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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

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# Digestion

Abstracts

## 2001: A Brain Gut Odyssey

July 11–15, 2001, Oxford, UK

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Guest Editors

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 Se

Gut to Brai

The Neuroi

The Brain-I



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## Contents

<b>Oral Presentations</b>	01–028
<b>Poster Session I</b>	
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
<b>Poster Session II</b>	
Gut to Brain Signalling	P26–P37
The Neuroimmune Brain-Gut Axis	P38–P45
The Brain-Gut Axis: Painful Memories	P46–P61

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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-CGRP<sub>8-37</sub> (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. hCGRP<sub>8-37</sub> 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