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The neuroleptic antipsychotic derivate thioridazine has been shown to increase the susceptibility of a methicillin-resistant Staphylococcus aureus (MRSA) isolate towards dicloxacillin. The aim of this study was to investigate the combinatorial effect of the two drugs on a broad selection of staphylococcal strains by analyzing a large collection of MRSA strains carrying different types of SCCmec, as well as MSSA strains. Transcription and translation of the resistance marker PBP2a encoded by mecA within the SCCmec cassette were analyzed by primer extension and western blotting. We observed increased susceptibility to dicloxacillin in the presence of thioridazine in all tested MRSA isolates. In contrast to previously published results, the synergistic effect was also applicable to methicillin-susceptible S. aureus (MSSA). We conclude that the combination of dicloxacillin and thioridazine potentiates the killing effect against S. aureus in a broad selection of clinical isolates. Additionally, the study indicates that the killing effect by the combinatorial treatment is independent of PBP2a-mediated resistance mechanisms.