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Role of substance P and CGRP in PAR-2-induced rectal hyperalgesia in rats

Bruno Guiard, Nicolas Cenac, Rafael Garcia Villar, Nathalie Vergnolle, Anne-Marie Coelho, Jean Fioramonti, Lionel Bueno

► To cite this version:

Bruno Guiard, Nicolas Cenac, Rafael Garcia Villar, Nathalie Vergnolle, Anne-Marie Coelho, et al.. Role of substance P and CGRP in PAR-2-induced rectal hyperalgesia in rats. 2001 A Brain-Gut Odyssey, Jul 2001, Oxford, Angleterre, United Kingdom. Digestion, 2001, Digestion. 10.1159/000051897 . hal-01604751

HAL Id: hal-01604751

<https://hal.science/hal-01604751>

Submitted on 4 Jun 2020

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Abstracts

2001: A Brain Gut Odyssey

July 11–15, 2001, Oxford, UK

Digestion 2001;63:247–279

<https://doi.org/10.1159/000051897>
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H. Raybould, Davis, Calif., USA
F. Azpiroz, Barcelona, Spain

Contents

Oral Presentations

01–028

Poster Session I

The Brain I

Receptors

Potential for

Feeding, O

The Brain-I

Poster Session II

Gut to Brain

The Neuro

The Brain-II



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Article / Publication Details

Published online: June 29, 2001

Issue release date: 2001

Number of Print Pages: 33

Number of Figures: 0

Number of Tables: 0

ISSN: 0012-2823 (Print)

eISSN: 1421-9867 (Online)

For additional information:

<http://www.karger.com/DIG>

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Contents

Oral Presentations

01–028

Poster Session I

The Brain in the Gut

P1–P5

Receptors and Transmitters in the Brain-Gut Axis:

Potential for Novel Therapies

P6–P14

Feeding, Obesity and the Brain-Gut Axis

P15–P17

The Brain-Gut Axis: Sensations and Psyche

P18–P25

Poster Session II

Gut to Brain Signalling

P26–P37

The Neuroimmune Brain-Gut Axis

P38–P45

The Brain-Gut Axis: Painful Memories

P46–P61

"2001 A BRAIN-GUT ODYSSEY"
OXFORD, UK, July 11-15, 2001.

In: DIGESTION 63, p.275.

ROLE OF SUBSTANCE P AND CGRP IN PAR-2-INDUCED RECTAL HYPERALGESIA IN RATS

Intracolonic infusion to rats of the proteinase-activated receptor-2 (PAR-2) activating-peptide SLIGRL, induced delayed hyperalgesia to rectal distension (RD). This study investigates the involvement of substance-P (SP) and calcitonin gene-related peptide (CGRP) in PAR-2-induced visceral hyperalgesia.

Methods: Four groups (n=6-8) of male Wistar rats (250-300g) were equipped with an intracolonic (IC) catheter for SLIGRL (0.2mg/rat) or saline (0.25ml/rat) infusions, and electrodes for recording abdominal contraction (mean±SEM for 5-min episodes) as visceral pain index. RD was performed by 5min steps of 0.4ml (0 to 1.2mL). Groups 1&2 were infused with SLIGRL or saline (0.25mL/20min) respectively, and the NK1-antagonist SR140333 (1mg/kg-IP): first, SR140333 was administered 30min before SLIGRL or saline; second, 3 days later, SR140333 was administered 10h after SLIGRL or saline. Groups 3&4 were similarly infused with SLIGRL or saline respectively, and the CGRP receptor-antagonist human-CGRP₈₋₃₇ (100 µg/kg-IV), 20min before and 10h after SLIGRL or saline.

Results: SLIGRL (group 1) but not saline (group 2) induced 10h-delayed visceral hyperalgesia to RD (45.0±4.1 contractions vs 33.3±3.0 in basal conditions i.e. 36% increase; p<0.05). SR140333 inhibited SLIGRL-induced hyperalgesia when administered before (45.0±4.1 vs 31.2±4.5; p<0.05) but not after SLIGRL (45.0±4.1 vs 48.0±4.8; p>0.05).

Similarly, SLIGRL (group 3) but not saline (group 4) increased the number of abdominal contractions by 47% in response to RD (1.2mL) at 10h post-infusion. hCGRP₈₋₃₇ did not affect SLIGRL-induced hyperalgesia when administered either before or after SLIGRL.

Conclusion: NK1-receptor blockade prevents SLIGRL-induced visceral hyperalgesia which suggests that SP, but not CGRP, is involved in PAR-2-induced sensitization of primary afferent neurons.

B. Guiard, N. Cenac, R. Garcia-Villar, A.M. Coelho, J. Fioramonti, L. Bueno

N. Versnalle.

Author Index for abstracts

Digestion

Numbers refer to page number

- Abrahams, T.P. 259
Adelson, D.W. 268
Aja, S. 263
Akkermans, L.M.A. 277
Al-Chaer, E.D. 254
Altmann, C.A. 254
Avni, Y. 265
Aziz, Q. 254
- Babyatsky, M.W. 272
Baffi, M.C. 273
Ball, A.J. 269
Ballinger, A.B. 273
Bantick, S. 254
Barbara, G. 254
Barrachina, M.D. 271
Beckett, E.A.H. 250
Beckmann, C. 254
Bellinger, L.L. 252
Bielanski, W. 270
Bielefeldt, K. 267, 274
Bilski, J. 262
Bischoff, S. 251
Bonaz, B. 274, 275
Bonior, J. 262, 273
Booth, C.E. 267
Bradley, J.M. 249
Brammer, M.J. 254
Brinkman, B. 264
Brodacz, B. 270
Brown, D.R. 271
Browning, K.N. 272
Bruijnzeel, A.W. 277
Brzozowski, T. 261, 270
Bueno, L. 274, 275
Burr, R.L. 276
Burton, D. 264
- Cáin, K.C. 276
Calatayud, S. 271
Camilleri, M. 264
Cenac, N. 275
Chang, L. 276
Chen, C.-Y. 261
Christen, M.O. 275
Christensen, J. 258
Christofi, F. 250
Cieszkowski, M. 262
Clare, S. 254
Coelho, A.M. 275
Coen, S. 254
Cooke, H.J. 250
Corneliussen, B. 252
Coutinho, S.V. 253, 260
Csáti, S. 271
- Danzer, M. 269
De Giorgio, R. 250
Dembinski, A. 262
Dexing Zang 277
Dockray, G.J. 264
Drozdowicz, D. 270
D'Alessio, D.A. 252
- Ekkelenkamp, K. 277
El-Haj, T. 273
Eliakim, R. 272
Enck, P. 256, 265, 278
Ennes, H.S. 252
Esplugues, J.V. 271
- Falzone, M.R. 273
Fan, Q. 272
Farthing, M.J.G. 273
Feuerstein, C. 274
Fioramonti, J. 274, 275
Fournet, J. 274, 275
Fowler, C.J. 256
Frankhuijzen, A.C. 277
Fujita, M. 266
- García-Villar, R. 275**
García-Zaragoza, E. 271
Gaykema, R.P.A. 272
Gebhart, G.F. 267, 274, 275
Gietzen, D.W. 252
Glass, M.E. 266
Glatzle, J. 258, 268
Goehler, L.E. 255, 272
Green, B.T. 271
Gregory, J. 254
Grodd, W. 278
Grundy, D. 251, 267
Guerrini, S. 258
Gui, A. 265
Guiard, B. 275
- Hahn, E.C. 270
Hahn, E.G. 261
Hall, G. 265
Hamdy, S. 257
Hanna, R. 250
Hausmann, S. 265
Heitkemper, M.M. 276
Hermann, G.H. 272
Hicks, G.A. 267
Hinninghofen, H. 278
Hobson, A. 254
Holzer, P. 259, 268, 269
Holzer-Petsche, U. 270
Hornby, P.J. 259, 269
- Horváth, Gy. 270
Humphrey, P.P.A. 267
- Izbéki, F. 271
- Jarrett, M.E. 276
Javed, N. 250
Jaworek, J. 262, 273
Jehle, E.C. 278
Jinton, L. 252
Jocic, M. 268
- Kalogeris, T.J. 268
Kamp, E.H. 275
Kapur, R.P. 249
Kim, M. 250
Kinnamon, S.C. 253
Kirkup, A.J. 251, 267
Klose, J. 265
Klosterhalfen, S. 265
Konturek, P.C. 261, 270
Konturek, S.J. 261, 262, 273
Kot, M. 262, 273
Kroese, A.B.A. 249
Kuo, B. 264
Kuratani, K. 261
Kwiecien, S. 261, 270
- La Roche, B. 275
Lachey, J.L. 252
Lal, S. 264
Lamy, C. 274
Leja, A. 262, 273
Leray, V. 275
Leslie, F.C. 264
Linden, D.R. 249
Lippe, I.Th. 259
Liu, J. 265
Liu, M. 263
Lonovics, J. 271, 274
Lotze, M. 278
Lukovetski, E. 265
Lyte, M. 271, 272
- Majka, J. 262
Mandal, B.K. 264
Martínez, V. 263
Martínez-Cuesta, M.A. 271
Marvizón, J.C. 252, 253
Mawe, G.M. 249
Mayer, E.A. 252, 253, 276
Mckinzie, S. 264
McLaughlin, J. 251
McLaughlin, J.T. 264
McRoberts, J.A. 252, 253
- Miampamba, M. 259
Michel, K. 251
Michl, T. 268
Miftakhov, R.N. 258
Miller, J.C. 253
Million, M. 259, 260, 261
Miselis, R.R. 278
Mittal, R.K. 265
Moerschbaecher, J.M. 269
Moran, T.H. 263
Mulè, F. 273
Naliboff, B.D. 276
- Narain, C. 254
Nawrot, K. 262, 273
Ng, V.W.K. 254
Nimaggadda, K. 272
- Orr, W.C. 276
Otto, B. 265
Owyang, C. 260
Ozaki, N. 267, 274
O'Connor, M. 264
- Pachnis, V. 249
Painsipp, E. 269
Pajdo, R. 261, 270
Partosoedarso, E.R. 251, 259
Pawlik, M. 261, 270
Pawlik, W. 262, 273
Perscha-Lippe, I.Th. 269
Peters, S. 251
Ploghaus, A. 254
Poole, S. 273
Ptak, A. 270
- Quintana, E. 271
- Rawlins, J.N.P. 254
Raybould, H.E. 258, 268
Reeve Jr, J.R. 258
Rivier, J. 260, 263
Robin, C. 258
Robinson, D.R. 267
Rogers, R.C. 272
Ron, Y. 265
Rosztóczy, A. 274
Rouzade-Dominguez, M.L. 278
- Sablad, M.R. 253
Sanders, K.M. 250
Santos, J. 255
Saunders, P. 260

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- Schemann, M. 251
 Schey, R. 263
 Schicho, R. 259, 269
 Schuligoi, R. 268
 Seeley, R.J. 252
 Sendur, R. 262, 273
 Sharkey, K.A. 249
 Sinniger, V. 274, 275
 Slice, L.W. 258
 Smedh, U. 263
 Song, B. 252
 Stachura, J. 273
 Stam, R. 277
 Sternini, C. 258
 Stockhorst, U. 265
 Szlachcic, A. 262
- Taché, Y. 259, 260, 261, 263
 Tada, H. 266
 Takahashi, T. 266
 Takeda, T. 265
 Thomforde, G. 264
 Thompson, D.G. 254, 264
 Thompson, J. 276
 Tjwa, E.T.T.L. 249
 Tomaszewska, R. 273
 Tracey, I. 254
 Travagli, R.A. 272
 Tso, P. 253, 263, 268
- Vale, W. 260
 Valentino, R.J. 278
 Vanner, S. 255
- Varro, A. 264
 Vergnolle, N. 256, 275
 Viramontes, B. 264
- Wang, L. 260, 263
 Wang, X. 252
 Wang, Y.H. 268
 Ward, S.M. 250
 Wardi, J. 265
 Warzecha, Z. 262
 Wei, J.Y. 268
 Wiegant, V.M. 277
 Wietek, B. 278
 Wiley, J.W. 256
 Williams, S.C.R. 254
 Wise, R. 254
- Wittmann, T. 271, 274
 Wong, H. 258
 Wright, B. 272
 Wu, H. 249
 Wu, X.Y. 260
- Yaguez, L. 254
 Ying Li 260
- Zhang, J. 272
 Zhao, X. 278
 Zhao, Y. 260
 Zhiqiang Wang 277
 Zhixiang Shen 277
 Zittel, T.T. 258, 268