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A Review of Electrocochleography: Instrumentation Settings and Meta-analysis of Criteria for Diagnosis of Endolymphatic Hydrops

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This paper reviews the literature on instrumentation settings used for transtympanic (TT-ECOG) and extratympanic electrocochleography (ET-ECOG). There is wide variation with regard to the applied stimulus, the settings and interpretation of ECOG results. For most physicians, the presence of endolymphatic hydrops is indicated either by the summating/action potential (SP/AP) ratio for click stimuli or the SP amplitude after tone bursts. Different upper limits have been proposed to discriminate hydropic from non-hydropic ears. Based upon a meta-analysis and classification criteria obtained from multivariate statistics, the authors propose that an SP/AP ratio with click stimulation >0.35 using TT-ECOG, or >0.42 using ET-ECOG, is indicative of hydrops. With tone burst stimulation set at a repetition rate of 30–40 stimuli per second, a SP of < -2 μV using TT-ECOG for at least one frequency within the range 0.5–8.0 kHz is considered pathologic. *Key words*: *electrocochleography, endolymphatic hydrops, meta-analysis, instrumentation settings.*

INTRODUCTION

For more than 20 years, electrocochleography (ECOG) has been used in the assessment of inner ear dysfunction, e.g. for threshold level determination, perilymph fistula detection, input-output function measurement, and glycerol provocation tests. In the last decade, ECOG has mainly been applied in the diagnosis of endolymphatic hydrops (ELH).

ECOG measures cochlear potentials evoked by acoustic stimulation when an active electrode is placed near the round window of the cochlea. Three potentials are of interest: the action potential (AP), the cochlear microphonic (CM) and the summating potential (SP). The AP is an algebraic sum of the action potentials from the spiral ganglion and cochlear nerve. The CM is a potential originating in the hair cells that mimics the mechanical movement of the basilar membrane. At high intensities the basilar membrane vibrates asymmetrically around its midpoint; the excess displacement towards the scala tympani produces a constant direct current (DC) component, the SP.

In hydropic ears, the basilar membrane is distended towards the scala tympani and this may be the reason for the enlarged SP in ELH (1, 2). Many investigators agree that specific changes of the AP and SP, as well as the SP/AP ratio, are correlated with the presence of ELH (3–13).

Since the late 1960s, the large number of studies using ECOG have resulted in a wide variety of recommendations for instrumentation settings, electrode applications and diagnostic criteria. These different approaches have given rise to difficulties in comparing the results obtained. An additional difficulty has been the evolving definition of Meniere's disease as documented in the American Academy of Otolaryngology and Head and Neck Surgery (AAO-HNS) guidelines of 1972, 1983 and 1995 (14) which jeopardises comparison between studies.

In 1990, the Prosper Meniere Society approved a standard for settings and interpretation of TT-ECOG (15, 16). While the settings have been adopted by several investigators the interpretation criteria are still subject to debate.

This paper reviews the literature and discusses clinical ECOG instrumentation settings and methodology. A meta-analysis of the different diagnostic criteria characterising ELH is presented.

STIMULUS

The two types of stimuli used in ECOG are clicks of 100 μs and long tone bursts (16 ms). Almost all studies use click stimuli; however, tone bursts are additionally applied in three-quarters of the TT-ECOG publications reviewed (10, 11, 13, 15–24) and only in one third of the ET-ECOG reports (21, 23, 25–30).

Due to the synchronicity, clicks evoke sharp AP responses enabling reliable assessment of the signals. Also the latency shift between AP responses in rarefaction and condensation clicks yields information about cochlear function. Due to the high intersubject variability of the absolute AP and SP potentials, Eggermont (31) introduced the SP/AP ratio which is now applied by most clinicians in the diagnosis of ELH.

Nevertheless, there are two theoretical reasons for measuring cochlear function by the response to tone bursts. First, the frequency specificity of the stimulus and the tonotopicity of the cochlea enable measurement of potentials arising from different cochlear

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regions. Second, there is the intrinsic DC property of the SP making it apparent only as long as the stimulus lasts. A transient click stimulus with a duration of 100 μs is therefore not ideal for measuring the SP which, moreover, is covered by the AP. With tone bursts, the AP extinguishes by adaptation, thus making the SP clearly discernible (20, 30).

TT-ECOG VERSUS ET-ECOG

Several studies elaborate on the comparison between TT-ECOG and ET-ECOG (21, 23, 32–37). The main advantage of TT-ECOG is that the signal amplitude of the potentials is 5–10 times larger than in ET-ECOG. This yields a superior signal-to-noise ratio which is particularly crucial in tone burst responses where the absolute SP value is used as a clinical tool for discrimination of ELH. It is necessary to stress that different SP/AP ratios are recorded in the same patient when evaluated by the two techniques. This is because the SP value measured with TT-ECOG is four-fold greater than that of the ET-ECOG response, whereas the AP is six-fold greater with TT-ECOG than with ET-ECOG (35); the variation may be explained by different potential-generating sites. TT-ECOG responses are more stable, repeatable, sensitive and need less signal averaging (37).

A drawback of TT-ECOG is its more invasive nature as it requires microscopic needle placement. Nevertheless, most patients show equal tolerance for TT-ECOG and ET-ECOG (21).

PROCEDURE

Prior to initiation of ECOG the patient is fully informed about the procedure. The use of a standard ECOG protocol minimises methodological errors. Table I presents the most common electrode placements used in TT-ECOG and ET-ECOG.

After the ear lobes or mastoids and the forehead are cleansed with alcohol-soaked wipes, electrode gel is applied to reduce impedance. Disposable silver/silver chloride surface electrodes or their equivalent are then attached to the reference and common sites (Table I). Impedance between the surface electrodes is measured to verify secure attachment to the skin (impedance <10 kΩ). The impedance of the tympanic or transtympanic electrodes can vary significantly and is not always directly related to ECOG quality (36).

Next, a doughnut-shaped headset is securely fastened to the head. With TT-ECOG, the patient's eardrum and outer ear canal can be anaesthetised using topical lidocaine 10% which is then removed after 10 min using vacuum aspiration. Under an operating microscope, a Teflon-coated stainless steel needle is placed in the superior posterior quadrant of the eardrum close to the annulus, resting on the promontorium near the round window niche. The needle is kept in place by means of crosshairs attached to the doughnut.

Table I. *Electrode configuration for ECOG*

Electrodes	TT-ECOG	ET-ECOG
Active electrode	Near round window niche	Eardrum or outer ear canal
Reference electrode	Ipsilateral earlobe or mastoid	Ipsilateral/contralateral earlobe/mastoid
Common electrode	Forehead	Forehead

With ET-ECOG the electrode is applied to the external ear canal near to or on the eardrum and secured using foam (5) or a wick (38, 39).

After placement of the active electrode, a headphone is fixed to the head. To reduce stimulus artefacts and other electrical interference, the headphones should be shielded. The patient should be passive and relaxed during the recordings, i.e. resting on a bed or an easy-chair that supports the head.

ECOG SETTINGS

The settings most commonly used for clinical ECOG, as defined in the literature, are listed in Table II.

The high-pass filter (also called the low-frequency filter) is designed to eliminate low-frequency noise and EEG activity. The response can be improved by increasing the filter frequency but it may not influence the SP (DC) component of the signal. Setting the filter too high (e.g. >30 Hz) provokes a severe distortion of the click SP (40). A frequency of 3–5 Hz (12 dB/octave) is used by most clinicians.

The low-pass filter frequency (or high-frequency filter) serves to eliminate high-frequency noise and is mostly set to 3 kHz (range: 1.5–30.0 kHz). We recommend a setting of 5 kHz (12 dB/octave) together with averaging over a sufficiently large number of clicks and tone bursts to improve the signal-to-noise ratio. A notch filter (50–60 Hz) is recommended to eliminate mains supply interference.

The number of sweeps is closely related to signal quality. The signal-to-noise ratio increases with the square root of the number of averages but also with the amplitude of the potentials. Most TT-ECOG methods need less than 500 sweeps whereas ET-ECOG usually demands up to 2000 sweeps. With both techniques, repeated averaging of all signals is highly recommended to assess reproducibility and reliability. It is important to note that reproducibility deteriorates when needle or electrodes are incorrectly placed.

Table II. *ECOG settings*

Stimulus	Click	Long tone burst
Low-frequency filter	3–5 Hz	3–5 Hz
High-frequency filter	3–5 kHz	3–5 kHz
Sweeps	<500 (TT-ECOG) ±2000 (ET-ECOG)	<500 (TT-ECOG) ±2000 (ET-ECOG)
Stimulus duration	100 μs	2 ms ramp, 10–12 ms plateau
Stimulus frequency	broad band	0.5, (0.75), 1, 2, 4, 8 kHz
Time Window	10 ms	20 ms
Rate	11.4 per second	30–40 per second
Polarity	alternating, condensation, rarefaction	alternating
Intensity	90 ± 10 dB nHL	90 ± 10 dB nHL
Masking	no	no
Pre-stimulus delay	2 ms	0 ms
Sensitivity	250 μV	250 μV
Artefact rejection	on	on
Notch filter (50 or 60 Hz)	on	on

Click duration is set to 100 μs by almost all investigators. The reported tone burst frequencies are heterogeneous, ranging from only one frequency (26, 27) to five frequencies (15, 20, 37). Tone burst evoked signals at 500 Hz give information about the apical region of the cochlea and are of particular interest for ELH. Indeed at 500 Hz the basilar membrane is at its broadest and is more susceptible to the displacement found in the ELH state. To study the frequency-specific behaviour of the cochlea it is recommended that a broad range of frequencies be measured (0.5, 1, 2, 4 and 8 kHz). ELH can often be characterised by pathological SP values at only a few frequencies.

In most studies, tone burst ramps are set to 2 ms whereas plateau durations range from 10 to 12 ms. Some clinicians have chosen a ramp of 5 ms for a clear desynchronisation of the AP (30). The plateau should be at least 4 ms (41), but a longer plateau (e.g. 10 ms) is preferable for clear identification of the SP.

The time window of the averager is set at 10 ms for clicks and 20 ms for tone bursts by most investigators.

For most commentators, the repetition rate for click stimuli varies between 8 and 11.5 clicks per second. The rate has to be chosen such that the AP complex is not influenced by adaptation of the firing neurones. Rates that are multiples of 50 or 60 Hz and from the time window of the averager are to be avoided because of interference problems.

The reported repetition rates for tone bursts were much higher than for clicks since AP adaptation was not of any importance. Except for a few investigators (10, 13, 18, 24, 35), all TT-ECOG tone burst stimuli were administered at rates between 30 and 40 per second. ET-ECOG rates differed much more, ranging from 5.3 (37) to 200 stimuli/s (26). A rate of 37.4 was proposed following the Prosper Meniere Society's International Standards for TT-ECOG (15, 16).

An alternating click polarity was used in most studies on ECOG although some clinicians emphasised the importance of using rarefaction and condensation stimuli to detect abnormal wave forms (27, 30). We recommend the use of alternating polarity while seeking the appropriate intensity level but signals for the analysis of the SP/AP should be averaged separately with rarefaction and condensation clicks, and summed afterwards. The latency difference between the AP in both signals (which should not exceed 0.3 ms [30]) is a good indication of the cochlear partition quality. In cases where the AP and/or SP are barely discernible in the alternating click signal, inspection of the separate rarefaction and condensation signals may show a large AP latency difference, leading to a nonsensical combination in

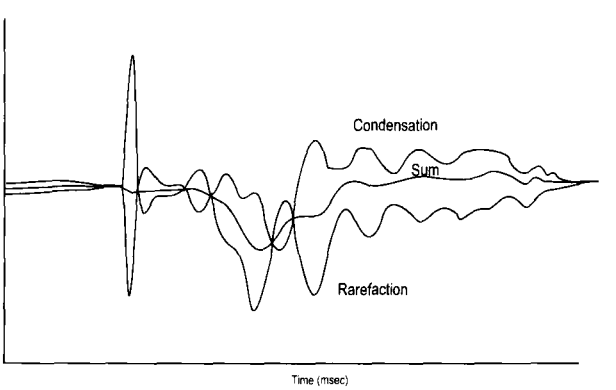

Fig. 1. TT-ECOG responses on rarefaction and condensation clicks. The summation (sum) of these signals produces the response that would be obtained by alternating clicks. Since the AP is not found at the same latency with both rarefaction and condensation responses, the sum produces no clear AP or SP.

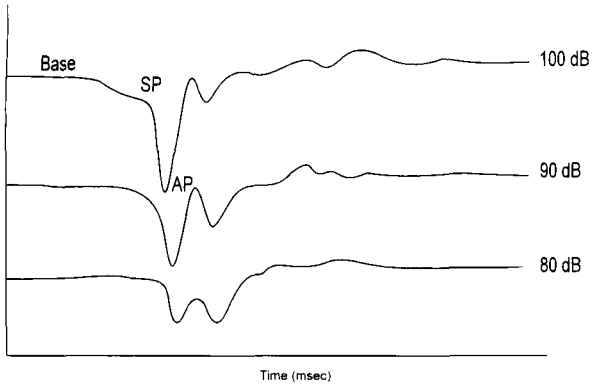

Fig. 2. TT-ECOG responses to alternating clicks at 80, 90 and 100 dB nHL. The SP is located at the shoulder of the AP trough, and is only seen at the highest intensity.

the summed signal. This is illustrated in Fig. 1 where the TT-ECOG responses are obtained from a patient with severe hearing loss.

Since the SP is only elicited at higher intensities, the levels should be set at 90 ± 10 dB normal hearing level (nHL) with TT-ECOG as well as ET-ECOG techniques. The intensity level which reveals the most discernible SP and AP should be used, as shown in Fig. 2. No masking is required in ECOG since the potentials are recorded near the generator.

The measurement of AP and SP are obtained by subtracting the potential amplitudes from the baseline level. It is therefore suggested that a pre-stimulus delay of 1–2 ms be set to determine the baseline with greater confidence. This is because the post-AP-SP complex may be contaminated by an auditory brainstem (ABR) response and is not always suitable for baseline determination.

INTERPRETATION OF PUBLISHED STUDIES

Click stimulation

The top curve in Fig. 2 shows a typical click response; the base, AP and SP are indicated. The SP/AP ratio, used as the discriminating factor between normal and hydropic ears, depends upon many influencing factors such as the technique of recording (TT-ECOG or ET-ECOG), the disease stage, level of hearing loss, and the fluctuating nature of the hearing loss. Although it is not clear how these different factors influence the cochlear potentials, some general conclusions can be drawn from the literature.

An SP/AP ratio of 0.33 has been used as the upper limit of normality in a number of TT-ECOG studies (15, 16, 21, 22, 42). In contrast, others have applied limits of 0.27 (35), 0.3 (18, 43–45), 0.32 (46), 0.37 (19), and 0.4 (13). A value of approximately 0.40 has been employed in ET-ECOG studies but there is a wide variation in practice e.g., values have included

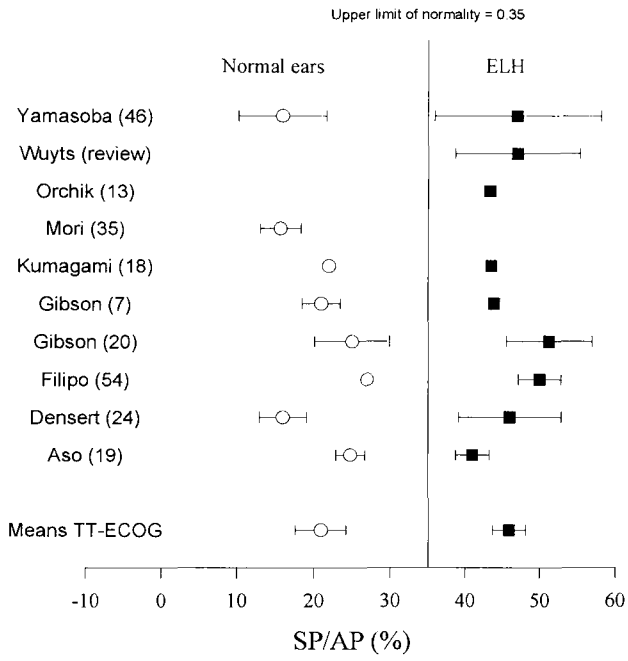

Fig. 3. Meta-analysis of the TT-ECOG SP/AP ratios obtained from the literature. The means and 95% confidence intervals (CI) are plotted for normal ears and those from patients with endolymphatic hydrops. When the standard deviation or the number of studies was not available, only the means are indicated. The overall mean SP/AP with its 95% CI is depicted at the bottom of each population group. The upper limit of normal is indicated.

0.25 (female patients [47]), 0.34 (5), 0.35 (48), 0.37 (49), 0.39 (male patients [47]), 0.40 (34), 0.43 (50, 51), 0.5 (8, 21) and 0.51 (52).

Meta-analysis

We performed a meta-analysis on the SP/AP ratios reported in different studies, applying parameter settings that are compatible with those listed in Table II, and assuming a normal distribution.

Fig. 3 shows the mean SP/AP ratios and the 95% confidence intervals (CI) for normal individuals and ELH patients that were obtained according to the procedures defined in Tables I and II. The mean SP/AP ratio for 17 ELH patients was 0.47 with a standard deviation (S.D.) of 0.17.

The mean SP/AP ratio for ELH patients included in 9 TT-ECOG studies was 0.459 (S.D. = 0.033) compared with 0.209 (S.D. = 0.046) for normal subjects (8 studies). Using the formula (Appendix 1) adopted from multivariate statistical analyses (53), we calculated that an SP/AP ratio (TT-ECOG) of 0.35 would discriminate between normal individuals and ELH patients. Fig. 3 shows the overall mean as well as the discriminatory value.

Eleven ET-ECOG studies reported data for normal subjects, yielding a mean SP/AP ratio of 0.241

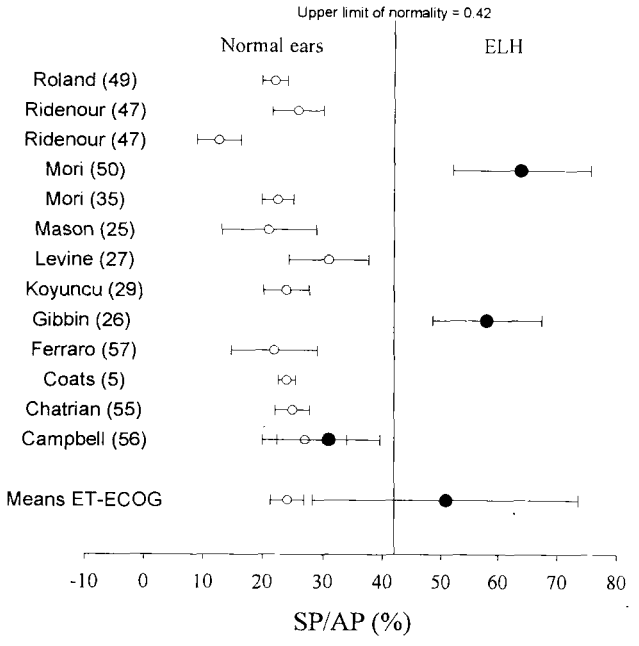

Fig. 4. Meta-analysis of the ET-ECOG SP/AP ratios obtained from the literature. The means and 95% confidence intervals (CI) are plotted for normal ears and those from patients with endolymphatic hydrops. When the standard deviation or the number of studies was not available, only the means are indicated. The overall mean SP/AP with its 95% CI is depicted at the bottom of each population group. The upper limit of normal is indicated.

(S.D. = 0.030). However, fewer data were available for the ELH group. The mean SP/AP ratio from 3 studies was 0.51 (S.D. = 0.18), making true discrimination questionable. We therefore calculated the 95% prediction interval (mean ± 2 S.D.) from the 11 studies which included normal data. The average SP/AP value was 0.42 (S.D. = 0.08) which can be regarded as an upper limit for normality since 95% of the normal SP/AP ratios were below this limit. Clearly, more data for ELH patients are required to permit the same classification criteria that were applied with TT-ECOG to be employed with ET-ECOG.

Fig. 4 shows the results of a meta-analysis of ET-ECOG data from ELH patients and subjects with no inner ear pathology. The means and 95% CI of the different studies are depicted together with the overall mean and the upper limit of normality.

These data confirm that TT-ECOG and ET-ECOG do not yield the same SP/AP values for identical populations, and that ET-ECOG shows a broader deviation around the mean.

Tone bursts

In tone burst evoked responses, most clinicians measured the SP amplitude at the mid-point of the stimulus response (20) (Fig. 5). Densert et al. pointed out that when the post-stimulus baseline was higher than the pre-stimulus value, the pre- and post-response baselines should be combined to find the SP mid-point (24). A number of other clinicians reported SP amplitudes at different frequencies, yet without mentioning upper limits to discriminate ELH (10, 13, 24). The SP cut-off level for discriminating hydropic from normal ears is rarely mentioned (15, 16, 22, 27, 30).

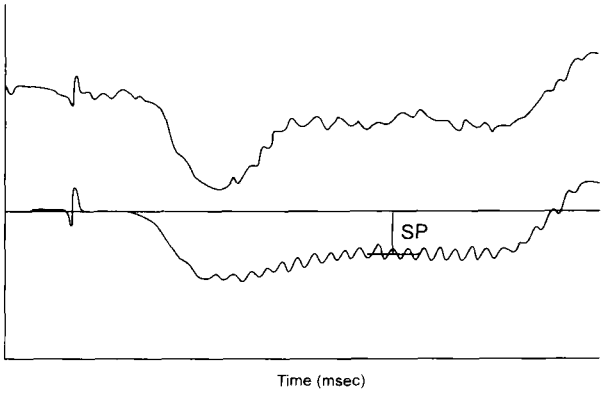

Fig. 5. Tone burst responses (TT-ECOG) at 1 kHz in a normal ear (top) and the ear of a patient with endolymphatic hydrops (bottom). The SP was determined from baseline to the plateau near the middle of the response at ±10 ms after stimulus onset.

A distinction must be made between TT-ECOG and ET-ECOG techniques since the amplitudes may differ by an order of magnitude. The lower signal amplitude with ET-ECOG limits the use of tone bursts to no more than a few frequencies. Very few studies reported normal values for tone burst stimuli (5, 10, 24, 37). Like ET-ECOG, the normal values with TT-ECOG were close to the baseline level or slightly positive (10, 37); currently, too few data exist with either technique to extract representative normal values. Table III lists the published SP upper limits of normality with TT-ECOG.

In normal individuals, a typical wave form has a SP close to the baseline (Fig. 5, *top trace*) whereas in ELH the SP only returns to baseline at the end of the stimulus (Fig. 5, *bottom trace*). Therefore with TT-ECOG, we suggest adopting the Prosper Meniere Society's International Standard (15, 16) proposing an SP upper limit of normality of $-2\ \mu V$ for all frequencies except 1 kHz when $-3\ \mu V$ should be chosen. More negative values suggest the presence of hydrops. With ET-ECOG, these limits may be even smaller but, due to lack of data, no values can be given.

CONCLUSION

To improve the diagnostic value of ECOG, consistent settings need to be applied in comparable patient

Table III. *TT-ECOG SP upper limit of normality*

Authors	500 Hz	1 kHz	2 and 4 kHz	8 kHz
Arenberg et al. (16)	–	> -3 μV:nl	> -2 μV:nl	> -2 μV:nl
Dornhoffer & Arenberg (22)	–	> -3 μV:nl	> -4 μV:nl	> -6 μV:nl
Gibson (20)	–	> -3 μV:nl	–	–
Hohman (45)	> -2 μV:nl	> -6 μV:nl	> -5 μV:nl	–

nl: normal; e.g.: if for a patient SP at 1 kHz = -1 μV it is considered normal.

populations. Further data are needed on the influence of disease stage, degree of hearing loss, and symptoms at the time ECOG is performed.

This review discusses the most common ECOG settings and proposes specific values based on the wide range found in the literature. ELH criteria are suggested on the basis of a meta-analysis of click and tone burst responses with TT-ECOG and ET-ECOG.

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APPENDIX 1

Given that μ_1 and σ_1 are the mean and standard deviations for normal individuals and that μ_2 and σ_2 are the equivalent for ELH patients, the discriminating value x is obtained by solving the equation:

$$-\frac{1}{2}\left(\frac{1}{\sigma_1^2}-\frac{1}{\sigma_2^2}\right)x^2+\left(\frac{\mu_1}{\sigma_1^2}-\frac{\mu_2}{\sigma_2^2}\right)x \geq \frac{1}{2}\ln\left(\frac{\sigma_2^2}{\sigma_1^2}\right)+\frac{1}{2}\left(\frac{\mu_1^2}{\sigma_1^2}-\frac{\mu_2^2}{\sigma_2^2}\right)$$