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Adaptively Optimized Combination (AOC) of Phased-Array MR Spectroscopy Data in the Presence of Correlated Noise: Compared With Noise-Decorrelated or Whitened Methods

Minjie Wu^{1,†}, Liang Fang^{1,†}, Charles E. Ray Jr.², Anand Kumar¹, Shaolin Yang^{1,2,3,*}

¹Department of Psychiatry, University of Illinois at Chicago, Chicago, Illinois, USA.

²Department of Radiology, University of Illinois at Chicago, Chicago, Illinois, USA.

³Department of Bioengineering, University of Illinois at Chicago, Chicago, Illinois, USA.

Abstract

Purpose—A method for adaptively optimized combination (AOC) of MR spectroscopic data from a coil array was recently introduced. The superior performance of the AOC method is evident when compared with the methods that assume uncorrelated noise between coil elements. However, it is unclear whether the AOC method represents the most optimal combination in the presence of correlated noise, when compared with the noise-decorrelated or whitened methods that specifically tackle the correlated noise between coil elements.

Methods—A new, unified theoretical framework was developed to illustrate the relationship between the AOC method and three noise-decorrelated or whitened methods, namely, noise-decorrelated combination (nd-comb), whitened singular value decomposition (WSVD), and improved WSVD (WSVD+Apod). Simulation-based comparisons and in vivo human brain experiments on a 3 Tesla (T) MRI scanner were performed using an 8-channel phased-array head coil.

Results—Compared with the noise-decorrelated or whitened methods, the AOC method consistently yielded the best combination in terms of the robustness against noise and maintaining the combined spectrum from distortion, and the superior performance was most evident at a low signal-to-noise ratio (SNR).

Conclusion—The AOC method represents the theoretical optimal combination in the presence of correlated noise between coil elements, whereas the three noise-decorrelated or whitened methods are asymptotically optimal.

Keywords

magnetic resonance spectroscopy; coil array; adaptively optimized combination; noise correlation

*Correspondence to: Shaolin Yang, PhD, Departments of Psychiatry, Radiology, and Bioengineering, University of Illinois at Chicago, 1601 W. Taylor St., Suite 512, Chicago, IL 60612, USA. Tel: 312-413-3818, shaolin@uic.edu.

[†]These authors contributed equally to this work.

INTRODUCTION

MR spectroscopy (MRS) provides unique information about the biochemical composition of a subject in a noninvasive manner (1–5). However, most metabolites in the human brain and body are present at low concentrations and/or with low MR sensitivity, so a low signal-to-noise ratio (SNR) is one of the primary factors that limits the clinical applications of MRS. Signal averaging is commonly used to increase the SNR, but leads to substantial increase of data acquisition time that may not be practical in some situations. Fortunately, state-of-the-art MRI scanners are generally equipped with multichannel receiving coils or phased-array coils (6,7); thus, phased-array MRS can be exploited to improve the SNR (8–19).

It is straightforward to equally weight the MRS data received from individual coil elements after aligning the phase to enhance the SNR (referred to as “equal weighting”). Alternatively, each coil element can be weighted by the signal magnitude (S), SNR (S/N), or ratio of the signal to the square of noise (S/N^2) of unsuppressed water or prominent metabolite signal received on individual coil elements. These methods are termed “signal (S) weighting” (10–13), “S/N weighting” (14), and “ S/N^2 weighting” (15), respectively.

Recently, a method for adaptively optimized combination (AOC) of MRS data from a coil array or phased-array coil was introduced (16). The superior performance of the AOC method is evident with significant improvement of SNR when compared with the aforementioned four methods (ie, equal weighting, signal weighting, S/N weighting, and S/N^2 weighting), and the improvement is especially noted in the presence of correlated noise between coil elements. Actually, the aforementioned four methods are based on the assumption that noise is uncorrelated between coil elements, and their performance is not optimal in the presence of correlated noise. Of note, although a coil array is designed with minimal mutual coupling (20,21), noise correlation between coil elements is still observed in practice (16–19,22,23).

There are three noise-decorrelated or whitened combination methods: noise-decorrelated combination (nd-comb) (17), whitened singular value decomposition (WSVD) (18), and a recently improved version of WSVD, ie, WSVD+Apod (19). These methods employ an explicit “prewhitening” process to remove noise correlation prior to weighted summation of spectroscopic data. These methods have yielded a combined spectrum with an improved SNR in the presence of correlated noise; however, it is unclear whether the recently developed AOC method remains the most optimal combination method in the presence of correlated noise when compared with these three noise-decorrelated or whitened methods.

In the present study, we performed a comprehensive theoretical analysis and comparison of the AOC method (16) and three noise-decorrelated or whitened methods (17–19) (ie, nd-comb, WSVD, and WSVD+Apod) in the presence of correlated noise. To facilitate examining the relationship between the AOC method and the noise-decorrelated or whitened methods, we transformed the original, quite different mathematical formulation of the four methods into a unified mathematical formulation, ie, “weighted summation of the noise-decorrelated or whitened spectroscopic data.” Under the new, unified theoretical framework, it is clearly shown that four methods differ primarily in obtaining the weighting vector for

the weighted summation, and the AOC method possesses obvious advantages in the robustness against noise and in maintaining the combined spectrum from distortion. Simulation-based comparisons were conducted, which verified the theoretical prediction of the performance of the four combination methods. And finally, in vivo human brain experiments on a 3 Tesla (T) MRI scanner using an 8-channel phased-array head coil were carried out to verify the theoretical and simulation-based prediction, which demonstrated that the AOC method consistently and robustly yielded the best performance in the presence of correlated noise between coil elements. In addition, we also compared these methods with the generalized least squares (GLS) method (27) that was proposed for coil combination in MRS with correlated or uncorrelated noise.

METHODS

Theory

Signal Model—Individual elements of a coil array usually have different coil sensitivities and spatial phase shifts as a result of different geometrical positions of the coil elements relative to the voxel of interest. In addition, the received spectroscopic data are inevitably contaminated by noise. Thus, the spectroscopic data, $y_i(t)$, received from the i th coil element, can be expressed as

$$y_i(t) = b_i x(t) + n_i(t), \quad [1]$$

where $x(t)$ denotes the metabolite resonance signal originating from the voxel; $b_i = |b_i|e^{j\theta_i}$ is a complex variable, in which $|b_i|$ and θ_i correspond to the coil sensitivity and spatial phase shift, respectively, of the i th element; and $n_i(t)$ represents the noise on the i th element. With a sampling frequency of f_s , the sampled spectroscopic data can be written as

$$y_i(p) = b_i x(p) + n_i(p), \quad [2]$$

where $p = f_s t$ indexes the samples. In the frequency domain, it becomes

$$Y_i(k) = b_i X(k) + N_i(k), \quad [3]$$

where $Y_i(k)$ denotes the k th spectral component of the spectroscopic data received by the i th coil element, $X(k)$ corresponds to the spectral component of the metabolite resonance signal, and $N_i(k)$ represents the spectral component of the noise. In a matrix/vector form, the time-domain or frequency-domain data received by the coil array can be expressed as

$$\mathbf{Y} = \mathbf{b}\mathbf{x} + \mathbf{N}, \quad [4]$$

where $\mathbf{Y}$ and $\mathbf{N}$ are $M \times P$ matrices with M being the number of coil elements and P the number of sampled or spectral data points; $\mathbf{N}$ represents the noise, $\mathbf{x}$ is a $1 \times P$ vector denoting the signal from the voxel in the time or frequency domain, and $\mathbf{b}$ is an $M \times 1$ vector corresponding to the coil sensitivities and spatial phase shifts.

It has been shown that electric and magnetic coupling can produce correlated noise between coil elements in a coil array (24,25). Therefore, correlated noise should be incorporated into

Equation [4]. Accordingly, in the simulation, the noise matrix $\mathbf{N}$ was generated by mixing M circular complex white noise sources (16,17), which can be expressed as

$$\mathbf{N} = (\mathbf{A} + \mathbf{B})\tilde{\mathbf{N}}, \quad [5]$$

where $\tilde{\mathbf{N}}$ is an $M \times P$ matrix associated with M uncorrelated and identically distributed Gaussian noises, each with P sampled points; $\mathbf{B}$ is an $M \times M$ diagonal matrix whose diagonal elements denote the noise variance on each coil element; and $\mathbf{A}$ is an $M \times M$ matrix with nonzero off-diagonal elements associated with the noise correlation between coil elements.

nd-comb—The nd-comb method (17) takes advantage of noise decorrelation between coil elements, which is also commonly referred to as “noise whitening.” Specifically, a linear transformation of MR spectroscopic data is first performed to project the data into a subspace where the noise across coil elements is orthogonal; then the S/N weighting method (14) is employed to combine the noise-decorrelated or whitened spectroscopic data to obtain the combined spectrum. Based on Equation [4], the noise correlation matrix can be written as

$$\mathbf{R}_N = \mathbf{N}\mathbf{N}^H, \quad [6]$$

where H denotes the conjugate transpose. Noise usually dominates in the latter part of the sampled spectroscopic data or in the spectral regions that are free of any metabolite resonance peaks, from where the samples of the noise can be obtained. The eigendecomposition of the noise correlation matrix is represented as follows:

$$\mathbf{R}_N = \mathbf{X}\mathbf{D}\mathbf{X}^H, \quad [7]$$

where $\mathbf{X}$ is a unitary matrix of eigenvectors, and $\mathbf{D}$ is a diagonal matrix of eigenvalues. Based on the eigendecomposition of the noise correlation matrix, the whitening transformation matrix is constructed as

$$\mathbf{W} = \mathbf{D}^{-1/2}\mathbf{X}^H \quad [8]$$

Applying the forward transformation of $\mathbf{W}$ to the acquired spectroscopic data as expressed in Equation [4], we obtained

$$\bar{\mathbf{Y}} = \bar{\mathbf{b}}\mathbf{x} + \bar{\mathbf{N}}, \quad [9]$$

where $\bar{\mathbf{Y}} = \mathbf{W}\mathbf{Y}$ denotes the noise-decorrelated or whitened spectroscopic data, $\bar{\mathbf{b}} = \mathbf{W}\mathbf{b}$ corresponds to the transformed coil sensitivities and spatial phase shifts, and $\bar{\mathbf{N}} = \mathbf{W}\mathbf{N}$ represents the transformed noise matrix in which the noise vectors are orthogonal, ie, $\bar{\mathbf{N}}\bar{\mathbf{N}}^H = \mathbf{I}_M$ ($\mathbf{I}_M$ is an $M \times M$ identity matrix). Finally, the nd-comb method performs the phasing and weighted summation of the noise-whitened spectroscopic data as follows:

$$\mathbf{z}_{\text{nd-comb}} = \mathbf{w}_{\text{nd-comb}}^H \bar{\mathbf{Y}}, \quad [10]$$

where $\mathbf{z}_{\text{nd-comb}}$ is a $1 \times P$ vector denoting the combined spectroscopic data obtained by the nd-comb method, and $\mathbf{w}_{\text{nd-comb}}$ is an $M \times 1$ complex weighting vector obtained by the S/N weighting method. Specifically, phase alignment is applied based on the selected reference resonance peak with a relatively high SNR in the noise-whitened spectrum, and the weighting coefficient is actually the SNR of the reference resonance peak.

WSVD—As an alternative noise-whitened method, the WSVD method (18) employs the same prewhitening processing as used in the nd-comb method (17), but obtains the combined spectroscopic data directly by decomposing the noise-whitened spectroscopic data matrix $\bar{\mathbf{Y}}$ as defined in Equation [9].

The singular value decomposition (SVD) of the noise-whitened spectroscopic data matrix $\bar{\mathbf{Y}}$ gives

$$\bar{\mathbf{Y}} = \bar{\mathbf{U}} \bar{\mathbf{\Sigma}} \bar{\mathbf{V}}^H, \quad [11]$$

where $\bar{\mathbf{U}}$ is an $M \times M$ unitary matrix, whose orthonormal columns are the left singular vectors of $\bar{\mathbf{Y}}$; $\bar{\mathbf{\Sigma}}$ is an $M \times P$ diagonal matrix, whose M diagonal elements, arranged in decreasing order, are the singular values of $\bar{\mathbf{Y}}$; and $\bar{\mathbf{V}}$ is a $P \times P$ unitary matrix, whose columns are the right singular vectors of $\bar{\mathbf{Y}}$. The combined spectroscopic data are obtained by taking the first right singular vector (ie, $\bar{\mathbf{v}}_1$), that is

$$\mathbf{z}_{\text{WSVD}} = \bar{\mathbf{v}}_1^H \quad [12]$$

WSVD+Apod—The recently published WSVD+Apod method (19), as an improved WSVD method, involves the use of an apodization on the noise-whitened spectroscopic data as follows:

$$\tilde{\mathbf{Y}} = \bar{\mathbf{Y}} \mathbf{A}, \quad [13]$$

where $\tilde{\mathbf{Y}}$ is an $M \times P$ matrix corresponding to the apodized spectroscopic data; and $\mathbf{A}$ is a $P \times P$ diagonal matrix, whose diagonal elements denote the apodization function (eg, an exponential decay). Applying SVD to the apodized spectroscopic data $\tilde{\mathbf{Y}}$ gives

$$\tilde{\mathbf{Y}} = \tilde{\mathbf{U}} \tilde{\mathbf{\Sigma}} \tilde{\mathbf{V}}^H. \quad [14]$$

Taking the first left singular vector (ie, $\tilde{\mathbf{u}}_1$) as the weighting coefficients of the original noise-whitened spectroscopic data $\bar{\mathbf{Y}}$, the combined spectroscopic data can be expressed as

$$\mathbf{z}_{\text{WSVD+Apod}} = \tilde{\mathbf{u}}_1^H \bar{\mathbf{Y}}. \quad [15]$$

AOC—Instead of using the noise-whitening processing, the AOC method (16), which was recently developed for adaptively optimized combination of MRS data from a coil array, directly weights the spectroscopic data as follows:

$$\mathbf{z}_{\text{AOC}} = \mathbf{w}_{\text{AOC}}^H \mathbf{Y}, \quad [16]$$

where $\mathbf{w}_{\text{AOC}}$ is an $M \times 1$ complex weighting vector, and $\mathbf{z}_{\text{AOC}}$ is a $1 \times P$ vector denoting the combined spectroscopic data. According to Equations [4] and [16], the SNR of the combined spectroscopic data is calculated as

$$\text{SNR} = \frac{\mathbf{w}_{\text{AOC}}^H \mathbf{R}_S \mathbf{w}_{\text{AOC}}}{\mathbf{w}_{\text{AOC}}^H \mathbf{R}_N \mathbf{w}_{\text{AOC}}}, \quad [17]$$

where $\mathbf{R}_S = (\mathbf{X}\mathbf{X}^H)\mathbf{b}\mathbf{b}^H$ is the signal correlation matrix. To maximize the SNR by the weighting vector $\mathbf{w}_{\text{AOC}}$, the method of Lagrange multipliers (26) is employed as follows:

$$L(\mathbf{w}_{\text{AOC}}) = \mathbf{w}_{\text{AOC}}^H \mathbf{R}_S \mathbf{w}_{\text{AOC}} + \lambda (\mathbf{I} - \mathbf{w}_{\text{AOC}}^H \mathbf{R}_N \mathbf{w}_{\text{AOC}}). \quad [18]$$

The differential with respect to $\mathbf{w}_{\text{AOC}}^*$ (* denotes conjugate) produces

$$\frac{\partial L(\mathbf{w}_{\text{AOC}})}{\partial \mathbf{w}_{\text{AOC}}^*} = \mathbf{R}_S \mathbf{w}_{\text{AOC}} - \lambda \mathbf{R}_N \mathbf{w}_{\text{AOC}}. \quad [19]$$

Setting Equation [19] to a zero vector yields

$$\mathbf{R}_S \mathbf{w}_{\text{AOC}} = \lambda \mathbf{R}_N \mathbf{w}_{\text{AOC}}. \quad [20]$$

Substituting $\mathbf{R}_S = (\mathbf{X}\mathbf{X}^H)\mathbf{b}\mathbf{b}^H$ gives

$$\mathbf{w}_{\text{AOC}} = \alpha \mathbf{R}_N^{-1} \mathbf{b}, \quad [21]$$

where α is a scalar defined as $\lambda^{-1} \mathbf{b}^H \mathbf{w}_{\text{AOC}} (\mathbf{x}\mathbf{x}^H)$. In practice, the complex vector $\mathbf{b}$, representing the coil sensitivities and spatial phase shifts, is unknown and needs to be estimated. In the AOC method, the unsuppressed water signal is selected as the reference for calculating the coil sensitivities and spatial phase shifts of individual coil elements as follows:

$$\mathbf{b} = \beta \mathbf{s}, \quad [22]$$

where $\mathbf{s}$ is an $M \times 1$ complex vector associated with the unsuppressed water signal received from the coil elements, and β is a scalar. Ignoring the universal scaling coefficient $\alpha\beta$, the weighting vector of the AOC method is written as

$$\mathbf{w}_{\text{AOC}} = \mathbf{R}_N^{-1} \mathbf{s}, \quad [23]$$

where the inversion of the full noise correlation matrix (ie, $\mathbf{R}_N^{-1}$) is incorporated into the coil weighting vector. According to Equations [16] and [23], the combined spectroscopic data obtained by the AOC method are given by

$$\mathbf{z}_{\text{AOC}} = \mathbf{s}^H \mathbf{R}_N^{-1} \mathbf{Y}. \quad [24]$$

GLS—In addition, An et al. applied the generalized least squares solution to a linear regression system, ie,

$$\mathbf{z}_{\text{GLS}} = \left(\mathbf{b}^H \mathbf{R}_N^{-1} \mathbf{b} \right)^{-1} \mathbf{b}^H \mathbf{R}_N^{-1} \mathbf{Y}, \quad [25]$$

to the coil combination in MRS, from which the name of the GLS method was derived (27).

Relationship between Different Coil Combination Methods—The three noise-decorrelated or whitened methods (ie, nd-comb, WSVD, and WSVD+Apod) employ the same prewhitening process, but are different in weighted summation of the resultant noise-whitened spectroscopic data. The nd-comb method weights the noise-decorrelated spectroscopic data by a factor contributed by the SNR and phase of the selected reference resonance peak in the noise-decorrelated spectra, as described in Equation [10]. In contrast, the WSVD method, as formulated in Equation [12], obtains the combined spectroscopic data directly from the SVD of the noise-whitened spectroscopic data matrix. In fact, based on Equation [11] and a few transformations (not shown here for simplicity), Equation [12] can be rewritten as

$$\mathbf{z}_{\text{WSVD}} = \bar{\mathbf{u}}_1^H \bar{\mathbf{Y}} \quad [26]$$

where $\bar{\mathbf{u}}_1$ is the first left singular vector in $\bar{\mathbf{U}}$. It suggests that we can also consider the WSVD method as a weighted summation of the noise-whitened spectroscopic data. Therefore, unlike the nd-comb method in which only the reference resonance peak is used to estimate the weighting vector, the WSVD method exploits the full noise-whitened spectroscopic data to estimate the weighting vector, which potentially results in a more optimized combination than the nd-comb method at a low SNR. However, it is probably less robust in the scenario of an extremely low SNR because of the overall, substantial noise contamination.

The WSVD+Apod method, as an improved version of the WSVD method, employs an apodization to suppress the high-frequency noise in the noise-whitened spectroscopic data (Eq. [13]), which can potentially improve the estimation of the weighting vector. Compared with the WSVD method, the WSVD+Apod method is expected to produce a more robust combination, especially at a low SNR.

Based on Equation [24] and $\mathbf{R}_N^{-1} = \mathbf{W}^H \mathbf{W}$, the combined spectrum obtained by the AOC method can be represented as

$$\mathbf{z}_{\text{AOC}} = (\mathbf{W}\mathbf{s})^H \bar{\mathbf{Y}} \quad [27]$$

It suggests that the AOC method can also be considered as a weighted summation of the noise-whitened spectroscopic data, analogous to the three noise-decorrelated or whitened methods. Moreover, the weighting vector is associated with the “transformed” unsuppressed water signal, which will provide superior performance of coil combination because of the extremely high SNR of the unsuppressed water signal.

Based on the new, unified mathematical formulation (Eqs. [10], [15], [26], and [27]) that has been summarized in Table 1, the four methods (ie, nd-comb, WSVD, WSVD+Apod, and AOC) differ primarily in obtaining the weighting vector of the noise-decorrelated or whitened spectroscopic data. In Equation [9], the whitened noise is uncorrelated across coil elements and identically Gaussian distributed. As demonstrated in (16), for this kind of noise the transformed coil sensitivity and spatial phase shift factor (ie, $\bar{\mathbf{b}} = \mathbf{W}\mathbf{b}$) represent the theoretical optimal weighting vector for combining the noise-decorrelated or whitened spectroscopic data. In fact, the weighting vector $\mathbf{W}\mathbf{s}$ in the AOC method is the theoretical optimal weighting vector $\mathbf{W}\mathbf{b}$, based on the assumption that the unsuppressed water signal is highly correlated with the coil sensitivities and spatial phase shifts (Eq. [22]). In contrast, in the nd-comb method the weighting vector (or the transformed coil sensitivities and spatial phase shifts) is estimated from a selected metabolite resonance peak in the noise-decorrelated spectrum. Although the prewhitening process turns the correlated noise into uncorrelated noise, prewhitening itself does not suppress the noise. The selected reference metabolite resonance peak is generally several hundred or a few thousand times lower than the unsuppressed water peak. Estimation of the weighting vector is therefore vulnerable to the individual noise fluctuations in the reference peak region, and the effect would be more acute when the noise level (reflected by the noise variance) increases. Moreover, estimation of the weighting vector, particularly the phase component, can be impaired by macromolecular resonances (from the background, also called the baseline) within the reference peak region. This is because the estimated phase information of an assumed “single” signal will be biased if the data are actually from two or more different signal sources. An alternative approach to reduce the vulnerability of coil combination to noise is to use multiple points or multiple peak areas. The logical end point of this approach is to use all of the available spectral data points, which may help to suppress the influence of noise. The WSVD and WSVD+Apod methods are among this kind of methods. They employ the first left singular vector of the noise-whitened or apodized noise-whitened spectroscopic data matrix as the weighting vector, which exploit the full spectroscopic data and result in a potentially more optimized combination than the nd-comb method at a low SNR. At a high SNR, the weighting vectors of three noise-decorrelated or whitened methods will approximate the theoretical optimal weighting vector; therefore, the three noise-decorrelated or whitened methods and the AOC method are expected to yield comparable results at a high SNR.

Additionally, in the original GLS method (Eq. [25]) (27), $(\mathbf{b}^H \mathbf{R}_N^{-1} \mathbf{b})^{-1}$ is a 1×1 universal scalar that is identical across coil elements. As well known, a common scaling factor in the

combination coefficients has no effect on the SNR of the combined spectrum. So we remove this universal scalar from the original formula of GLS, which will give the modified GLS formulation as follows:

$$\mathbf{z}_{\text{GLS}} = \mathbf{b}^H \mathbf{R}_N^{-1} \mathbf{Y}. \quad [28]$$

After replacing $\mathbf{R}_N^{-1}$ with $\mathbf{W}^H \mathbf{W}$ in $\mathbf{z}_{\text{GLS}} = \mathbf{b}^H \mathbf{R}_N^{-1} \mathbf{Y}$, the combined spectrum obtained by the modified GLS formulation can be written as

$$\mathbf{z}_{\text{GLS}} = (\mathbf{W}\mathbf{b})^H \bar{\mathbf{Y}}. \quad [29]$$

This new mathematical formulation suggests that the modified GLS method, like the other four methods, can also be considered as a weighted summation (by the weighting vector $\mathbf{W}\mathbf{b}$) of the noise-decorrelated or whitened spectroscopic data ($\bar{\mathbf{Y}}$). In the original GLS paper (27), a metabolite peak with a relatively high SNR (such as *N*-Acetyl aspartate (NAA)) in the water-suppressed spectra was chosen as the reference for calculating the coil sensitivity and spatial phase shift of a coil elements in nd-comb and GLS; in this situation, the nd-comb method ($\mathbf{z}_{\text{nd-comb}} = \mathbf{w}_{\text{nd-comb}}^H \bar{\mathbf{Y}}$) and the modified GLS method ($\mathbf{z}_{\text{GLS}} = (\mathbf{W}\mathbf{b})^H \bar{\mathbf{Y}}$) as introduced above are theoretically equivalent. This is because the forward noise-decorrelating or whitening transformation matrix $\mathbf{W}$ is a linear transformation matrix, the transformed complex coil sensitivity (with the spatial phase shift) derived from the reference resonance peak in the original spectroscopic data is equivalent to the complex coil sensitivity (with the spatial phase shift) derived from the same reference resonance peak in the transformed (ie, noise-decorrelated or whitened) spectroscopic data. In addition, in the original GLS paper (27), the coil sensitivity and spatial phase shift factor was calculated through “the integral of the complex-valued spectral signal” over the reference peak. However, integration of complex-valued spectral signal over the reference peak region could be problematic from the perspective of signal processing; it works only when the phase of each spectral point is identical over the reference peak region, which, however, is not the case in practice, considering the contribution from the noise and the overlap from the macromolecular and metabolite signals within the reference peak region. Our results showed that using the integral of the complex-valued spectral signal over the reference peak region could significantly degrade the performance of the GLS (data not shown for simplicity). Therefore, an alternative method of calculating the reference signal should be employed in GLS. Finally, in the original GLS paper (27), using the unsuppressed water peak as the reference to calculate the coil sensitivity and spatial phase shift was also discussed; however, it was not recommended by the authors of that paper. If the unsuppressed water peak is used as the reference, the following relationship may hold with a high success rate in practice as a result of the high SNR of the unsuppressed water signal:

$$\mathbf{b} = \beta \mathbf{s},$$

where s is an $M \times 1$ complex vector associated with the unsuppressed water signal received from the coil elements, and β is a scalar. Only under these conditions (including the means of calculating the reference signal) are the modified GLS method (ie, Eq. [28]) and the AOC method intimately related. To simplify the presentation of the results (ie, Figs. [2], [3], and [5]) and discussion, the nd-comb results will also represent the results of modified GLS when the water-suppressed metabolite (such as NAA) resonance peak is chosen as the reference, and the AOC results will also represent the results of modified GLS when the unsuppressed water peak is chosen as the reference. However, both statements hold true only if an alternative calculation method, other than the original method (ie, the integral of the complex-valued spectral signal over the reference peak region), is used to calculate the reference signal in the modified GLS; otherwise, the GLS method will yield much worse performance especially at a low SNR.

Simulation-Based Evaluation of Coil Combination Methods in the Presence of Correlated Noise—Computer simulations were performed to compare the performance of the different coil combination methods in the presence of correlated noise between coil elements. The simulated MR spectroscopic signal consisted of two Lorentzian resonance components, which were modeled as

$$x(p) = \sum_{q=1}^2 a_q e^{j\theta_q} e^{(-d_q + j2\pi f_q)p/f_s} \quad [30]$$

where f_s is the sampling frequency, and a_q , θ_q , d_q , and f_q denote the amplitude, phase, damping factor, and resonance frequency of the q th sinusoid, respectively. The parameters of two resonance peaks are given in Table 2. The sampling frequency was set to 2500Hz and the number of sampling points to 2048. The synthetic spectroscopic data from the assumed eight coil elements were then generated by scaling and shifting the model signal with selected amplitudes and phases, as well as adding correlated noise between coil elements based on Equation [5]. Finally, the synthetic multichannel spectroscopic data were combined using the different coil combination methods. In the nd-comb method, the resonance peak associated with creatine CH_3 was used as the reference resonance peak to calculate the S/N weighting vector. An exponential decay was applied for the apodization in the WSVD+Apod method. In the AOC method, it was assumed that the unsuppressed water resonance has a sufficient SNR, so it could be used to accurately determine the coil sensitivities and spatial phase shifts of individual coil elements. To evaluate the performance of the different methods in maintaining the combined spectra from distortion, a metric measuring the spectral distortion was defined, which was the difference in the ratio of the creatine CH_2 peak area to the creatine CH_3 peak area between the combined spectrum and the original model spectrum.

Monte Carlo simulations were performed to evaluate the performance of the different coil combination methods in terms of mean and standard deviation (SD) of the spectral distortion at different SNRs. The SNR of the simulated spectroscopic data was set from -22 to 16 dB, whereas the noise correlation between coil elements remained unchanged. At each SNR

level, the noise-added MR spectroscopic data were simulated 300 times, and the mean and SD of the spectral distortion were calculated for each combination method.

Evaluation of Coil Combination Methods in Human Brain Experiments—To compare the performance of the different coil combination methods in human brain experiments, two volunteers were recruited and written informed consent was obtained from each subject in this institutional review board–approved study. ^1H -MRS scans were performed on a Philips Achieva 3T scanner (Philips Medical Systems, Best, the Netherlands) with an 8-channel phased-array head coil (SENSE-Head-8). A single-voxel PRESS sequence was applied with the following parameters: repetition time (TR)/echo time (TE)=3000/35 ms, 2048 complex data points, spectral bandwidth = 2000Hz, 128 averages with a 16-step phase cycling, and the unsuppressed water data were acquired at the beginning of the MRS scan. The voxel ($2 \times 2 \times 2\text{cm}^3$) encompassed the rostral anterior cingulate cortex (ACC).

Raw in vivo human brain spectroscopic data were processed offline using MATLAB (MathWorks, Natick, Massachusetts, USA). The data from each coil element were averaged over 1 and 128 repetitions to generate the human spectroscopic data with a low SNR and a high SNR, respectively. The resultant multichannel MR spectroscopic data were then combined using the different methods described previously.

RESULTS

Simulated Experiments

Figure 1 shows the simulation-based comparison of the different combination methods in the presence of correlated noise between coil elements and at a high SNR. Figure 1a demonstrates the noise correlation matrix, in which the nonzero off-diagonal elements indicate the noise correlation between coil elements. Figure 1b shows the spectra from individual elements of an eight-channel coil array. The combined spectra are demonstrated in Figure 1c, in which the original model spectrum that was used to generate the simulated spectroscopic data is also depicted as the reference. The combined spectra obtained by the five methods demonstrated negligible difference from the original model spectrum, which verifies that at a high SNR, the five methods are comparable in the presence of correlated noise between coil elements.

Figure 2 shows the simulation-based comparison of the different combination methods in the presence of correlated noise between coil elements and at a low SNR. Figure 2a demonstrates the noise correlation matrix. Figure 2b shows the individual spectra from eight coil elements, which exhibited high levels of noise and had no clear spectral pattern of signal. Figure 2c shows the noise correlation matrix after prewhitening processing, which is a scalar matrix. It indicates that the whitened noise, with identical variances, was orthogonal across coil elements, and the noise correlation between coil elements had been eliminated. By projecting the spectroscopic data onto a subspace where the noise between coil elements is orthogonal (described by Eq. [9]), noise-decorrelated or whitened spectra were obtained and are demonstrated in Figure 2d, which can be regarded as the spectra acquired by “virtual” coil elements that are free from noise correlation between coil elements. The noise-

decorrelated or whitened spectra were still dominated by noise. Figure 2e demonstrates the apodized spectra after applying an exponential decay to the noise-decorrelated or whitened spectra (described by Eq. [13]), which shows that the apodization significantly suppressed the high-frequency noise in the noise-decorrelated or whitened spectra. Figure 2f shows the combined spectra obtained by the different combination methods, which demonstrate significant differences between the performances of these methods. Specifically, the basic spectral pattern of signal was largely missing in the combined spectrum obtained by the WSVD method, whereas the combined spectra obtained by the other three methods exhibited a relatively clear spectral pattern of signal (ie, two creatine resonance peaks). In addition, the combined spectrum obtained by the nd-comb method had a certain degree of distortion (ie, the ratio between two creatine resonance peak areas was different from that of the original model spectrum shown in Fig. 1c). In contrast, the combined spectra obtained by the WSVD+Apod and AOC methods demonstrated a more appropriate ratio between the two creatine peaks.

Figure 3 demonstrates the means and SDs of spectral distortion of the combined spectra obtained by the different combination methods using Monte Carlo simulations. Figure 3a shows the relationship between the mean of spectral distortion and SNR. As SNR increases, the means of the spectral distortion yielded by the different methods asymptotically approximate zero, which further verifies that the different combination methods are comparable at a high SNR. At a low SNR, the mean spectral distortion of the AOC method fluctuates around zero, which suggests that the AOC method represents an unbiased combination. In contrast, the means of the three noise-decorrelated or whitened methods deviated from zero. Specifically, at an extremely low SNR (eg, -22 dB), the spectral distortion of the WSVD method is more severe than those of the nd-comb and WSVD+Apod methods, which is evidenced by the observation that the combined spectrum obtained by the WSVD method has no clear spectral pattern of signal (Fig. 2f). As SNR increases, the spectral distortion by the WSVD+Apod methods reduced substantially, followed by the WSVD method and the nd-comb method. Figure 3b shows the SDs of spectral distortion yielded by the different combination methods as a function of SNR. The SDs of the spectral distortion by the different combination methods asymptotically approximate zero at high SNRs. At low SNRs, the AOC method yields the smallest SD, followed by the nd-comb, WSVD+Apod, and WSVD methods, respectively.

Human Experiments

Figure 4 demonstrates the spectroscopic data acquired from a voxel encompassing the rostral ACC of a human subject. The spectroscopic data from each coil element were averaged using 128 repetitions. Figure 4a shows the noise correlation matrix of the spectroscopic data received by an 8-channel phased-array head coil. Some off-diagonal elements were nonnegligible, indicating noise correlation between the coil elements. Figure 4b shows the spectra received from individual coil elements, which were at relatively high SNRs. Figure 4c demonstrates the combined spectra obtained by the different combination methods. There was no remarkable difference among these combined spectra, suggesting that the performances of the different combination methods are comparable at a high SNR.

Figure 5 shows two versions of combined spectra obtained by the different combination methods using the spectroscopic data acquired from a voxel encompassing the rostral ACC of a human subject. One version was calculated using one repetition (in blue) and the other version using 128 repetitions (in red, the reference for comparison). It demonstrates that at the low SNR, the AOC method yielded the smallest distortion of metabolite resonance peaks, followed by the WSVD+Apod and WSVD methods, and the combined spectrum obtained by the nd-comb method presented the largest distortion of the metabolite resonance peaks (eg, the creatine and choline resonance peaks at 3 and 3.2ppm, as marked by arrows).

DISCUSSION

We compared the AOC method with the three noise-decorrelated or whitened methods (nd-comb, WSVD, and WSVD+Apod) in combining the phased-array MRS data in the presence of correlated noise between coil elements by theoretical analysis, computer simulation, and in vivo human experiments. Compared with the three noise-decorrelated or whitened methods, the AOC method consistently yielded the best performance in terms of the robustness against noise and maintaining the combined spectrum from distortion at a low SNR; in contrast, the performances of these methods were comparable at a high SNR.

The relationship between the AOC method and the three noise-decorrelated or whitened methods, as well as the GLS method, was first examined through theoretical analysis and comparison. To facilitate a better comparison, we transformed the original, quite different mathematical formulations of these methods into a unified theoretical framework, ie, a weighted summation of the noise-decorrelated or whitened spectroscopic data, which is summarized in Table 1. It shows that these coil combination methods differ primarily in obtaining the weighting vector for combining the noise-decorrelated or whitened spectroscopic data, which provide the underlying substrates for the observed differential performance of these methods.

Of note, the performances of the different combination methods were evaluated based on the measure of spectral distortion (ie, the difference in the ratio of two creatine peak areas between the combined spectrum and the original model spectrum), instead of SNR, in the Monte Carlo simulation. As shown in Figure 3, the AOC method produced minimal spectral distortion (an unbiased zero mean and the smallest SD of the spectral distortion) compared with the three noise-decorrelated or whitened methods. It has been recognized that unconstructive weighted summation of phased-array spectroscopic data would lead to cancellation or loss of the signal, which is usually evaluated by SNR-related metrics. However, the fact that unconstructive summation would also cause distortion of the combined spectra has largely been ignored until recent years. Such distortion would have detrimental effects on the quantification of metabolites.

The results of simulation-based comparisons were consistent with the theoretical prediction. As shown in Figures 1 and 3, these methods yielded comparable performance at a high SNR; however, at a low SNR, their performance differed significantly (shown in Figs. 2 and 3). Why are the performances of these methods more different at a low SNR? Or alternatively,

why do the weighting vectors of these methods (in Table 1) have differential sensitivity to noise? We will discuss more of the underlying reasons next.

The weighting vector of the nd-comb method is estimated from a selected reference resonance peak where the signal is strong (eg, the NAA peak at 2.01ppm repetitions). However, the intensity of the selected strong metabolite reference resonance peak is still several hundred or a few thousand times lower than that of the unsuppressed water peak. This will inevitably introduce a risk of impaired estimation of the weighting vector if any data point within the reference peak region is degraded by the noise, and the effect would be more significant when the noise level (reflected by the noise variance) increases. In addition, estimation of the weighting vector can also be impaired by macromolecular resonances from the background (ie, baseline), because the estimated phase of an assumed single signal will be biased if the data are actually from two or more different signal sources with nonnegligible intensities. Summation of multichannel spectroscopic data with wrongly aligned phase across coil elements will lead to a complicated phase in the combined spectrum with a mixture of the absorption and dispersion spectral modes, which will ultimately bring about spectral distortion if the distortion cannot be completely corrected for. In contrast, at a high SNR, these issues will be less serious; therefore, the estimation of the weighting vectors, and therefore the coil combination, will not be significantly impaired. Because of these reasons, the nd-comb method is sensitive to noise, and is suboptimal at a low SNR.

Instead of relying on a single reference resonance peak within a limited spectral range, the WSVD and WSVD+Apod methods exploit the full noise-whitened spectroscopic data to estimate the weighting vectors (see Table 1), which reduces the effects of noise and result in a generally more reasonable combination at a low SNR than the nd-comb method. This has been confirmed in Figure 3a, in which the mean spectral distortions yielded by the WSVD and WSVD+Apod methods (measured by the amount of deviation from the ideal ratio of two creatine peak areas) were smaller than that of the nd-comb method at most of the low SNRs examined. However, as shown in Figure 3a, the spectral distortion metric was actually larger in WSVD than nd-comb at extremely low SNRs. The reason for this exception lies in the WSVD method itself. The WSVD method makes a “Rank 1 approximation” (13) of the noise-whitened multichannel spectroscopic data, and the combined spectroscopic data is obtained from the first left singular vector that corresponds to the maximum singular value of the noise-whitened spectroscopic data matrix and is assumed to be associated with the spectroscopic resonance signal. When the noise is far stronger than the spectroscopic resonance signal, the maximum singular value will not correspond to the spectroscopic resonance signal but to the noise instead, and the same for the first singular vector, which led to a complete failure of coil combination (as demonstrated in Fig. 2f) and brought about the largest spectral distortion at an extremely low SNR (< -20 dB) as shown in Figure 3a. In contrast, the WSVD+Apod method first employs an apodization to suppress the noise (primarily high-frequency noise) in the noise-whitened spectroscopic data, and then exploits the apodized spectroscopic data to estimate the weighting vector, thereby resulting in a more robust coil combination at a low SNR than the WSVD method (demonstrated in Fig. 2f and Fig. 3a).

The AOC method possesses both advantages of the nd-comb method and the WSVD/WSVD+Apod methods, but avoids the problems of these methods in terms of the sensitivity to noise at a low SNR. In AOC, the unsuppressed water signal is used as the reference for calculating the coil sensitivities and spatial phase shifts of individual coil elements, and inversion of the full noise correlation matrix (ie, R_N^{-1}) is also incorporated into the coil weighting vector. Under the new, unified theoretical framework, as introduced in this paper and summarized in Table 1, the AOC method can also be considered as a weighted summation of the noise-decorrelated or whitened spectroscopic data, and the weighting vector is associated with the transformed, unsuppressed water signal, which, because of its extremely high SNR, helps to provide a superior performance of coil combination for MRS. Because the unsuppressed water signal is several hundred or a few thousand times stronger than the metabolite resonance signals and also the macromolecular resonances from the background (or baseline), the estimation of the weighting vector from the unsuppressed water peak in AOC will be significantly less impaired by the noise and the overlap of metabolite and macromolecular resonances, compared with the nd-comb method. As shown in Figure 3, the AOC method performs better than the WSVD and WSVD+Apod methods at moderate and low SNRs in terms of spectral distortion and the sensitivity to noise. In contrast, although the WSVD and WSVD+Apod methods use the first left singular vector (obtained by SVD of the full noise-whitened spectroscopic data matrix and the apodized noise-whitened spectroscopic data matrix, respectively) as the weighting vector, the estimation will inevitably be affected by the noise at a very low SNR. At an extremely low SNR, the WSVD method may completely fail and bring about significant spectral distortion in the combined spectrum.

In addition to theoretical analysis and simulation-based comparisons, we also evaluated the different combination methods in in vivo human experiments, in which ^1H -MRS data were acquired from a voxel encompassing the rostral ACC. In the scenario of a high SNR, the AOC method yielded comparable performance with the three noise-decorrelated or whitened methods (Fig. 4), whereas the AOC method outperformed the three noise-decorrelated or whitened methods in maintaining the combined spectrum from distortion at a low SNR (Fig. 5). This indicates that the in vivo human experiments are consistent with our theoretical analysis and simulation-based comparisons.

A low SNR is not uncommonly observed when applying MRS in practice. Therefore, it is important to choose an appropriate coil combination method at a low SNR and in the presence of correlated noise between coil elements. When the unsuppressed water data are available, we recommend the AOC method for the optimal combination of MRS data received from a coil array. When the unsuppressed water data are not available, we recommend, based on the recent report (19), the WSVD+Apod method for the asymptotically optimal combination of multichannel MRS data.

CONCLUSIONS

In the present study, a comprehensive comparison of the AOC method with the three noise-decorrelated or whitened methods (nd-comb, WSVD, and WSVD+Apod) in the presence of correlated noise between coil elements was performed. The theoretical analysis, computer

simulations, and in vivo human experiments demonstrated that the AOC method yielded the best performance in the robustness against noise and maintaining the combined spectrum from distortion.

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FIG. 1.

Simulation-based comparison of the combination methods in the presence of correlated noise between coil elements and at a high SNR. (a) Noise correlation matrix. (b) Spectra received from individual coil elements. (c) Combined spectra obtained by the five methods, along with the original model spectrum. Note that there is negligible difference between those combined spectra and the original model spectrum.

FIG. 2.

Simulation-based comparison of the combination methods in the presence of correlated noise between coil elements and at a low SNR. (a) Original noise correlation matrix. (b) Spectra received from individual coil elements. (c) Noise correlation matrix after noise-prewhitening processing. (d) Noise-whitened spectra from virtual coils element that are free of noise correlation. (e) Apodized spectra after applying an exponential decay to the noise-whitened spectroscopic data. (f) Combined spectra obtained by the different methods.

FIG. 3. Means and standard deviations (SDs) of the spectral distortion of the combined spectra yielded by the different methods based on Monte Carlo simulations. (a) Means of the spectral distortion yielded by the different methods as a function of SNR. (b) SDs of the spectral distortion yielded by the different methods as a function of SNR.

FIG. 4. Results of the spectroscopic data acquired from a voxel encompassing the rostral ACC of a human subject (the spectroscopic data from each coil element were averaged using 128 repetitions). (a) Noise correlation matrix. (b) Spectra received from individual coil elements. (c) Combined spectra obtained by the five methods. Note that at a high SNR, there was no remarkable difference among the combined spectra yielded by the five methods.

FIG. 5.

Two versions of combined spectra obtained by the different methods using the spectroscopic data acquired from a voxel encompassing the rostral ACC of a human subject. One version was calculated using one repetition (in blue), and the second version using the full 128 repetitions (in red): (a) nd-comb; (b) WSVD; (c) WSVD+Apod; (d) AOC.

New, Unified Mathematical Formulation of Five Combination Methods of Phased-Array MR Spectroscopy Data in the Presence of Correlated Noise between Coil Elements

Table 1

Method	Formula	Weighting vector of the noise-whitened spectroscopic data
nd-comb	$\mathbf{z}_{\text{nd-comb}} = \mathbf{u}_{\text{nd-comb}}^H \bar{\mathbf{Y}}$	The SNR and phase of a selected reference resonance peak with a relatively high SNR in the noise-whitened spectrum
WSVD	$\mathbf{z}_{\text{WSVD}} = \bar{\mathbf{u}}_1^H \bar{\mathbf{Y}}$	The first left singular vector obtained by SVD of the noise-whitened spectroscopic data matrix
WSVD+Apod	$\mathbf{z}_{\text{WSVD+Apod}} = \bar{\mathbf{u}}_1^H \bar{\mathbf{Y}}$	The first left singular vector obtained by SVD of the apodized noise-whitened spectroscopic data matrix
modified GLS	$\mathbf{z}_{\text{GLS}} = (\mathbf{W}\mathbf{b})^H \bar{\mathbf{Y}}$	The vector associated with either the transformed water-suppressed metabolite signal or the transformed unsuppressed water signal, depending on the selection of the reference peak
AOC	$\mathbf{z}_{\text{AOC}} = (\mathbf{W}\mathbf{s})^H \bar{\mathbf{Y}}$	The vector associated with the transformed unsuppressed water signal

Table 2

Parameters of Two Resonance Peaks in the Model Spectrum

Peak q	a_q	θ_q/rad	d_q	f_q/Hz
1 (creatine, CH_3)	15	0	10	132
2 (creatine, CH_2)	10	0	10	56