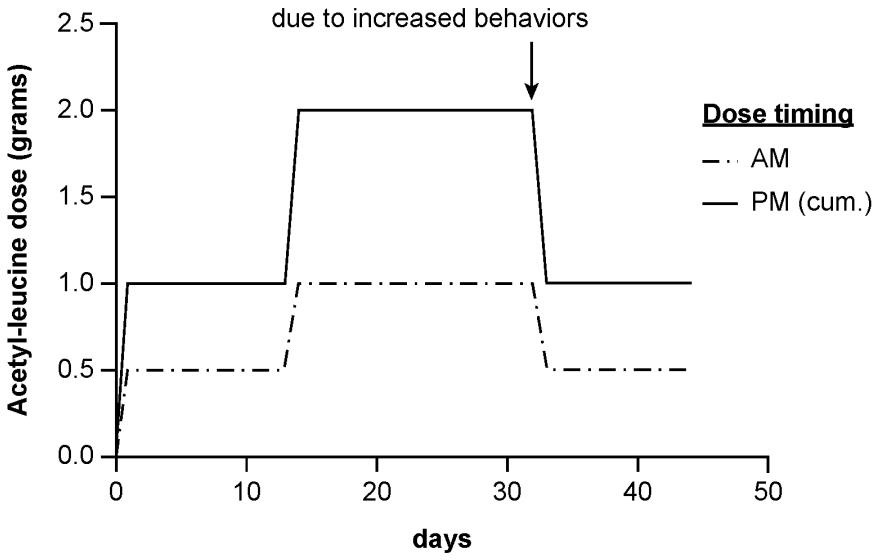

due to increased behaviors
Acetyl-leucine dose (grams)
2.5
2.0
1.5
1.0
0.5
0.0
0
10
20
30
40
50
days
Dose timing
AM
PM (cum.)

FIG. 7A

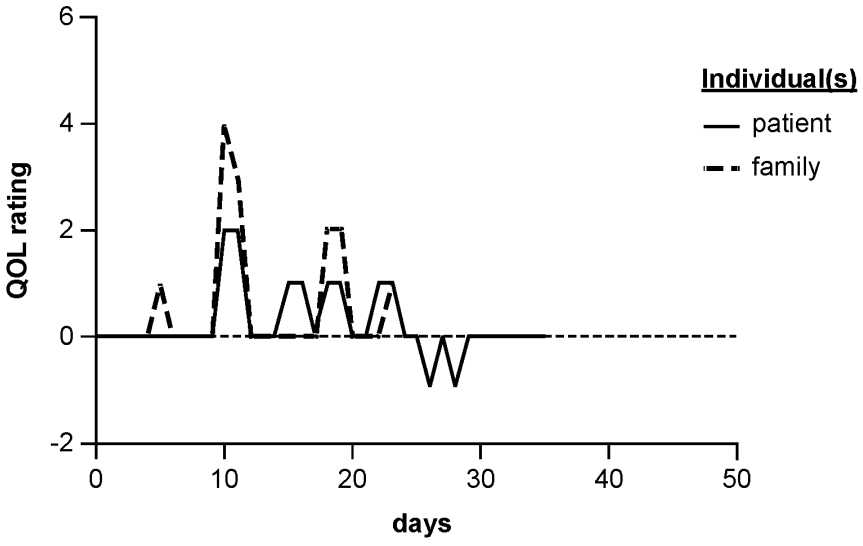

QOL rating
6
4
2
0
-2
0
10
20
30
40
50
days
Individual(s)
patient
family

FIG. 7B

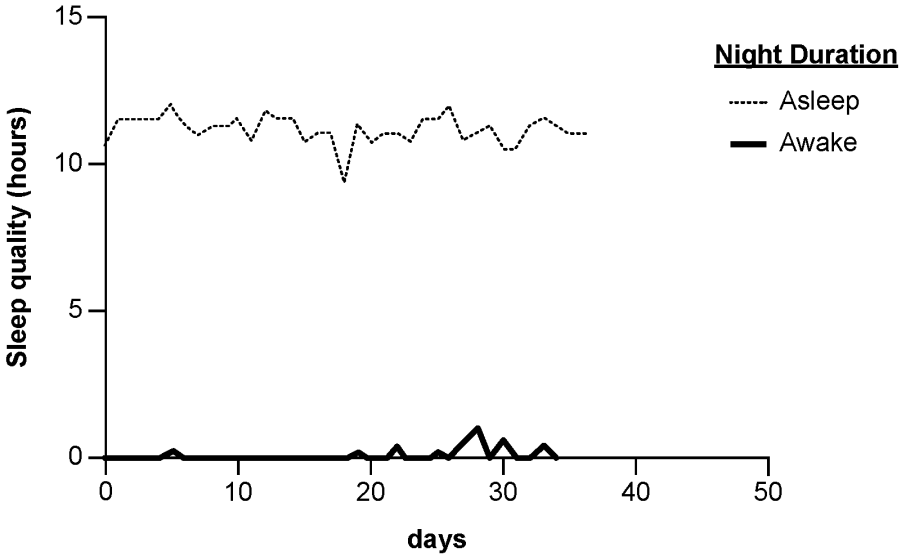

Sleep quality (hours)
15
10
5
0
0
10
20
30
40
50
days
Night Duration
Asleep
Awake

FIG. 7C

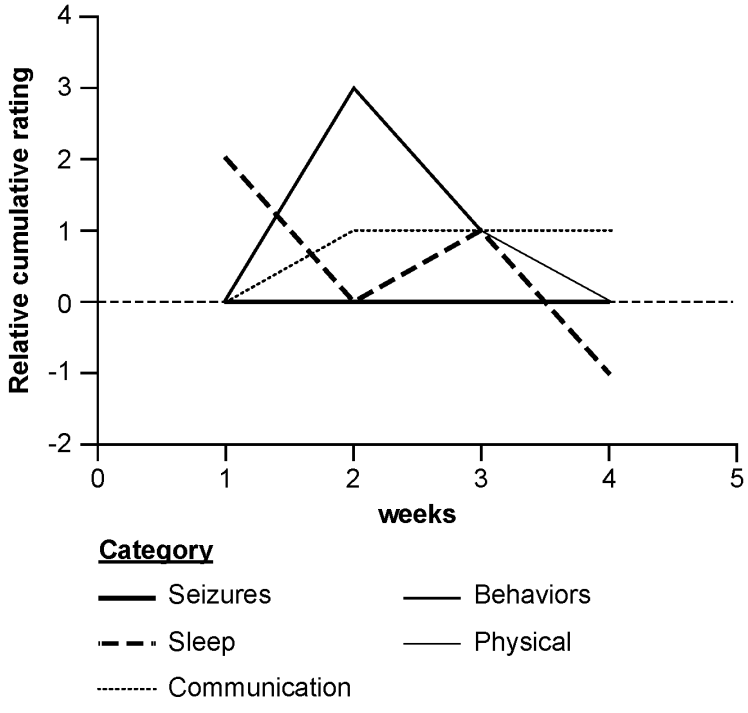

Relative cumulative rating
4
3
2
1
0
-1
-2
0
1
2
3
4
5
weeks
Category
Seizures
Behaviors
Sleep
Physical
Communication

FIG. 8A

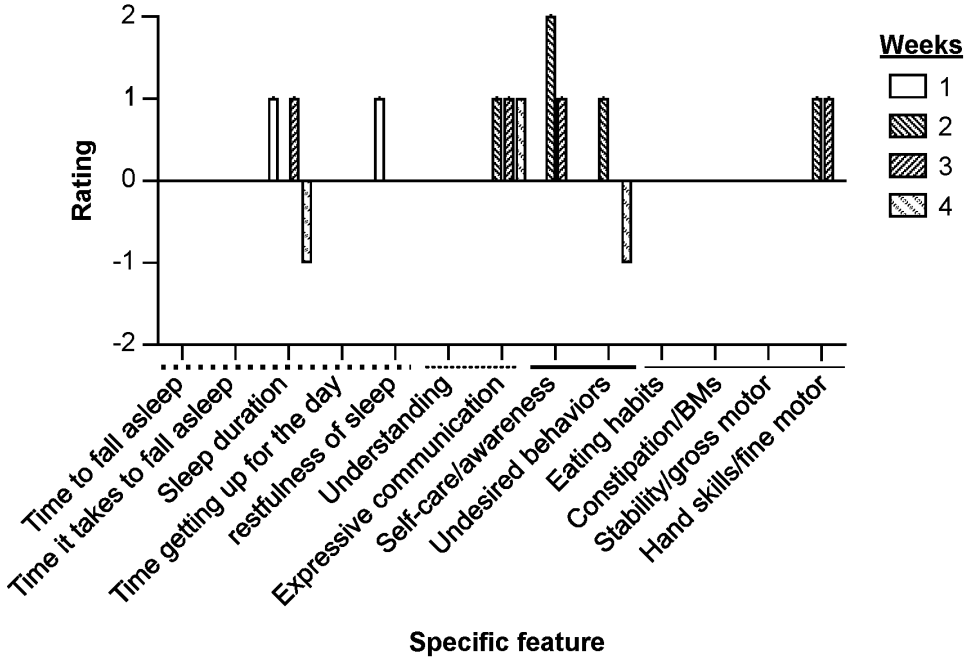

Rating
2
1
0
-1
-2
Weeks
1
2
3
4
Time to fall asleep
Time it takes to fall asleep
Sleep duration
Time getting up for the day
restfulness of sleep
Understanding
Expressive communication
Self-care/awareness
Undesired behaviors
Eating habits
Constipation/BMs
Stability/gross motor
Hand skills/fine motor
Specific feature

FIG. 8B

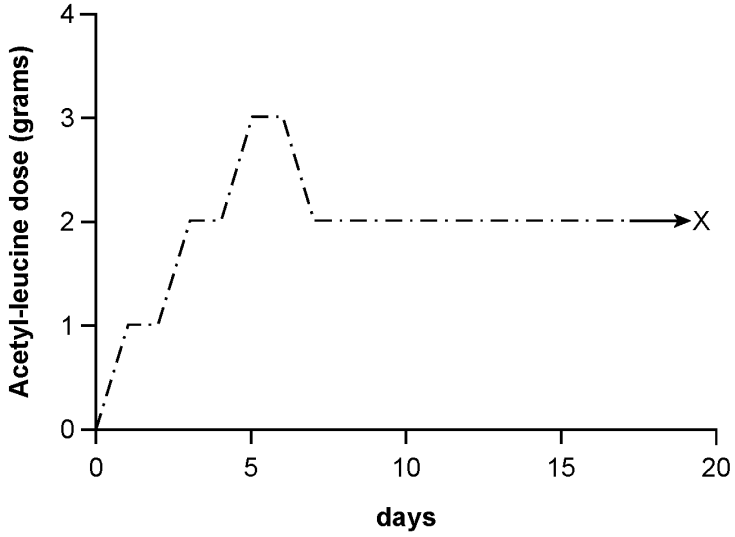

Acetyl-leucine dose (grams)
4
3
2
1
0
X
0
5
10
15
20
days

FIG. 9A

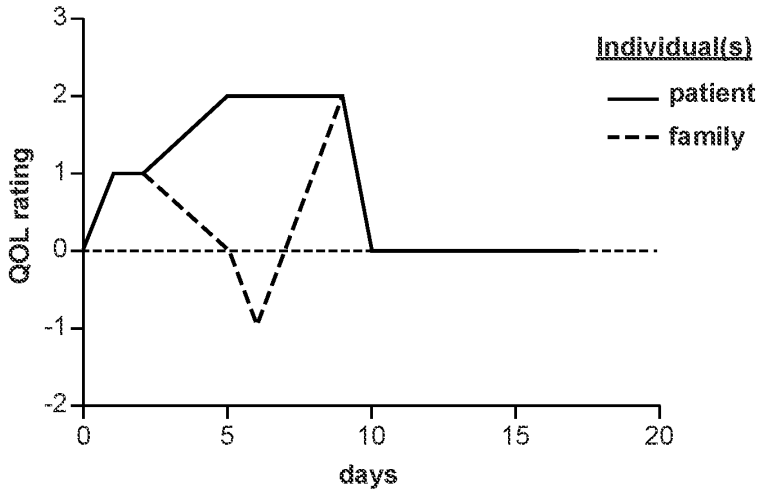

Individual(s)
patient
family
QOL rating
3
2
1
0
-1
-2
0
5
10
15
20
days

FIG. 9B

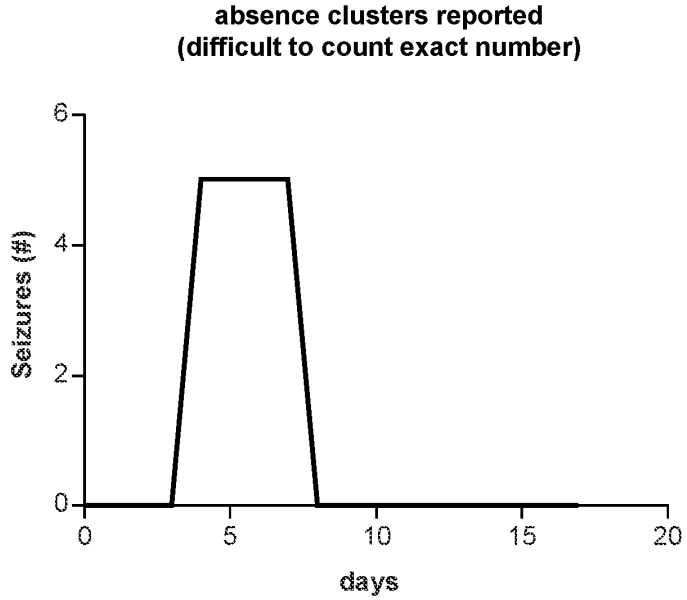

absence clusters reported
(difficult to count exact number)
Seizures (#)
6
4
2
0
0
5
10
15
20
days

FIG. 9C

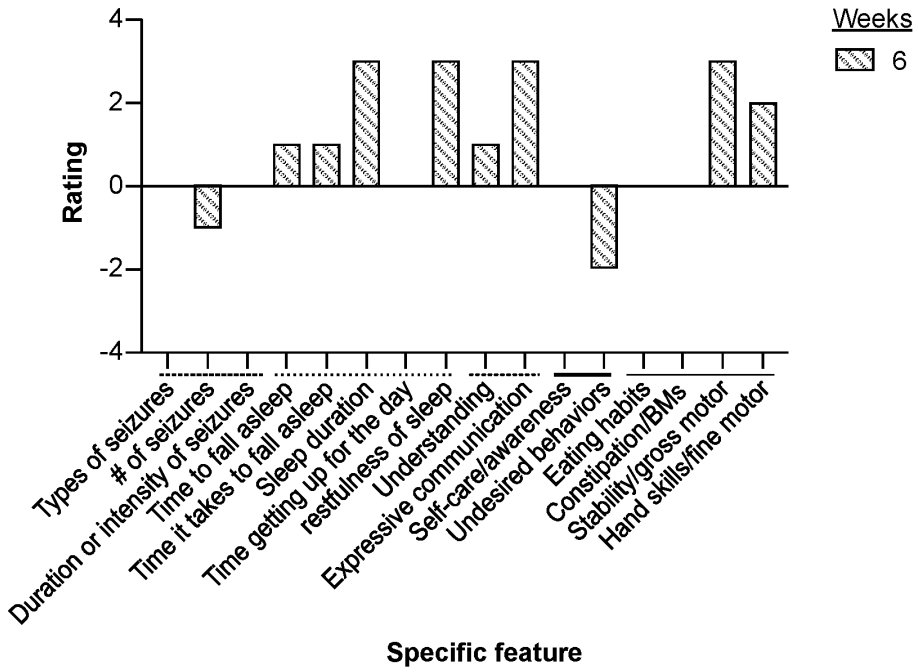


FIG. 10

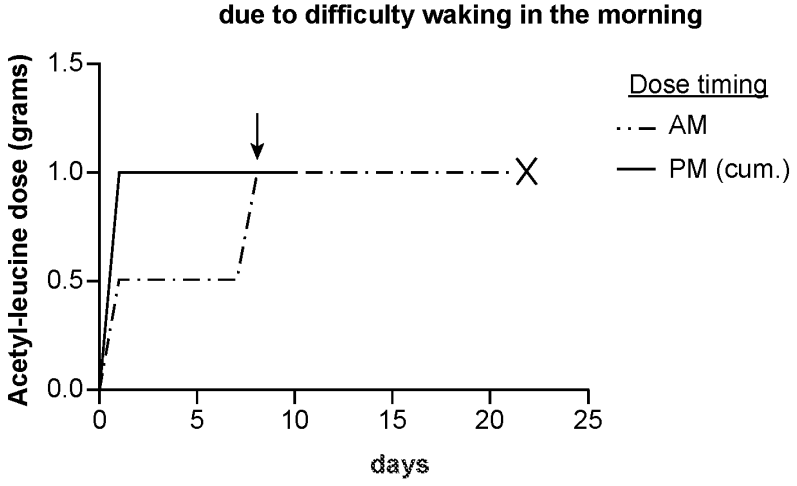


FIG. 11A

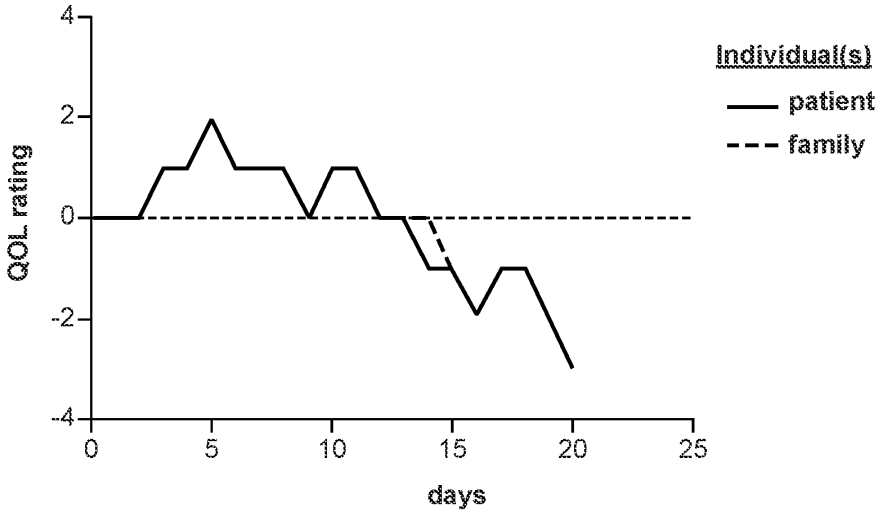


FIG. 11B

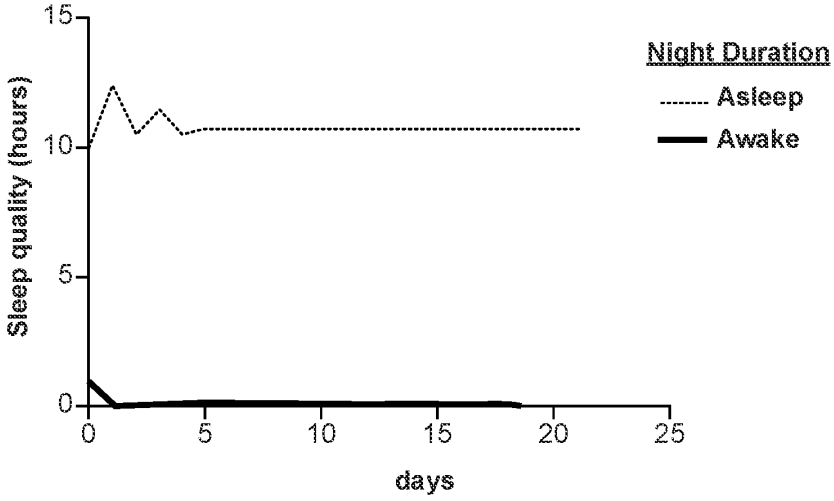


FIG. 11C

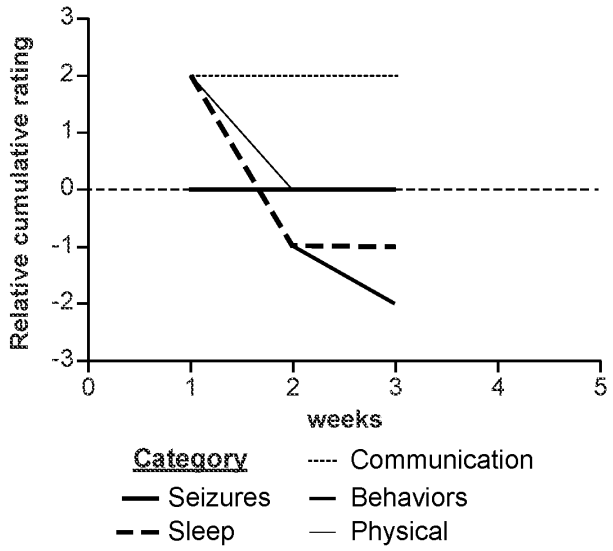


FIG. 12A

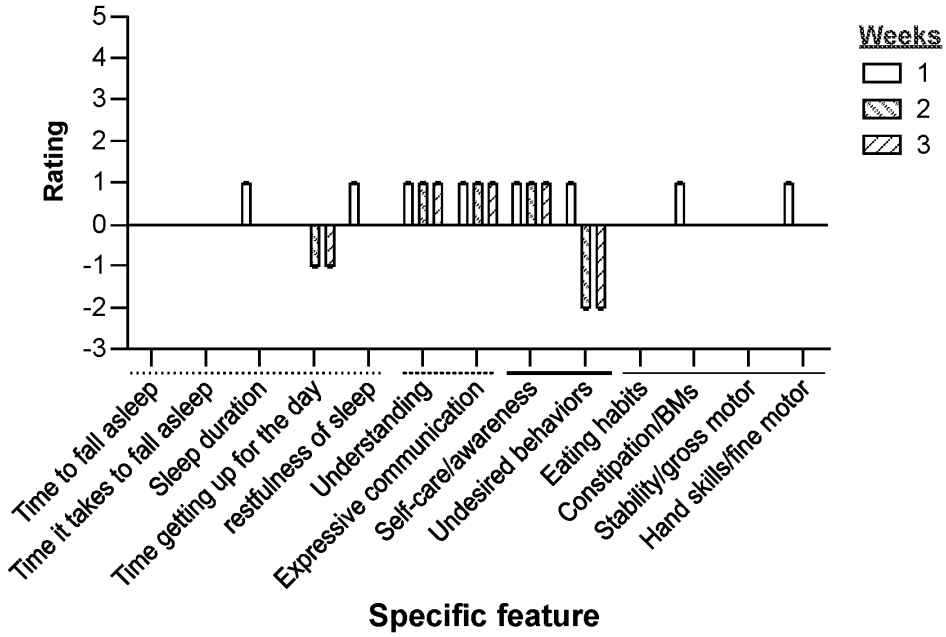


FIG. 12B

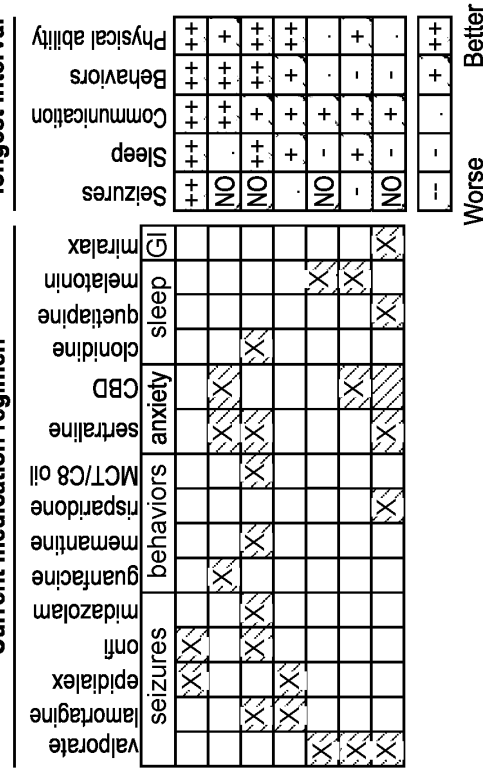

Current medication regimen
NAL effect at longest interval
valporate
lamotragine
epidiolex
onfi
midazolam
guanfacine
memantine
risperidone
MCT/C8 oil
sertraline
CBD
clonidine
quetiapine
melatonin
miralax
seizures
behaviors
anxiety
sleep
GI
Case #
Sex
Age
Weight (lbs)
SYNGAP1 mutation
Weeks on NAL
NAL dose (g)
Seizures
Sleep
Communication
Behaviors
Physical ability
Initial M 8 50 PT, c490 C>T 12 2
2 M 8 59 PT, c.490 C>T 8 1 - 1.5
3 F 21 135 PT, c.1167_1168delAG 6 0.5 - 1
4 F 6 55 PT, c.1760_1792del33 4 1 - 2
5 F 13 79 MS, c.662A>T 6 1 - 2
6 M 7 60 PT, c.333del 6 1 - 3
7 F 9 88 PT, c.3233_3236delTCAG 3 1
PT = protein truncating
MS = missense
Worse
Better

FIG. 13

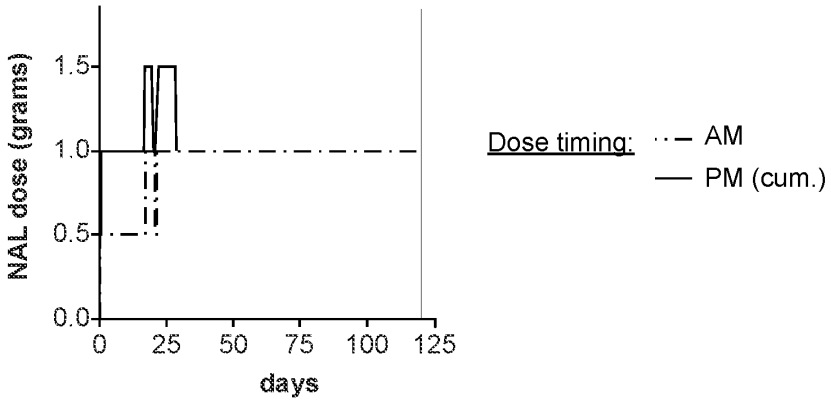


FIG. 14A

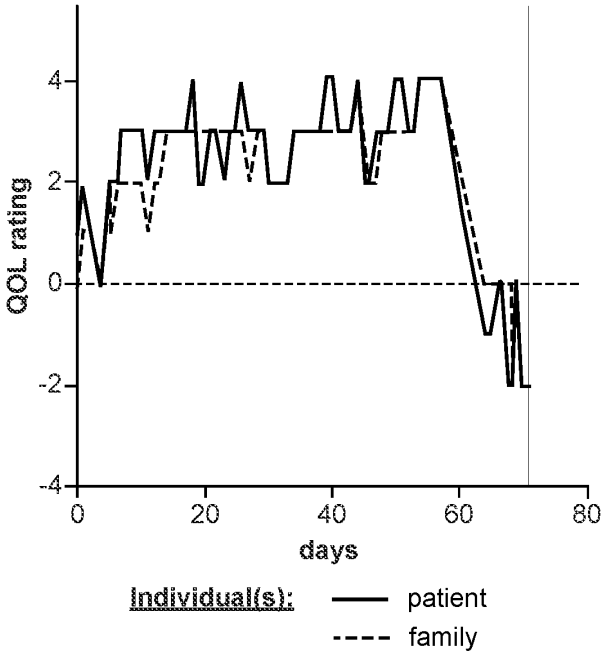


FIG. 14B

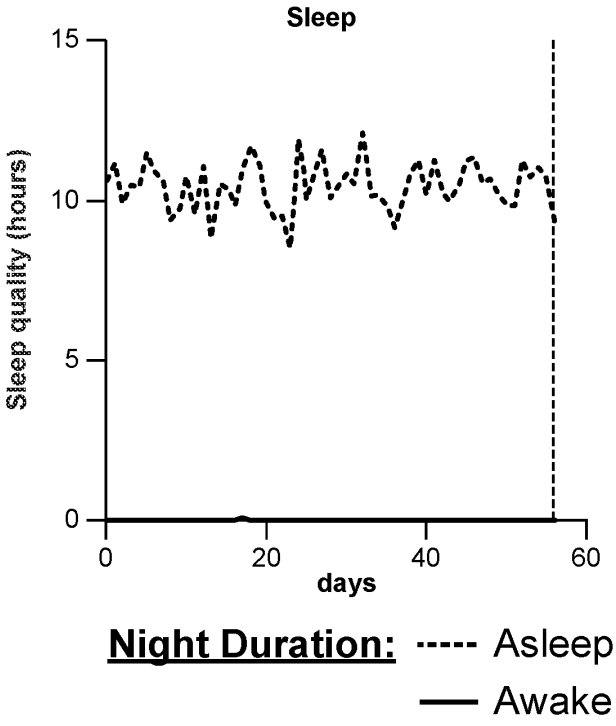


FIG. 14C

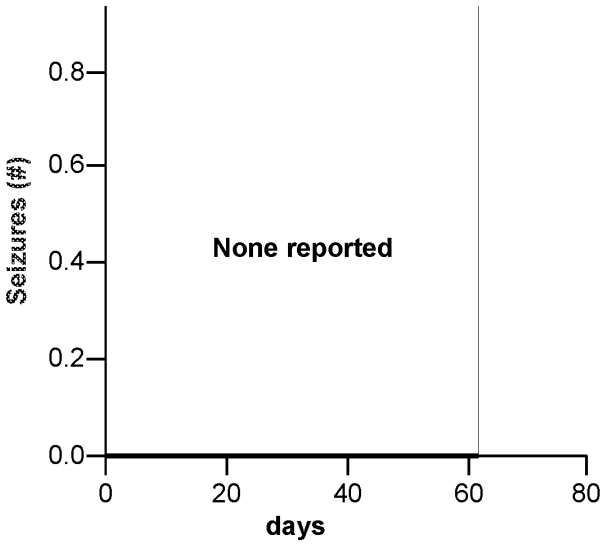


FIG. 14D

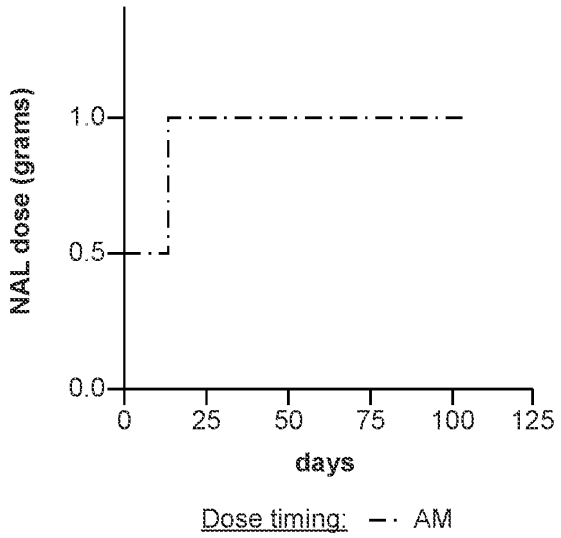


FIG. 15A

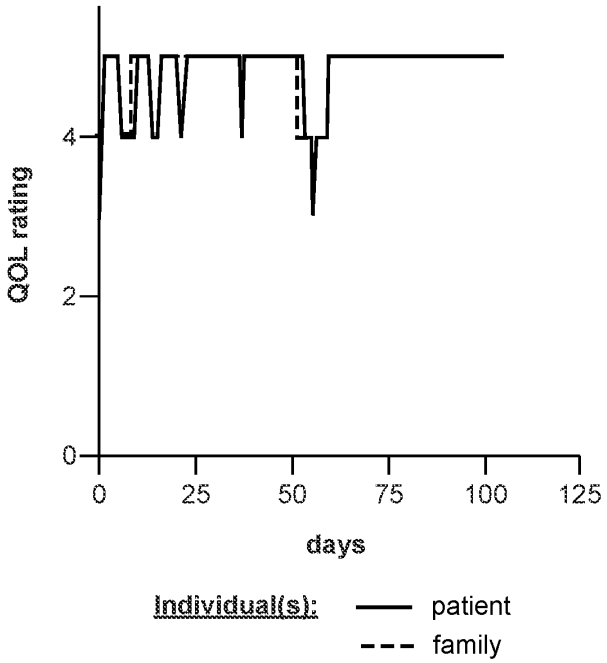


FIG. 15B

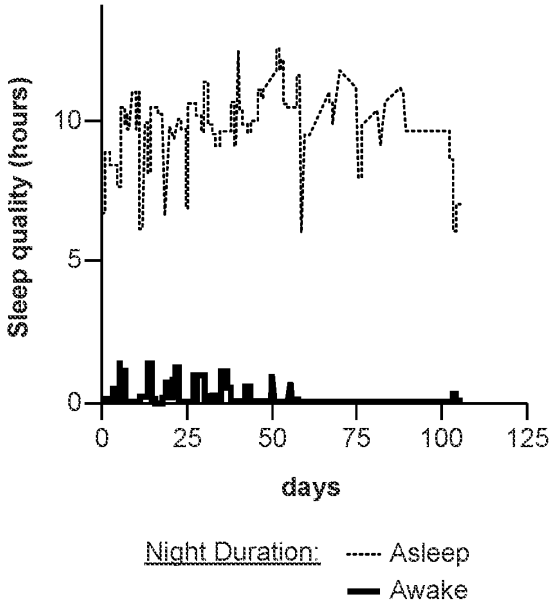


FIG. 15C

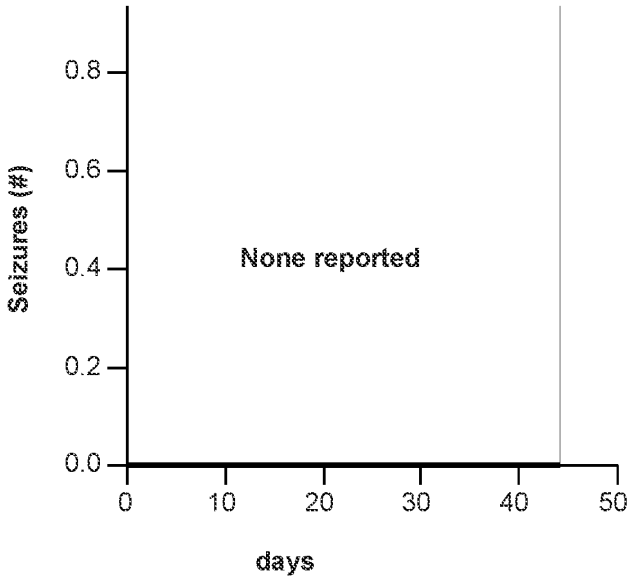


FIG. 15D

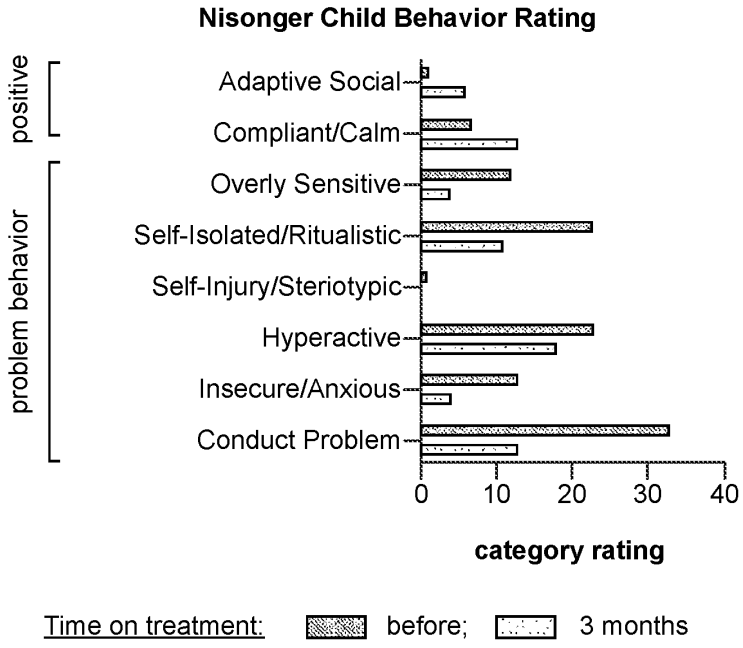


FIG. 15E

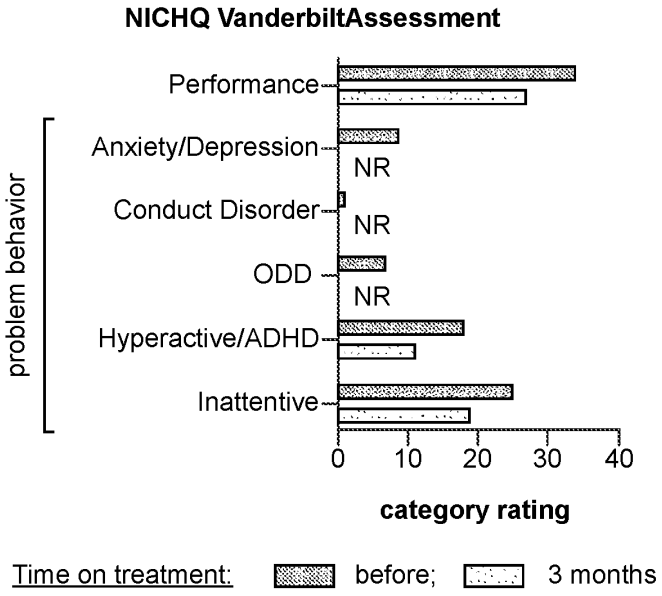


FIG. 15F

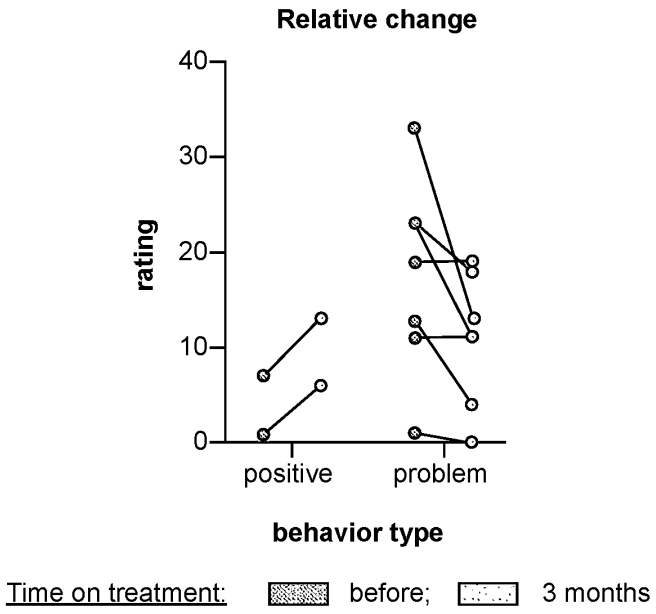


FIG. 15G

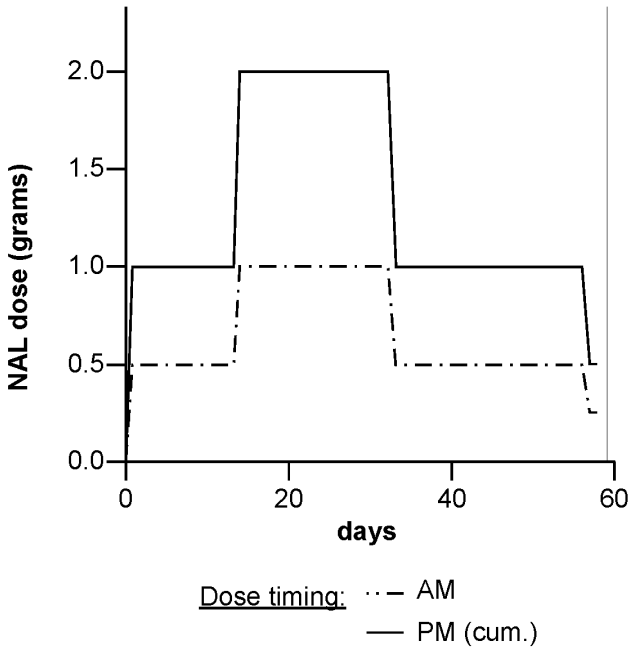


FIG. 16A

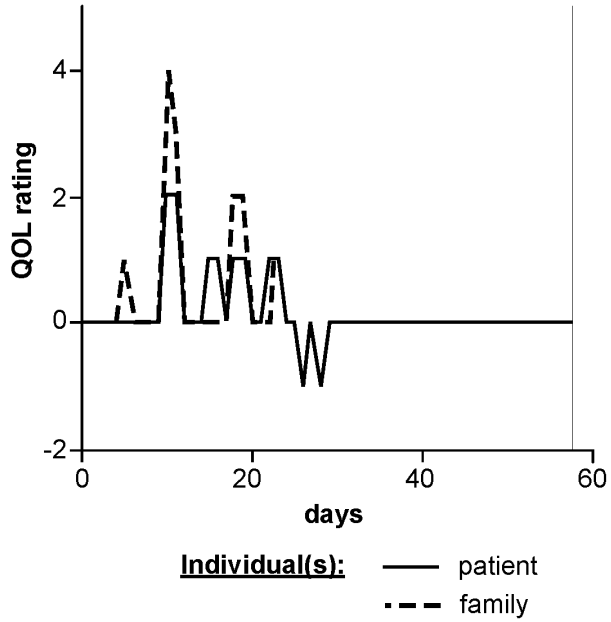


FIG. 16B

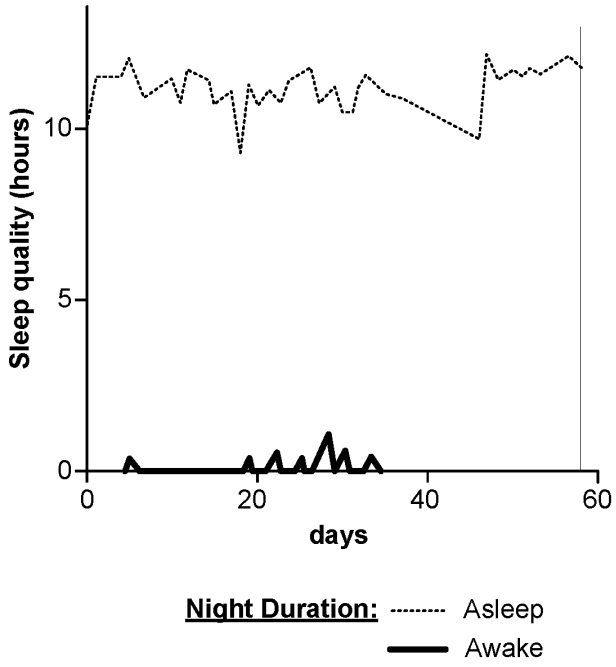


FIG. 16C

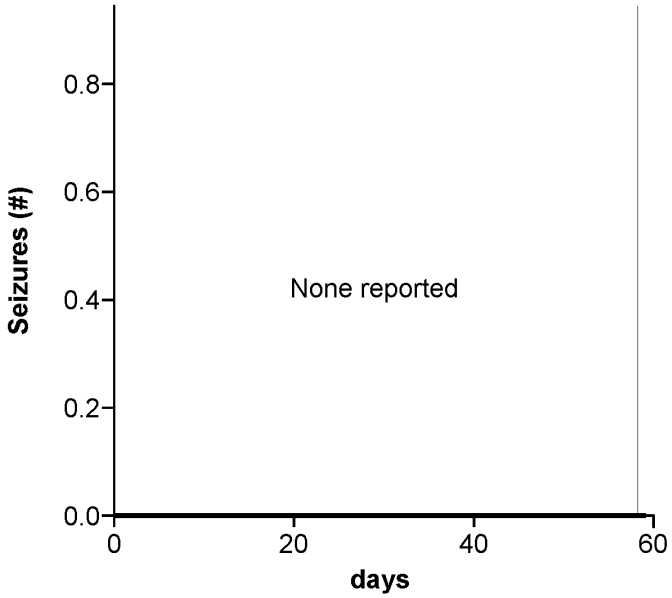


FIG. 16D

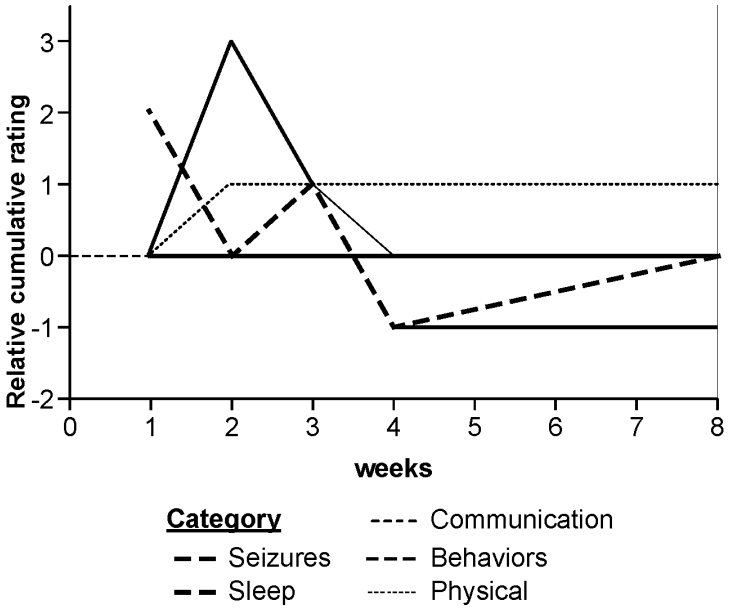


FIG. 16E

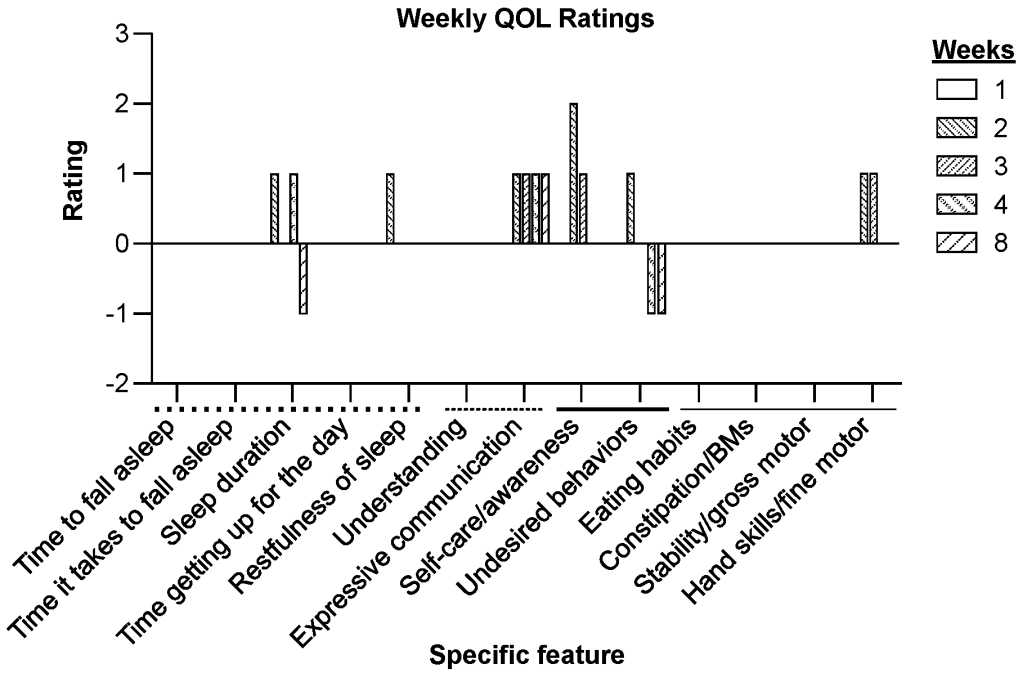


FIG. 16F

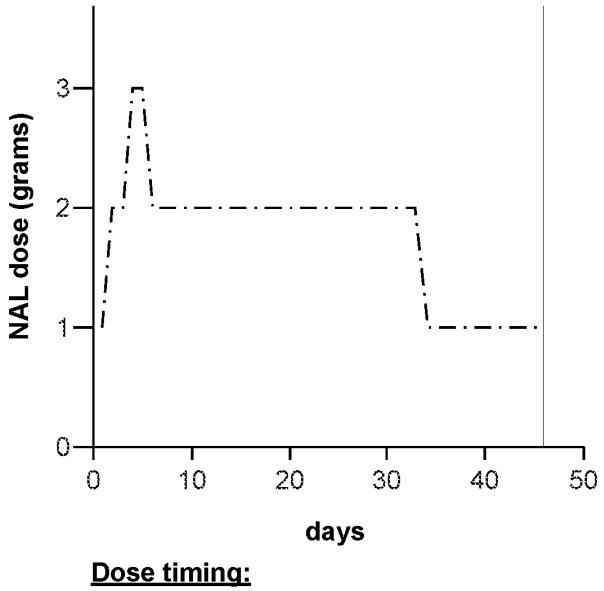


FIG. 17A

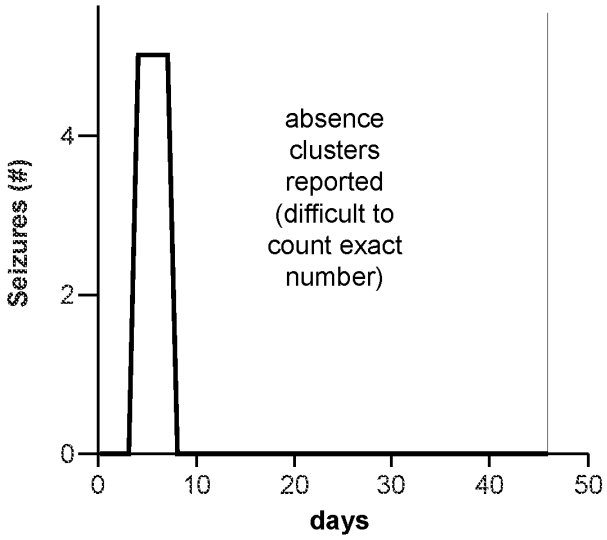
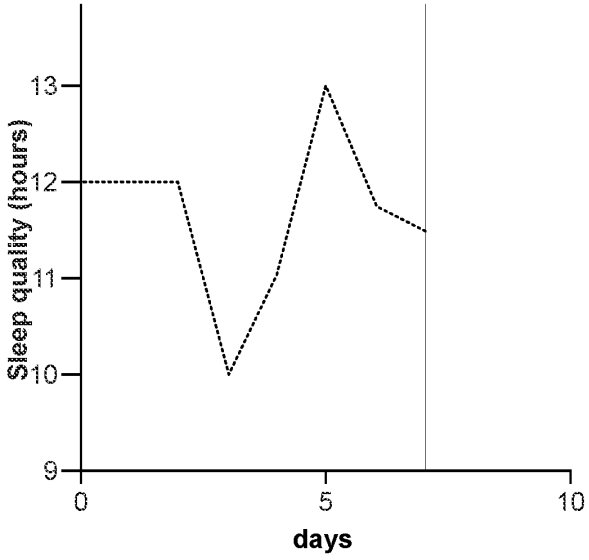


FIG. 17B



Night Duration:

FIG. 17C

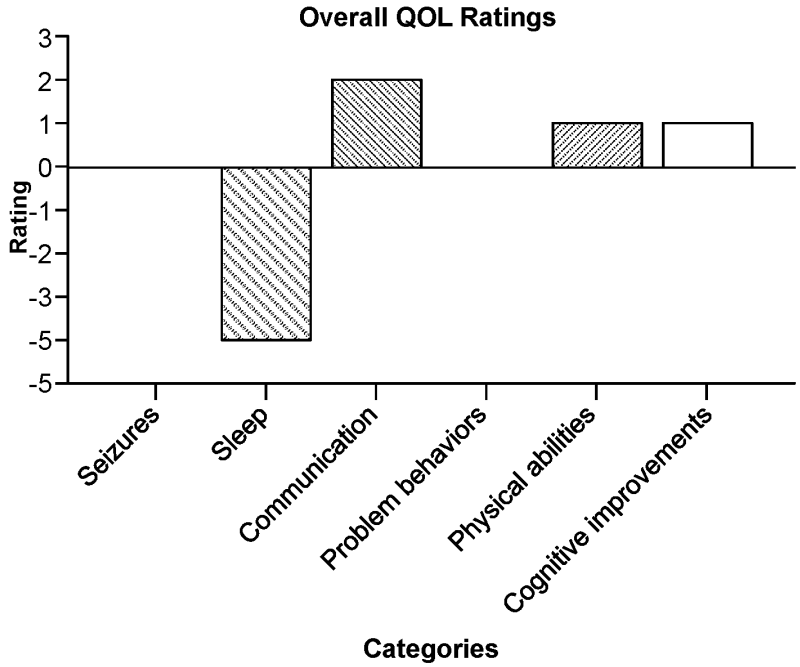


FIG. 18

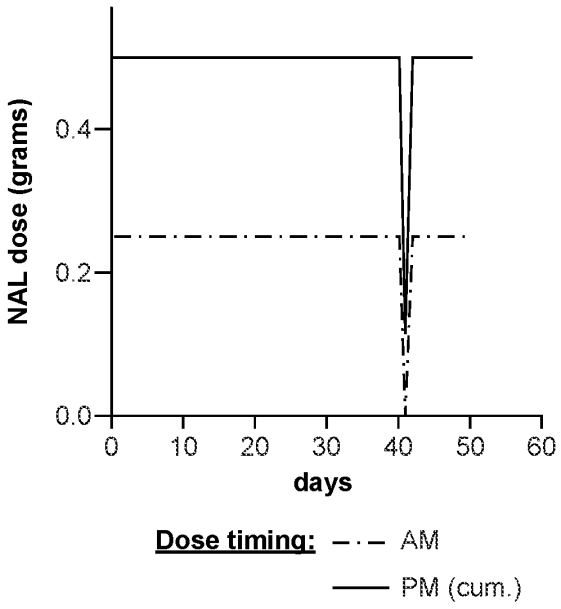


FIG. 19A

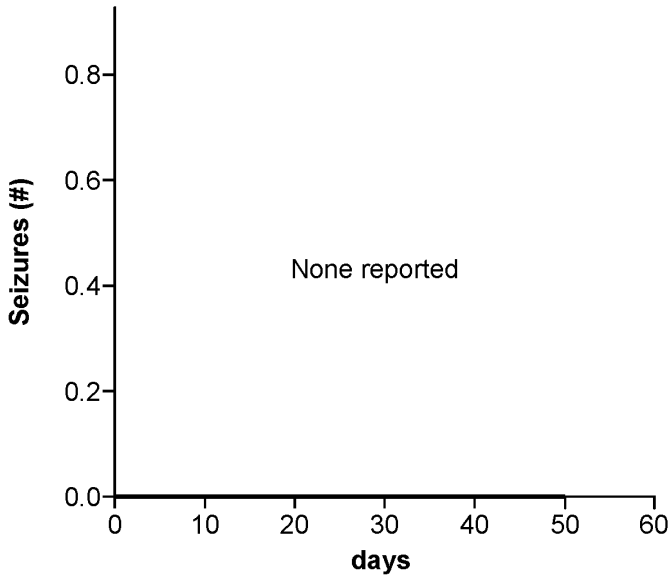


FIG. 19B

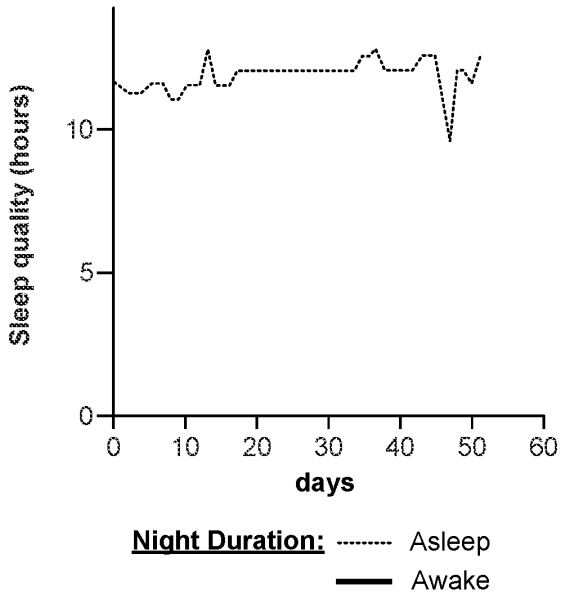


FIG. 19C

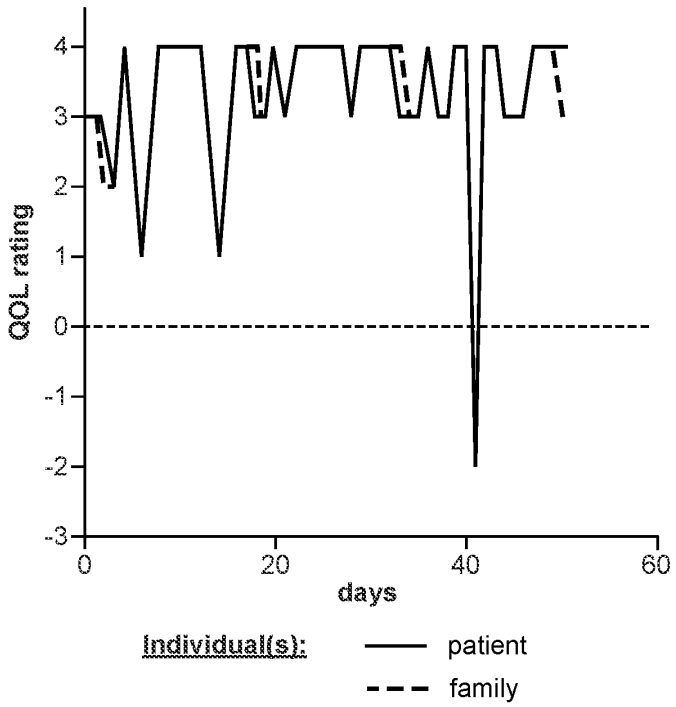


FIG. 19D

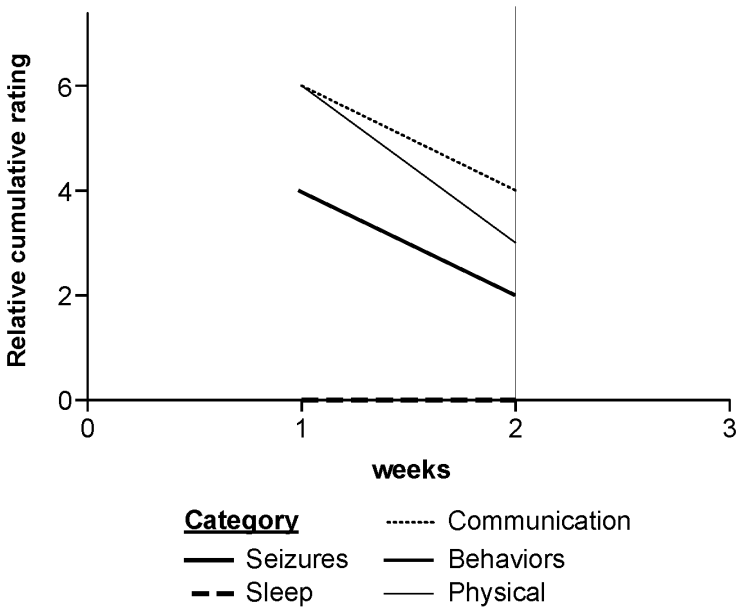


FIG. 19E

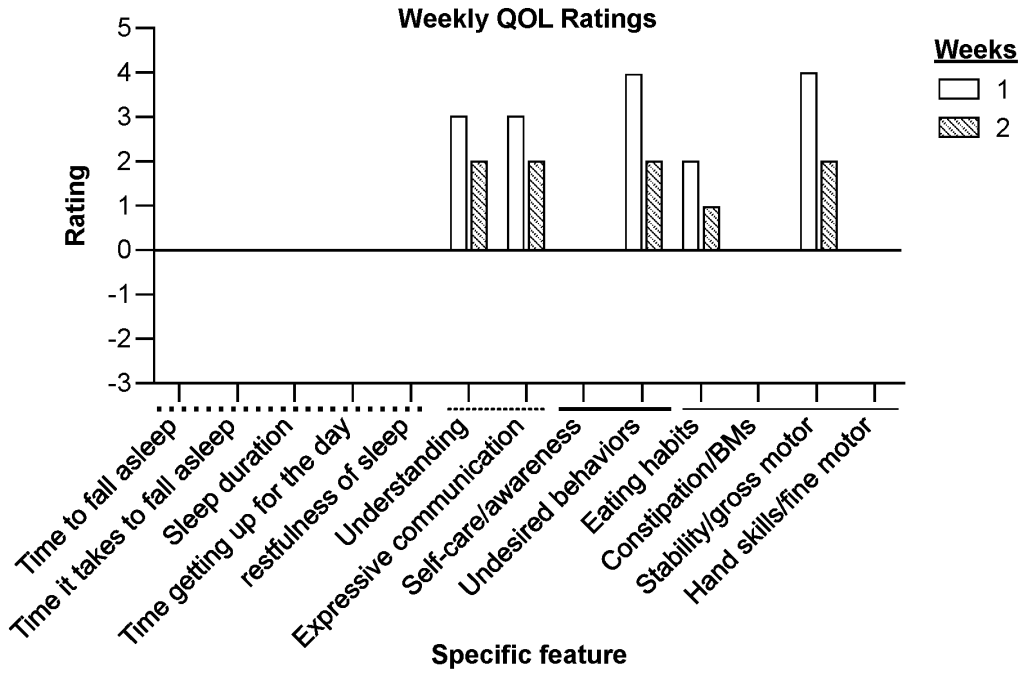


FIG. 19F

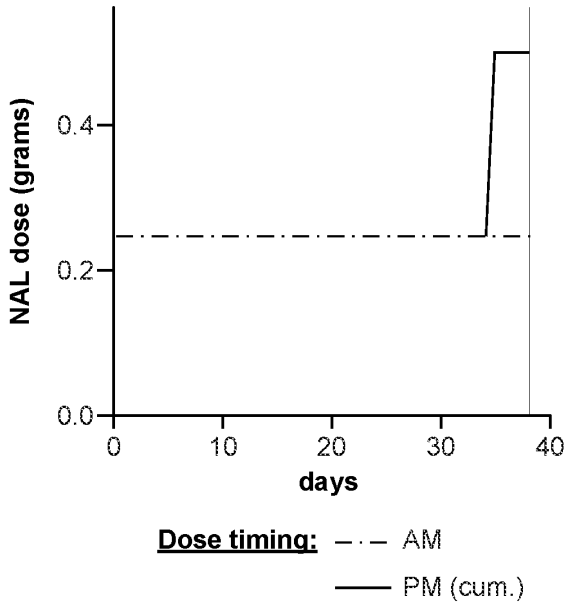


FIG. 20A

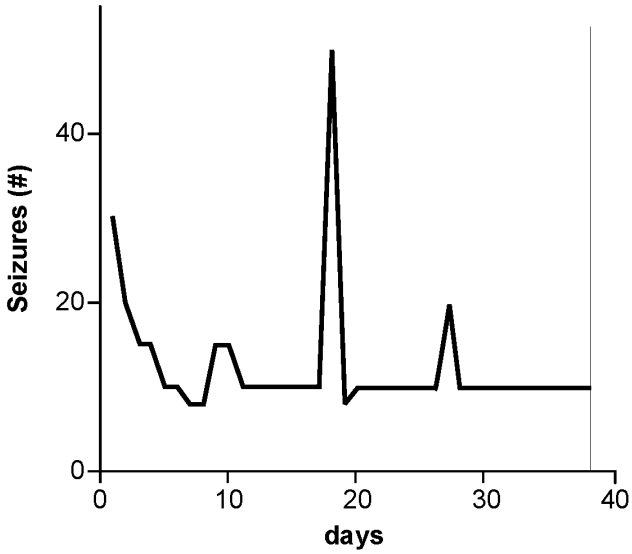


FIG. 20B

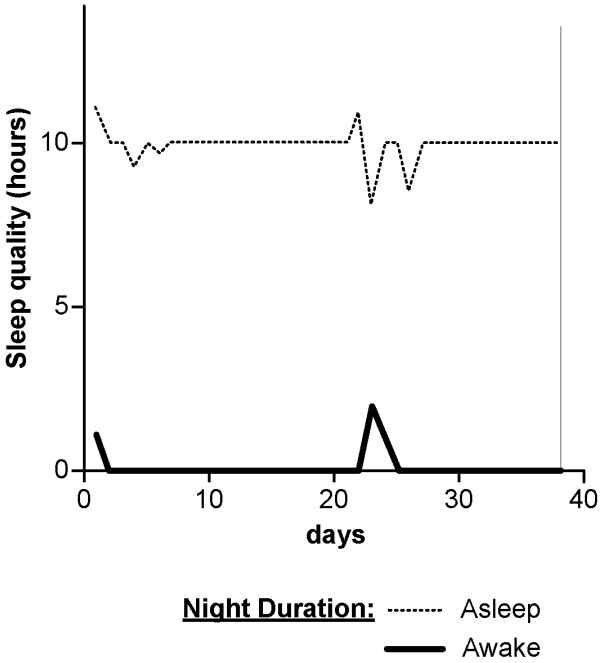


FIG. 20C

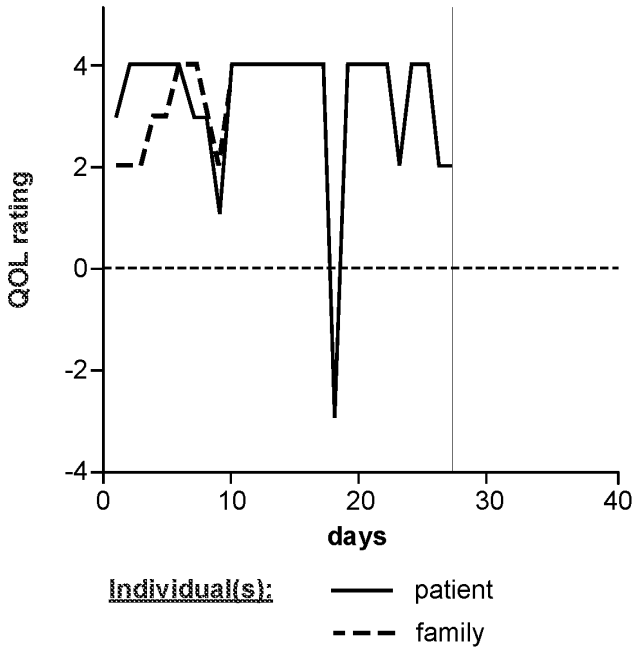


FIG. 20D

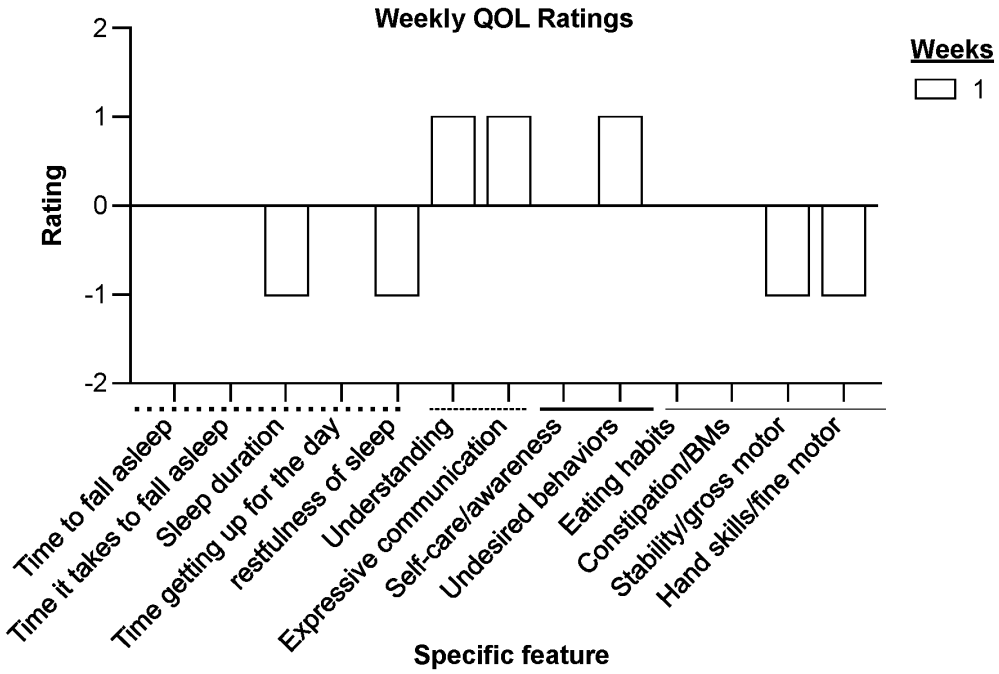


FIG. 20E

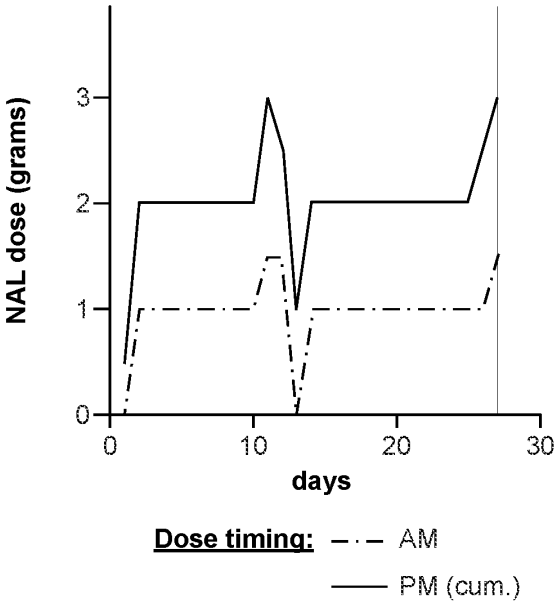


FIG. 21A

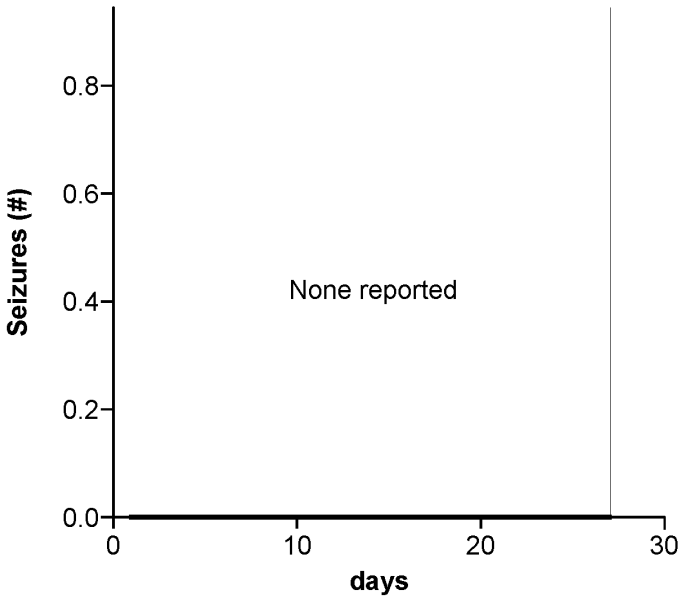


FIG. 21B

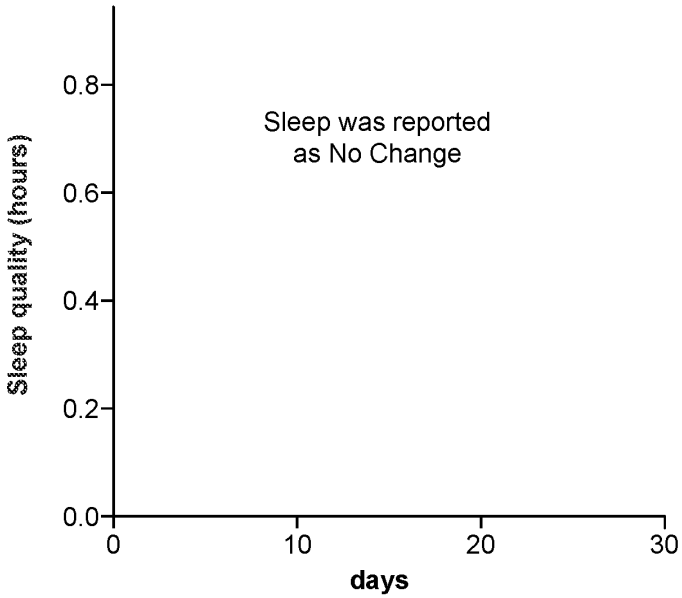


FIG. 21C

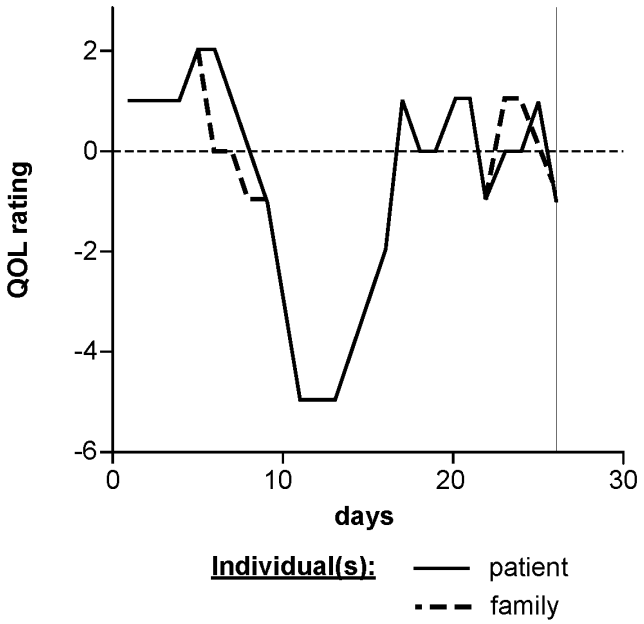


FIG. 21D

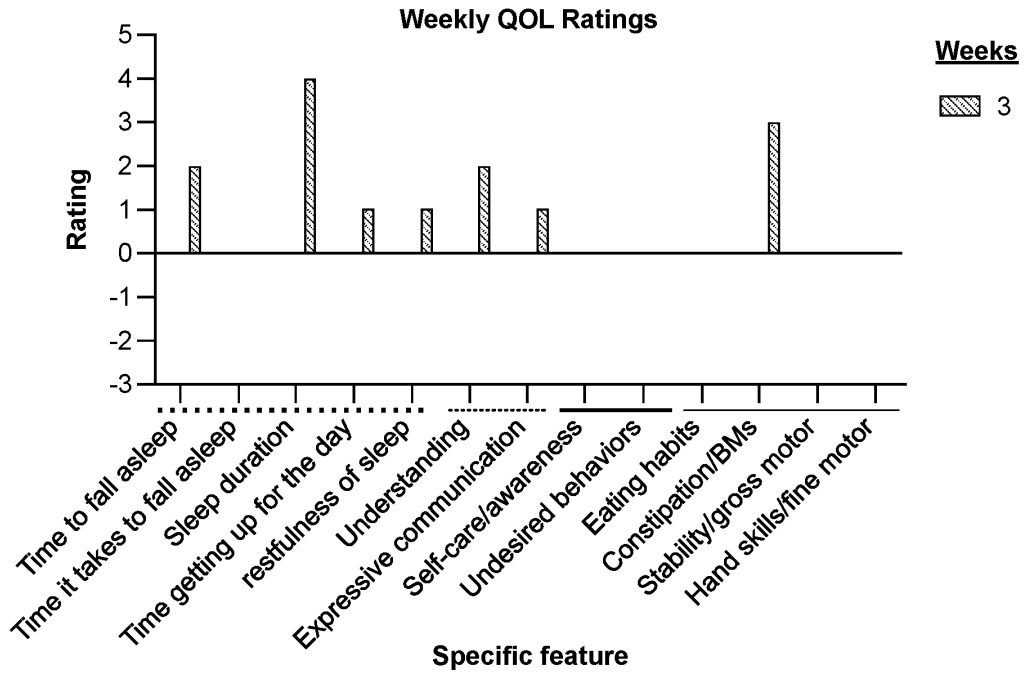


FIG. 21E

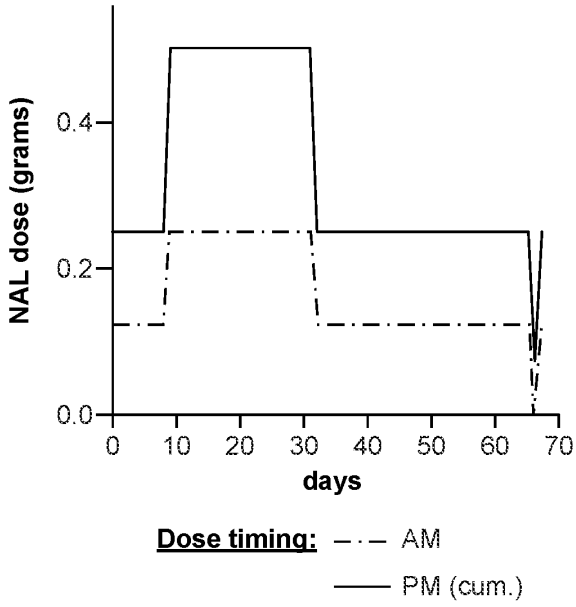


FIG. 22A

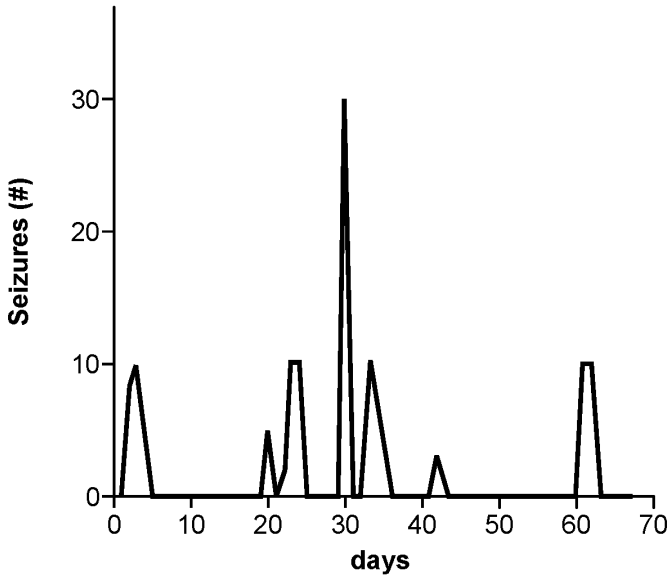


FIG. 22B

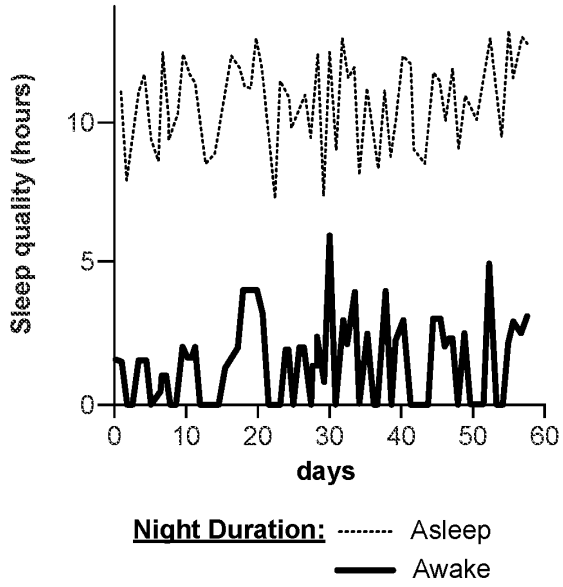


FIG. 22C

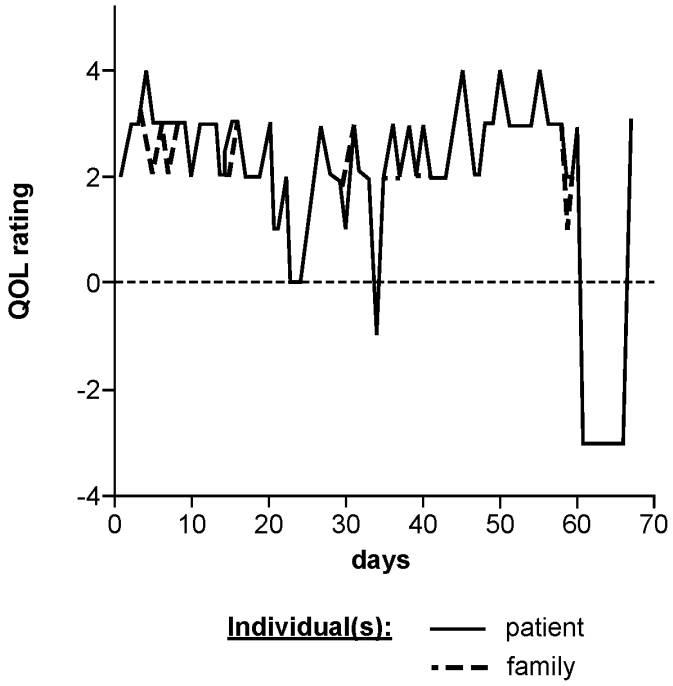


FIG. 22D

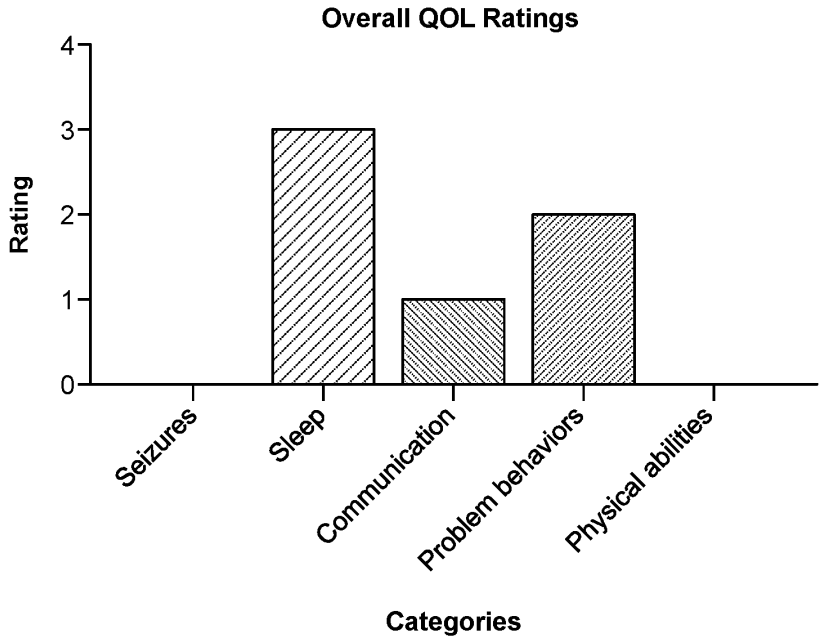


FIG. 23

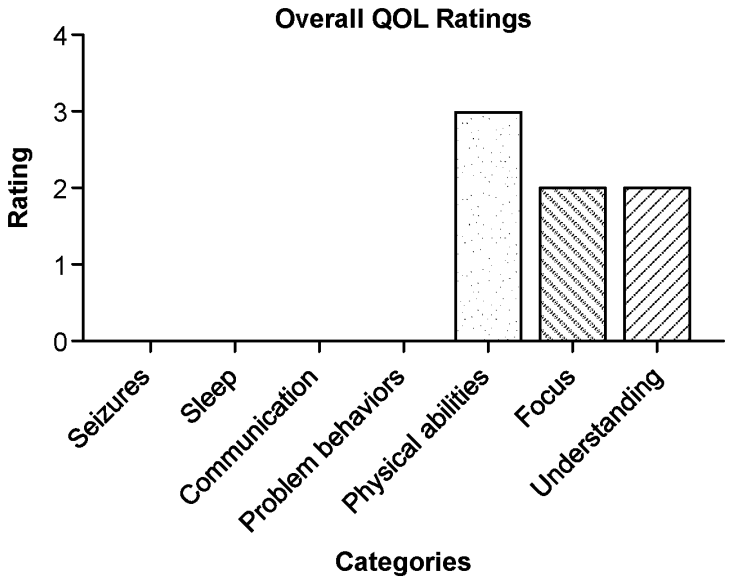


FIG. 24

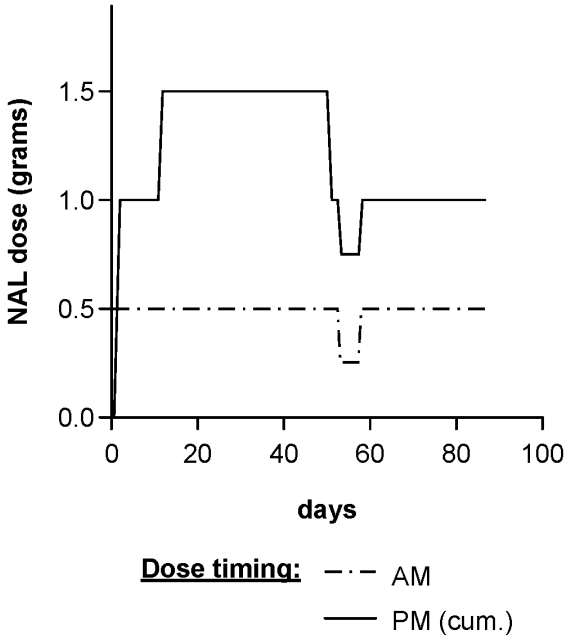


FIG. 25A

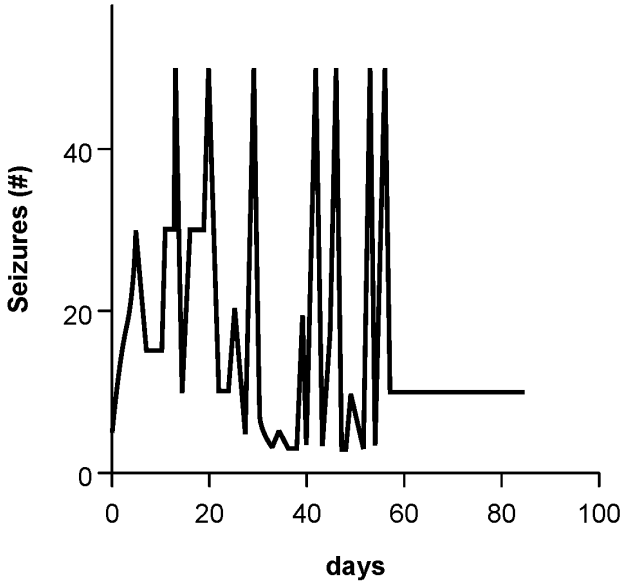


FIG. 25B

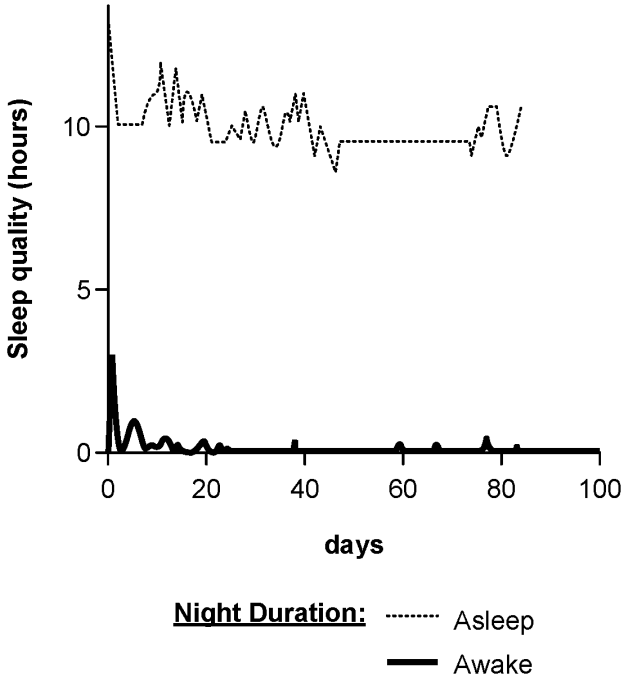


FIG. 25C

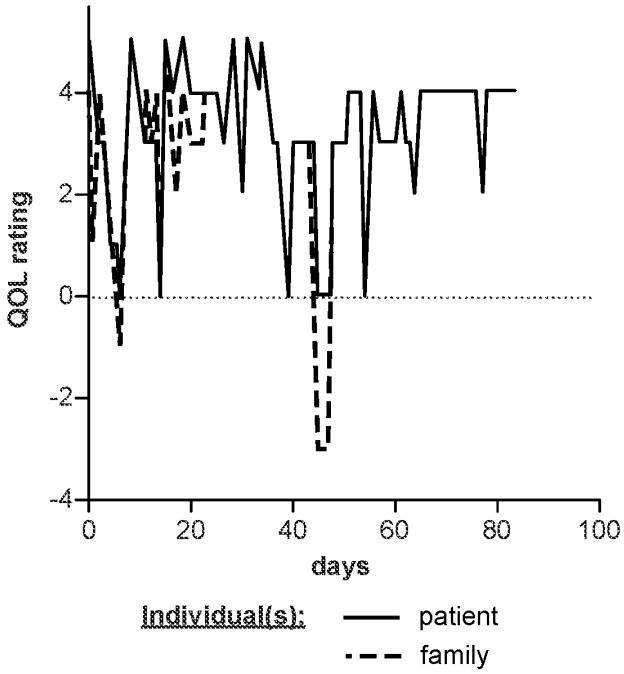


FIG. 25D

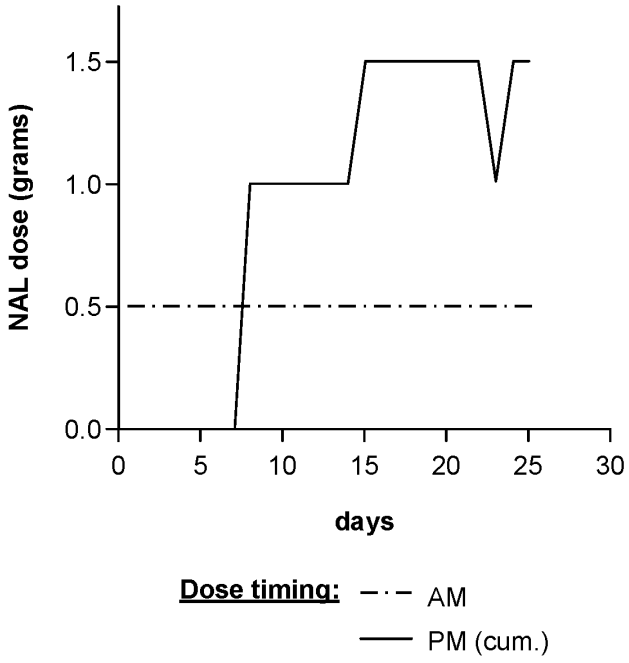


FIG. 26A

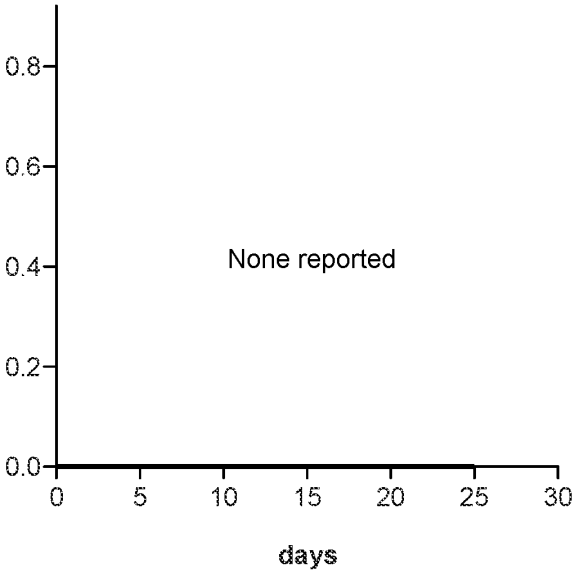
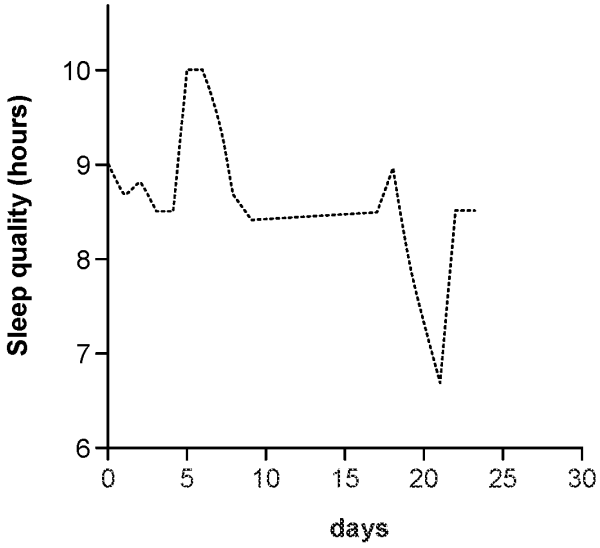


FIG. 26B



Night Duration: --------- Asleep

FIG. 26C

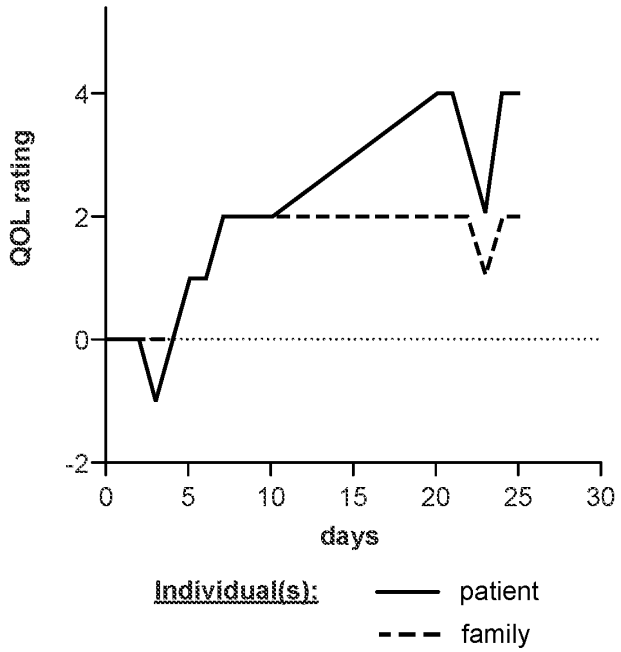


FIG. 26D

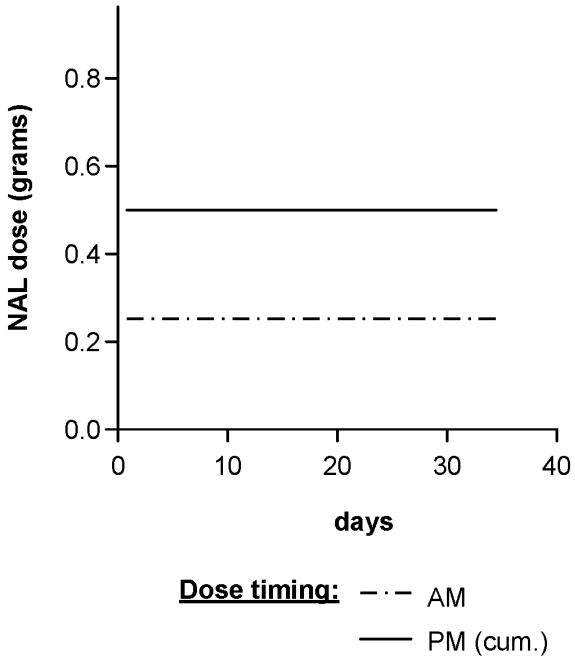


FIG. 27A

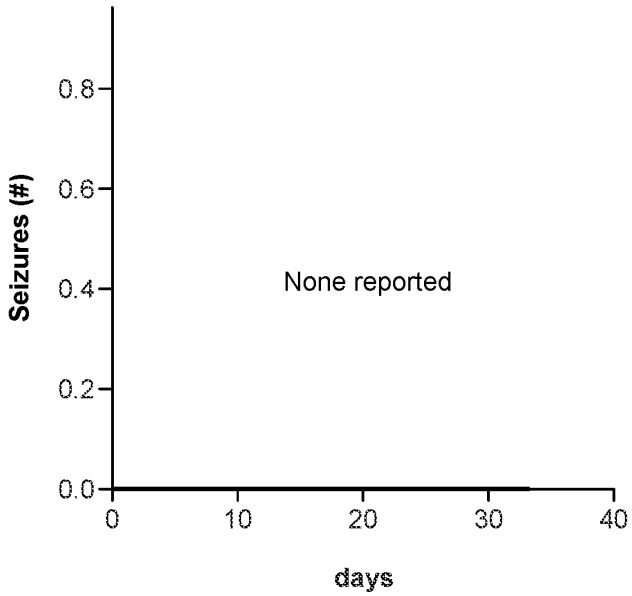


FIG. 27B

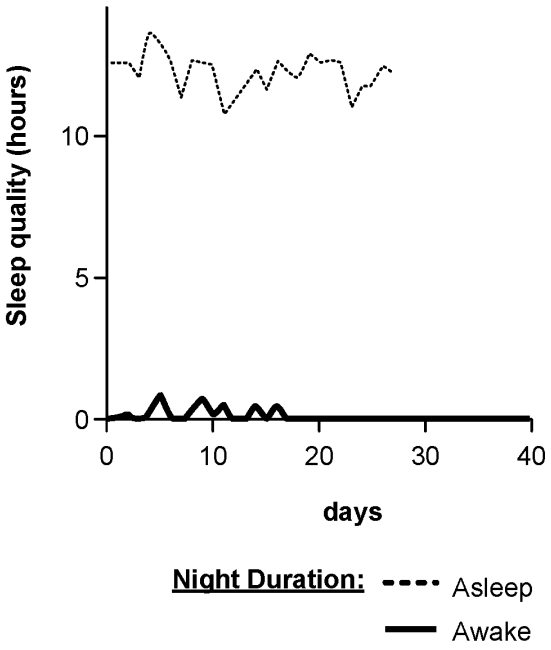


FIG. 27C

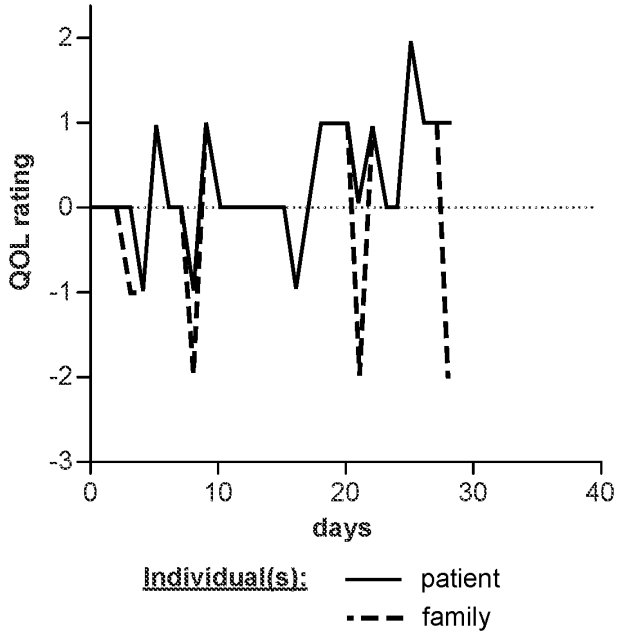


FIG. 27D

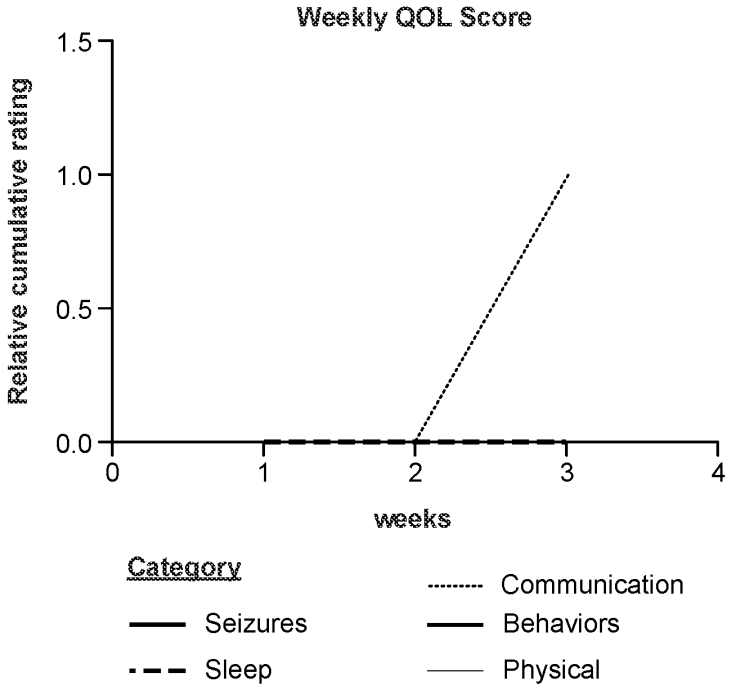


FIG. 27E

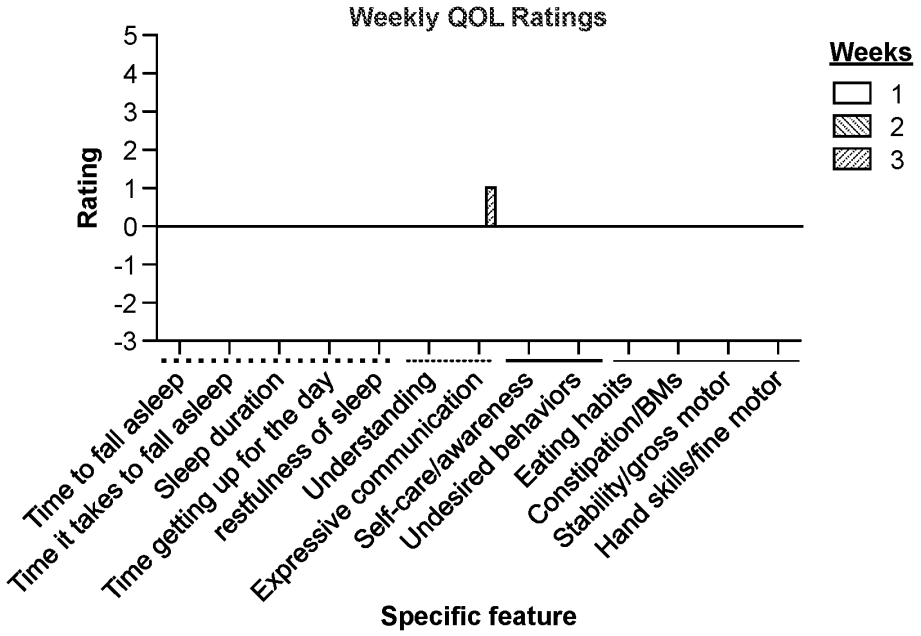


FIG. 27F

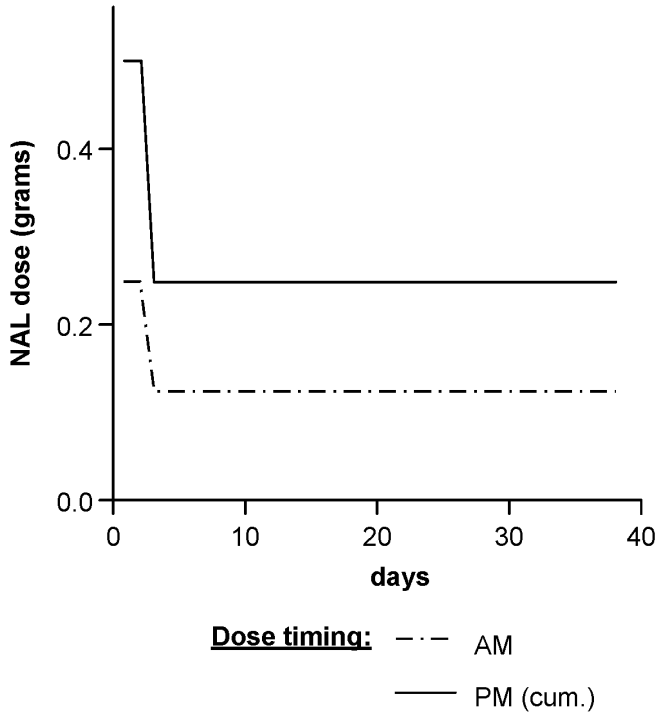


FIG. 28A

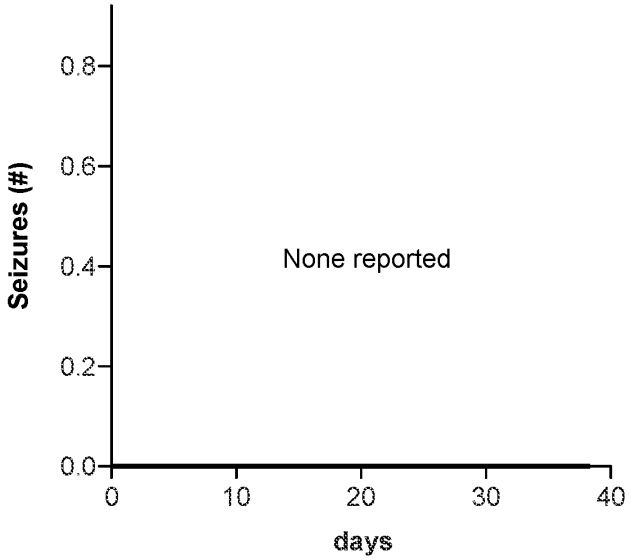


FIG. 28B

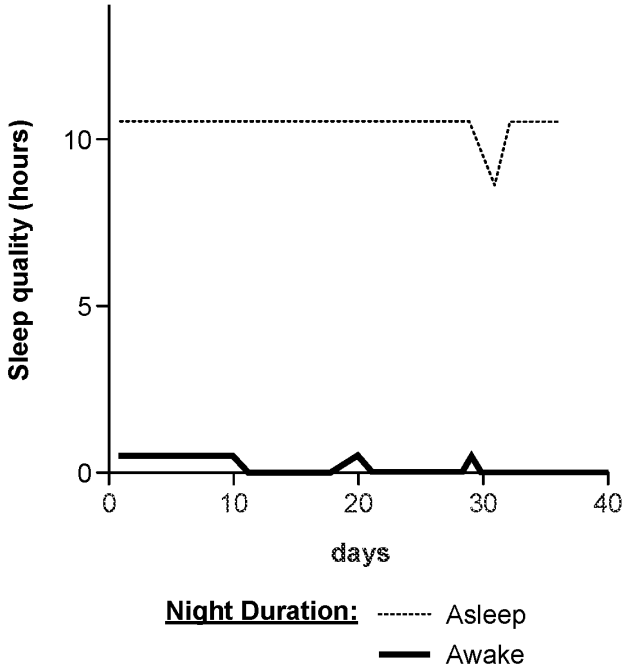


FIG. 28C

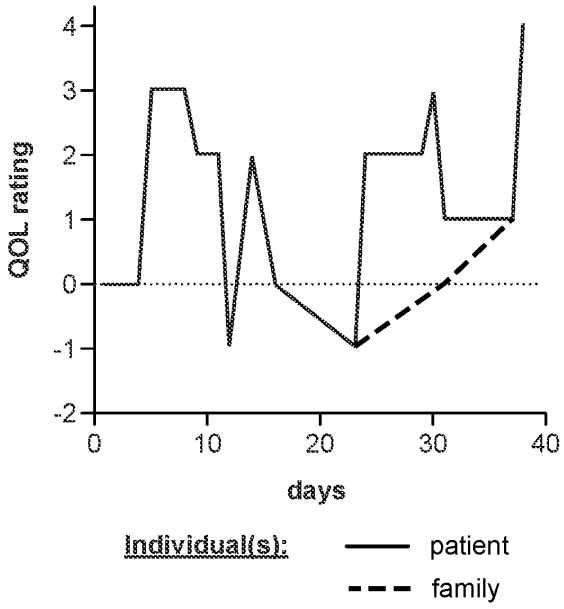


FIG. 28D

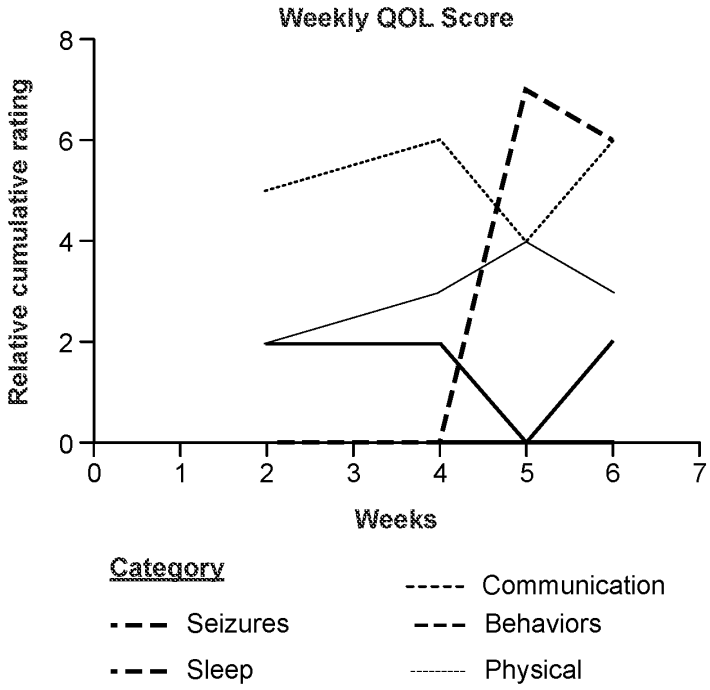


FIG. 28E

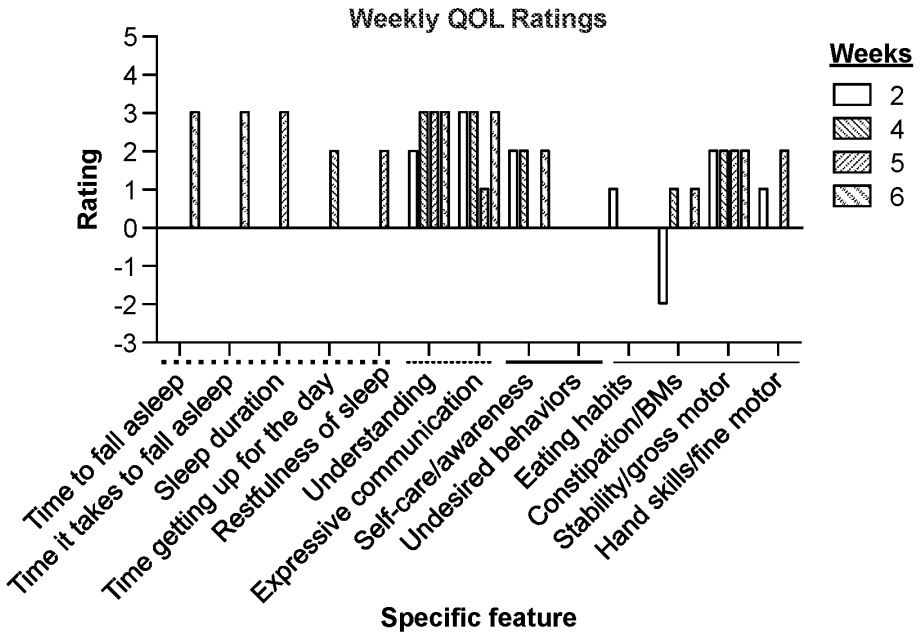


FIG. 28F

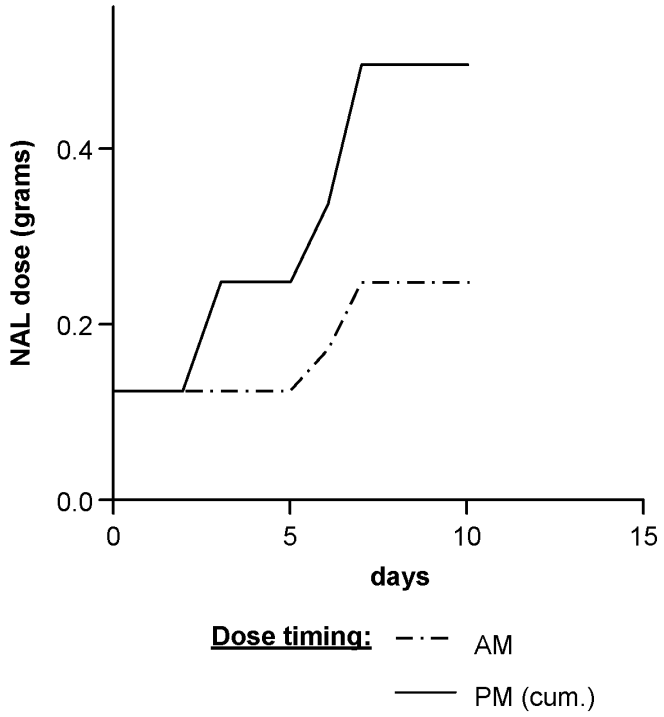


FIG. 29A

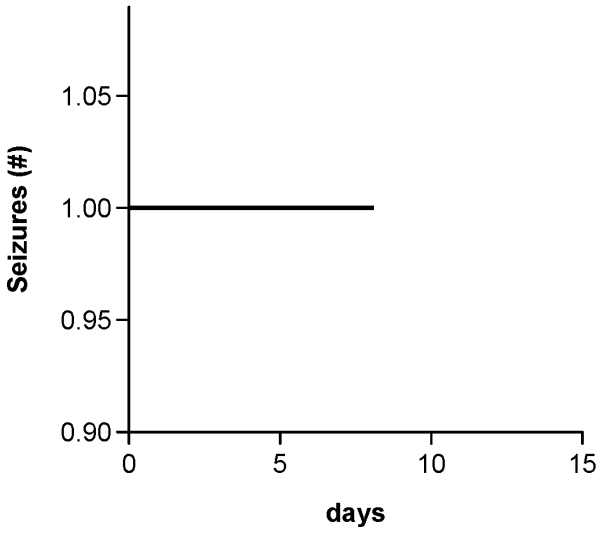


FIG. 29B

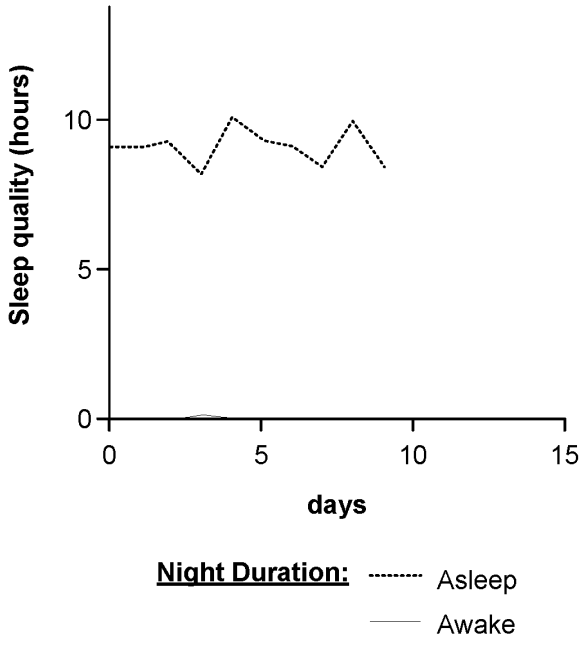


FIG. 29C

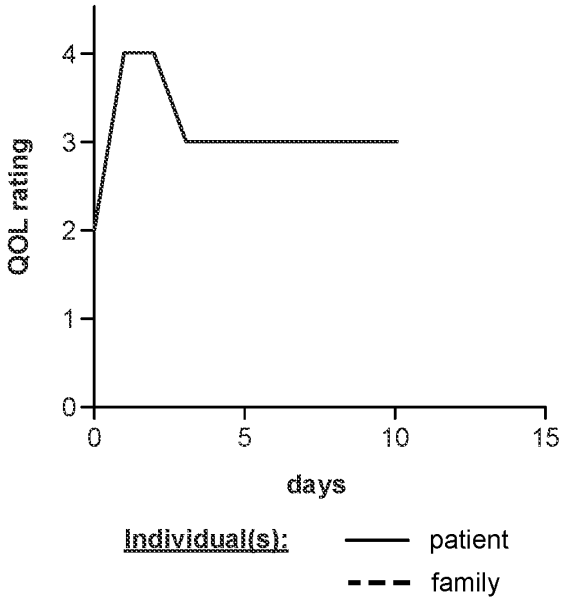


FIG. 29D

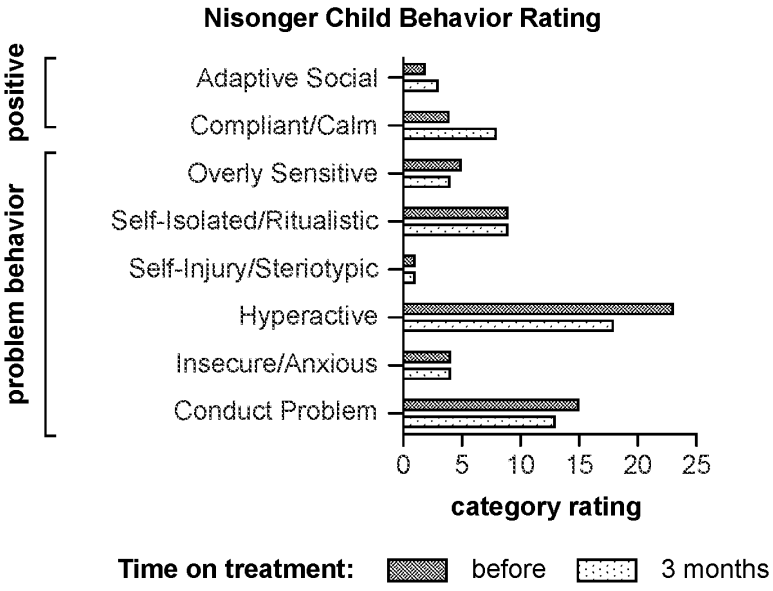


FIG. 30A

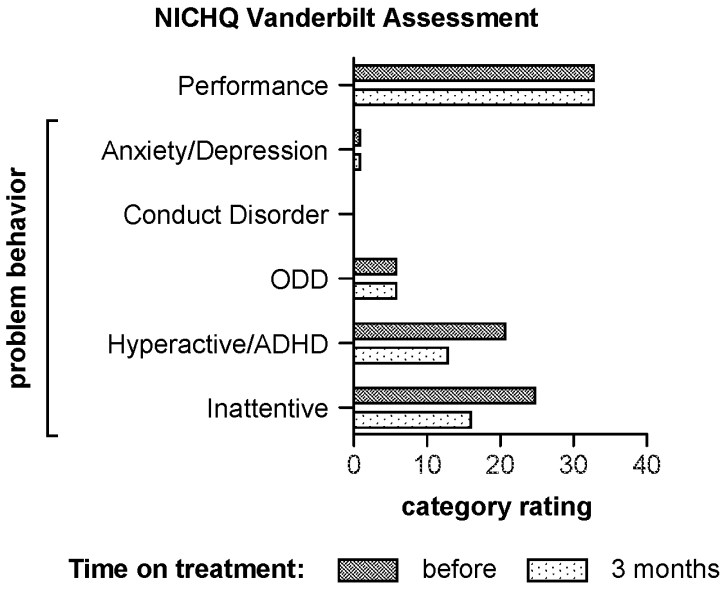


FIG. 30B

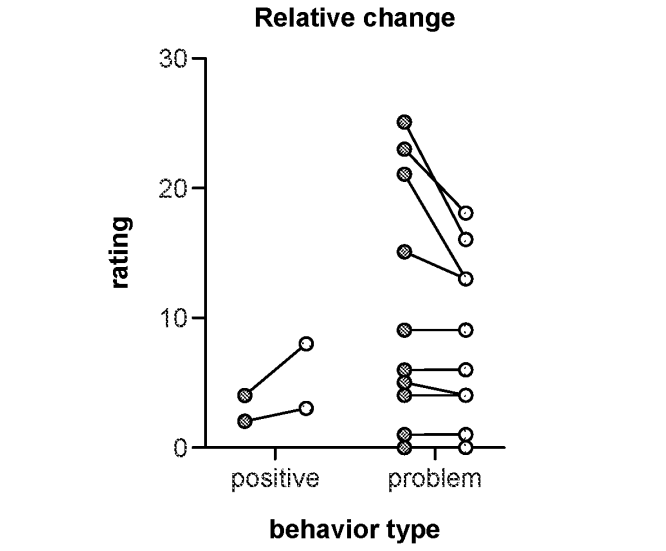


FIG. 30C