Title: Do TRPC channels support working memory? Comparing modulations of TRPC channels and working memory through G-protein coupled receptors and neuromodulators

Authors: Antonio Reboreda, Frederik M. Theissen, Maria Valero-Aracama, Alberto Arboit, Mihaela A. Corbu, Motoharu Yoshida

PII: S0166-4328(17)30994-4
DOI: https://doi.org/10.1016/j.bbr.2018.02.042
Reference: BBR 11317

To appear in: *Behavioural Brain Research*

Received date: 13-6-2017
Revised date: 27-2-2018
Accepted date: 27-2-2018

Please cite this article as: Reboreda A, Theissen FM, Valero-Aracama M, Arboit A, Corbu MA, Yoshida M, Do TRPC channels support working memory? Comparing modulations of TRPC channels and working memory through G-protein coupled receptors and neuromodulators, *Behavioural Brain Research* (2010), https://doi.org/10.1016/j.bbr.2018.02.042

Do TRPC channels support working memory? Comparing modulations of TRPC channels and working memory through G-protein coupled receptors and neuromodulators

Antonio Reboreda[1,2*], Frederik M Theissen[2], Maria Valero-Aracama[3], Alberto Arboit[2], Mihaela A Corbu[4], Motoharu Yoshida[1,2,5*]

Affiliations:

[1]Leibniz Institute for Neurobiology (LIN) Magdeburg.
Brenneckestraße 6, 39118 Magdeburg, Germany.

[2]German Center for Neurodegenerative Diseases (DZNE) Magdeburg.
Leipziger Str. 44 / Haus 64, 39120, Magdeburg, Germany.

[3]Institute of Physiology and Pathophysiology, Friedrich-Alexander-Universität Erlangen-Nürnberg. Universitätsstraße 17, 91054 Erlangen, Germany.

[4]Ruhr University Bochum (RUB). Universitätsstraße 150, 44801, Bochum, Germany.

[5]Center for Behavioral Brain Sciences, 39106, Magdeburg, Germany.

*Corresponding authors: aprieto@lin-magdeburg.de; motoharu.yoshida@lin-magdeburg.de

Highlights:

- Brain areas involved in working memory show persistent firing *in vivo* and *in vitro*.
- TRPC channels support persistent firing in individual neurons.
- GPCRs that improve WM (e.g. G_q-PLC) generally activates TRPC channels.
- Neuromodulatory receptors that improve WM generally activates TRPC channels.
- These observations support the idea that TRPC channels underlie working memory.

Abstract

Working memory is a crucial ability we use in daily life. However, the cellular mechanisms supporting working memory still remain largely unclear. A key component of working memory is persistent neural firing which is believed to serve short-term (hundreds of milliseconds up to tens of seconds) maintenance of necessary information. In this review, we will focus on the role of transient receptor potential canonical (TRPC) channels as a mechanism underlying persistent firing. Many years of *in vitro* work have been suggesting a crucial role of TRPC channels in working memory and temporal association tasks. If TRPC channels are indeed a central mechanism for working memory, manipulations which impair or facilitate working memory should have a similar effect on TRPC channel modulation. However, modulations of working memory and TRPC channels were never systematically compared, and it remains unanswered whether TRPC channels indeed contribute to working memory *in vivo* or not. In this article, we review the effects of G-protein coupled receptors (GPCR) and neuromodulators, including acetylcholine, noradrenalin, serotonin and dopamine, on working memory and TRPC channels. Based on comparisons, we argue that GPCR and downstream signaling pathways that activate TRPC, generally support working memory, while those that suppress TRPC channels impair it. However, depending on the channel types, areas, and systems tested, this is not the case in all studies. Further work to clarify involvement of specific TRPC channels in working memory tasks and how they are affected by neuromodulators is still necessary in the future.